ETHICS

Children of the 90s II: challenges for the ethics and law committee

S E Mumford

Introduction

The first article in this series of two discussed the decision to establish a separate ethics committee for ALSPAC, a major longitudinal study of pregnancy and childhood, and the committee's initial role in formulating policies for ethical conduct in obtaining data from questionnaires, biological samples, and clinical and environmental tests.[1] This second article considers the consequences of some of these policy decisions in light of challenging issues that have arisen in the course of the study. As in the first article, the intention is to provide strategies that others may find useful when dealing with similar dilemmas.

Questionnaire design: "Did anyone have sexual intercourse with you before you were 16?"

The methodology of the ALSPAC study was explained in the first of these papers[1 2]; many of the data are gleaned from a series of detailed questionnaires. In one of the early questionnaires, a team investigating the aetiology of child abuse wanted to include a series of questions to explore the nature and extent of the link between parents who abuse their children and those who were themselves abused. Researchers hoped to ask the 14000 ALSPAC mothers several questions about any childhood sexual experiences they might have had. The ethics and law committee identified two concerns with this proposal: first, that some participants might find enforced recall of, and answering questions about, unhappy experiences distressing; and secondly, that some might find the questions offensive. That in turn raised the spectre of irate or shocked participants going to the media, with potentially damaging consequences for the study as a whole.

The committee asked for additional evidence about this project and its methodology. The psychologists responsible claimed that asking these questions was the only means of obtaining accurate and reliable information. Child abuse is a serious problem and the committee was convinced that a prospective study might shed important new light on its origins. However, responsibility to participants was its primary concern. Did this merit removal of the sensitive questions?

The committee took the view that the study's existing provisions to care for participants, such as the telephone hotline,[1] were probably sufficient to meet its responsibilities for the few people whose distressing childhood memories might be strongly evoked or exacerbated by this questionnaire. It was decided that the sensitive questions could be included. However, the committee followed the guidelines of the Royal College of Physicians[3] which state that if research questions may cause distress or resentment, it is appropriate to seek participants' consent in advance. It was suggested that these questions be presented in a separate section at the end of the questionnaire. Before that section, participants were warned that the next set of questions would be about early sexual experience and told: "If you would rather not answer them, we quite understand. Just stop now and send the questionnaire back as usual."

ANONYMITY OR ACCESS?: THE REFUGEE'S COT

The conflict between the protection of privacy and confidentiality and the need for access to information is one of the most common ethical dilemmas in epidemiology.[4] Initial statements to participants had guaranteed that their names and questionnaire answers "could not be linked." But when the committee chose that phrase, not all its members fully appreciated the computer technology involved. It was, in fact, technically possible to make links, although only one person knew how this might be done and that person was under strict instructions not to do so. It was also relatively easy for information to be requested from the computer in such a way as to identify a very small group of participants—for example, by asking for the files of all those who had said their child was blind. The possibility of making links presented new challenges to the guarantee of anonymity which had been given to participants.

The first request to "break the code" was both innocuous and emotionally compelling. A refugee mother had written a note at the bottom of her questionnaire, asking for help in finding a cot for her baby. She had not signed her name. ALSPAC might easily have helped her and the child by identifying who she was and contacting her: it could be argued that there was a moral duty to do so. Yet, this would have been a public admission that the code could— and would—be broken. If the study's duty was to breach its promise of anonymity to

Department of Law
University of Bristol
Wills Memorial Building
Queens Road
Bristol BS8 1RJ
S E Mumford

Correspondence to:
S E Mumford

help this child, then what of the children whose mothers had confessed to various forms of neglect in response to ALSPAC questionnaires? There is a general problem with anonymity, in that it may lead to "missed opportunities to promote health education and care."[5] However, the committee had decided that a guarantee of anonymity was the best way to collect truthful information that might help child health as a whole. It chose to stand by its original policy and hoped that the refugee mother would find a cot in some other way.

A more enduring issue of anonymity arose when various research groups became interested in studying subgroups of participants, identifiable by their questionnaire answers. For example, all those who had breastfed their babies, or who smoked, or whose children had language problems might be of interest to different researchers. Some teams might wish to interview or examine the participant or child, others to search for links between answers to an assortment of questions. If the computer could be asked to generate the names of all those who had answered a question in a particular way, then these groups could be studied further.

The danger to participants' interests lay in the fact that if the computer could be asked to generate the names of breastfed children, it could also be asked to generate the names of those whose mothers had admitted taking drugs. It would also be obvious to any small group selected for a follow up study that they had been identified as a result of their questionnaire responses. On the other hand, if this sort of subsidiary study were not permitted, researchers would have to review the cases of all 14000 children to study a problem affecting perhaps only a very few. This would render many projects financially unfeasible.

