

### What is already known on this topic

Hysterectomy is one of the most widely undertaken procedures in the healthcare systems of developed countries

Laparoscopic assisted hysterectomy is being used as an alternative to conventional (abdominal or vaginal) hysterectomy

The differential cost of the conventional and laparoscopic procedures has been assessed only in observational studies and small trials

### What this study adds

Laparoscopic hysterectomy is more costly than conventional hysterectomy, though additional costs are lower in comparison with abdominal than with vaginal hysterectomy

The laparoscopic procedure has a small beneficial effect in terms of quality adjusted life years (QALYs)

Laparoscopic hysterectomy is unlikely to be considered cost effective relative to vaginal hysterectomy. Its cost effectiveness relative to the abdominal procedure is finely balanced

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## Autopsy after termination of pregnancy for fetal anomaly: retrospective cohort study

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### Abstract

**Objective** To study trends in termination of pregnancy for fetal anomaly over 10 years and to assess the contribution of autopsy to the final diagnosis and counselling after termination.

**Design** Retrospective study with cases from a congenital anomaly register and a defined unselected population.

**Data sources** Pregnancies resulting in termination for fetal anomaly identified from the Oxford congenital anomaly register. Details about the prenatal diagnosis and autopsy findings were retrieved from case notes.

**Results** Of the 57 258 deliveries, 309 (0.5%) were terminated because of prenatally diagnosed abnormality. There were 129/29 086 (0.4%) terminations for fetal anomaly carried out in 1991-5 and 180/28 172 (0.6%) in 1996-2000. The percentage of fetuses that underwent autopsy fell from 84% to 67%. Autopsy was performed in 132 cases identified by ultrasound scan, with no evidence for abnormal

karyotype. In 95 (72%) the autopsy confirmed the suspected diagnosis and did not add important further information, two cases were not classified, and in 35 (27%) the autopsy added information that led to a refinement of the risk of recurrence (reduced in 17, increased in 18); in 11 of these 18 cases it was increased to a one in four risk.

**Conclusions** Though there has been an increase in the rate of terminations of pregnancy for fetal anomaly, there has been a decline in the autopsy rate. When a prenatal diagnosis was based on the results of a scan only, the addition of information from a autopsy by a specialist paediatric pathologist provided important information that changed the estimated risk of recurrence in 27% of cases and in 8% this was to a higher (one in four) risk.

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## Introduction

When a serious anomaly is suspected prenatally some parents request termination of pregnancy. This request may be based on the results of investigations that imply that the baby will almost certainly have a lethal anomaly—for example, anencephaly—or one likely to cause long term morbidity—for example, spina bifida. In other instances the implications of the investigations are less clear—for example, a fetus with mild cerebral ventriculomegaly. After termination of pregnancy the accuracy of the prenatal prediction and the implications for future pregnancies, particularly when based on ultrasound scan findings only, may be obtained from the autopsy examination.

After the adverse publicity surrounding paediatric autopsies at Alder Hey Hospital<sup>1</sup> it is now widely acknowledged that parents need a full explanation to make an informed decision. Currently there is little quantitative information about the likelihood of autopsy being of practical use to parents and their families by modifying the assessment of the recurrence risk.

The prenatal diagnosis unit in Oxford is a tertiary referral centre. Since 1991 anomalies suspected prenatally and those presenting postnatally have been recorded on the Oxford congenital anomaly register (OXCAR) with the outcome of each pregnancy. We used 10 years of data reported to the register<sup>2-3</sup> to assess how often information from the autopsy changes the suspected prenatal diagnosis and hence the advice given

to parents about risks of recurrence; to ascertain the rates of termination of pregnancy and autopsy over 10 years in cases of prenatally suspected anomalies; to report on the range of anomalies for which termination of pregnancy was carried out and their severity; and to estimate the reduction in prevalence of conditions associated with long term morbidity because of prenatal diagnosis and termination of pregnancy.

