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Academic medicine campaign

Obstacles to conducting epidemiological research in the UK general population

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Experiences from a national case-control study of Creutzfeldt-Jakob disease show the tensions between protecting individual patients' confidentiality and the access required for the benefit of public health

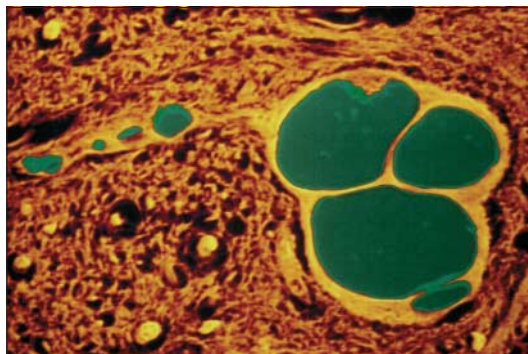
Case-control studies are a powerful epidemiological method for identifying risk factors for disease. They are generally complex to design and execute. However, the difficulties of conducting such studies have been substantially increased by concerns about confidentiality and access to medical records. These barriers could be deleterious to the public's health. In this article, we report some of the problems we faced in conducting a national case-control study of Creutzfeldt-Jakob disease.

Data protection in the United Kingdom

Advances in computer technology have given rise to fears about access to patients' records. The UK response was to supplement doctors' common law duty of confidentiality to their patients with the Data Protection Act 1998. Much debate has ensued about the extent to which medical research could be impeded, including issues surrounding informed consent, patient confidentiality, anonymisation, and access to data.^{1,2} The subsequent updating of guidance on confidentiality by various professional organisations has produced inconsistencies, adding to the confusion about what constitutes ethically acceptable research.³⁻⁵ Fears have been expressed that epidemiological research will be severely hampered, and disease surveillance was severely threatened in England and Wales before the introduction of section 60 of the Health and Social Care Act 2001.⁶

UK case-control study of Creutzfeldt-Jakob disease

The National Creutzfeldt-Jakob Disease Surveillance Unit was conducting a national case-control study of all cases of sporadic Creutzfeldt-Jakob disease before variant Creutzfeldt-Jakob disease was identified in the United Kingdom in 1996.⁷ The study compared the exposure history of patients with Creutzfeldt-Jakob disease with that of controls recruited from inpatients at the same hospitals as the cases. We considered



Vacuole in brain of person with Creutzfeldt-Jakob disease: issues of confidentiality are hampering research

hospital controls suitable for comparison with cases for many potential risk factors. However, they were likely to be unrepresentative of the general population with respect to their exposure to medical procedures.

The discovery of variant Creutzfeldt-Jakob disease made identification of iatrogenic risk factors a priority. We therefore decided to recruit controls likely to be more representative of the general population in this respect—namely, people registered with the same general practitioner as each case.

Research ethics committee approval

With the Data Protection Act 1998 in its infancy and uncertainty surrounding its interpretation, there was concern about how the study could be carried out without breaching patient confidentiality. We submitted an application to a multicentre research ethics committee in July 1998 and obtained approval, after some amendments, in October 1998. Under the revised protocol, we would write to the general practitioners of patients with Creutzfeldt-Jakob disease and ask them to take part in the study. If they agreed, the general practitioners would be asked to write (using pre-prepared letters) to 20 people of similar age and

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sex to the case, randomly selected from their patient database. These individuals were asked to consent to be contacted by the National Creutzfeldt-Jakob Disease Surveillance Unit. We then wrote to those who consented, inviting them to participate in the study and to nominate a relative to be interviewed. (Because cases are typically too unwell to participate, a relative is interviewed, and so we had to do the same for controls.) The relatives of the controls who agreed were approached, and if they also consented, a nurse practitioner visited and interviewed them at a convenient location.

As a condition of our ethical approval, we also had to approach 213 local research ethics committees. This was because at that time no provision was made for studies that did not have local researchers. The task was cumbersome, partly because there was no uniformity in what was required by each local ethics committee or in how they discharged their responsibility.^{2 8-10} Since 2000, studies with no local researcher and that meet certain conditions are not required to seek approval from local research ethics committees, although the above concerns still apply to studies with local investigators.

Recruiting controls

By September 2003, we had written to 333 general practices (relating to 109 variant and 224 sporadic cases). Of these, 328 replied and 243 agreed to take part in the study (85 (78%) and 158 (71%) for variant and sporadic cases, respectively). Some of the practices that refused to participate did not give a reason. Others just stated that they did not want their patients to participate, some were concerned about a potential breach of patient confidentiality, and others contacted the families of the cases, who expressed concern about the practice participating.

The table summarises the response rates of potential controls and their relatives written to by their general practitioner. Overall, 37% (1033/2804) of potential controls replied to their general practitioner's letter, of whom 702 consented to be approached directly by the surveillance unit. Of 637 controls written to by the unit by September 2003, 466 consented to take part in the study. Of the 448 relatives contacted to ask for their consent to be interviewed, 397 (89%) consented. Thus the overall response rate was 16%.

During 2000, when it was apparent that the response rate was low, two senior researchers attended

a multicentre research ethics committee meeting to put the case for telephoning people who had not responded to a reminder letter from their general practitioner. We proposed that the initial letter from the general practitioner would indicate that if the person did not reply to a reminder letter within a certain time they would be telephoned by a researcher from the surveillance unit. The ethics committee refused this approach on the grounds of breaking patient confidentiality.

Effect of restrictions

It is now difficult to recruit community based controls from general practices without introducing scope for a substantial degree of selection bias, partly because of the status of patient confidentiality in Europe and the United Kingdom. In our study, an additional barrier was created because we could not approach people unless they had sent written consent to their general practitioner. We believe this was partly responsible for the poor initial response rate of 37%.

