

MEDICAL ETHICS

Informed Consent in International Research: Perspectives from India, Iran and Nigeria

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ABSTRACT

The amount of international biomedical research is increasing and much of this is happening in developing countries. It is important to place adequate focus on the issue of obtaining voluntary informed consent. Researchers need to understand local socio-cultural realities and also respect local cultural beliefs and indigenous research guidelines. Through examples from India, Iran and Nigeria the authors highlight the diversity within and between developing country situations. Emphasis is placed on the importance of informed consent in research as well as clinical practice settings, and the need to be enterprising and innovative in obtaining it.

International biomedical research continues to grow, especially in clinical sciences, and is often welcomed by economically developing countries. Conducting research in developing countries raises ethical concerns related to issues like standard of care and post-trial obligations. Many of these issues are currently being debated by researchers and bioethicists.

An important component of conducting research in any setting is obtaining informed consent. We will therefore focus on the issue of informed consent in our article. Three subsections in this article will highlight the challenges and specific considerations for informed consent in India, Iran and Nigeria. We will reiterate the importance of understanding local socio-economic-political-cultural and religious realities before starting international research. We also highlight the need to understand the diversity within each country. We then give some practical suggestions for researchers planning to work in developing countries, especially in the area of informed consent.

PERSPECTIVES FROM INDIA

A researcher must be aware that Indian patients or research participants may prefer to involve their families or communities in the consent process in addition to giving individual consent. However, no assumptions may be made about the choices of the particular patient or research participant relating to consent or privacy.

India is a diverse country with a large land mass, multiple languages, and a variety of cultures. It is a booming economy with a strong industry base in biotechnology and information technology and is a hub for outsourcing services. There are numerous hi-tech private hospitals now in development which will provide treatment and healthcare services to foreigners who want cheaper treatments or shorter waiting times than in their own countries. The Indian government is promoting this kind of 'healthcare tourism'.

India also has a strong pharmaceutical industry, with indigenous research and development (R&D) capacities. The liberal patent laws of the 1970s, which protected product patents but not process patents, allowed many of the Indian pharmaceutical companies to produce and supply generic medications at a much lower cost than multinational drug companies. Many of the low cost generic anti-retroviral medications used to treat people living with HIV/AIDS across the world are produced in India. There is uncertainty about the future of generic drug production in India now, since the World Trade Organization intellectual property regulations became enforced in January 2005. These regulations might not allow generic drug production in critical public health areas in India.

In spite of all these economic advances, large socio-economic inequities exist in India. India has a dual healthcare system – public and private. The private 'for profit' healthcare system is available in all parts of India, ranging from

private medical practitioners at the village level to hi-tech hospitals in metropolitan centres like Mumbai where facilities could compete with the best in the world. The public healthcare system is among the most under-funded in the world – as a proportion of the GDP, public healthcare spending is a mere 1.3 percent, while private out-of-pocket expenditure (both for services as well as drugs and devices etc.) is 4.8 percent (World Health Report 2005). The government disinvestment in health is further encouraged by policies of lending agencies like the World Bank and the International Monetary Fund. These agencies promote a ‘user fees’ system in public health care facilities which forces poor families to be further burdened. Expenditure on healthcare is a leading cause for debt accrual in Indian families.

A large proportion of the Indian population is still illiterate. The country’s literacy for its population aged seven years and older stands at 65.38 percent according to the 2001 national census. There is a high level of trust in health care providers. In addition to allopathic health care providers, there are many indigenous medical practitioners. There are also many other systems of medicine such as the ancient Ayurveda, homeopathy, and Unani system of medicine. Often individuals access health care from more than one health care system.

Poverty is a reality in both rural and urban settings, and the only option for these populations is to access health care from the public health care system. The public health care system is under-resourced in terms of infrastructure, staff as well as medications. This adversely affects the standard of care that is publicly available. There is a high volume of patients at all levels of public health care and overcrowding exists in outpatient, as well as inpatient departments.