The committee's solution was to permit the computer to generate names of particular groups on the basis of their answers, but only in such a way as to make individual identification virtually impossible. Target individuals selected by the computer would have to be matched by an equal number of controls in a random manner. However, in the case of a group such as blind children this might still mean a tiny number of affected children plus a tiny number of matched controls. It would still be clear that the code had been broken and anonymity would be lost. So the committee proposed a second condition: that additional "control" subjects would have to be added until the size of the group studied by anyone using this identification method reached at least 500.

There are still unanswered questions in this area: Was it necessary for the committee to guarantee anonymity as well as confidentiality? Were these guarantees important to participants? And has the committee achieved the right balance between the desire to protect parents' anonymity and their children's welfare?

Taking biological samples:"midwives are paid 10 pence for each placenta collected"

In many British hospitals the extremely modest incentive of 10 pence is provided to the midwife for each placenta she collects. Placentas are used for a variety of therapeutic, pharmaceutical, and research purposes. The matter is rarely discussed with the mother; it is assumed that most women will be sufficiently preoccupied with other matters as not to be particularly interested in what happens to the placenta. However, the recent growth of interest in the ownership of biological material has raised questions about ALSPAC's own use of umbilical cord and maternal blood.

ALSPAC requires prior written consent from the mother before any blood is used.[1] As well as protecting autonomy, it was hoped that this precaution would vitiate any legal claim that material "belonging" to the mother or child had been wrongfully taken. However, when arrangements began to be made for ALSPAC's 28 000 samples of DNA to be stored and worked on by collaborators, the question of ownership needed to be re-examined. If ALSPAC is to make good its claim to provide a high level of ethical surveillance, then it requires adequate control over the use of the biological samples.

Questions of ownership are primarily matters of law rather than ethics. The recent cases of *Dobson v North Tyneside Health Authority*[6] and *R v Kelly*[7] have given authority to a previously obscure[8 9] tradition in English law that there is no "property" in the human body. Once bodily tissue has been removed, it is considered to have been "abandoned." However, the courts in both the Dobson and Kelly cases accepted the proposition that, if body parts and substances have undergone some application of human skill, they can become the subject of property in the ordinary way. This strengthens ALSPAC's case for ownership of DNA samples they have extracted and prepared.

Have the participants themselves any proprietorial claim over their own bodily tissue? It scarcely seems likely that a woman would want a right in law to the possession of her blood or placenta. The question would only arise if she was unhappy about the use to which it had been put or wanted to have some share in profits in the improbable eventuality that her blood or DNA led to financial profit. For example, in the American case of *Moore v Regents of the University of California*,[10] cells taken from a man's diseased spleen were used to make commercially valuable cell lines. When he was called back to provide more blood, he grew suspicious and took legal action against the hospital, demanding compensation for the blood removed without proper consent—and for a share in the profits. The court granted him the former but denied the latter, stating that he did not "own" his cells.

If the blood used by ALSPAC had been taken without consent to the research, an English court might rule differently and favour the mother's claim to ownership. It might hold that the mother's "abandonment" of her tissue had

been conditional on its appropriate destruction. In that case, the tissue in question might be destroyed at the mother's behest. However, even then, it is highly unlikely that she would receive any more than nominal financial compensation for its unlawful taking. Any profits would probably be allocated so as to represent the proportional contribution in money or money's worth expended by the parties.[11] Very little would go to the mother.

With proper consent, the biological samples used in ALSPAC are no longer simply "stolen," nor are they abandoned unthinkingly. Hence the best analogy in this context may be to describe the cord or maternal blood—as a sort of gift from the mother to ALSPAC.[12] In any dispute between ALSPAC and those storing or working on the samples, it might also be held that gifts may be conditional—and the ALSPAC guarantees would likely form part of the conditions. The policy of requiring carefully informed written consent was confirmed.

Reports of clinical and environmental tests: "Your house is only mildly radioactive"

The committee chose initially to tell parents that Children of the Nineties was an anonymous research project designed to benefit children of the future; individual findings would not be passed on to them. This policy was challenged as new collaborators joined ALSPAC. For example, the National Radiological Protection Board (NRPB) wished to study the effects of radon gas in the home, but wanted to apply its own guidelines and tell people when the radon readings in their houses exceeded national recommended levels.

It is clearly arguable that information discovered about an individual or population should not be withheld from anyone who may be significantly affected.[13] Part of the benefit to the community of a study is being informed of the results.[5 14] But others have questioned whether participants would really want to have their lives complicated by the intervention of researchers bringing unsolicited bad news.[15] Although unexpected and unwanted findings may result from any medical investigation, those who are tested in clinical situations are at least expecting to be told something. Furthermore, the clinical significance of varying levels of radon is itself one of the questions under investigation; there is, as yet, no conclusive evidence that the NRPB recommendations actually delineate safe from unsafe.