Another problem was that the ethical approval required general practitioners to send detailed written information about the study. An important part of the process of recruiting people into studies is explaining to them why the study is important and what is being asked of them. This is particularly true when the study is as complicated as ours. We believe that relying on letters, with no early opportunity for the researchers to interact directly with potential participants, contributed to the low response rate.

Our study has an excess of healthcare workers in the control group, which may bias our results. Because of the potential for selection bias resulting from the low response rate, and the complicated logistics involved, we have had to explore other approaches to recruiting controls.

Balancing costs to the individual with benefits to society

We believe that if valid epidemiological research is to continue, a balance must be found to ensure an appropriate degree of patient confidentiality without making it impossible to conduct research into questions with overall benefit for society. The potential gain to the wider public from the results of individual studies must be considered. In addition, we need a debate about the efficient use of public funds for research in relation to patient confidentiality. The cost of recruiting each control in this study was considerable (about £1100 (€1650, \$2000) compared with £300 for each case), but the low response rate will inevitably limit our conclusions. Should the effective use of public funds be given more weight in the ethics committee decision making process?

Alternative ethical approaches

Alternative approaches to recruiting community controls include using publicly available databases, picking random houses in a street, or asking cases (or their relatives) to nominate a relative or friend. Each of these has advantages and disadvantages. The use of publicly available databases—for example, telephone

Recruitment of controls and their relatives for a case-control study of variant and sporadic Creutzfeldt-Jakob disease (CJD) by the national surveillance unit

| | No of people (% of those written to) | | |
|---|--------------------------------------|--------------|-----------|
| | Variant CJD | Sporadic CJD | Total |
| Controls written to by general practitioner | 1673 | 1131 | 2804 |
| Replied to letter | 409 (24) | 624 (55) | 1033 (37) |
| Consented to be contacted | 312 (19) | 390 (34) | 702 (25) |
| Controls written to by unit | 304 | 333 | 637 |
| Replied to letter | 228 (75) | 262 (79) | 490 (77) |
| Consented to participate | 220 (72) | 246 (74) | 466 (73) |
| Relatives written to by unit | 214 | 234 | 448 |
| Replied to letter | 193 (90) | 213 (91) | 406 (91) |
| Consenting to participate | 188 (88) | 209 (89) | 397 (89) |

Summary points

Issues of patient confidentiality are hampering epidemiological research

Wider debate is required about the use of medical records to identify eligible individuals

Ethics committees should weigh the benefits to society against costs to the individual when considering studies

Use of public funds should be considered as part of the cost to society if a study cannot recruit participants by the most effective method

directory listings or the postcode address file, raises an interesting issue. People on these databases can be (and are) approached by researchers or salespeople without any ethical approval, although research funded within the health service will usually require that ethical approval is obtained. However, health researchers are not permitted to contact directly individuals who have not replied to a letter from their general practitioner because their name has been obtained from a general practice list.

If we had contacted individuals who had not responded to a letter from their general practitioner (to which they could have responded indicating that they did not wish to be contacted) would this have constituted an unacceptable breach of patient confidentiality or an unacceptable infringement of their privacy? Further debate is needed on how to strike an appropriate balance between an individual's rights and freedoms and the right of the community or society to answer important questions. Perhaps patients of general practitioners should have the opportunity to opt out of being contacted for health research purposes in the same way as some private companies

offer customers the opportunity to indicate that they do not want their names passed on to other interested parties.

This study would not have been possible without the cooperation of the relatives of patients with Creutzfeldt-Jakob disease and controls and their relatives. We thank research staff at the unit for collecting data (M Zeidler, G Stewart, M A Macleod, C Henry, A Lowman, S Cooper, C Heath, K Murray) and N Attwood for database management.

Contributors and sources: HJTW is an epidemiologist and public health specialist. BSB and ML are research nurses who visit and interview the relatives of controls in the study. SNC and PGS have been involved in epidemiological research into Creutzfeldt-Jakob disease for many years. DE is a medical statistician. RGW set up the surveillance unit in 1990 and was its director for many years. The article arose from a number of discussions around the problem of the low response rate. HJTW analysed the data and prepared the first draft of the manuscript. DE, SNC, PGS, RGW reviewed the data. All authors contributed to writing and redrafting the article. HJTW is the guarantor.

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When Dr Mopp tried to get into research

Initially, it had all seemed so easy and straightforward. Working in a large children's hospital, I thought it would be useful to survey paediatric nurses and doctors about their knowledge of popular children's television characters. Knowing one's Tweenies from one's Fimbles always helps in communicating with a wary preschool child, and it would be interesting to find out just how much paediatric healthcare professionals knew about these things. Filling out a little questionnaire would be a bit of fun for everyone involved. But fun and research don't always make easy friends, as I was soon to learn.

One of my colleagues wisely suggested that it would make sense to survey a few young hospitalised children as a control group. This sounded like good advice, but that's when the trouble started. In order to be able to ask a few children whether they recognised Tinky

Winky or Jake, I was told I had to apply for approval from the ethics committee. In order to obtain this approval, I had to seek statistical advice. The statistician asked me to do a pilot study first to establish how many children would be needed for my project. Having done so, I finally filled out the rather lengthy ethical approval application form. After all this, I was told today that the form has changed as from this month to a new nationwide form.

If you never read this study written up in any journal don't be surprised. Mind you, I will add it to my portfolio as an extremely interesting learning experience in politically correct research.

Markus Hesseling *specialist registrar in paediatrics, Alder Hey Children's Hospital, Liverpool*