

# Hospital ethics approval for a population-based case–control study of very preterm birth

Lyndsey F Watson, Jo-Anne Rayner and Judith M Lumley

## Abstract

**Aim:** To describe the process involved in obtaining ethics approval for a study aiming to recruit women from all maternity hospitals in Victoria, Australia.

**Design:** Observational data of the application process involving 85 hospitals throughout Victoria in 2001.

**Results:** Twenty-three of the 85 hospitals had a Human Research Ethics Committee (HREC) constituted in accordance with the National Health and Medical Council requirements; 27 agreed to accept decisions from other hospitals having HRECs and 27 relied on ethics advisory committees, hospital managers, clinical staff, quality assurance committees or lawyers for ethics decisions. Four of the latter did not approve the study. Eight hospitals no longer provided maternity services in the recruitment period. The process took 16 months, 26 000 sheets of paper, 258 copies of the application and the cost was about \$30 000. Approval was eventually obtained for recruitment at 73 hospitals.

**Discussion:** Difficulties exist in obtaining timely ethics approval for multicentre studies due to a complex uncoordinated system. All hospitals should have explicit protocols for dealing with research ethics applications so that they can be processed in a straightforward and timely manner. To facilitate this, those without properly constituted HRECs should be affiliated with one hospital that has an HREC.

*Aust Health Rev* 2007; 31(4): 514–522

**Lyndsey F Watson**, BSc, MSc, Senior Research Fellow

**Jo-Anne Rayner**, RN, BNursing, GradDipWomHlth, MWomHlth, Research Fellow

**Judith M Lumley**, MA, MBBS, PhD, GradDipChildDev, FaFPHM, FFPH (UK), Director  
Mother and Child Health Research, La Trobe University, Melbourne, VIC.

Correspondence: Ms Lyndsey F Watson, Mother and Child Health Research, La Trobe University, 324–328 Little Lonsdale Street, Victoria, Melbourne, VIC 3000.

[l.watson@latrobe.edu.au](mailto:l.watson@latrobe.edu.au)

## What is known about the topic?

Researchers are concerned about delays and duplication associated with obtaining ethics approval for multicentre studies.

## What does this paper add?

This paper describes the process involved in obtaining ethics approval for a population-based observational study in Victoria in 2001. It describes the delay and resource use in detail.

## What are the implications for practitioners?

This experience highlights the need for revision to the ethics approval processes. Ethical and design issue decisions made by one human research ethics committee should be accepted by others, with allowance for local resources. There is a need for rationalisation of the ethics application form with the aim of making its submission electronic and for grants to include an allocation for the ethics application process in multicentre studies.

ETHICS APPROVAL for research studies is now an appropriate and generally rigorous process to ensure ethical practice and respect for research participants. In Australia, the National Health and Medical Research Council (NHMRC) requires all institutions or organisations receiving NHMRC funding to establish a Human Research Ethics Committee (HREC) and to subject all research involving humans, whether related to health or not, to ethical review by that committee. This and other statutory requirements are contained in the 2007 NHMRC National Statement on Ethical Conduct in Human Research (hereafter, National Statement),<sup>1</sup> as are guidelines for HRECs. The required HREC composition is at least eight members and as far as possible equal numbers of men and women; at least one third of the members should be external; and including two lay persons, one experienced in professional care or counselling, a person who performs pastoral care, one lawyer and two current researchers (National Statement, pp. 80–1).<sup>1</sup> HRECs are also required

to establish working procedures concerning frequency of meetings, timely consideration and review of research protocols, methods of decision making, and reporting of adverse occurrences (National Statement, pp. 81–2).<sup>1</sup> Compliance with the National Statement is to be ensured by audit of activities of HRECs by the Australian Health Ethics Committee (AHEC) and annual reporting to the NHMRC by institutions and their HRECs (National Statement, p. 96).<sup>1</sup> Currently, over 200 institutions report to AHEC. Nevertheless, within this framework, each institution can develop its own process for approving studies to be conducted in its own jurisdiction.

Multicentre research (where a study is conducted at more than one institution) has increased as much as nine-fold in the last 20 years.<sup>2</sup> It usually involves a complex and lengthy process since researchers are required to obtain individual approval from each institution, complete different application forms, provide varying numbers of copies, comply with different committee deadlines, and adjust their study protocols in various ways to suit the requirements of different institutions. However, not all hospitals have HRECs constituted as defined by the National Statement since they do not have NHMRC funding and are not initiators of research. For population-based epidemiological studies problems arise when researchers attempt to recruit from these hospitals.

