Chapter 7

Standards of care

Introduction

7.1 This chapter examines the ethical considerations that arise when researchers determine the standards of care to be provided for participants in research. In particular, we focus on whether participants in the control group of a research trial should be provided with a universal standard of care, regardless of where the research is conducted (see Box 7.1). This issue was highlighted in 1997 in the dispute about the standard of care to be provided to those involved in clinical trials investigating the prevention of the transmission of HIV from mother to child (see Box 1.2).

7.2 Research conducted in developing countries should be relevant to the healthcare needs of that country (see Chapter 2). However, debate has arisen about how the requirement that research be relevant should be balanced against the need to avoid exploitation of participants in research in developing countries. The debate arises in the following way. Some argue that when research is externally sponsored, participants in developing countries should receive the same standard of care and treatment as would participants in the country sponsoring the research. In contrast, others claim that the requirement that participants be offered the same standard of care and treatment, whether or not they live in developed or developing countries, would prevent some forms of research from being carried out which could lead to improved healthcare in developing countries. For example, researchers may seek to determine whether a new treatment for a disease is better than the one currently available in a developing country. To do this they may want to compare the new treatment with the current treatment that is available within that country, rather than with another, but much more expensive treatment that is available in developed countries.

> ### BOX 7.1   Standards of care
>
> We are aware that use of the term 'standard of care' has been criticised in the context of research related to healthcare because of its ambiguity.[1] Rather than introduce a new term, we have chosen to adopt the term 'standard of care' in the Report, and define it as: 'the nature of the care and treatment that will be provided to participants in research'.[2] We use the term simply as a generic description of the range of preventive or curative treatments (or lack of them) and diagnostic interventions which are made available to participants.
>
> We use the term 'universal standard of care' to indicate the best current method of treatment available anywhere in the world for a particular disease or condition. For most diseases and conditions such a standard of care is routinely available to only a small proportion of the world's population.
>
> ---
>
> 1 See for example, National Bioethics Advisory Commission (NBAC) (2001) **Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries. Volume I: Report and Recommendations of the National Bioethics Advisory Commission**: 9 and Benatar SR and Singer PA (2000) A new look at international research ethics, **British Medical Journal**, 321 824–6.
> 2 While the term 'standard of care' is used in law to refer to the standard of treatment that a court would conclude that a reasonable physician would provide in the circumstances, the term is used here to describe what happens in practice, whether or not it could be considered to be reasonable or appropriate.

Existing guidance

7.3 The existing international and national guidance embraces a range of interpretations about what standard of care should be provided during the conduct of research (see Table 7.1 and Appendix 1 Table 2). The Declaration of Helsinki (2000) is the primary source of guidance on which the majority of other guidance draws. It is, therefore, our starting point. The relevant provisions are set out in Table 7.1. In the context of developing countries, the best current method of treatment (paragraph 29) is frequently not accessible and the majority of people are 'economically and medically disadvantaged' (paragraph 8). The difficulties that can arise when meeting the requirement of comparing a new treatment to the best current method of treatment while also recognising the needs of the economically and medically disadvantaged are discussed below.

Table 7.1

Primary sources of international guidance on standards of care

Source	Text
CIOMS 'International Ethical Guidelines for Biomedical Research Involving Human Subjects' (1993)[1]	Research in developing countries should be 'responsive to the health needs and the priorities of the community in which it is to be carried out'. **Guideline 8** 'If there is already an approved and accepted drug for the condition that a candidate drug is designed to treat, placebo for controls usually cannot be justified'. **Commentary on Guideline 14**
WHO 'Guidelines for Good Clinical Practice (GCP) for trials on pharmaceutical products' (1995)	'The investigator is responsible for adequate and safe medical care (or dental care, where appropriate) of subjects during the trial …' **Principle 4.1** 'In accordance with Sections 4.1 and 4.3 of these guidelines, the investigator must ensure the safety of the trial subjects. This includes providing the best possible care for subjects experiencing any trial-related adverse events and conducting a thorough investigation to determine causality'. **Principle 7.1**
International Conference on Harmonization (ICH) Harmonised Tripartite Guideline. Guideline for Good Clinical Practice (1996)	'Clinical trials should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with GCP and the applicable regulatory requirement(s)'. **Principle 2.1** 'During and following a subject's participation in a trial, the investigator/institution should ensure that adequate medical care is provided to a subject for any adverse events … related to the trial'. **Principle 4.3.2**
World Medical Association 'Declaration of Helsinki' (2000)	'The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic and therapeutic methods.' **Paragraph 29** 'Even the best proven prophylactic, diagnostic and therapeutic methods must continuously be challenged through research for their effectiveness, efficiency, accessibility and quality.' **Paragraph 6** 'The particular needs of the economically and medically disadvantaged must be recognised'. **Paragraph 8**
UNAIDS 'Ethical Considerations in HIV Preventive Vaccine Research' (2000)	'As long as there is no known effective HIV preventive vaccine, a placebo control arm should be considered ethically acceptable in a phase III HIV preventive vaccine trial'. **Guidance Point 11** 'Care and treatment for HIV/AIDS and its associated complications should be provided to participants in HIV preventive vaccine trials, with the ideal being to provide the best proven therapy, and the minimum to provide the highest level of care attainable in the host country in light of … circumstances listed.'[2] **Guidance Point 16**

