

The ethics of research related to healthcare in developing countries

a guide to the Report

Introduction

Developing countries urgently need research to help relieve the enormous burden of disease that they carry. It is vital that those in wealthy countries, both in the public and private sector, help fund this research. However, the inequalities that exist between developed and developing countries create significant risks of exploitation when externally sponsored research is carried out.

Following a number of international controversies, the Nuffield Council on Bioethics established a Working Party to

consider the issues. The Report, *The ethics of research related to healthcare in developing countries*, was published in 2002. A follow-up Discussion Paper, based on a Workshop held in Cape Town to discuss practical issues faced when implementing guidance, was published in 2005.

This summary sets out some of the arguments and recommendations which are discussed in more detail in the main Report.

[Notes in square brackets throughout refer to chapters and paragraphs in the Report]

Context

Background

The need for research

Each year £35-40 billion is spent on healthcare research worldwide. But only 10 percent of this is devoted to the health problems of 90 percent of the world's population. Developing countries urgently need research to help prevent and treat diseases such as TB and malaria. But many countries have limited funds and a lack of trained staff to conduct their own research. It is vital that the public and private sectors in developed countries should sponsor research to help bridge this gap [Chapter 2].

Social and cultural issues

Misunderstandings can occur when sponsors of research are unfamiliar with the cultural traditions of the country in which it is conducted. There will often be cultural differences between those organising or funding the research and the participants, for example, differing perspectives on respect for family and individuals, and the role of the community.

Prospective participants in research may have experience of very different traditions of healthcare and hold varying beliefs about illness and disease. Views about the causation of illness may differ from the 'western' medical model. Participants will often be unfamiliar with the concept of research and may be sensitive to some practices, such as taking blood samples. It is critically important that the local social, cultural and economic context is taken into account when research is designed [Chapter 3].

Ethical framework

We recognise that it would not be possible to formulate a robust set of guidelines for all situations. However, we identify four principles which should be taken into account by anyone who is designing or conducting healthcare research in developing countries [Chapter 4]. These are:

- the duty to alleviate suffering;
- the duty to show respect for persons;
- the duty to be sensitive to cultural differences; and
- the duty not to exploit the vulnerable.

Setting priorities

National resources for research are often lacking in developing countries and it is therefore particularly important for each country to ensure that research is appropriate and relevant for its health needs.

We recommend that all countries should set national priorities for healthcare research. If external sponsors propose research which falls outside the national priorities, the research should be justified to the appropriate research ethics committees [paras 2.31-2.32].

Guidelines

When planning research in developing countries, researchers and sponsors may be subject to a wide range of national and international guidance, guidelines, declarations and regulations, including:

- **World Medical Association (WMA):** *Declaration of Helsinki*, last revised 2000; Note of Clarification on Paragraph 29, Dec 2002; Workgroup Report on the revision of Paragraph 30, May 2004.
- **The Council for International Organizations of Medical Sciences (CIOMS)** in collaboration with the **World Health Organization (WHO):** *International Ethical Guidelines for Biomedical Research Involving Human Subjects*, last revised 2002.
- **Council of Europe (CoE):** *Additional Protocol to the Convention on Human Rights and Biomedicine concerning Biomedical Research*, prepared by the Steering Committee on Bioethics (CDBI) of the Council of Europe adopted by the Committee of Ministers, June 2004.
- **European Council and European Parliament (EU):** *Directive 2001/20/EC on the approximation of the laws, regulations and administrative provisions of the Member States relating to implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use*, April 2001, brought into force by May 2004.
- **The European Group on Ethics in Science and New Technologies (EGE):** *Opinion Nr 17 on the ethical aspects of clinical research in developing countries*, published in Jan 2003.

However, there have been criticisms that these guidelines are often inconsistent and inappropriate for the developing country setting. Interpreting and applying international guidance in a specific context is often extremely difficult. We recommend that developing countries produce their own national guidance to promote ethically sound research [Chapter 5].

[For a full list of guidance, see Appendix 1. Further comparison of the guidelines on the issues of consent, standards of care, ethical review, and after the research is over, is given in *The ethics of research related to healthcare in developing countries: a follow-up Discussion Paper, Appendix 1.*]

Consent

For research to be ethically acceptable, participants should be given the relevant information in a comprehensible manner, and must take part voluntarily. However, differences in social and cultural contexts in developing countries mean that some procedures may be ineffective or inappropriate. The way in which information on the potential risks and benefits of research is provided is particularly important [Chapter 6].

Who should give consent?