Implications for Informed Consent

Informed consent is presently a central precept of clinical medicine and research involving humans. The commentary for CIOMS guideline 4 on individual informed consent states that:

“Informed consent is a decision to participate in research, taken by a competent individual who has received the necessary information; who has adequately understood the information; and who, after considering the information, has arrived at a decision without having been subjected to coercion, undue influence or inducement, or intimidation.”¹

The Indian Council for Medical Research (ICMR) guidelines for informed consent mandate similar requirements for the process. Institutional ethics committees, equivalent to Research Ethics Boards (REBs) in the West, are expected to follow the ICMR guidelines for reviewing research proposals, though they may also take international guidelines like CIOMS into consideration. Though most ethics committees are located within academic institutions, in recent years many commercial for-profit ethics committees have also

been formed in India, paralleling the phenomenon of increased outsourcing of clinical trials to India.

The requirement of informed consent has several implications on the way health care in India is structured. The upper and middle socioeconomic classes are literate and often pay for their health care. They can arguably fulfill the conditions of informed consent in the same way as their counterparts in developed countries. Illiteracy and the different languages spoken by the investigators can make it difficult to obtain informed consent from the lower socioeconomic classes. However, note that while potential research participants from the lower classes may be illiterate, they are not ‘uneducated’. Individuals often have life experiences which empower them. A researcher must be innovative in creating a consent process for communicating information which ensures that potential research participants understand the purpose of the research before consenting. To overcome language differences, researchers should be prepared with translated consent forms, and have available local interpreters who are trusted by the community. The onus of providing evidence for voluntariness and understanding lies with researchers.

With the Consumer Protection Act becoming applicable to the ‘for profit’ healthcare system in India, physicians are treated as service providers and patients as consumers.² Patients may now make claims on the basis of a lack of informed consent. While informed consent has to be obtained in the public health care system too, physicians in government service are exempt from the Consumer Protection Act. This is symptomatic of the consumer model of health care that is gaining ground in many developing countries.

Power hierarchies continue to exist between patients and health care providers and thus patients might not feel empowered enough to say no to research being carried out by their physicians. Research participants may not understand the differing roles of physicians as caregivers and researchers who are not caregivers.

An important difference from the focus on individual rights in the West is the importance of family involvement in all aspects of life in India. Most individuals will not agree to participate in research or even to major clinical procedures without discussing it with one or more members of their families. Gender differences may mean that women do not feel empowered enough to agree to participate in research until they obtain the permission of their spouses.

Privacy is still an important value. Overcrowding might make it difficult to maintain the privacy and confidentiality of patients and research participants. However, some individuals may still insist on privacy, even from their own families. This might be especially pertinent in the case of research into sexually transmitted infections such as HIV/AIDS because of the intense stigma related to these infections.

Researchers from other countries should also understand the importance of respecting and following indigenous

national guidelines for research. The biomedical guidelines are available on the website of the Indian Council of Medical Research and the guidelines for social science research in health from the CEHAT website.^{3,4} It would be wise to be familiar with these guidelines before initiating research in India.

With the variety of regional, sociocultural and economic differences, obtaining informed consent in India might seem a difficult task and an impediment to research. Researchers should remember however, that the process of obtaining true voluntary informed consent, even if it seems tedious, engenders respect for the research participants, and empowers local communities with information related to research.

PERSPECTIVES FROM I.R.IRAN

One of the most important issues in the field of biomedical ethics is informed consent. Although there are many differences between Western and Eastern societies in terms of obtaining informed consent from patients or potential research participants, the main goal and ideas are the same in both cultures, that is, respect of individuals and the value of life.

The rich cultural values and religious beliefs of Iranians have inspired many ethical discussions and debates. Over centuries, many Iranian physicians have published on ethical issues in the field of medicine. Ethical principles are also emphasized in Islamic teachings. These principles are based on the Quran and the tradition of the Prophet Mohammad. One of the valuable teachings of the Prophet Mohammad is the goal to expand and improve ethical virtues.