Some attempts have been made to streamline the process for multicentre studies. In the United Kingdom, the Multicentre Research and Ethics Committees were formed in 1997, yet there continue to be concerns regarding complexity and delay.<sup>3–6</sup> In New Zealand, the National Ethics Advisory Committee's review has enabled the rule of "one study, one review" for multicentre studies to streamline the review process.<sup>7</sup> In Australia, guidelines for the simplification of ethical review of multicentre research were included in the National Statement (Chapter 5.3),<sup>1</sup> with notes in the Human Research Ethics Handbook<sup>8</sup> which are under review.<sup>9</sup> Key points included were: researchers coming to a prior agreement with one HREC to take the primary role in the ethical and

scientific assessment of the protocol; that the primary researcher inform all other Australian sites at which the research is to be conducted, that HRECs communicate with and give advice to other HRECs; and that HRECs accept assessments by another organisation. These recommendations failed to recognise that the responsibility of deciding that an external review was satisfactory was that of the institution and not its HREC and that research institutions' history of institutional autonomy left them deeply resistant to devolving or sharing their responsibilities for ethical review.<sup>10,11</sup> AHEC identified legal issues, indemnity and monitoring obstacles as the reasons for the failure of HRECs to use the provisions in the National Statement.<sup>11</sup> Nevertheless, consultations and workshops and some individual efforts on mutual acceptance continue in an attempt to improve the situation.<sup>12,13</sup>

Some success has occurred in simplifying the production of application forms. Within Victoria, the HREC of the Victorian Government Department of Human Services (DHS) together with leading hospitals developed a common core application form (CAF) which, with a variety of additional modules, aimed to reduce the work involved in seeking ethics approval for multicentre research projects. The CAF was introduced in 2000.<sup>14</sup> Although it allowed some rationalisation, its uptake was voluntary and individual institutions still required additional institution-specific sections. Currently the AHEC and a working party from institutions in at least five states are developing a national web-based ethics application form (the NEAF).<sup>15</sup> Submitting applications to individual institutions is still required. In addition, Victorian state privacy legislation was introduced in 2001 and became operational in July 2002, resulting in some new, unclear, misunderstood, and untested issues associated with patient rights.<sup>16,17</sup> One impact has been to make HRECs and other institutions cautious about patients' rights, to be proscriptive about allowing outsiders (non-staff personnel) to approach patients, and to opt out of research to avoid risk.

At the time this privacy legislation was introduced, we undertook a multicentre population-

based study of very preterm birth, the Early Births Study, in Victoria. This paper describes the process we were involved in to obtain approval to conduct our study.

## Methods

The Early Births Study was designed to be population-based, recruiting the entire case population of women having a singleton or twin pregnancy in Victoria who gave birth from 20 to 31<sup>+6</sup> weeks' gestation over 2 years — from April 2002 to April 2004, regardless of outcome — live birth, fetal death, or termination of pregnancy. Controls were a selection of women having a singleton birth from 37 completed weeks' gestation and all women having twins from 37 weeks, in the same period as case recruitment. A semi-structured questionnaire was administered by interview to all women agreeing to be in the study.

The case population was sourced primarily from the three tertiary level hospitals where it was expected that more than 85% of women would either give birth or have their infants cared for after a very preterm birth. The control sample was selected using a successful method,<sup>18</sup> with a random sample of 1500 birthdays and hospitals of term singleton births from the Victorian Perinatal Data Collection (VPDC) database for 1999 projected forward to the time of recruitment. This method enabled foreknowledge of where and when controls eligible for recruitment would occur and allowed hospital staff to be advised in advance of how many women would be asked to participate and at what times. It meant that almost all hospitals providing maternity care in Victoria would be chosen as sites for recruitment requiring multiple applications for ethics approval.

Before funding for the study was released we required ethics approval from the university HREC overseeing the researchers and administering the National Health and Medical Research Council funding grant. We also required approval from the HREC of the DHS, which oversees all public hospitals in Victoria, as well as approval from the individual hospitals. Once the hospitals

had been selected, it was necessary to identify who was responsible for the application and what was required in the application, including the number of copies and submission deadlines. Tracking the process was monitored and quantified using an MS Excel spreadsheet (Microsoft Corporation, Redmond, Wash, USA).