Researchers are often faced with difficult choices when considering who should make decisions about taking part in research. For example, in some communities it is customary for male members of the family to make decisions on behalf of wives and children.

For consent to be genuine, it must be freely given. We conclude that consent to participate in research must be obtained from each person individually. However, we also recommend that it may sometimes be appropriate to obtain agreement from the community or assent from a senior family member before approaching a prospective participant [para 6.22].

How should consent be obtained?

Participants should be provided with information that covers the nature and purpose of the research, the procedures involved, and the potential risks and benefits. However, long and complex consent forms are likely to confuse, rather than inform, people. Potential participants should be given the opportunity to ask questions about the proposed research [paras 6.4-6.17].

We recommend that information sheets and consent forms should be accurate, concise, clear, simple, specific to the proposed research and appropriate for the social and cultural context [para 6.40].

How should consent be recorded?

Problems may arise when recording consent with illiterate populations. In other situations, participants may be unwilling to sign consent forms because of concern that they are signing away rights. It is the substance of the process for obtaining consent which is important, rather than the procedures to record the consent itself.

Researchers should obtain written consent where appropriate. We recommend that when written consent is not feasible, verbal consent is acceptable, provided that it is formally documented and witnessed. The process must be approved by a research ethics committee [para 6.40].

Are inducements acceptable?

Where healthcare facilities are lacking in developing countries, some people may agree to take part in research because they believe it is their only way to receive improved healthcare. Researchers need to be aware that the offer of treatment during a trial might count as an inducement. In addition, other benefits such as financial payments, to compensate for time or travel costs, may act as incentives. An inducement may be considered inappropriate if it encourages someone to take greater risks than they would otherwise consider acceptable.

Inducements to take part in research must be appropriate to the local context. We recommend they should be considered by the local research ethics committee [para 6.32].

Standards of care

A particularly controversial issue concerns the 'standard of care' that should be provided to participants during research in developing countries. Much of the debate has focused on the level of care provided to the control (or comparison) group in clinical trials. Should participants in developing countries receive the same standard of care that participants in wealthier countries would receive if the research was conducted there? [Chapter 7]

What level of care should be provided for those in the control group?

Some argue that when research is externally sponsored, participants in developing countries should receive the same standard of care as participants would receive if the research was conducted in the sponsor's country. Others argue that this could prevent some forms of potentially beneficial research from being undertaken. In some instances, the medical facilities to provide such treatment are not available. In addition, the research findings based on the universal standard may not be relevant to developing countries. For example, if researchers are investigating whether a new treatment for a disease is better than the one currently available in a developing country, it is more appropriate to compare the new treatment with the currently available one, rather than a more expensive treatment available only in developed countries.

We conclude that wherever appropriate, participants should be offered the best standard of care available in the world for the disease being studied. But this is not always appropriate or possible. In these situations, we recommend that – as a minimum – participants should be offered the best treatment available from the national public health system. The standard of care must be defined in consultation with those who work within the country and must be justified to the research ethics committee [paras 7.29-7.31].

Definitions:

- Universal standard of care: the best current method of treatment available anywhere in the world for a particular disease or condition.
- Non-universal standard of care: the treatment available in a defined region.

Provision of care to all trial participants

Research into preventive measures

When research into preventive measures is conducted, what standard of care should be offered to patients who develop the disease once the research is completed? This issue was debated in the context of research to develop a vaccine to prevent HIV infection.

We conclude that when research into preventive measures is conducted, wherever appropriate, participants who develop the disease being studied should be offered a universal standard of care for the disease. Where this is not appropriate, the best available intervention as part of the national public health system should be offered, as a minimum [paras 7.32-7.33].

Care for other conditions

During research into some diseases, participants may develop other conditions that are not related to the disease being studied. In some cases, researchers may not have the expertise to treat the condition effectively and appropriate treatment may not be available locally.

We recommend that before research begins, agreement should be reached about the standard of care that should be provided to participants who develop other diseases. Again, we conclude that – as a minimum – participants should be offered the best treatment available from the national public health system [paras 7.34-7.35].

After the research is over

Is it ethically acceptable to conduct research in a country that may not be able to afford to provide the treatment if it is effective? This is not always a straightforward issue. For example, sometimes the cost of treatments can drop dramatically after research, or an agreement may be reached with a pharmaceutical company that the treatment will be provided for free for a certain period. Providing access will depend on several factors, including whether alternatives exist, the relative burden of the disease and the costs of supplying treatment [Chapter 9].

Should an intervention be provided after the trial?