The following discussion about informed consent is based on personal experience in the Family Health and Population Department of the Undersecretary for Health in the Ministry of Health and Medical Education of I.R.Iran.

Legislative Considerations

The Declaration of Helsinki is rooted in the principle of respect for human dignity and self-determination, and serves to protect the rights and welfare of human subjects from potentially unethical research. Its spirit is consistent with the recommendations of Islam and Iranian culture. However, legislation has yet to be formerly developed in I.R.Iran to address this issue.⁵

In 1999, the Iranian Ministry of Health and Medical Education (MOH&ME) required the establishment of Research Ethics Committees (RECs) in each Medical University.⁵ Similarly around this time, the office of the Study for Humanistic and Islamic Sciences on Medicine and Medical Ethics implemented a survey. Based on the results of this survey and the cultural and religious beliefs of Iranian society, MOH&ME drafted an act named the Protection Code for Human Subjects in Medical Research.⁶ The most important provisions of this act include the requirement of informed consent; the need to review the risks and benefits of each research study; the protection of research partici-

pants' rights; confidentiality of participants' information; compensation for injury; and preservation of the rights of fetuses, prisoners, and individuals with mental illnesses.

Sociocultural Considerations

Problems regarding informed consent are usually created when the researchers and the potential participants are from different cultural and religious backgrounds. Although it is not common for foreign researchers to come to I.R.Iran, obtaining informed consent has its own challenges, even when conducting national studies or programs. For example, some problems arise when researchers start to talk to potential participants without first increasing awareness of the study and educating individuals at the community level.

Our approach in the MOH&ME is through the Primary Health Care (PHC) Network. The PHC in I.R.Iran is a comprehensive network through which we have good access to all communities in different parts of the country, even remote rural areas. In this system each village has a health house and two health personnel, one man and one woman, named *Behvarze*. They are trusted members of the local community and know community members well. *Behvarzes* are key informants when conducting research or implementing health programs. They can act as mediators for the consent process by explaining scientific and technical parts of research or health programs in a simple way. They can also act as consultants and translators when conducting research among populations with a low literacy rate, like the elderly for example.

One of the misconceptions in the West is a notion that women may not provide consent in I.R.Iran. Iranians have respect for the family as a social value and family members consult and support each other. In therapeutic research, obtaining consent from the male or female participant is sufficient. However, based on the ethical codes, when a spouse participates in non-therapeutic research and the consequences might affect marital life, obtaining consent from both partners is necessary. For example, the author was directly involved in a Breast Cancer Study in which written informed consent was obtained from female participants. There was not a single woman who refused to participate in the study or withdrew from it due to the lack of their husband's permission.

Another example is the Family Planning Program, which is one of the most successful health programs in I.R.Iran. In some religious countries the use of contraception is problematic, but various kinds of free contraceptive methods are available in rural and urban public health centers in order to decrease the maternal mortality rate, and improve women's health and family planning. However, to perform either a vasectomy or a tubal ligation, written informed consent from both partners is necessary.

In many countries the literacy rate of women is considered to be an important factor in obtaining informed consent. The high literacy rate among Iranian women is another positive and helpful point in this regard. It should be noted that

in 2004 more than half of the students entering university were women.⁷

Ethnic diversity is another cultural challenge in obtaining informed consent. Turk, Kurd, Lor, Arab, Baluchee, and Fars are different communities with different languages and cultures in different parts of the country. Local personnel should be involved in creating effective communication with these groups and obtaining informed consent.