[1]This guidance is currently being modified and the revised edition is expected to be published in 2002.
[2]Circumstances include: level of care and treatment available in the sponsor country, highest level of care available in the host country, highest level of treatment available in the host country (including the availability of antiretroviral therapy outside the research context in the host country), availability of infrastructure to provide care and treatment in the context of research, potential duration and sustainability of care and treatment for the trial participant.

Defining the best current method of treatment

7.4   When considering what the Helsinki Declaration requires, a clear understanding of the complexities of defining 'best current' method of treatment is needed. One definition of the best current method for a particular disease might be that which is most effective. However, achieving agreement about the most effective method is often far from straightforward. First, there may be a divergence of views within a particular medical community about what constitutes the best method of treatment. Even the evidence from controlled trials may be inconclusive or subject to debate, leaving scope for disagreement about which method of intervention is the 'best'. Secondly, even if one medical community reaches a consensus about what constitutes the best current method of treatment, there may be disagreements among different medical communities. For example, the UK and US have different views about the methods used to screen for lung cancer (see Box 7.2).

7.5   Although there may be some debate about what constitutes the best current method of treatment available anywhere in the world, there is usually less room for debate about which is the better

when comparing the methods available in developing countries as against developed countries. Because of the greater resources available, in many instances it will be unarguable that the care available in developed countries for a particular condition is better, i.e. more effective, than that widely available in a developing country. In light of this disparity, the issue we address is what standard of care should be provided to participants in research when there is a discrepancy in the standard of care in the country in which the research is conducted and the country sponsoring the research.

> **BOX 7.2 Screening for lung cancer**
>
> At present a trial is being planned in the UK and other European countries to determine whether a novel form of screening for lung cancer will reduce mortality by detecting the cancer. In the trial, one group will receive the new form of screening (low dose spiral computed tomography), while the control group will receive no screening. In a similar trial planned in the US, this new form of screening will be compared to screening using a chest x-ray. In contrast to the US, the view held in the UK, and in some other European countries, is that there is no evidence that a chest x-ray is an effective method of screening.

The appropriate standard of care for control groups in clinical trials

7.6   The different approaches that have been proposed when deciding the level of care that should be provided for those in the control group of a clinical trial can be divided into two broad categories:

● universal: the best treatment available anywhere in the world, wherever the research is conducted

● non-universal: the treatment available in a defined region.

Our aim in making this distinction is to separate the universal or global 'best' from all other levels of care, be they local, regional or national.

7.7   The approach of those who are in favour of a universal standard of care being provided to the control group in clinical trials is set out in a widely quoted editorial by Marcia Angell in the **New England Journal of Medicine**:

> I believe that our ethical standards should not depend on where the research is performed … Furthermore I believe the nature of investigators' responsibility for the welfare of their subjects should not be influenced by the political and economic conditions of the region. It would follow that these conditions should not be used to justify providing a lower standard of care for some subjects than they would have received had they taken part in the same study in a different place. In practical terms any other position could lead to the exploitation of people in developing countries, in order to conduct research that could not be performed in the sponsoring countries.[1]

7.8   Marcia Angell sets out at least three principles: one concerned with the importance of avoiding the exploitation of people in developing countries; one concerned with the responsibilities of researchers and sponsors or research; and one concerned with the need to avoid making the standard of care depend upon the local context. We address each of these in turn.

