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Review

Ultrasound screening in pregnancy: a systematic review of the clinical effectiveness, cost-effectiveness and women's views

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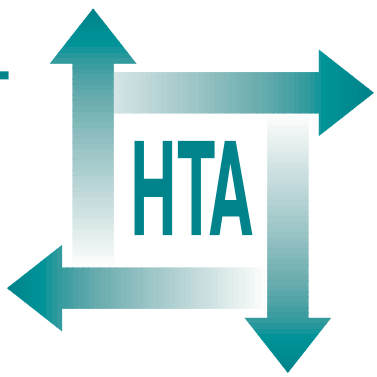
Health Technology Assessment
NHS R&D HTA Programme



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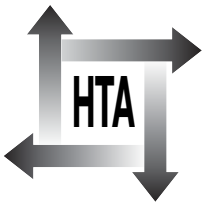

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Ultrasound screening in pregnancy: a systematic review of the clinical effectiveness, cost-effectiveness and women's views

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The Standing Group on Health Technology advises on national priorities for health technology assessment. Six advisory panels assist the Standing Group in identifying and prioritising projects. These priorities are then considered by the HTA Commissioning Board supported by the National Coordinating Centre for HTA (NCCHTA).

This report is one of a series covering acute care, diagnostics and imaging, methodology, pharmaceuticals, population screening, and primary and community care. It was identified as a priority by the Population Screening Panel and funded as project number 93/30/03.

The views expressed in this publication are those of the authors and not necessarily those of the Standing Group, the Commissioning Board, the Panel members or the Department of Health. The editors wish to emphasise that funding and publication of this research by the NHS should not be taken as implicit support for the recommendations for policy contained herein. In particular, policy options in the area of screening will be considered by the National Screening Committee. This Committee, chaired by the Chief Medical Officer, will take into account the views expressed here, further available evidence and other relevant considerations.

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Contents

List of abbreviations

ASD	Arial septal defect*
AVSD	atrioventricular septal defect*
CAML	congenital adenomatous malformation of the lung*
CDH	congenital diaphragmatic hernia*
CI	confidence interval
CNS	central nervous system
CPC	choroids plexus cyst
CVS	chorionic villus sampling
GP	general practitioner
ICER	incremental cost-effectiveness ratios
ICU	intensive care unit*
MeSH	medical subject headings
NT	nuchal translucency
OR	odds ratio
RADIUS	Routine Antenatal Diagnostic Imaging Study
RCOG	Royal College of Obstetricians and Gynaecologists
RCR	Royal College of Radiologists
RCT	randomised controlled trial
RPD	renal pelvic dilatation
SD	standard deviation
SURUSS	Serum, Urine and Ultrasound Screening Study
T1, 2, 3	first, second and third trimesters*
VSD	ventricular septal defect*
WMD	weighted mean difference*

* Used only in tables and figures

Executive summary

Objectives

- To update the pre-existing Cochrane review of ultrasound for routine fetal assessment in early pregnancy.
- To compile new Cochrane reviews of
  – routine ultrasound in late pregnancy
  – routine Doppler® ultrasound in pregnancy.
- To review the literature on the detection of fetal abnormalities by ultrasound screening examinations during pregnancy.
- To conduct a primary study to assess the consequences of a routine two-stage ultrasound regimen in pregnancy in a teaching hospital (clinical pathways).
- To compile literature reviews of (a) women's views on undergoing routine ultrasound examination and (b) estimates of costs and cost-effectiveness of routine ultrasound examinations.
- To conduct a primary study of costs of a routine two-stage ultrasound regimen in early or mid-pregnancy in a UK teaching hospital.
- To refine and update a decision model of cost-effectiveness of options for routine scanning for fetal anomalies.

Methods

Full details of search strategies for systematic reviews are in the appendices. Other methods are described in individual sections of the full report, as are methods for the primary studies of clinical pathways and costs.

Results

Routine ultrasound before 24 weeks:

- leads to earlier diagnosis of multiple pregnancies but has not been shown to have an important positive impact on the outcome of multiple pregnancies
- is associated with fewer inductions of labour for 'post-term' pregnancy
- reduces perinatal mortality rate if detection of fetal malformations is an important objective and a high level of diagnostic expertise exists and if termination of pregnancy for fetal abnormality is widely accepted in the population screened.

