Research involving patients

SUMMARY AND RECOMMENDATIONS OF A REPORT OF THE ROYAL COLLEGE OF PHYSICIANS

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Summary

The careful study of disease as it occurs in patients, and the equally careful scrutiny of the effects of treatment, are an indispensable part of the continuing process of improving the efficiency of diagnosis and the effectiveness of treatment. Most patients realise that experience gained from their own case may contribute to their personal benefit or to that of society and, if asked, readily agree to take part in research into their condition. Accordingly, a patient who willingly participates in research has the status of a volunteer similar to that of a healthy person so that some of the questions relating to selection, consent, conduct of research and compensation in the event of injury are similar to those addressed in the College’s report on Research in healthy volunteers, published in 1986. It is important to realise, however, that the patient is in a position of at least partial dependence which may affect the degree of voluntariness of collaboration, and also that there is a risk that enthusiasm on the part of the researcher could lead to undue persuasion or incomplete declaration of the facts. Furthermore, the patient’s ability to give consent to participate in research may be impaired by illness. For these and other reasons, the College has prepared a separate report addressing the special problems of Research involving patients.

A balance has to be struck between the benefits which may flow from properly conducted research, and the risk of infringing the autonomy, or of causing harm to the individual patient. The report provides guidance for all concerned—including patients, researchers, doctors, nurses and other health workers, sponsors of research, Research Ethics Committees and the institutions in which research takes place. The general public, too, may find this report useful.

This report should be read in conjunction with the second edition of the College’s Guidelines on the practice of ethics committees in medical research involving human subjects, which is being published at the same time as this report. The Guidelines describe the contribution and working of medical Research Ethics Committees and are designed to assist those committees in their work. Necessarily, many of the issues are common to these two publications, particularly those concerned with consent given by patients to participate in a research study, and the conduct and monitoring of research on human subjects.

This report considers all forms of research in patients, whether they involve the study of treatment which may benefit individual patients (therapeutic research) or the acquisition of knowledge which can be of no immediate benefit to the patient (non-therapeutic research). The discussion of medical research in this document includes research involving surgical procedures. It does not include fetal tissue.

Particular attention is paid to potentially vulnerable groups of patients such as unborn babies, children, elderly people, patients suffering from mental illness or handicap, and patients in custody. The report also gives consideration to special cases such as research in severely ill or unconscious patients, or research into sudden unexpected events in which it may be difficult to obtain consent for the investigation. Arrangements for compensation in the event of injury occurring as a result of participating in research are also considered, as is the need to protect the patient’s confidentiality.
Recommendations

Research involving patients is in the interests of patients and of society and should proceed without unnecessary impediment. Certain safeguards are, however, necessary to protect the patient from suffering physical or emotional harm or breach of confidentiality in the course of research.

Role of Research Ethics Committees

1. All research involving patients should be approved by a local Research Ethics Committee. This applies to research undertaken in hospitals and in other institutions, research conducted in general practice and elsewhere in the community and research carried out by doctors and non-medical health or other workers. Recommendations on the composition and function of Research Ethics Committees are set out in Chapter 4 of the full report.

Assessing the aims, quality, risks and benefits of research

2. The Research Ethics Committee should be satisfied that the question addressed by the research activity is a worthwhile one and Research Ethics Committees should examine the overall design of proposed research that comes before them.

3. Research Ethics Committees must assess whether, in proposed research, the risk or inconvenience caused to the patient is justifiable in relation to the value of the information sought.

4. Research Ethics Committees and investigators have a duty to ensure that the risks inherent in proposed research have been reduced to the minimum necessary to achieve the research objective.

5. Investigators must ensure that the study protocol effectively excludes special groups of patients in whom the risk of participation would be particularly great.

6. As a general rule, research involving patients should not incur risk greater than minimal. An exception to the general rule may be justified where there is great potential benefit to the individual participating in therapeutic research (that is, research which offers the prospect of direct benefit to the patient taking part). Non-therapeutic research involving greater than minimal risk might be approved by a Research Ethics Committee but only under rare circumstances where: i. the risk of the research procedure is still very small in comparison to the risks already incurred by the patient as a consequence of the disease itself; ii. the disease under study is a serious one; iii. there is great potential benefit in terms of the importance of the knowledge gained; iv. there is no other means of obtaining the knowledge; and v. the subject understands well what is involved and wishes to participate.

Selection of patients and use of medical records

7. Any list of patients’ names should be confidential to the person or institution responsible for its construction.

8. Where records are used as a starting point in the recruitment of patients, the person who approaches the patient should normally be the individual who was responsible for the clinical care at the time that the patient’s relevant case records were generated.

9. Research work based upon scrutiny of medical records should continue without unnecessary impediment, but great care is required to avoid causing harm or distress to patients or their relatives, particularly through breach of confidentiality. Research which will involve access to personal medical records should receive approval by the local Research Ethics Committee.