---

1   Angell M (2000) Investigators' responsibilities for human subjects in developing countries, **New England Journal of Medicine**, 342(13) 967–9.

Avoiding exploitation

7.9   The Working Party is firmly of the view that the need to avoid exploitation is imperative. As we have stated in Chapter 4, it is a fundamental ethical principle that those involved in research in developing countries, including research teams, pharmaceutical companies and governments, should not take advantage of the vulnerabilities created by poverty or a lack of infrastructure and resources. However, as discussed below, the Working Party considers that insisting upon a universal standard of care may not always be the best way to respect this principle.

7.10   At first sight, justice might seem to require that we treat people identically, regardless of context, because justice demands equal respect. If showing respect for the participants in a particular research project in the developed world demands that they receive a particular intervention, it would seem to follow that parity of respect means that participants in similar research conducted in the developing world should receive the same intervention. To apply a lower standard of care would thus be not only to take advantage of the participants' vulnerabilities, but also to commit an additional wrong by perpetuating an injustice. However, the principle of equal respect does not imply that we must behave towards others in a uniform manner, since features of individuals and of their circumstances will differ. Parity of respect requires us to address the specific needs and circumstances of individuals in determining how to behave towards them. What we mean by equality is not that people must always be treated identically, but that 'for *every* difference in the way men are treated, a [relevant] reason should be given'.[2] Thus, the context of the research in different countries must be critically assessed to establish whether or not it provides a morally relevant reason for offering a different standard of care (see paragraphs 7.17–7.18).

Responsibilities of researchers and sponsors

7.11   The goal of research related to healthcare is to gain information about diseases and to discover better methods of prevention, diagnosis and therapy that can be applied to benefit the wider community. Raising the quality of healthcare available to those in developing countries to the standard that exists in developed countries is necessarily a long-term goal. Given current inequities, it will clearly not be possible, in the short term, to improve the health of their populations to the level of their counterparts in the developed world. Research on improving preventive and therapeutic methods in developing countries is necessarily conducted within this context.

7.12   Some commentators have argued that by failing to extend to those participating in research in a developing country, the level of treatment that would be given in the sponsors' own, more wealthy country, external sponsors thereby harm the participants in research. Indeed, a central argument against the perinatal HIV-transmission trial (see Box 1.2) put forward by Lurie and Wolfe was that the conduct of the research would 'lead to hundreds of preventable HIV infections in infants'.[3] One response to this argument is to suggest that in not providing a universal standard of care, research sponsors do not harm the participants, they merely fail to benefit them; that is, they do not put participants in a worse position, but neither do they improve their position. However, this cannot be the end of the matter.

7.13   The fundamental duty to alleviate suffering has a natural extension, namely a duty to provide a positive benefit, though defining the extent of the duty to benefit in a given situation is a

---

2   See Williams B (1973) The Idea of Equality, in Williams B **Problems of the Self**, Cambridge University Press, New York, for a clear exposition of the view that what we mean by equality is not that people must always be treated identically, but that 'for *every* difference in the way men are treated, a reason should be given' that is relevant.

3   Lurie P and Wolfe SM (1997) Unethical trials of interventions to reduce perinatal transmission of the human immunodeficiency virus in developing countries, **New England Journal of Medicine**, 337: 853–6.

challenging task.[4] In many research projects, it will be the case that the greater wealth of the sponsoring country or institution means that there will not be a financial barrier to offering a higher level of care than that which is available locally to those in a specific research study. The Working Party notes that a person's duty to benefit another is related to his or her capacity to do so, whether financial or practical. If a particular benefit cannot be provided for reasons of practical constraint, the duty to do so is weakened. Conversely, if a country's wealth allows it to confer a benefit on the inhabitants of another country when that country cannot do so itself, the wealthier country has a stronger duty to provide that benefit.

7.14 In some research projects, the care provided to participants in developing countries can be higher than the national standard without significantly affecting the requirement to conduct research relevant to that country's health needs or the economic constraints on sponsors. This is most likely to be the case with respect to the treatment of conditions that arise among participants in research during the course of a study. For example, consider a trial of a new vaccine for malaria that is conducted in an area where there are high levels of drug-resistance to the disease. The main aim of the research may be a comparison of the incidence of malaria in the two arms of the trial (new vaccine and control), but researchers may be able to make available medicines that may not be available nationally for the treatment of cases of malaria. However, the desirability and sustainability of such measures should be fully discussed with local health services in advance, to ensure that the otherwise unavailable treatment does not lapse as soon as the research is completed (see Chapter 9).