Routine ultrasound after 24 weeks:

- has not been shown to confer any clear benefit to mother or baby, except that assessment of placental appearances may, as an adjunct to fetal measurement, help reduce perinatal mortality.

Routine Doppler ultrasound in pregnancy:

- has not been shown to be of benefit and may even increase the risk of adverse outcome.

Detection of fetal abnormality by screening ultrasound examinations:

- detection rates vary with the organ system affected, with generally high rates of detection of abnormalities of the CNS, and low rates for skeletal and cardiac abnormalities
- similar variations are seen at both second and third trimester examinations
- data on the value of first trimester anomaly screening are lacking.

Clinical pathways:

- largely unrecognised consequences of routine ultrasound examinations exist that have health service resource implications as well as the potential to alarm women. Specifically:
  – 2.5% of booking scans are repeated
  – 7.6% of anomaly scans are repeated
- women present for antenatal booking at different gestations; hence, the coverage of any one scan regimen may be incomplete.

Women's views

- Ultrasound is very attractive to women and partners; this may be because it provides early visual confirmation of pregnancy and contact with their babies, and reassures about fetal well-being.
- Such features may augment the potential for anxiety, shock and disappointment when the scan shows a problem. Recent changes in the use of ultrasound may lead to more findings of uncertain clinical significance, which is likely to have important psychological and social consequences for women.
- Women's earlier fears, that ultrasound might harm the fetus, do not feature in later research, although this may be partly due to researchers not asking about fears.
- Reports of a reduction in anxiety after ultrasound examination are likely to reflect

increased anxiety before the scan rather than a real benefit of ultrasound.
- There is no reliable evidence of reduced smoking or any other positive health behaviour as a consequence of routine ultrasound.
- Trials comparing ultrasound with no ultrasound have not considered its psychological or social impact on both parents and babies.

Costs and cost-effectiveness

Literature review

- There are few good quality economic evaluations and primary cost studies of ultrasound scanning in pregnancy. Only one economic evaluation conducted alongside an RCT was included in the review.
- Routine scanning in the second trimester was shown to be relatively cost-effective.
- The skill of ultrasonographers in detecting anomalies and the time taken to perform a scan have a significant effect on the relative cost-effectiveness.

Primary costing study

- Costs to women of attending ultrasound examinations were significant compared with NHS service costs.
- It is important to include women's costs in economic evaluation of routine ultrasound screening, particularly where cost shifting may occur, because any change in the provision of routine ultrasound may shift the costs away from the provider on to women and their families and influence attendance.

Decision-analysis modelling

- The initial eight options considered were reduced to three dominating options:
  – one second trimester scan alone
  – one third trimester scan alone
  – a combination of one second trimester scan followed by one third trimester scan.
- More representative cost data are required before precise estimates of the additional costs and benefits of alternative screening options can be determined.
- One second trimester scan emerged as a clear reference case, being one of the cheapest options yet still detecting a significant number of anomalies.
- When termination is acceptable and available, a third trimester scan alone or the combination of one second with one third trimester scan, although comparable in economic terms, may be impractical because of the delay in identifying anomalies.
- The interaction of an anomaly scan(s) with a first trimester scan for dating purposes was not assessed.