One of the basic issues pertaining to informed consent is the individual's awareness of their rights as a research participant. Most, particularly those in rural areas, do not want to know details about procedures and will provide consent immediately after understanding that the researchers are physicians. They believe that all personnel of the health sector are trying to improve their health and place their confidence in what they say. This emphasizes the need for ethical virtues in physicians who conduct research. Researchers must discuss important aspects of the study without rushing potential participants and ensure that they understand the option to refuse to participate without affecting the regular medical care offered to them or their families.

To summarize, it is often argued that bioethics is a Western secular concept and that its implementation in an Eastern religious country would be difficult. I believe that the basic and overall spirit of bioethics in Western and Eastern cultures - that is, the protection of human rights, welfare, dignity, and autonomy - are the same.

Informed consent is one of the tools for achieving the common goal of self-determination. Examples of how informed consent is obtained in I.R.Iran show that achieving this goal is not difficult because the cultural values and religious beliefs are in fact supportive of the principle of self-determination rather than barriers.

PERSPECTIVES FROM NIGERIA

Conducting human research within the limits of international regulations can present enormous challenges to both the investigator and research participants. Features of many developing countries such as poverty, endemic diseases and illiteracy often influence the conduct of research in these areas. The ethical and scientific oversights of some foreign researchers in the preparation and conduct of research involving participants in developing countries call for a critical review. The controversial Trovan study conducted by Pfizer in Nigeria is analyzed as a case in point in this paper.

In 1996, a group of researchers from Pfizer in the United States conducted a clinical trial of the antibiotic Trovan during an outbreak of cerebrospinal meningitis in Kano, in Northern Nigeria. Various allegations of impropriety have since been made.^{8,9} About fifty Nigerian families claim that Pfizer violated the ethical principles of autonomy and non-maleficence ('do no harm'). Among the 200 stricken children enrolled in the experiment, eleven died and others suf-

fered from severe meningitis-related complications such as deafness, blindness, seizure, and in one case, an inability to walk or talk.⁹ Many Nigerians believe that the trial drug was unsafe, inadequately pre-tested and caused many serious side effects among the children.

Based on reviews of the Trovan study by Ahmad and Stevens, a variety of ethical flaws can be seen.^{8,9} First, parents of the children who participated in the trial allege that they were not informed of the procedure or risks of the study. Although Pfizer officials insist that they received verbal informed consent from the largely illiterate population. Second, the study design also suggests substandard practice. Despite the availability of chloramphenicol, the first-line treatment for bacterial meningitis, only one-third of the recommended dose was given to the children in the controlled arm of the study. In the treatment arm, Pfizer tested oral instead of intravenous Trovan, which is the standard therapy in the US.

The study has been trailed by a myriad of allegations, which are sub-judice in the US. If the local ethical review board had done a sufficiently thorough review, the study would not have been approved.⁹

Implications

The history of abuse in research entails a history of racism, class injustice, exploitation and other forms of bias and discrimination. The Trovan study created the perception in some that researchers do not care about the safety of research participants. This may lead to difficulties in enrolling participants from the community in genuine scientific research in the future. Besides being unethical, research conducted in the fashion of the Trovan study also yields scientifically unreliable data.

Sociocultural Factors Influencing Research in Nigeria

The centrality of informed consent in local and international research cannot be overemphasized. Even though there has been consensus among nations to adopt international regulations guiding research, each society has distinctive sociocultural features which influence the level of adherence among researchers. Knowledge of the peculiar sociocultural factors in an unfamiliar research setting can influence the process by which informed consent is obtained. This is significant in determining the extent to which the consent for research guarantees understanding, voluntariness, and authorization.¹⁰ Research in Nigeria is no doubt influenced by these factors.

Nigeria is socioculturally diverse in terms of language, religion, economy, and tradition. A great percentage of the population is highly vulnerable due to structural inequalities, racism, poverty, low literacy, and gender disparity. These factors invariably impart significant influence on the conduct of research involving humans. Local and international researchers therefore need to understand the specific characteristics and values of the setting and the people to be

recruited as research participants. This unique heterogeneity makes it imperative for would-be researchers to fashion practical scientific methods in order to conduct ethically acceptable research in Nigeria.