7.15 It must be noted, nonetheless, that the most effective way to discharge the duty to alleviate suffering with respect to a particular research participant will not necessarily be to provide them with a universal standard of care during the conduct of research. For example, patients with chronic diseases may not be better off in the long term if they receive a standard of care during a research project which cannot be sustained once the project ends. In other words, the question of what standard of care and treatment should be made available during the conduct of research may not be separable from the question of what care is made available once the research is completed. Should participants require long-term care, the two issues necessarily overlap.

Unsafe practices

7.16 Researchers will be obliged to raise the standard of care above the national standard when that national standard is unsafe. In the example from South-East Asia set out in Box 7.3, the re-use of equipment for taking blood was the routine local practice. Researchers have a duty to prevent avoidable harm to participants in research. The use of unsafe or harmful practices, even if they

---

BOX 7.3 Research in South-East Asia

Research studies in one South-East Asian country required a lancet to be used to take a blood sample. In that country it was common practice for lancets to be re-used after being dipped in alcohol. In most countries, lancets are not re-used because of the high risk of cross-infection. Health professionals in the country were aware of the risks inherent in the multiple use of lancets, but a period of famine had just ended and there were very limited financial resources to purchase new equipment. Researchers wanted disposable lancets to be used in the study. To avoid creating internal difficulties within the hospital, it was therefore necessary to provide an adequate supply of such lancets for the whole of the hospital.[1]

---

1   Personal communication, Working Party fact-finding meeting.

---

4   For a thought-provoking attempt to set out the limits of this obligation, see Unger P (1996) **Living High & Letting Die: our illusion of innocence**, Oxford University Press, New York.

are routine locally, is unacceptable. It follows that adopting a non-universal rather than a universal standard of care in research does not provide a justification for employing unsafe practices.

The importance of the research context

7.17 In paragraph 7.10 we noted that equal respect for participants in research does not necessarily entail that they should receive equal treatment, regardless of where the research may be conducted. Instead, the circumstances in which the research will be conducted must be critically assessed to establish whether or not the variations in circumstances provide a morally relevant reason for offering a different standard of care.

7.18 We take the view that, in determining the appropriate standard of care to be provided to participants in the control group of a research trial, a number of factors should be considered by sponsors, researchers, and research ethics committees. These include:

- the appropriate research design(s) to answer the research question; (in some situations only one research design may be appropriate to answer the research question, in others a number of research designs, in which different standards of care are offered to the control group, may be possible)
- the seriousness of the disease and the effect of proven treatments
- the existence of a universal standard of care for the disease or condition in question and the quality of the supporting evidence
- the standard(s) of care in the host and sponsoring country(ies) for the disease being studied
- the standard(s) of care which can be afforded by the host and sponsoring country(ies) for the disease being studied
- the standard(s) of care which can effectively be delivered in the host country(ies) during research
- the standard(s) of care which can be provided in the host country(ies) on a sustainable basis.

BOX 7.4   Treatment of schistosomiasis with praziquantel

For some diseases there is widespread agreement about the standard of care that will be provided for those infected, wherever they are in the world. For example, cost-effective control tools, based on treatment with praziquantel, are available for treating schistosomiasis. This has resulted in prolonged, sustainable national control programmes in endemic countries such as Brazil, China, the Philippines and Egypt, and eradication or near eradication of the disease in countries such as Puerto Rico, Venezuela, Saudi Arabia, Tunisia and Morocco. Africa now accounts for an estimated 80% of the remaining cases of the disease and WHO is committed to reviving control of the disease in Africa, with a simple morbidity control package including affordable access to praziquantel at all levels of healthcare.[1]

---

1   See http://www.who.int/ctd/schisto/index.html.

7.19 Taking the above considerations into account, in some circumstances, it will be clear that a control group in a clinical trial should receive a universal standard of care, wherever they live (see Box 7.4). For example, if research were to be conducted in any developing country into a new treatment for schistosomiasis, we consider that the control group in such research should at least be offered praziquantel or a medicine with the same efficacy. We base this view on the fact that an effective, proven treatment for schistosomiasis exists and has been approved and implemented in affected countries around the world. The treatment has been demonstrated to be affordable and feasible to deliver, in a sustained manner in developing countries. Any future research is likely to focus on forms of care that are better than this treatment, and thus it will be an appropriate comparison for the control group to receive.