Conclusions

Implications for policy and practice

- There is evidence that routine ultrasound in early pregnancy provides:
  (i) better gestational age assessment
  (ii) earlier detection of multiple pregnancies
  (iii) detection of clinically unsuspected fetal malformation at a time when termination of pregnancy is possible. These effects have not been shown to improve ultimate fetal outcome. No convincing evidence of benefit from routine examination in late pregnancy (> 24 weeks) was found, whether using imaging or Doppler ultrasound.
- Clinicians, women and health planners need to decide if these effects are sufficient to justify routine ultrasound. Clinicians in the UK seem convinced of the benefits, given the very widespread use of the technique. As seen from the systematic review of women's views, imaging is popular with women (provided the appearance of the baby is normal). The study in Liverpool indicates that the average cost to the hospital of providing a 20-week anomaly scan is £15. This seems modest in the UK but will be prohibitively high in many developing countries.
- If routine ultrasound is to be offered before 24 weeks, what timing is optimal? The Royal College of Obstetricians and Gynaecologists' (RCOG) Working Party report of 1997 recommended a two-stage regimen of booking ultrasound at about 12 weeks, followed by a second ultrasound anomaly scan at 20 weeks – the regimen offered at Liverpool Women's Hospital. When this report was initially drafted, no comparative information was available about the clinical impact of different regimens. Since then, an RCT comparing the two-stage regimen with a 20-week scan alone has demonstrated less need for readjustment of dates at the mid-pregnancy scan in the two-stage group (with possible consequences for timing serum screening, if available) and less anxiety among the women. Again, clinicians, women and health planners have to decide whether such benefits justify the costs.
- The systematic review of the effectiveness of anomaly detection has highlighted substantial variation in, and limits to, detection rates of certain structural abnormalities. This information should be made available to

clinicians and women, and may also be relevant to the medico-legal arena. Given these limits, the RCOG Working Party's recommendations, that ultrasound examinations should be conducted only by appropriately trained personnel and using equipment no more than 5 years old, seem appropriate. Quality control mechanisms should be set in place to audit performance. The system of reporting suspected anomalies to regional fetal anomaly registers should be encouraged where these exist.
- A number of inefficiencies in the routine ultrasound screening programme were identified (including the need for repeat scans and that not all women book at early gestations), some of which are unavoidable, but which have implications for both its clinical and cost-effectiveness.

Research recommendations

Within each category below, the research recommendations are prioritised.

Guidelines on research methods

All future work evaluating uses of ultrasound in pregnancy should take account of the following methodological points.

- Published reports from clinical departments of detection rates of fetal abnormalities by ultrasound screening may not represent general standards. General detection rates should be assessed by linkage with high-ascertainment fetal abnormality registers at a regional level.
- Reporting of costs and cost-effectiveness of routine ultrasound screening should take account of recommended standards for economic evaluation.
- New or extended uses for pregnancy ultrasound should be evaluated in psychological and social, as well as healthcare efficiency and clinical terms.
- Studies of women's views of ultrasound, clinical effectiveness and costs of technologies should report the date and place of the research and describe the clinical contexts and purposes for which ultrasound was used for those research participants.

Priorities for research

Effectiveness of newer applications of ultrasound screening and alternative forms of care

Some forms of ultrasound screening are being introduced into routine practice without strong evidence on effectiveness; others are promising but need more evaluation.

- Nuchal translucency scanning and other types of ultrasound screening for anomalies during the first trimester of pregnancy are topical and controversial issues in obstetric care. None of the limited number of reports on these topics met our criteria for inclusion in systematic reviews and have therefore not been considered in detail. Researchers should be encouraged to study rigorously not only the effectiveness of detection of anomalies but also adverse clinical sequelae, psychological impact on women and their partners, and economic consequences. Until these data are available, the evidence does not support screening in the clinical service.
- More representative data are required on the clinical and psychological effects and cost implications of first trimester anomaly scanning.
- The possible value of routine mid-pregnancy uterine Doppler ultrasound to predict pre-eclampsia, intrauterine growth restriction and other adverse outcomes should be assessed in randomised trials.
- A single trial has suggested that placental texture grading during the third trimester may be helpful; this merits further study.

Documenting current practice, clinical pathways, costs and outcomes

In order to develop relevant guidance for the NHS, more needs to be known about current practice.

- Research is needed to assess the effects and costs of detection of fetal abnormalities amenable to *in-utero* intervention and neonatal surgery on substantive outcomes, such as short- and long-term morbidity and mortality for both mother and child, including parental psychological consequences.
- The findings of the primary studies of costs and clinical pathways undertaken to augment anticipated gaps in knowledge in this review need to be repeated and validated in other settings.
- Further evaluation is required on the impact of changes in routine antenatal care practice and its influence on family economy, clinical attendance or healthcare efficiency.

Defining options for screening

Developments in ultrasound technology provide information with uncertain implications.

