

Research based on archived information and samples

RECOMMENDATIONS FROM THE ROYAL COLLEGE OF PHYSICIANS COMMITTEE ON ETHICAL ISSUES IN MEDICINE

In 1996 the College published *Guidelines on the Practice of Ethics committees in Medical Research involving Human Subjects* (3rd edition) which includes a section on unintrusive research. The recommendations published here are intended to clarify the issues surrounding this category of research as they relate to consent to the use of archived information and samples.

Properly designed and conducted medical research benefits society. Ethically sound research should therefore be encouraged and protected. Such research frequently involves the co-operation of research subjects, both patients and healthy volunteers. Those who participate in research as subjects, usually do so for the general good, although on some occasions there may be hope of self-benefit.

There is an inevitable tension between the requirement for research and the rights of individual research subjects. Patients, and to a lesser extent healthy volunteers, are vulnerable to exploitation and must be protected. Several important international agreements govern the protection of human subjects of medical research¹ and a considerable body of theory and practice in medical ethics has been built up.

Amongst the guiding principles, in the UK and internationally, are that research on human subjects should in general be undertaken only on the basis of individual consent*; and that such research should be subject to approval by an independent, credible and publicly accountable Research Ethics Committee.

The RCP has supported moves towards clear guidelines governing clinical research, and has played a leading part in developing the role of Research Ethics Committees in the UK.

We endorse the fundamental principle of ethical and legal medical research, enshrined in the Helsinki Declaration, and in the Nuremberg Codes of Conduct, that no research should be conducted on human beings without appropriate consent (Informed consent of the individual or special arrangements for those who cannot give valid consent such as children and those with mental incapacity). However, these codes were framed in the context of intrusive research and no modification relating to non-intrusive research has been made in the subsequent revisions of the Helsinki Declaration.

We therefore are concerned that emerging legislation or regulation designed to protect the rights of patients (see Appendix) should not inhibit the conduct of some types of harmless research which have previously been conducted without difficulty and have formed the basis of important

medical advances. We are not aware of evidence that a significant proportion of UK citizens wish to restrict this type of 'non-intrusive' medical research which includes:

- the retrospective use of existing medical records for analysis of disease prevalence, clinical features, prognosis, response to treatment etc.
- the use of biological samples that have been previously taken during the course of medical diagnosis or treatment, at autopsy, or for research, and are in excess of requirement for their original purpose; eg, 'left over' portions of blood samples or tissue biopsies.

In these instances the information or biological sample has already been obtained so there is no additional hazard to the research subject from physical intervention. In some such studies, data or samples are anonymised at a very early stage of the research process, so that individual research subjects are not identifiable even to the researcher. The risk of psychological harm or invasion of individual privacy is thereby eliminated.

There is however the possibility of invasion of privacy and psychological harm if data or samples have not been anonymised before they are given to an investigator. This is avoided by observing the principle of collective confidentiality², which applies to all members of the medical team when involved in clinical work, teaching, audit and research, and by anonymising the data before publication. Publishing information or photographs from which the research subjects can be identified requires consent by individual subjects.

Extension of the requirement for universal consent to the non-intrusive research referred to above would bring to a halt all research on existing archived material, some of which has been collected over decades and has been used, and is being used, to make important contributions to medicine. The resources of medical information and medical samples, already in existence, for which such consent has not been sought are enormous. To attempt to contact very large numbers of people, often long after the event in question, and seek such consent, would be impractical, and probably unethical, since it would certainly involve in some instances a considerable and unexpected intrusion into people's lives.

One option would be to abandon all such research, but in our view that would be unethical because we believe that the medical profession have a duty to improve health care by appropriate research and a responsibility to those who have provided information or samples in the course of clinical

management, to use these effectively and not, by discarding them, waste the valuable information they could yield.

Use of existing archived material

We have therefore reached the view that the kinds of non-intrusive medical research on human subjects that we have described may be ethically conducted without the express consent of the individual patients or subjects. Amongst the conditions to be fulfilled are:

- The material must be anonymised at the earliest possible stage consistent with obtaining the information necessary for the research. The minimum level of anonymisation is that which precludes identification of individuals from the output of the research;
- There would be no inconvenience or hazard, psychological or physical, to the subjects.
- Where doubt exists as to the intrusive nature of proposed research, the benefit of that doubt should always lie on the side of seeking the appropriate consent; we have no wish to see any relaxation of the legal and ethical requirement to obtain the consent of research subjects in most situations.
- The appropriate Research Ethics Committee should have reviewed and agreed the research protocol, and specifically agreed to exempt the research from the general requirement for individual consent from each research subject.