7.20 In contrast to the case above, there are situations in which it is clear than even if there were an agreed universal standard of care for a disease, it may not be possible for this standard to be provided to the control group in a research project. In some cases the universal standard of care will not be able to be provided because of practical considerations. For example, if a treatment was sought for a condition such as liver cancer (which often develops in carriers of hepatitis), the universal standard of care includes surgery to remove the tumour or a liver transplant. While the sophisticated infrastructure required to provide such treatments is available in developed countries, (including intensive care units, trained surgeons and healthcare staff) it is very limited or absent in the majority of developing countries. If researchers sought to develop a form of treatment for liver cancer which would be affordable, deliverable and sustainable in developing countries, it is unlikely that it would be possible to provide a universal standard of care to the control group in the research.

7.21 Practical constraints may not be the only factor preventing delivery of a universal standard of care in research. For example, when research into preventing the perinatal transmission of HIV was conducted in the Cote d'Ivoire in 1995, researchers were not able to provide women in the control group with the universal standard of care which involved administration of the medication in pregnancy, intravenous infusion during labour and delivery, and administration of the medicine to the infant four times a day for six weeks. This complicated regimen, which requires voluntary counselling and testing for HIV to be performed early in pregnancy, has limited application for many developing countries where women have poor access to antenatal care and may only seek assistance from healthcare workers after the onset of labour.

7.22 In the two cases outlined above, even though a universal standard of care cannot be provided to participants, it can be convincingly argued that the research should nevertheless be conducted because it offers the opportunity of developing responses to important healthcare needs in developing countries.

7.23 We have set out contrasting cases in which it can be said to be respectively appropriate or inappropriate, to offer a universal standard of care to participants who are in control groups. However, the decision about whether or not a universal standard of care is called for is usually not so straightforward. It involves a careful consideration of the various factors outlined in paragraph 7.18. In circumstances where it is apparent that a universal standard of care is not appropriate, further analysis of these factors will be required to determine what the appropriate standard of care should be.

7.24 In some circumstances, differing research designs may each provide relevant information about a particular disease or intervention. Researchers and research ethics committees will need, therefore, to consider which design is the most suitable. A number of respondents to our public consultation and in our fact-finding meetings stressed the importance of involving local researchers when designing research and determining appropriate standards of care. An awareness of the standards of care currently being used within developing country(ies) and of information sought by local providers of healthcare will increase the likelihood of research being relevant to local needs and producing results that are likely to be applicable in developing countries.

7.25 It should be borne in mind that any definition of the 'best treatment' which may be available in a country is subject to change over time, in response to the results of research, and will affect the standard of care that it is appropriate to offer to participants in research. For example, in initial trials investigating perinatal HIV transmission in Thailand which involved testing a short course of therapy (see Box 1.2), a trial design in which the control group received a placebo was considered to be acceptable. Since this research has demonstrated the effectiveness and feasibility of the short course treatment in Thailand, further research which provides the control

group in the research project with anything less than the short course of treatment would be unethical. Currently, trials to assess the potential additional efficacy of new medicines or combinations of medicines in preventing perinatal transmission of HIV in a developing country setting provide a short course regimen of proven efficacy to the control group.[5]

Defining a non-universal standard of care

7.26 Where it is not appropriate to require that a universal standard of care be provided to the control group, in the light of all the relevant circumstances, questions arise about what standard of care should be provided. For example, should it be a national, regional or local standard? Should it be the level of care available in a local hospital, a district hospital, tertiary institution or within the private sector? The ultimate goal of research must be to provide information about treatment and other interventions which can then be used by national governments to ensure that improvements are made in the provision of healthcare. Thus, for policy reasons, it seems sensible to take the particular country as the unit of focus, as it is national governments which, by and large, take responsibility for the health of their citizens and which make decisions about the provision of healthcare. With knowledge of the resources available to them, governments make decisions about the level of care which they can provide for the prevention and treatment of specific diseases or conditions. In that context, they set targets for the level of care that they will strive to achieve, often recognising that it will not be possible to meet this goal.