- There is continuing controversy about the significance of ultrasound 'soft markers' and their relationship to, in particular, chromosomal abnormalities. There should be ongoing

clinical research into the significance and implications of detection of all sonographic soft markers in unselected and low-risk populations. These findings should be interpreted in the light of other screening programmes for chromosomal abnormalities (e.g. biochemical screening).

Ethical and cultural issues

Current practice is not based on a strong basis of knowledge of women's needs and understanding of ultrasound.

- Ways of improving women's understanding of the information gained from ultrasound should be developed and evaluated.
- There is scope for further investigation into the values women attach to their own time and to attending for a scan in different circumstances.
- Comparative research into the ways in which prenatal ultrasound is carried out and experienced in different countries and cultures would be valuable.

Cost-effectiveness

This is not constant over time and regular updating of models should be based on research as recommended above.

- Further development of economic models of cost-effectiveness of ultrasound screening in pregnancy should include assessing the effects of including a first or second trimester dating scan, and considering longer-term consequences and changing evidence on technologies, effectiveness and outcomes.

Chapter 1
Background

There has been little debate, rightly or wrongly, about the usefulness of ultrasound examination in those clinical situations in which there are clear reasons to suppose that such an investigation might provide important information which would complement clinical assessment. The many examples would include:

- antepartum haemorrhage, primarily to identify or exclude placenta praevia
- clinical suspicion that a fetus was small for gestational age, because of the well-recognised perinatal risks that can be avoided by early delivery
- polyhydramnios, because the excessive amount of amniotic fluid may result from a structural malformation in the fetus.

What is much more controversial is the routine use of ultrasound in **all** pregnancies, a procedure that has become standard practice in many countries. The use of ultrasound in the UK is not routinely documented in NHS statistics and so the only source of evidence on current practice is from surveys and clinical audit. Two national studies of pregnancy ultrasound use in the UK have been found.[1,2] Both found that women are offered at least one scan in pregnancy. The Royal College of Obstetricians and Gynaecologists (RCOG)/Royal College of Radiologists (RCR) survey[2] found that 77% of hospitals offered a routine dating scan, while 82% offered a second trimester anomaly scan (at 18–20 weeks). Only 5% of departments undertook an additional routine third trimester scan.

An RCOG Working Party suggested in 1984[3] that, in the UK, a single routine ultrasound examination, ideally between 16 and 18 weeks of pregnancy, might be beneficial. A stronger recommendation came from an RCOG Study Group in 1991[4] – endorsing a routine 'anomaly scan' at 18–20 weeks. This was an 'expert-based' rather than evidence-based recommendation. A further RCOG report on routine ultrasound was published in 1997.[5] This Working Party, chaired by Professor MJ Whittle, reviewed the evidence available at that time, including systematic reviews. Their report:

- supported the offer of a routine anomaly scan to women at 18–20 weeks, although it indicated that the exact regimen would hinge on specific objectives and financial considerations
- did not endorse nuchal translucency (NT) scanning as that was still being evaluated
- did support a 'booking scan' before and in addition to the anomaly scan
- emphasised the need for women to make informed decisions about whether they wished to undergo routine ultrasound
- highlighted the dearth of knowledge about costs and cost-effectiveness of routine ultrasound, and recommended economic research
- stressed the need for ultrasound to be performed by appropriately trained personnel using modern equipment (< 5 years old), safe practice (applying the ALARA [as low as reasonably achievable] principle) and audited performance.

The RCOG Working Party[5] also listed issues that required further research, including population impact of screening, continuing surveillance of safety, psychological impact of positive prenatal diagnosis, effects of prenatal invasive procedures and neonatal surgery.

This study has sought to fill, where possible, the gaps in knowledge identified by the RCOG Working Party. The primary tool has been the systematic review.

All interventions in pregnancy have the capability of doing harm as well as good, and there are many procedures that have been discarded after systematic evaluation of their impact, for example, routine enemas and pubic shaving in labour. Routine ultrasound has been less easy to evaluate because it is a relatively new technology in which there have been vast improvements in imaging capabilities within a short time. Thus, an individual study may have little relevance within a few years as technical advances expand clinical application. However, assumptions cannot be made about safety, both in the sense of potential damage by ultrasound energy (although relevant studies have been generally reassuring), or of inappropriate clinical intervention based on routine ultrasound findings, or of unnecessary distress produced by findings of unclear significance. In addition, all countries are grappling with increasing demands

for limited health resources, and it is a particular responsibility of health planners to ensure that such screening procedures are cost-effective as well as being clinically effective.