## Methods

From the OXCAR register we identified all women with an OX postcode who were booked for delivery between 1 January 1991 and 31 December 2000 inclusive at the John Radcliffe or attached community hospital and in whom the outcome of pregnancy was recorded as termination. We excluded women booked into and referred from other hospitals and those with an OX postcode who would have delivered at another district hospital. The study population was therefore unselected. The total number of deliveries occurring in the same population and time period was obtained from the Oxford Maternity Data System. We reviewed autopsy reports, clinical notes, and laboratory and ultrasound reports.

We identified those cases in which a structural anomaly was diagnosed by scan, there was no evidence for abnormal karyotype, and an autopsy was carried out. Two investigators reviewed the autopsy findings to determine whether they altered the suspected prenatal diagnosis and the assessment of the risk of recurrence (table).

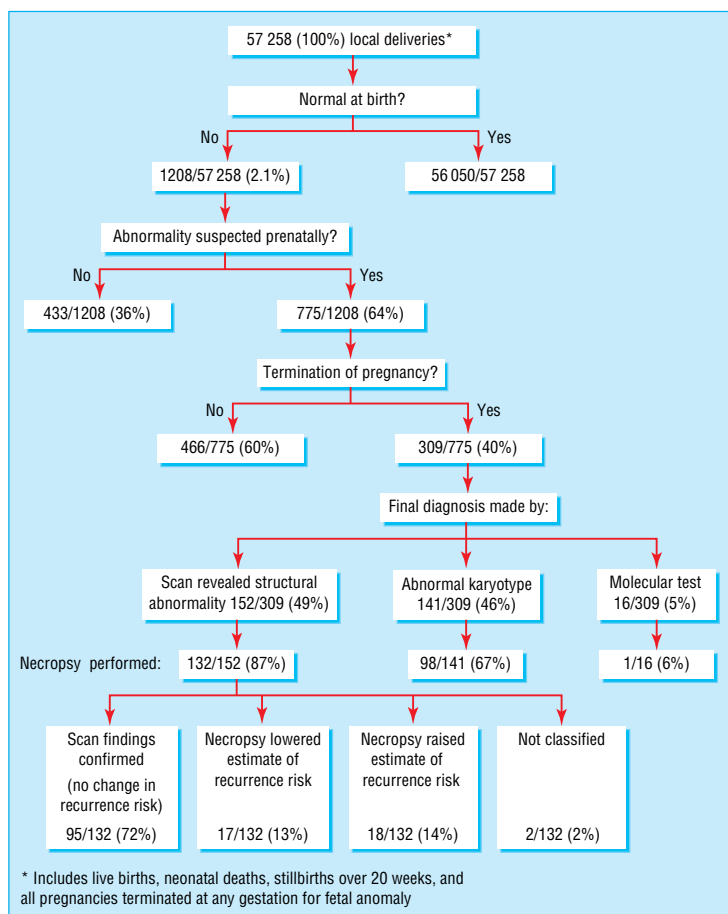
## Results

The figure provides an overview of the prenatal diagnosis of congenital anomalies and termination of pregnancy.

The rate and number of terminations for suspected fetal anomaly increased during the study period, from 129 (129/29 086 (0.4%)) during 1991-5 to 180 (180/28 172 (0.6%)) during 1996-2000. In the same time periods the number of prenatal diagnoses made (with abnormality present at birth) increased from 41% to 46%. The number of terminations of pregnancy in which autopsy was carried out fell from 84% in the first five years to 67% in the second five years.

Of the 57 258 births, 309 (0.5%) were terminated because a fetal anomaly had been suspected or diagnosed prenatally. Chromosome anomalies accounted for 141 (46%) of these. Neural tube defects and other central nervous system defects were the most common structural defects, accounting for 66 (21%) cases. One hundred and fifty five (50%) fetuses were considered to have defects which probably would have proved lethal, and in 154 the defects were compatible with survival beyond a year. See [bmj.com](http://bmj.com) for details of the final postnatal diagnosis and their lethality.

During the 10 years of the study there were 1208 fetuses or babies with a malformation. Of these, 601 had a malformation compatible with survival with long term morbidity. The crude reduction in prevalence of congenital malformations associated with long term morbidity is 26% (that is, 154/601). The true reduction in prevalence would be lower than this because some of the pregnancies would have ended in miscarriage. See [bmj.com](http://bmj.com) for details of the calculation and assumptions made.