Recruitment of patients

10. Arrangements should be made to exclude patients who may be at increased risk from proposed research procedures.

11. Excessively frequent requests to patients to participate in research should be avoided.

12. Patients should be invited to participate in research as volunteers in the same way as healthy individuals are invited to volunteer.

13. In the course of inviting a patient to participate in research, an investigator must make it clear that the patient is free to decline to participate without giving a reason, that a decision to decline will be accepted without question or displeasure and that the patient will then be treated as though the matter had not arisen and without any disadvantage to future care.

14. The patient participating in research should understand that he will remain free to withdraw at any time, that no reason need be given for the withdrawal, that the withdrawal will be accepted without question, without incurring displeasure and without any disadvantage to future care.

Consent

15. Patients should know that they are taking part in research.

16. Research involving a patient should only be carried out with the patient’s consent. We have found it necessary to describe exceptions to this general rule in the case of some innocuous observations of behaviour, research based on anonymous specimens or on medical records and some research into unheralded emergencies.

17. The simple procedure of seeking oral consent after an oral explanation may need to be supported by additional measures.

A Patient Information Sheet may be used to back up the oral description of what is involved.
18. Research involving minimal risk or greater than minimal risk should be described in a Patient Information Sheet which is given to patients when they are invited to participate and retained by them. The Information Sheet should be submitted to the Research Ethics Committee for approval.

19. The use of written consent and a consent form is recommended in research projects associated with minimal or more than minimal risk or with significant discomfort. The Consent Form should be submitted to the Research Ethics Committee for approval.

Research involving children

20. Research which could equally well be done on adults should never be done on children.
21. Children should be consulted when the question of their participation in research arises.
22. Even if an investigator believes that a child is capable of giving consent the approval of a parent or guardian should be obtained before any research procedure is contemplated on a child under the age of 16 years. It may also be desirable to obtain parental consent in some older children.
23. Where the research is for the benefit of children generally, and the child is incapable of giving consent, the investigator can properly rely on the consent of a parent or guardian. If, when the parental approval has been obtained, a child objects to the procedure itself, the investigator and the parent or guardian should reconsider whether it is appropriate to proceed.

Research involving the mentally handicapped

24. Research should never be carried out in mentally handicapped patients which could equally well be undertaken in adults who are not mentally handicapped.
25. Research in mentally handicapped patients should be limited to that which is related to mental handicap.
26. Research in mentally handicapped patients is subject to the usual constraints affecting all research in patients.
27. Many mentally handicapped patients are capable of giving consent but consideration should be given to the use of simple tests of competence and to the use of 'two part' consent forms in which the first part comprises a test. Even if consent is forthcoming it is good practice to obtain the consent of the next-of-kin after proper explanation of the intended research. A strong ethical case can be made out for therapeutic and non-therapeutic research involving only minimal risk in mentally handicapped patients not competent to give consent. The best guidance might be that there should be agreement by close relatives and that the individual should seem to consent to the procedure, but the legal status of such research remains uncertain.

Research involving the mentally ill

28. Research should never be carried out in mentally ill patients which could equally well be undertaken in adults who are not mentally ill.
29. Research in mentally ill patients should be limited to that which is related to the mental illness.
30. Research in mentally ill patients is subject to the usual constraints affecting all research in patients. Most patients with mental illness are competent to make up their own minds as to whether they wish to take part in research and to comprehend the implications of the research.
31. The Research Ethics Committee must be convinced that the inclusion of patients who are incompetent to give consent is acceptable and that it arises because the research is specifically directed to the condition of patients who might be incompetent.
32. Where competence is in doubt or absent, due to psychosis, dementia or other causes, and in all patients detained under the Mental Health Act irrespective of competence, a procedure which seeks what is in effect a mixture of consent by the patient and consent by a relative or nominated individual may be the most satisfactory arrangement. The same considerations affect therapeutic and non-therapeutic research in mentally handicapped and mentally ill individuals who are incompetent to give consent; the legal status of such research is at present uncertain.

Research involving prisoners

33. Research should not be undertaken solely in prisoners who are patients unless the fact of being imprisoned is itself an essential component of the research topic.

Research involving severely ill patients

34. Where the severity of a patient's illness renders him incompetent to give consent to participate in research the principles which should apply resemble those applicable to mentally handicapped and mentally ill patients.
35. In research involving severely ill patients the researcher should obtain as competent consent as
possible. No patient who refused or, if incapable of refusing, resisted should be included or continued in research. A near relative should be informed of the nature of the research and the details of what is involved and should concur. In general, the patient should be told about the participation in research later, when he recovers sufficiently to comprehend. The same considerations that affect therapeutic and non-therapeutic research in mentally handicapped individuals who are incompetent to give consent may also apply in mentally ill patients incompetent to give consent; the legal status of such research is at present uncertain.