Suggested applications of routine ultrasound have included (in chronological order) the following.

- Measurement of fetal NT during the late first trimester as a means of screening for Down's syndrome and other chromosomal abnormalities[6] and cardiac malformations.[7] This is a recent innovation, currently being investigated in an ongoing HTA-funded project (the Serum, Urine and Ultrasound Screening Study – SURUSS) and will receive little attention in this report.
- A 'booking scan', usually performed at about 12–14 weeks, with the primary aims of establishing gestational age, viability, and detecting multiple pregnancies (and chorionicity if a multiple pregnancy is detected). Although some gross fetal malformations will also be detected during this investigation, this is not its primary aim.
- An 'anomaly scan', usually performed at about 20 weeks, which does have the primary aim of detecting structural malformations in the fetus. This may include a deliberate search for so-called 'soft markers' – features that, in themselves, have little or no functional significance but which may indicate an increased risk of chromosomal abnormality, for example, choroid plexus cysts (CPCs), echogenic bowel, or echogenic cardiac foci ('golf balls') in the fetal heart.
- A Doppler® ultrasound study of the maternal uterine arteries at about 22 weeks to identify any increased risk of the subsequent development of pre-eclampsia and fetal growth restriction.
- Third trimester ultrasound measurements of the fetus or imaging of the placenta or Doppler study of the umbilical arteries, primarily to investigate clinically unsuspected fetal growth restriction. This option also includes detecting anomalies (whether meant to or not), which may also trigger interventions pre- or postnatally.

This study had three main parts: clinical effectiveness, women's views and cost-effectiveness. All three rely on the concept of the systematic review as a scientific, replicable method of explicitly describing objectives, the search strategy for relevant literature, and the methods for processing information and deriving conclusions.[8] In some areas there was a need for primary research to supplement literature-based data, and these studies were performed in the Liverpool Women's Hospital, one of the largest maternity units in the UK, where two of the research team are based.

Chapter 2

Systematic review of clinical effectiveness of routine ultrasound in pregnancy

Introduction

The use of ultrasound imaging in pregnancy has become an integral part of antenatal care in most parts of the world. While there has been little debate about its value in clinical situations for which there are specific indications, there is an increasing realisation that initial assumptions about its value as a screening tool in low-risk pregnancy may have been optimistic, and this has led to much uncertainty and controversy. The issues are complex and include questions about its effect on hard outcomes such as perinatal morbidity and mortality, the use of available resources, and the short- and long-term psychological and social consequences for individuals and society at large.

The aim of this part of the review was to assess the clinical effectiveness of routine ultrasound screening in pregnancy, identifying those areas in which the evidence is lacking and where further research is required, and providing clinical information for the economics section of the review. This was undertaken in three parts.

1. Updating and performing systematic reviews of the existing literature on randomised trials to determine the clinical effectiveness of routine ultrasound in pregnancy, using the well-established methods for systematic reviews developed by the Cochrane Collaboration. (see below).
2. Systematically reviewing all the literature on routine ultrasound screening in pregnancy, including non-randomised studies, with particular reference to detection, management and outcome of the abnormal fetus. (see chapter 3).
3. Studying the patterns which emerge from the routine two-scan regimen at the Liverpool Women's Hospital, with the intention of obtaining information about the clinical pathways that develop as a result of routine ultrasound and which may be missing from the literature review. (see chapter 4).

Systematic reviews of randomised trials

Three systematic reviews, detailed below, have undergone the peer review process of the Cochrane Collaboration's Pregnancy and Childbirth Group. Details are available electronically on the Cochrane Library CD-ROM or on the Internet at http://www.update-software.com/ccweb/.

Ultrasound for fetal assessment in early pregnancy

The abstract that follows is taken from the pre-existing Cochrane review, which has recently been updated – see appendix 1 for the full review.