## Results

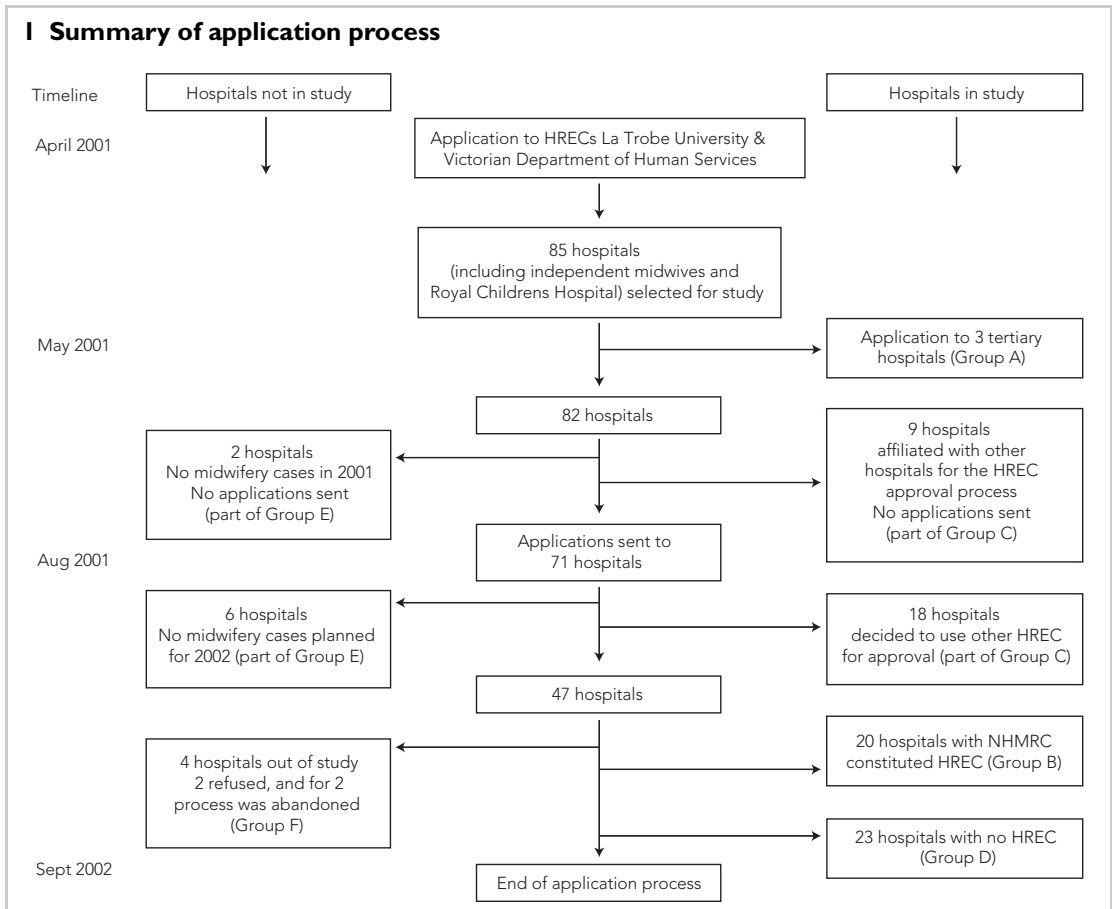
In April 2001, HREC applications for study approval were sent to La Trobe University (LTU) and the DHS. By May, with approval in principle from the University and the appointment of the study coordinator, seeking approval for individual hospital participation started.

### **Hospital participation**

The selection of a control sample from the VPDC database comprised 83 hospitals providing maternity care in Victoria in 1999 and some homebirths (hereafter included as a hospital for simplicity), representing 80% of the 104 maternity units but at least 99% of births before 32 weeks' gestation. These, as well the Royal Children's Hospital — where mothers whose babies were transferred to the neonatal intensive care unit might be recruited — needed to be approached. Approval was sought from 87 institutions and the process is described below for the 85 hospitals involved (Box 1 and Box 2). In 17 hospitals just one control had been selected for recruitment, in 15 hospitals between two and five had been selected, and in a further 11 hospitals only, between six and nine controls had been selected.