7.27 The Working Party is of the view that in externally-sponsored research, the level of care that ought to be offered to participants should, as a minimum, be the standard that the country endeavours to provide nationally. In many circumstances, it may be appropriate for researchers to offer a higher level of care than this, while still conducting research that is relevant to the local setting. Exceptionally, it may be appropriate to provide a level of care that falls below the national standard. The ethical justification for this, however, will need to be carefully argued and accepted by local authorities and ethical review bodies before such research can be conducted (see paragraph 7.30).

7.28 We have previously noted that defining the 'best treatment' is not straightforward (see paragraphs 7.4–7.5, 7.25). Similarly, it may not be easy to identify a single 'national standard' of care. In many countries, the 'best' levels of care may be available within private healthcare systems, although in most developing countries these provide care for only a small proportion of the population, while most people are served by the public health service. In setting the national standard of care, it would seem appropriate to concentrate on what can be provided within the public health system, as this is under the direct control of national governments. The challenge in defining the national standard of care may be greater in large countries (with regional differences in access to healthcare) than in small countries. In some circumstances it may be appropriate to use a regional standard (within a country) rather than the national standard. However, again this will need to be carefully justified.

7.29 We conclude that discussion with clinicians, researchers and representatives of government and health authorities within the host country is essential so as to establish what the best national level of treatment available as part of the national public health system is. **We recommend that in setting the standard of care for the control group of a particular research project the context in which the research is to be conducted be carefully evaluated. A suitable standard of care can only be defined in consultation with those who work within the country and must be justified to the relevant research ethics committees. Wherever appropriate, participants in the control group should be offered a**

---

5   For example a study in South Africa is comparing the efficacy of two new medicines alone, and in combination with a zidovudine only short course regimen.

universal standard of care for the disease being studied. Where it is not appropriate to offer a universal standard of care, the minimum standard of care that should be offered to the control group is the best intervention available for that disease as part of the national public health system. A summary of the reasoning behind this conclusion is given in the Box 7.5.

Deviations from the national standard

7.30 In exceptional circumstances, research may be proposed which involves the use of a standard of care that is lower than the best available intervention as part of the host country's public health system for the disease being studied. For example, researchers may wish to demonstrate that what is deemed to be the best treatment available through the host country's public health system is ineffective, or even harmful, by comparing it to a placebo, or an apparently lesser standard of care. Alternatively, researchers may wish to show that the best available intervention in the host country as part of the public health system for a particular disease is so beneficial that it should be made more widely available within the country (see Box 7.6). Prophylactic chemotherapy to prevent tuberculosis (TB) is widely recognised to be the best treatment for individuals who are HIV positive in countries in which TB is endemic. However, it is not possible to provide this treatment in many African countries that can barely maintain their current TB Control Programmes. Research to investigate how to implement prophylaxis for TB might compare current practice (normally no prophylaxis) with other approaches. If an aim of research into healthcare is to improve current forms of treatment, then there may be circumstances in which it is justified to compare current local practice with a new treatment, in the local setting.

BOX 7.5 Summary of arguments about standards of care

The principle of not exploiting those who are vulnerable lends support to the adoption of a universal standard of care so that people in different countries receive the same care and treatment during research.

However, in some circumstances it may not be possible to adopt a universal standard of care. In other circumstances, providing a universal standard of care to the control group may not provide research results that are relevant to the country in which the research is conducted.

In an ideal world, variations in healthcare resources throughout the world would be eliminated. But the duty to undertake research requires us to act even in a non-ideal world where resources are limited and not equally distributed.

Therefore, the challenge is to fulfil this duty to undertake research in a way that is consistent with the principle of not exploiting those who are vulnerable.

This can be achieved by requiring the standard of care to be universal where possible, or at least that which is available as part of the national public health system of a country, and by improving standards wherever feasible.