The Report considers the provision of post-trial treatment to three groups of people: members of the control group, all of the research participants, and the wider community. The possibility of providing successful interventions to the wider community is often the most contentious issue.

We acknowledge that it may not be possible to ensure post-trial access in all cases. However, we conclude it is not ethically acceptable for research to begin without a decision being made as to whether members of the control group will receive an effective intervention. Researchers should also endeavour to secure post-trial access to successful interventions for all trial participants. The possibility of providing a treatment in the wider community should be considered before research is begun and we recommend that possible options should be clarified as early as possible [paras 9.27, 9.31 and 9.48-9.49].

Who should be responsible for making a successful intervention available?

We consider that the provision of new medicines or improved healthcare is primarily the responsibility of national governments. We recognise that sponsors may not be in a position to make long-term commitments before beginning a trial. However, researchers and sponsors should address the issue before starting research. They may also play a role by contributing to the development of local healthcare facilities [para 9.36].

Where participants have chronic diseases, who should be responsible for providing continuing care after the research is over?

Participants in research may have conditions that require continuing treatment. In such cases, it may be suggested that there is an obligation to continue to provide an intervention that has been shown to be effective. Researchers should try to secure post-trial access for effective interventions for all participants before the trial begins.

The Report also considers questions relating to adverse affects that occur as a result of an intervention under evaluation; long-term surveillance of participants after the research is over; the responsibilities of researchers, sponsors, international agencies and governments; and the continued provision of a higher level of healthcare [Chapter 9].

Ethical review

Research ethics committees

An effective system for ethical review of research proposals is a crucial safeguard for participants. However, properly functioning research ethics committees (RECs) are often absent, ineffective or under-resourced in developing countries. In addition, there may not be enough trained and independent people to serve on a committee.

What types of review should be required?

We recommend that each proposal should receive three levels of assessment:

- relevance to healthcare priorities within the country;
- scientific validity; and
- ethical acceptability.

Appendix 1 outlines some of the issues to be considered when reviewing research proposals.

We recommend that scientific and ethical review should, where possible, be undertaken separately because they serve different purposes. This may, but will not necessarily, require the establishment of two committees [paras 8.4-8.5].

Where should ethical review take place?

All developing countries should have a properly functioning system for the independent ethical review of research. If an independent national REC is the most appropriate way to review externally-sponsored research, we recommend that the Government should be responsible for establishing and funding the committee [para 8.16].

It is important that both the country in which the research is to be conducted and the sponsor providing funding should be satisfied about the ethical acceptability of research. We therefore recommend that externally-sponsored research projects should be reviewed both in the local country(ies) and in the sponsor's country(ies). There should be mechanisms in place to allow the committees to negotiate if there is disagreement between them [paras 8.22-8.25].

Who should fund research ethics committees?

Many RECs in developing countries have very limited financial and administrative support. Some may receive funding from government, while others levy fees for reviewing protocols.

It is crucial that RECs are independent. We conclude that there is a need for creative approaches for providing support for RECs, without compromising their independence. Sponsors should be responsible for meeting the costs of reviewing externally sponsored research in an appropriate manner [para 8.20].

Developing capacity

Local expertise in healthcare-related research is generally very limited. Externally sponsored research has the potential to allow regional scientists to develop skills and expertise. Partnerships between scientists from developed and developing countries can help to build capacity. The development of expertise in ethical review is also urgently required.

We recommend that sponsors of research should require that the development of local expertise in healthcare is an integral component of research proposals [para 9.52]. Consideration should also be given to longer-term issues – it is important to ensure that improvements to healthcare facilities are sustainable once the research is over [para 9.12]. We recommend that international organisations should help to strengthen research ethics committees by expanding initiatives that assist with training and monitoring [para 8.29].



Summary

- *There is an urgent need for externally sponsored research in developing countries. However, rigorous ethical safeguards must be in place to prevent the exploitation of those who take part in the research. The Report aims to provide a framework for anyone who is designing or conducting healthcare research in developing countries.*
- *Research must be appropriately planned, taking account of the local context, and effectively reviewed on scientific and ethical grounds. Externally sponsored research also provides the opportunity to assist developing countries to strengthen expertise in conducting and reviewing research.*

Copies of the Report are available to download from the Council's website:
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To order a printed copy, please email bioethics@nuffieldbioethics.org

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Nuffield Council on Bioethics
28 Bedford Square
WC1B 3JS

Telephone: +44 (0)20 7681 9619
Fax: +44 (0)20 7637 1712
Internet: www.nuffieldbioethics.org