### **Determining responsibility for the application**

Finding a person in each hospital responsible for administering the ethics application entailed searching hospital websites, downloading application forms if available and telephoning hospitals. In May 2001, applications were sent to the three tertiary hospitals which accounted for 20% of planned controls (305 women) and the majority of cases. It had been hoped that the majority of other hospitals would approve the study once



approval from tertiary hospitals had been obtained. In the first round of enquiries to these hospitals, we learnt that two no longer offered maternity services and nine others were affiliated with or agreed to accept another hospital's ethics approval process. In August 2001 further applications were sent to 71 hospitals. Subsequently, six hospitals informed us that they would not be offering maternity services in 2002. Approval decisions for the remaining hospitals were made between August 2001 and September 2002. Eighteen hospitals eventually agreed to accept the decisions of other hospitals, and four refused to participate in this research study. Forty-three hospitals approved the study; 20 of which had HRECs constituted as specified by the 1999 National Statement<sup>19</sup> applicable at that time. All

nine metropolitan public hospitals and all seven rural Level 2 hospitals had HRECs, while only six each of the 17 rural public hospitals and the 12 private hospitals had HRECs. One hospital established an HREC as a result of our study application.

Where hospitals had HRECs, including four that used HRECs from affiliated hospitals not providing maternity care, working procedures for obtaining ethics approval existed. This meant that submission and meeting dates (varying from monthly to quarterly), notification of cancelled or aborted meetings, numbers of applications required, timely decisions and notifications of such were available to us. Four hospitals requested fees to process our application — one for a payment of \$3300, mistakenly terming the

## 2 Resources required for ethics approval for the Early Births Study, by hospital approval category

| Hospital group                            |  | All hospitals Hospitals in group |        |         |
|---|--|----------------------------------|--------|---------|
|   |  | Total                            | Median | Range   |
| <b>All hospitals</b>                      | <b>n=85; 61 used the common application form</b> |                                  |        |         |
| Controls                                  | Original number allocated                        | 1500                             | 9      | 1–131   |
|   | Number recruited                                 | 1495                             | 12     | 0–132   |
| Cases                                     | Estimated number                                 | 1972                             | 2      | 0–576   |
|   | Number recruited                                 | 1290                             | 1      | 0–467   |
| Applications                              | Months taken for approval or refusal             |                                  | 3.7    | 0–13    |
|   | Number of copies of application sent             | 258                              | 1      | 0–29    |
|   | Total number of pages used                       | 26350                            | 96     | 0–3509  |
| <b>A Tertiary</b>                         | <b>n=3; 2 used the common application form</b>   |                                  |        |         |
| Controls                                  | Original number allocated                        | 305                              | 129    | 45–131  |
|   | Number recruited                                 | 306                              | 129    | 45–132  |
| Cases                                     | Estimated number                                 | 1320                             | 416    | 328–576 |
|   | Number recruited                                 | 977                              | 288    | 222–467 |
| Applications                              | Months taken for approval                        |                                  | 3.3    | 2.4–13  |
|   | Number of copies of application sent             | 32                               | 2      | 1–29    |
|   | Total number of pages used                       | 3798                             | 192    | 96–2180 |
| <b>B HREC, NHMRC constituted</b>          | <b>n=20; 14 used the common application form</b> |                                  |        |         |
| Controls                                  | Original number allocated                        | 568                              | 30     | 8–67    |
|   | Number recruited                                 | 562                              | 29     | 0–67    |
| Cases                                     | Estimated number                                 | 238                              | 8      | 0–34    |
|   | Number recruited                                 | 68                               | 2      | 0–13    |
| Applications                              | Months taken for approval                        |                                  | 3.3    | 0.7–12  |
|   | Number of copies of application sent             | 172                              | 6.5    | 1–22    |
|   | Total number of pages used                       | 16280                            | 672    | 96–2180 |
| <b>C Agreeing to use other HREC</b>       | <b>n=27; 16 used the common application form</b> |                                  |        |         |
| Controls                                  | Original number allocated                        | 376                              | 4      | 1–77    |
|   | Number recruited                                 | 383                              | 5      | 1–79    |
| Cases                                     | Estimated number                                 | 204                              | 2      | 0–66    |
|   | Number recruited                                 | 126                              | 0      | 0–67    |
| Applications                              | Months taken for decision                        |                                  | 3.3    | 1.1–10  |
|   | Number of copies of application sent             | 23                               | 1      | 0–3     |
|   | Total number of pages used                       | 2783                             | 96     | 37–288  |
| <b>D No formal HREC</b>                   | <b>n=23; 19 used the common application form</b> |                                  |        |         |
| Controls                                  | Original number allocated                        | 207                              | 8      | 1–36    |
|   | Number recruited                                 | 244                              | 9      | 1–38    |
| Cases                                     | Estimated number                                 | 198                              | 2      | 0–144   |
|   | Number recruited                                 | 118                              | 1      | 0–96    |
| Applications                              | Months taken for approval                        |                                  | 4.7    | 0.4–11  |
|   | Number of copies of application sent             | 21                               | 1      | 0–1     |
|   | Total number of pages used                       | 2835                             | 96     | 37–288  |
| <b>E No maternity services in 2002–04</b> | <b>n=8; 4 used the common application form</b>   |                                  |        |         |
| Controls                                  | Original number allocated                        | 33                               | 2      | 1–13    |
|   | Number recruited                                 | 0                                |        |         |
| Cases                                     | Estimated number                                 | 4                                | 0      | 0–2     |
|   | Number recruited                                 | 0                                |        |         |
| Applications                              | Months taken for decision                        |                                  | 0      | 0–0     |
|   | Number of copies of application sent             | 5                                | 1      | 0–1     |
|   | Total number of pages used                       | 296                              | 59     | 0–59    |
| <b>F Refused</b>                          | <b>n=4, 4 used the common application form</b>   |                                  |        |         |
| Controls                                  | Original number allocated                        | 11                               | 2.5    | 1–5     |
|   | Number recruited                                 | 0                                |        |         |
| Cases                                     | Estimated number                                 | 8                                | 0      | 0–8     |
|   | Number recruited                                 | 0                                |        |         |
| Applications                              | Months taken for refusal                         |                                  | 7.3    | 7–7     |
|   | Number of copies of application sent             | 4                                | 1      | 1–1     |
|   | Total number of pages used                       | 356                              | 59     | 59–177  |