Summary chart of prenatal screening and termination of pregnancy for congenital abnormality in Oxford, 1991-2000, inclusive

Contribution of autopsy in 132 cases of termination of pregnancy due to structural anomalies detected at scan with no evidence for abnormal karyotype and autopsy performed

Category	Contribution of autopsy	No (%) of cases	Example
1	Prenatal diagnosis confirmed; scan and autopsy findings identical	72 (55%)	Scan=isolated anencephaly; autopsy =isolated anencephaly
2	Prenatal diagnosis confirmed; autopsy added some information which did not change recurrence risk	23 (17%)	Scan=anencephaly; autopsy =anencephaly + unilateral renal agenesis
3a	Autopsy added information that reduced estimate of recurrence risk	17 (13%)	Scan=anencephaly; autopsy =amniotic band
3b	Autopsy added information that increased estimate of recurrence risk	18 (14%)	Scan=cystic kidneys; autopsy =infantile polycystic kidney disease
4	Other (see text)	2 (2%)	

The table shows an assessment of the contribution of the autopsy findings to the final diagnosis made for the purpose of counselling after termination of pregnancy. Autopsy findings led to a refinement of the risk of recurrence (category 3) in 35 (27%) cases. In 11/18 (61%) (category 3b) of those in which the autopsy findings led to an increase in the estimated risk of recurrence this was to a probable one in four risk for subsequent pregnancies. Two cases (category 4) could not be classified; termination of pregnancy had been carried out at the parents' request before test results (subsequently normal) had been reported.<sup>2</sup>

## Discussion

### Autopsy rates

In an unselected population over a 10 year period there has been a decline in the number of fetal autopsies carried out despite an increase in the number of terminations of pregnancy after prenatal suspicion of fetal abnormality. Though this decline preceded the adverse publicity surrounding events at Alder Hey Hospital, it has accelerated since.<sup>1</sup> A fall in autopsy rates has also been reported by others.<sup>4</sup>

### Contribution of the autopsy to estimation of recurrence risks

When parents make a difficult decision to terminate a pregnancy because of suspected fetal abnormality most want to know if the prenatal suspicions are verified and what the implications are for further pregnancies for themselves and their wider families. We have shown that when the final prenatal diagnosis was made by ultrasound scan, in 27% of cases the information from the autopsy examination led to a refinement of the risk of recurrence, and in 8% this was increased to a one in four risk. We believe that these data may be of particular value to parents, and to those counselling them. Our study of an unselected population took place at a tertiary referral centre with autopsy performed by specialist paediatric pathologists. Care should be taken in extrapolating these data to other centres, especially those without access to a specialist paediatric pathologist.

A study of neonatal autopsy found a similar proportion in which new information was revealed,<sup>4</sup> although this is not directly comparable with our study of termination of pregnancy because of the influence of postnatal events and management. Another study of 300 fetal autopsies, found the autopsy examination changed the prenatal "hypothesis" in 20%, provided extensive additional information in 41%, and confirmed the prenatal hypothesis in 39%.<sup>5</sup>

### Contribution of prenatal diagnosis to reduction in prevalence of non-lethal congenital anomalies

We have now added four more years of data to our previous report from the same population.<sup>2</sup> Recalculation of the crude reduction in prevalence of congenital anomaly associated with long term morbidity because of termination of pregnancy shows it to have increased from 20% to 26%.

### Benefits of autopsy

Quantifying the value of autopsy is not easy. For example, renal cystic disease may be difficult to define on a scan because of a lack of amniotic fluid, and the differentiation between infantile polycystic kidney disease (recurrence risk 25%) and cystic renal dysplasia (recurrence risk 3%) may require histological examination.