Support for the principle that research based on medical records or stored samples could be conducted without subject consent, with appropriate safeguards, was unanimous but opinion was divided on the need for ethical approval. The majority of the Committee supported the view that, in today's climate, research on patient data or tissues was more securely conducted if a Research Ethics Committee had approved the research and waived the need for specific consent from individual subjects. However the minority view was expressed that, since non-intrusive research conducted by doctors did not contravene any fundamental principle or human right, it did not need review by a Research Ethics Committee, subject to specific safeguards set out in the report of a working group established by the Royal College of Physicians of London³. This is the policy of the USA as set out in federal regulations⁴ and in the UK the use of medical records and samples for audit, which cannot be clearly differentiated from research⁵, does not require consent or ethical approval.

Information archived in the future

The past decade in particular has seen a considerable increase in the public profile of biomedical research which, combined with the advent of very efficient information technology, has led to increasing concern to safeguard the rights and privacy of patients and research subjects (see Appendix).

There are therefore arguments in favour of ensuring that those providing medical information or giving samples for diagnostic or research purposes are made aware that this information or biological material may subsequently be used for further research, and are given the opportunity either to agree with or to opt out of such research.

Recommendations on informing patients about the use of their health records in medical research and allowing 'opting out of consent' were made in 1985⁶ and are included in Department of Health guidance⁷ but are not widely applied in the Health Service. The Nuffield Council on Bioethics also urged health service providers to consider the inclusion of relevant clauses in operation and autopsy consent forms relating to later use of left over biological material⁸ which are, again, not widely used.

When a patient consults a doctor, is admitted to hospital or has a blood or tissue sample taken, it is not possible to predict whether the information or sample will become important for research at a later date, and this event occurs many millions of times a year in the UK. Pilot studies showing that the proposed guidance can be followed in clinical practice is an essential prerequisite to universal adoption.

Recommendations

We recommend:

- 1 That the use of archived data and material for research must be preserved.
- 2 That the Department of Health and British government should not subscribe to legislation or codes of conduct that will seriously impede such research to the ultimate detriment of patients.
- 3 That the appropriate authorities pilot and, if successful, implement practicable measures to ensure that patients and healthy volunteers are made aware that the information and samples they provide may be used for research and are given the opportunity to dissent from such use.*
- 4 That once such measures are in use, information and samples provided by those who have dissented be exempted from use in research.
- 5 Notwithstanding Recommendation 4 above, in exceptional circumstances information and samples may be used where a patient has dissented, where in the view of a Research Ethics Committee the research is clearly warranted in the public interest.
- 6 That information and material archived before full implementation of these measures remain accessible for research under the conditions set out above (see 'Use of existing archived material').

*Minority view put forward by Professor N Wald:

Agreement on the importance of preserving records based research and of making the public aware of this is unanimous but there is disagreement over whether patients should have the right to prevent their records being used

confidentially for research. The selective removal of data could invalidate the research. There is a view that it is unreasonable to allow individuals to do this when the use of their data is at no cost or harm to themselves. There is no good reason to alter the long accepted principle that medical records can properly be used for research without explicit patient consent if confidentiality is preserved. The proposal of setting up a mechanism to override a patient's refusal on a public interest justification is unsatisfactory because all medical research by its nature is in the public interest and it would be misleading to create a category of research that purports to be otherwise. It is also not satisfactory to appear to give patients a choice which can later be rescinded without their involvement.

Appendix: Relevant recommendations of other bodies

UK data protection legislation makes specific provisions in relation to research⁹ though research data were excluded from the recent Review of Patient Identifiable Information¹⁰. The Data Protection Directive of the European Union also makes an exception for medical research¹¹. The Council of Europe Convention on Human Rights in Biomedicine and the Explanatory Report¹² emphasise that appropriate information and consent procedures will depend on the use to which specimens are to be put, so that consent would be required if sensitive information is to be collected about identifiable individuals, but in other circumstances general information to patients to allow them to express opposition in advance would be sufficient. This article deals with the use of removed tissue; patient records are dealt with in the Council of Europe 1997 Recommendation on Medical Data. The Protocol to the Convention on medical research may address both issues. The proposed UN international guidelines on HIV/AIDS and human rights state that (apart from unlinked sero-surveillance) HIV testing of individuals should be performed only with the specific informed consent of that individual¹³. In the Netherlands the use of human tissue in

research is dependent on having obtained prior consent¹⁴. In the USA legislation requiring prior consent for use of archived material varies between states and has provoked serious concern about its effect on future research¹⁵.

References

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- 9 The Data Protection Act 1984; Data Protection Act 1998. London: HMSO.
- 10 Caldicott Committee. *Report on the review of patient-identifiable information*. London: Department of Health, 1998.
- 11 Directive 95/46 of the European Parliament and the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data. *Official Journal of the European Communities*, 1995 (L281);**38**:31-55. 23 November 1995.
- 12 *Convention for the protection of human rights and dignity of the human being with regard to the application of biology and medicine: Convention on human rights and biomedicine*. [Together with explanatory report]. Strasbourg: Council of Europe, 1996.
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