study a “trial” — but after negotiation we only paid \$100 to one to cover costs of photocopying and distribution. Eight HRECs, four in rural Victoria, requested our attendance at a meeting. On all occasions, although time-consuming, the visit facilitated understanding of the project and discussion of perceived problems, contributing to satisfaction with the process, rapid resolution of problems and subsequent approval of the study.

For hospitals without HRECs the application process was difficult as it was inconsistent and uncoordinated. Responsibility was variously passed between Chief Executive Officers, boards of management, Medical Directors, Directors of Nursing, clinical research committees or quality assurance committees. Private hospitals with no HREC referred the application to their indemnifiers or insurers. Hospitals not responding to the application were contacted after 2 months. Ten hospitals required a second application as the first had been mislaid; one hospital mislaid the application three times. Additional problems occurred when personnel changed (in four hospitals), responsible persons were on leave (in three hospitals) or private hospitals were sold (three hospitals). Verbal approval was given by ten hospitals with no written approval forthcoming despite repeated attempts on our part.

### ***The ethics application form***

The CAF, available electronically, was recommended for use by 20 of the 29 hospitals with NHMRC-constituted HRECs. Two other hospitals had application forms that were not available electronically, which meant that they had to be completed by hand. All other hospitals, except one, accepted one copy of the CAF or accepted another hospital's ethics approval process. In all, 61 hospitals received at least one CAF.

There was no uniformity in style or length of the other attachments required with the application, or with the number of copies required by hospitals. The standard CAF plus generic attachments amounted to 59 pages. Twenty-one hospitals required the inclusion of their hospital logo and site-specific telephone contacts on all documentation. Therefore, specific approach letters,

participant information, consent forms, and participant protocols for distress were developed for each participating hospital. Fifteen hospitals with HRECs required multiple copies of applications, ranging from 2 to 29, with a median of 13 copies.

### ***Time taken for the ethics application/ approval process***

Time between initial approach and approval varied from 12 to 386 days; the approval dates occurred between May 2001 and September 2002 (a 16-month period). The median time for approval for hospitals with HRECs was 3.3 months compared with 4.7 months for hospitals without HRECs. Nevertheless, some hospitals in both groups took a year to grant approval.