The solution proposed by the committee was an attempt to combine truthfulness with sensitivity. In the radon project, those living in the three or four houses which, to date, have been found to have radon levels in excess of those recommended by the NRPB have been sent a letter. This informs participants that a "somewhat higher level than normal" of radon gas has been detected in their home, but explains that the precise significance of this finding is as yet unknown. It goes on to tell them that they may wish to contact the NRPB for a repeat reading and for further information about what is known about radon and what can be done to reduce the level. Thus no one is made to worry or obliged to take action, while those who do wish to make further enquiries are given the information that will enable them to do so.

The problem did not end with radon. Testing for radon shares a common ethical problem with several other analyses. Blood tests may reveal a high or low haemoglobin concentration. Those analysing the ultrasound scans and the results of cognition tests can tell when something "looks unusual." But like a high or low radon reading, the precise significance of these findings is not yet clear. Is there a responsibility for researchers to inform the participants of the bare finding—when that is all that can be provided?

One of the reasons for carrying out the study's procedures is to test the tests. What is the significance of a particular red blood count? Can the cognition test given at six months really predict later IQ scores? It is hard to know whether participants would find it helpful to be told: "Your child has a lower haemoglobin than most," and then to hear that no one knows whether this is problematic or quite innocuous. On the other hand, as it is through the courtesy of the participants that access is gained to their children and their houses, it is arguable that any information gleaned is ethically if not legally "theirs" and ought to be supplied to them or to their doctor, if only in its raw form. Doctors might not yet know how low a concentration of haemoglobin really is dangerous, but the child's general practitioner should at least be given the choice whether to intervene and be given some perspective on the information presently available on the subject.[16]

What is done with the information may vary with the test in question. The provision of iron supplements may follow a "low" red blood count. Intervention in the radon case is somewhat more complicated; the recommended method of reducing radon levels involves substantial building work. But with the knowledge that something might be amiss, participants could take further advice from experts and even choose to move house. In the case of cognition testing, however, there is no useful intervention available. Should parents still be told? The evidence may eventually show that the unusual finding is clinically insignificant. In the meantime, it will cause most parents concern. Many will modify their treatment of the child to conform to expectations that he or she may be cognitively impaired. And in terms of the study, this will have the same scientific effect as taking up the floor boards or giving an iron supplement. It will affect the results of the research.

That may well be ethically appropriate. It is clearly right to intervene—and abandon the research—if to do so would have a demonstrable benefit to health. And yet to intervene where there is no need to do so, to stand in the way of proper research because of an unproved hunch, would seem wrong as well. To cause unnecessary worry to parents would seem even worse. It may be ethically permissible to withhold results if they cannot benefit

individuals and they cannot be harmed by not knowing.[17]

A different problem arose in some of the other ALSPAC projects. Although their findings might well be of some use to children and their parents, the only way to afford these projects was for the data collection to be carried out over a period of time and the samples or information analysed together at a later date. This might mean that by the time the results were analysed and a problem was detected, it would be too late to intervene to the benefit of the child in question.

Argument based on the prohibitive cost of ethical safeguards has not deterred the committee from rejecting other protocols. However, the CIOMS guidelines seem to allow for situations in which participants are told that it will not be possible to give them results.[14] The committee took the view that the projects could, in principle, go ahead. However, it also seemed clear that the disclosure of results to participants was increasingly recognised as a normal ethical obligation stemming from the principle of respect for autonomy.[18] The committee decided that in cases of clinical testing where the abnormal findings would be immediately available—for example, in tests of vision or hearing—the policy of non-disclosure should be abandoned and the parents given access to relevant information. In any case where the research was intended to detect conditions that posed serious, reversible threats to health and these conditions might not manifest contemporaneous clinical symptoms, the research would have to be planned in such a way as to permit parents to be notified.

When ALSPAC research reaches the stage where its findings are ready to be reported to the world at large, the study follows recommendations[15 19 20] that its first obligation is to present the results to those who have provided the data. ALSPAC fulfils this responsibility by sending regular newsletters to all participants with highlights of recent study findings and the opportunity to receive information on all papers making use of ALSPAC data.

At the end of the Nineties…

Nine years after its inception, the committee continues to meet regularly. As the study children become older, pressures grow to collect more and more information about them. The children themselves are reaching an age at which their own views and opinions will begin to eclipse those of their parents in importance; the committee has already revised some of its guidelines on consent. A future article will discuss these emerging issues. Members of the committee have also become aware of how little is known about participants' own perceptions of the safeguards others have selected for their protection.[21] The committee's own research agenda therefore includes a study which will ask both adults and children what they think of the choices we have made on their behalf.

Of course, the essential responsibility of the ALSPAC ethics and law committee remains unchanged: to seek an appropriate balance between reaping the benefits of this important study and doing research in a way that is acceptable to the community from whom its subjects come and for whom the research is done.

The author is secretary to the ALSPAC Ethics and Law Committee.

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