Research involving pregnant patients

36. Research in pregnant patients should only be undertaken if pregnancy is an essential part of the research.
37. Research into pregnancy and childbirth requires special consideration since two individuals, mother and child, are inevitably involved and the rights and concerns of the father may need to be taken into account.

Research involving elderly patients

38. The participation of elderly patients in research is desirable. Elderly patients present special problems because of their altered metabolism, the frequency of multiple ailments, and their reduced tolerance of invasive procedures. In general, elderly patients should be assumed to be competent to give consent unless there is evidence to the contrary. It should not be thought that, because of their age, they need to know any less about the intended research than a younger patient.

Initiation of research without consent

39. There are some circumstances in which it is justifiable to initiate research without the consent of the patient. These are described in detail in the full Report. Such circumstances do not affect the duty of the investigator to obtain the prior approval of the Research Ethics Committee in the usual way.

Inducements to patients

40. Improved care should not be offered as an inducement to participate.
41. Payments to patients are generally undesirable but are occasionally acceptable in studies which are lengthy and tedious. Payments to patients should not be for undergoing risk and should not be such as to persuade patients to volunteer against their better judgement.
42. Any payments to be made to patients should be reviewed by the Research Ethics Committee.

Inducements to researchers

43. Personal expenses incurred by a doctor in the course of undertaking research involving patients may be reimbursed by the sponsor of the research. It is proper for doctors engaged in research to be paid a fee for their services but doctors should not be paid a fee for carrying out research work in sessions for which they are already being paid from another source.
44. The physician responsible for the project or trial is responsible for informing his employer of payments, for ensuring that proper accounting procedures are adopted with independent audit and for fulfilling all legal requirements. Financial arrangements should be made through the finance office of a health authority or a university and the accounts supervised by the financial officers.
45. Payments made to doctors must be reasonable in terms of the time and effort given to the trial and openly declared.
46. Payments made to doctors on a per capita basis (ie according to the number of patients that they recruit to a study) are unethical. Even fees paid to an institution on a per capita basis may lead to undue pressure to recruit patients.
47. All financial arrangements and also ad hoc payments should be divulged to Research Ethics Committees.
48. In the conduct of 'post-marketing surveillance' of medicines, the Guidelines drawn up between the Association of the British Pharmaceutical Industry, the British Medical Association, the Committee on Safety of Medicines and the Royal College of General Practitioners should be followed.

Randomised controlled therapeutic trials

49. The randomised controlled therapeutic trial has proved extremely valuable as a tool for examining the effectiveness of treatments and we give special attention to it because of its importance and because of the special ethical issues it raises. We discuss amongst other things the use of placebo treatments, double-blind procedure and randomisation. Detailed recommendations are set out in Chapter 7 of the main report.

Conduct of research

50. The ordinary requirements of patients — both medical and others — should not be neglected in the course of the involvement in research and the identity of the person in overall clinical charge of the patient's care must be clear.
51. Where research activities will be delegated by the investigator, the investigator should delegate only to individuals who have the necessary skills and experience.
52. The confidentiality of personal data must be preserved during the conduct of research.
53. The rights of patients, other doctors and sponsors to have access to the results of research require special consideration.
54. The results of research should be published free from any interference by financial sponsors of the research.

**Monitoring the conduct of research**

55. Research Ethics Committees should require investigators in charge of approved research projects to submit a brief report of progress at least annually.

56. Investigators should be requested to send copies of any published reports to the Research Ethics Committee.

57. Ways in which patients and health workers may approach the Research Ethics Committee when there is concern about the conduct of research should be devised and made known. It will sometimes be appropriate for this information to be included on the Patient Information Sheet.

**Arrangements for compensation**

58. Although the chances of harm coming to patients in the course of carefully conducted research are very small, it is important that proper arrangements are made to compensate patients in the event of such harm occurring.

59. Bodies that sponsor research, including both publicly funded bodies (such as the Research Councils, the Department of Health and the National Health Service) and the pharmaceutical industry, should now so arrange their affairs as to implement the principle that injury due to participation in research sponsored by them or conducted by their staff with the approval of a Research Ethics Committee shall be compensated by a simple, informal and expeditious procedure.

60. In the event of any significant injury the patient must be entitled to receive compensation regardless of whether there may or may not have been negligence or legal liability on any other basis.

**Acknowledgements**

The College thanks all those organisations and individuals who gave oral and written evidence. Their names are given in the full report.

The full report *Research involving patients* is available from the Royal College of Physicians, price £8.00. For information on other medical ethics publications see the panel below.

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### Medical Ethics Publications

*Guidelines on the practice of ethics committees involved in medical research involving human subjects* (2nd edition)

- Price: £8.00 (UK)  
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