BOX 7.6 STD and HIV research

In one country, a national programme for the treatment of sexually transmitted diseases (STDs) was not widely implemented, so that, in many regions, the availability of antibiotics to treat STDs, as contemplated in the programme, was limited. Research was conducted in which randomised communities received either existing care, or the antibiotic treatment for STDs recommended in the national programme. The rationale for this research was to demonstrate that if the national programme was widely available, it would reduce both the level of infection with STDs and HIV. Once this finding was demonstrated, the evidence that treating STDs would also reduce the level of HIV infection provided an incentive for the government to make the national programme for treating STDs widely available. The research also demonstrated that it was possible to implement the national programme on a large scale.[1]

1   Grosskurth H, Mosha F, Todd J, Mwijarubi E, Klokke A, Serkoo K *et al*. (1995) Impact of improved treatment of sexually transmitted diseases on HIV infection in rural Tanzania: randomised controlled trial, **The Lancet** 346(8974) 530–6.

7.31 Research on the management of outbreaks of disease in isolated places may necessarily involve standards of care that are lower than the best which are available nationally. For instance, research on the management of an outbreak of meningococcal meningitis in Northern Nigeria may have to accommodate thousands of people being cared for in the open, the performance of lumbar punctures and the administration of single-dose antibiotic therapy under conditions that are clearly less than the national standard. Denying these communities the opportunity to participate in research denies them improvements in healthcare and new ways to manage sick patients in settings with very limited resources.

Research into preventive measures

7.32 In some forms of research, such as those designed to determine the incidence of a disease in a population, or to prevent participants from contracting or developing a disease, the standard of care received by participants who develop the disease will not be immediately relevant to the research.[6] This is because the research is focused on preventing participants from contracting the disease, rather than the subsequent effects of and possible treatments for the disease. Under these circumstances, however, there is still a need to consider the standard of care which a patient should receive because the disease, once diagnosed, may have serious implications for the individual. The issue was the subject of extensive consultation in the developing countries in which the research to develop a vaccine to prevent infection with HIV was to be undertaken. Following these consultations the UNAIDS guidance on ethical considerations in research on a HIV preventive vaccine recommends:

> Care and treatment for HIV/AIDS and its associated complications should be provided to participants in HIV preventive vaccine trials, with the ideal being to provide the best proven therapy, and the minimum to provide the highest level of care attainable in the host country in light of the circumstances listed below. A comprehensive care package should be agreed upon through a host/community/sponsor dialogue, which reaches consensus prior to initiation of a trial, taking into consideration the following:

> ● Level of care and treatment available in the sponsor country

> ● Highest level of care available in the host country

> ● Highest level of treatment available in the host country, including the availability of antiretroviral therapy outside the research context in the host country

> ● Availability of infrastructure to provide care and treatment in the context of research

> ● Potential duration and sustainability of care and treatment for the trial participant. **Guidance Point 16**[7]

7.33 **We endorse Guidance Point 16 of the UNAIDS guidance on Ethical Considerations in HIV Preventive Vaccine Research. 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 under study. Where it is not appropriate to offer a universal standard of care, the minimum standard of care that should be offered is the best available intervention as part of the national public health system for that disease.**

---

6   For example, in vaccine trials and studies of other measures to prevent diseases such as malaria and AIDS, research will be designed to test the effectiveness of the proposed intervention. This assessment can be made by determining how many of those who receive the intervention go on to develop the disease being studied.

7   UNAIDS (2000) **Ethical Considerations in HIV Preventive Vaccine Research. UNAIDS Guidance Document**: Guidance Point 16.

Care for other conditions

7.34 During research into some diseases, participants may develop a condition that is related to the condition under study. For example, in certain regions individuals with STDs are more likely to become infected with HIV than those without (see Box 7.6). In addition, during research, participants may develop an entirely unrelated condition. In some circumstances, it may be relatively easy for researchers to treat the condition or refer participants to a local health centre where treatment can be provided. In other cases, researchers may not have the expertise to treat the condition effectively and appropriate treatment may not be available locally as part of the public health system.

7.35 As discussed in paragraph 7.13, in addition to researchers' duty not to harm participants in research, there is a duty to benefit participants where possible. Thus, where it is feasible for researchers to diagnose and treat an illness which arises, or to ensure that effective treatment is available at a local level, they have a duty to do so. This is a complex issue and decisions will need to be made on a case-by-case basis following discussion with clinicians, researchers and representatives of government and health authorities within the host country. **We recommend that before research begins, agreement should be reached about the standard of care that should be provided to participants in research who already have or who develop diseases other than the disease being studied. We conclude that the minimum standard of care that should be offered is the best intervention available as part of the national public health system. Any proposal which contemplates care of a lower standard deviation must be justified to the relevant research ethics committees.**