The direct benefits of autopsy to parents are not limited to refining the risk of recurrence. Even after autopsy, sometimes a definitive diagnosis cannot be made. In such cases the storage of fetal samples for possible future genetic analysis provides the hope of an accurate diagnosis (which may have ramifications for the wider family) at a later date. In most cases in which the scan findings are confirmed parents can gain comfort that their baby had the prenatally suspected condition. The finding of additional malformations, as well as in some cases changing the diagnosis, may be helpful in targeting tests in a subsequent pregnancy. A wider importance of autopsy is in its value for quality control for prenatal diagnosis, teaching, and research.

The decline in autopsy rate has been the subject of much debate since the adverse publicity concerning

### What is already known on this topic

After prenatal diagnosis of fetal anomaly some parents opt for termination of pregnancy

The rate of decline in the uptake of autopsy has accelerated since adverse publicity at Alder Hey Hospital

### What this study adds

The number of pregnancies resulting in termination after prenatal diagnosis of fetal anomaly has increased over a 10 year period

When termination of pregnancy occurs after identification of structural anomalies on scan and there is no evidence for abnormal karyotype, new information from autopsy changes the estimated risk for a recurrence in more than a quarter of cases; in 8% this is increased to a one in four risk

autopsies and organ retention. Parents should be provided with full information and not be coerced into accepting an autopsy examination, and these discussions should be with an appropriately trained professional. Our study provides important information for parents. If a termination has been carried out because of anomalies detected by ultrasound scan, by declining an autopsy, parents will remain ignorant of information that might change the recurrence risk in one in four cases and have a one in 13 chance for missing confirmation of a high (one in four) recurrence risk.

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## Comparison of requirements of research ethics committees in 11 European countries for a non-invasive interventional study

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The Declaration of Helsinki states that every experimental procedure involving human subjects should be approved by a research ethics committee.<sup>1</sup> All signatory countries must enact the declaration but can also add local requirements which do not reduce the protection. Research ethics committees are well established, though they have been criticised.<sup>2</sup>

I aimed to describe how countries vary in their requirements for research ethics committees for exactly the same trial protocol. The study was nested within a trial, in 11 signatory countries, of a leaflet intervention aimed at improving the involvement of older patients during consultations with their general practitioners. The trial outcome measures were questionnaires for the general practitioners and their patients before and after the intervention. The documents relevant to research ethics committees comprised the letter of invitation, information leaflet, and questionnaires for patients (patient's pack); the similar, but different general practitioner's pack; and the intervention consultation leaflet.

### Participants, methods, and results

I piloted a questionnaire, based on experiences in previous multinational studies,<sup>3</sup> and then sent it to the researcher in each country (see [bmj.com](http://bmj.com)). The questionnaire asked for details of processes in getting approval from research ethics committees for the trial. I received responses from all partners—Austria, Belgium, Denmark, France, Germany, Israel, the Netherlands, Portugal, Slovenia, Switzerland, and the United Kingdom (table).

In Belgium, application was made to one research ethics committee. In Slovenia, the application also needed the protocol in English. In the United Kingdom, the 20 copies of the application needed all

documents. Changes to the UK patient invitation letter required by the committee were resubmitted for chair's approval. The whole process took 10 weeks.

In all countries where researchers made applications, in addition to office costs, the researcher's time was used to prepare the application. This was two days in Slovenia and five days in the United Kingdom. In Israel, although approval of the research ethics committee was not needed, one day of researcher's time was taken in discovering this.

### Comment

Countries clearly differ in their requirements for approval by a research ethics committee for an identical study. If all countries are meeting the principles of the Declaration of Helsinki, then the striking variations mean we are too careful in some countries or too lax in others. The United Kingdom has an arduous process for gaining ethical approval for a non-invasive intervention study.

The risks of inappropriate requirements include unnecessarily delayed studies and extra costs without any increased protection for participants. Disintegration of study protocols is also a high risk, and, therefore, UK partners may be unwelcome in international studies.

In countries where researchers do not apply for approval of a research ethics committee they are not being unethical. In the Netherlands, guidelines distinguish between studies where approval is and is not necessary.<sup>4</sup> Not all medical research needs all the principles of the Declaration of Helsinki—for example,



The questionnaire completed by researchers is on [bmj.com](http://bmj.com)