### ***Resources used***

The resources required were extensive. All applications were paper-based, and with repeat applications a total of 258 applications were sent. This included a set of documents of 37 pages sent to all HRECs after final approval, using at least 26 000 sheets. Postage and delivery costs were around \$1000, phone calls (around 5 per hospital) were at least \$500, and travel costs \$1000.

The major cost, however, was that associated with study staff. The Project Co-ordinator was employed at 0.5 for the 16 months of this process although she was also involved in other aspects of the study (such as the interview schedule development). We had planned to commence the recruitment in January 2002, but delayed until April, during which time three research interviewers already employed had to be paid. If the study had started on time, there would have been a saving to the study of about \$25 000.

This total cost of \$30 000 did not include the additional cost associated with liaising with hospitals (travel, accommodation and time for hospital in-service sessions and face-to-face interviews of women, postage of documents, telephone costs), all of which was covered by the study budget. This included a set of 37 pages sent to all HRECs after final approval. At least 26 000 sheets were used.

### **Issues raised by hospital HRECs**

For hospitals with HRECs, queries were raised about recruitment, particularly of women whose baby had died. For a few, the study design was not understood. The study was complex, with different recruitment processes for cases and controls, and even though most hospitals were unlikely to recruit cases they were required to understand and approve the protocol should a very preterm birth occur. The issue of who should approach women was queried by 10 HRECs; and issues of confidentiality associated with changes to the privacy legislation were raised by five HRECs. Other issues raised by HRECs included concerns about the qualifications and ability of the research staff to conduct interviews with case mothers, defining an acceptable process for contacting women who had had a perinatal death, the inclusion of questions on intimate partner violence (one HREC refused permission to include these questions), the possibility of causing women distress, interviewing teenage mothers and medical record extraction.

For hospitals without HRECs, assigning a person responsible for the ethics approval decision, understanding the study design and implications for the hospital were the major issues. However, where the CAF was used, the preparation of each application was simplified.

### **Follow-up contact with HRECs and hospitals**

During 2002 and 2003 annual ethics reports had to be sent to all hospitals with HRECs, and for three this was required bi-annually. In 2004 when recruitment had finished a final report was sent to all participating hospitals summarising recruitment success. LTU, DHS and six hospitals require annual reports until the primary outcomes are published (expected early 2008). All hospitals will be sent study findings when available.

### **Discussion**

Obtaining ethics approval to undertake this population-based study was a very resource-intensive

process. However, we considered it essential to our study design since participation from every hospital selected was required to minimise bias. We approached 85 hospitals (including the independent midwives group) to obtain ethics approval; 73 approved our study and eight no longer offered maternity services in the recruitment period. Only four hospitals did not participate. The effort required on our part to obtain approval was out of proportion in many instances, given that for more than half the hospitals less than 10 women had been selected for inclusion in the study. In the end, women were recruited from all hospitals that gave approval, and were interviewed from all but one. Generally, clinical staff were supportive and cooperative, as were the women they recruited, even when the approval process had been problematic.

Rationalisation and evolution of ethical review of research is occurring in Australia and overseas. In both the United Kingdom<sup>5</sup> and United States<sup>20</sup> centralised review boards initially review multicentre trials. Once this body has granted final approval, local investigators submit the approved documents to their local review boards. This system has led to longer start-up times and dissatisfaction for researchers.<sup>21,22</sup> Two models in Canada (in Alberta and at McGill, Ontario) attempting affiliation agreements between review boards may obviate the need for local review. These rely on a binding agreement among institutions and require a level of trust.<sup>23</sup> In any event, the process is slow, and for all institutions issues of legal responsibility need to be investigated.