Most of the Western bioethical principles do not fit directly if imported without filtration. This does not mean that sub-standards are acceptable, but rather a careful blending of the set standards in international research with the sociocultural values of the study population is required.

One of the greatest challenges for researchers in Nigeria is developing an effective mechanism to inform participants about the purpose, method, risks and benefits of the research. Without adequate caution, consent forms may appear too technical, lengthy, or difficult to understand. Due to widespread illiteracy, especially in the rural areas, risks and benefits are often unclear or misconstrued; this does not imply that those individuals are of low intelligence. Many of the words used in research and Western societies do not have perfect translations in local Nigerian languages. Similarly, many Western terms are not freely used in local conversations because of cultural taboos. For instance, among the Yorubas of south western Nigeria, it is not culturally permitted to use certain words such as sexual intercourse among unmarried persons in the open. In the traditional Yoruba language, terms such as "sleep together" are used in place of sexual intercourse, which in back-translation does not precisely mean sexual intercourse. The meaning of most scientific terms and chemical names can often be lost in interpretation. Even common words such as snow are abstract, as it is not a feature of the tropical climate in Nigeria. Interpreting a consent form and research protocol therefore demands a more rigorous validation of participants' understanding of the information to ensure comprehension.

Different settings present different institutional challenges in obtaining informed consent to conduct research in Nigeria. In the south west, the line of authority in community research differs in nomenclature and hierarchical arrangement. Beyond obtaining the host country's ethics board approval, foreign researchers also need to obtain approval from the local ethics board. In order to recruit participants, the "baale" or the community heads are consulted. He in turn consults the "oloyes" or the local chiefs, who in turn consults compound heads and family heads. The family head is the contact person to the household.

Being a male dominated society, women often need to obtain their spouse's permission before participating in research. In a study on consent forms in Nigeria, one woman respondent was quoted as saying, "It is not going to be dangerous once my husband did not say I should not do it. If the community's opinion disproves it, then one may not open up to the questions the researchers will be asking."¹¹ The variations in Christian-Muslim philosophies of life also influence Nigerians' attitude toward research. Muslim women may be more reluctant to participate in clinical trials compared to women from other parts of the country.

As a result of poverty or corruption, some people would give consent exclusively for financial reward. Researchers need to be conscious of this, making deliberate efforts that participants' consent is based on an informed and autonomous decision.

Legislation

International regulations such as the Nuremberg code, Declaration of Helsinki, and CIOMS guidelines, are operational in Nigeria. The Federal Ministry of Health and Human Services, the National Agency for Drug Administration and Control (NAFDAC), among others, also have additional guidelines which are enforced, especially in intrusive studies.

CONCLUSION

In international settings, particularly in resource-poor nations, individuals and communities participating in public health studies may be vulnerable to coercion because of their poverty and high levels of illiteracy. Strict local and international REB review and monitoring is suggested. Local or foreign research should be valuable to participants and society, and ethical standards of both the host and foreign country must be upheld. These standards must be strictly adhered to when conducting research in developing countries, irrespective of participants' race, socioeconomic status, or religion.

Before conducting international research, it might be useful to review publications like the Nuffield Council Report on the ethics of clinical research in developing countries.¹² However, it would also be important to refer to local guidelines (if existing), and respect them during this process. Context, culture, and beliefs can differ within countries and it is best to be cognizant of this in advance; spend time with local researchers and communities to gain mutual understanding.

An important component of research involving human subjects is informed consent, and adequate stress should be placed on it. Whether it is poor underserved populations in India, patients in Iran or sick children in Nigeria, respect for the research participants is paramount, and is reflected in part through the quality of informed consent. Researchers need to be patient, meticulous and innovative to make sure that informed consent is truly voluntary, and that there is adequate understanding of the process among the participants.

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