Our experience has shown an inconsistent and uncoordinated ethics application process. It resulted in duplication of effort by researchers and unnecessary processing by hospitals. This experience is not new, both overseas<sup>1,4-6,24,25</sup> and in Australia.<sup>26,27</sup> There is a need for both formalisation and rationalisation of processes. A group of hospitals lying outside the scrutiny of AHEC proved most problematic. This applies to hospitals not receiving NHMRC funding. We recommend:

- That all hospitals have explicit working procedures to deal with research ethics applications and that these include a time limit for decision making. For hospitals with HRECs this already exists. For others, including private hospitals, explicit agreement for association with another institution that has an HREC should exist. This situation is most likely to occur with observational studies that endeavour to include whole populations. In our case, these other hospitals were particularly difficult to deal with. They were unable to be clear about who would take responsibility and took longer to grant approval. Many eventually accepted another hospital's decision. The decision not to participate in the study was made by the hospital managers with little or no understanding of public health research.
- That where approval for multicentre research is being sought, the recommendations in the National Statement<sup>1</sup> be adopted.
- That ethical and design issue decisions made by another HREC be accepted, but with the allowance that local resources and administration aspects of each hospital be considered.
- That rationalisation of the ethics application form continue, with the aim of making its submission electronic. The use of the CAF simplified the document preparation and enabled in the Early Births Study to provide a well-prepared comprehensive document to all hospitals by replication. However, it did not obviate hospital-specific requirements or reduce paperwork and duplication or expedite the decision-making process. No hospital accepted electronic submission of the ethics application.
- Firm guidelines on timely processing of applications. In the study, approval granted by tertiary hospitals with HRECs did not expedite approval from the other 71 hospitals. Hospital HRECs had no procedures in place to accept other HREC approval or to communicate effectively with us. The time taken in our study was unacceptable — with a median of 3.7 months and up to 12 months. At the time we had hoped to start recruitment, only about half the approvals sought had been granted.

- That specific grant allocation for ethics applications in multicentre studies be allowed by funding bodies.

The recent introduction of new Victorian privacy legislation, which increased caution among some ethics committees and hospitals, delaying approval in some institutions, was an additional impediment. The primary purpose of ethical review of research is that participants be accorded the respect and protection that is due to them and that research is fostered that is of benefit to the community (National Statement p. 1).<sup>1</sup> It makes no sense to have one without the other,<sup>28</sup> and if nothing is done clinical research could wither.<sup>29</sup> As with others,<sup>30</sup> we found that the balance against research is even worse for multicentre studies in public health.

Our experience adds to the increasing disquiet about good epidemiological studies having a future in the current Australian clinical environment.

## Acknowledgements

Funding for this study was provided by: Faculty of Health Sciences, La Trobe University (1998, 2003), National Health and Medical Research Council (2001–2003), SIDS and Kids Victoria (2002), Telstra Community Development Fund (2003). No funding body had any access to the data, or any role in the analysis or interpretation of the findings.

Many people contributed to the Early Births Study. We would like to thank all the following for their participation and support: clinical staff at Victorian hospitals; women who participated in Early Births Study; the Early Births Reference Group; staff at the Victorian Perinatal Data Collection Unit; associate investigators James King and David Henderson-Smart; the research team who undertook the recruitment and interviews: Sally von Bibra, Meg Chesterman, Rowena Morris, Stephanie Lenko, Mary-Ann Davey, Anne Harbison, Simone Quinton, Leanne Rich, Kathryn Browne-Yung and Jo-Anne Rayner; and the administrative assistants: Kasey Gibson and Martine Kilby.

## Competing interests

The authors declare that they have no competing interests.



## References

- 1 National Health and Medical Research Council. National statement on ethical conduct in human research. Canberra: Commonwealth of Australia, 2007. Available at: <http://www.nhmrc.gov.au/publications/synopses/e72syn.htm> (accessed May 2007).
- 2 McWilliams R, Hoover-Fong J, Hamosh A, et al. Problematic variation in local institutional review of a multicenter genetic epidemiology study. *JAMA* 2003; 290: 360-6.
- 3 Strobl J, Cave E, Walley T. Data protection legislation: interpretation and barriers to research. *BMJ* 2000; 321: 890-2.
- 4 Nicholl J. The ethics of research ethics committees. *BMJ* 2000; 320: 1217.
- 5 Lewis JC, Tomkins S, Sampson JR. Ethical approval for research involving geographically dispersed subjects: unsuitability of the UK MREC/LREC system and relevance to uncommon genetic disorders. *J Med Ethics* 2001; 27: 347-51.
- 6 Glasziou P, Chalmers I. Ethics review roulette: what can we learn? *BMJ* 2004; 328: 121-2.
- 7 Begg A. Reform of ethical review in New Zealand. *Australas Epidemiologist* 2005; 12.1: 18-21.
- 8 National Health and Medical Research Council. Human Research Ethics Handbook — commentary on the National Statement. Canberra: Commonwealth of Australia, 2005. Available at: [http://www.nhmrc.gov.au/publications/hrecbook/01\\_commentary/contents.htm](http://www.nhmrc.gov.au/publications/hrecbook/01_commentary/contents.htm) (accessed May 2007).
- 9 National Health and Medical Research Council, Australian Research Council, Australian Vice-Chancellors' Committee. Review of the National Statement on Ethical Conduct in Research Involving Humans. First consultation draft. Canberra: Australian Government, 2004.
- 10 Breen KJ, Hacker SM. Comment: privacy legislation and research. *Med J Aust* 2002; 177: 523-4.
- 11 Breen KJ. Ethical review of multi-centre research: obstacles to reform. *Australas Epidemiologist* 2005; 12.1: 21-4.
- 12 Sarson-Lawrence M, Alt C, Mok MT, et al. Trust and confidence: towards mutual acceptance of ethics committee approval of multicentre studies. *Intern Med J* 2004; 34: 598-603.
- 13 Rosenthal MA, Sarson-Lawrence M, Alt C, et al. Ethics committee reviews and mutual acceptance: a pilot study. *Intern Med J* 2005; 35: 650-4.
- 14 Victorian Department of Human Services. Human Research Ethics Committee. Making an application. Melbourne: DHS, State Government of Victoria, 2006. Available at: [http://www.health.vic.gov.au/ethics/single/common\\_app\\_form.htm](http://www.health.vic.gov.au/ethics/single/common_app_form.htm) (accessed May 2007).
- 15 National Health and Medical Research Council, Australian Research Council, Australian Vice-Chancellors' Committee. National Ethics Application Form for submitting research proposals to human research ethics committees. Canberra: Australian Government, 2006. Available at: <https://www.neaf.gov.au/Default.aspx> (accessed May 2007).
- 16 Carapetis JR, Passmore JW, O'Grady KA. Privacy legislation and research. *Med J Aust* 2002; 177: 523.
- 17 Skene LL. Comment: privacy legislation and research. *Med J Aust* 2002; 177: 524.
- 18 Draper ES, Kurinczuk JJ, Abrams KR, Clarke M. Assessment of separate contributions to perinatal mortality of infertility history and treatment: a case-control analysis. *Lancet* 1999; 353: 1746-9.
- 19 National Health and Medical Research Council. National statement on ethical conduct in research involving humans. Canberra: Commonwealth of Australia, 1999.
- 20 Koski G, Aungst J, Kupersmith J, et al. Cooperative research ethics review boards: a win-win solution? *IRB* 2005; 27: 1-7.
- 21 Tully J, Ninis N, Booy R, Viner R. The new system of review by multicentre research ethics committees: prospective study. *BMJ* 2000; 320: 1179-82.
- 22 Randal J. Growing pains: central review board project still developing. *J Natl Cancer Inst* 2003; 95: 636-7.
- 23 Enzle ME, Schmaltz R. Ethics review of multi-centre clinical trials in Canada. *Health Law Rev* 2005; 13: 51-7.
- 24 Hearnshaw H. Comparison of requirements of research ethics committees in 11 European countries for a non-invasive interventional study. *BMJ* 2004; 328: 140-1.
- 25 Ward HJ, Cousens SN, Smith-Bathgate B, et al. Obstacles to conducting epidemiological research in the UK general population. *BMJ* 2004; 329: 277-9.
- 26 Lumley J. Gate keeping by ethics committees. In: Brown V, Preston G, editors. Choice and change: ethics, politics and economics of public health. Canberra: Public Health Association of Australia, 1992.
- 27 Roberts LM, Bowyer L, Homer CS, Brown MA. Multi-centre research: negotiating the ethics approval obstacle course. *Med J Aust* 2004; 180: 139.
- 28 Chalmers D, Pettit P. Towards a consensual culture in the ethical review of research. Australian Health Ethics Committee. *Med J Aust* 1998; 168: 79-82.
- 29 Warlow C. Clinical research under the cosh again. *BMJ* 2004; 329: 241-2.
- 30 Skene L. Proliferating ethics committees and privacy legislation: new fetters on scientific research. *Australas Epidemiologist* 2005; 12.1: 16-18.

(Received 15/12/06, revised 6/05/07, accepted 5/06/07) □