Background

Advantages of early pregnancy ultrasound screening are considered to be more accurate calculation of gestational age, earlier identification of multiple pregnancies, and diagnosis of non-viable pregnancies and certain fetal malformations.

Objective

The objective of this review was to assess the use of routine (screening) ultrasound compared with the selective use of ultrasound in early pregnancy (i.e. before 24 weeks).

Search strategy

The Cochrane Pregnancy and Childbirth Group Trials Register and the Cochrane Controlled Trials Register (up to July 1998) were searched.

Selection criteria

Adequately controlled trials of routine ultrasound imaging in early pregnancy.

Data collection and analysis

One reviewer assessed trial quality and extracted data. Study authors were contacted for additional information.

Main results

Nine trials were included. The quality of the trials was generally good. Routine ultrasound examination was associated with earlier detection

of multiple pregnancies (twins undiagnosed at 26 weeks, odds ratio (OR) 0.08, 95% confidence interval (CI), 0.04 to 0.16) and reduced rates of induction of labour for post-term pregnancy (OR, 0.61, 95% CI, 0.52 to 0.72). There were no differences detected for substantive clinical outcomes such as perinatal mortality (OR, 0.86, 95% CI, 0.67 to 1.12). Where detection of fetal abnormality was a specific aim of the examination, the number of terminations of pregnancy for fetal anomaly increased.

Reviewers' conclusions

Routine ultrasound in early pregnancy appears to enable better gestational age assessment, earlier detection of multiple pregnancies and earlier detection of clinically unsuspected fetal malformation at a time when termination of pregnancy is possible. However, the benefits for other substantive outcomes are less clear.

Routine ultrasound in late pregnancy (> 24 weeks' gestation)

The following abstract of a Cochrane review was recently published in the Cochrane Library – see appendix 2 for the full review.

Background

Diagnostic ultrasound is used selectively in late pregnancy when there are specific clinical indications. However, the value of routine late pregnancy ultrasound screening in unselected populations is controversial. The rationale for such screening would be the detection of clinical conditions which place the fetus or mother at high risk, which would not necessarily have been detected by other means such as clinical examination, and for which subsequent management would improve perinatal outcome.

Objectives

To assess the effects on obstetric practice and pregnancy outcome of routine late pregnancy ultrasound, defined as greater than 24 weeks' gestation, in women with either unselected or low-risk pregnancies.

Search strategy

The Cochrane Pregnancy and Childbirth Group Specialised Register of Controlled Trials and the Cochrane Controlled Trials Register were searched.

Selection criteria

All acceptably controlled trials of routine ultrasound in late pregnancy (defined as after 24 weeks).

Data collection and analysis

The principal reviewer assessed trial quality and extracted data, under supervision of the co-reviewer.

Main results

Seven trials recruiting 25,036 women were included. The quality of trials overall was satisfactory. There was no difference in antenatal, obstetric and neonatal intervention or morbidity in screened versus control groups. Routine late pregnancy ultrasound was not associated with improvements in overall perinatal mortality. Placental grading as an adjunct to a third-trimester examination scan was associated with a significant reduction in the stillbirth rate in the one trial that assessed it. There is a lack of data with regard to long-term substantive outcomes such as neurodevelopment. There is a lack of data on maternal psychological effects.

Reviewers' conclusions

Based on existing evidence, routine late pregnancy ultrasound in low risk or unselected populations does not confer benefit on mother or baby. There is a lack of data about the potential psychological effects of routine ultrasound in late pregnancy, and the effects on both short- and long-term neonatal and childhood outcome. Placental grading in the third trimester may be valuable but whether reported results are reproducible remains to be seen, and future research into late pregnancy ultrasound should include evaluation of placental textural assessment.

Routine Doppler ultrasound in pregnancy

The following abstract is of a Cochrane review published in the Cochrane Library – see appendix 3 for the full review.

Background

Doppler ultrasound study of umbilical artery waveforms helps to identify the compromised fetus in 'high-risk' pregnancies and, therefore, deserves assessment as a screening test in 'low-risk' pregnancies. One of the main aims of routine antenatal care is to identify the 'at-risk' fetus in order to apply clinical interventions which could result in reduced perinatal morbidity and mortality.

Objectives

To assess the effects on obstetric practice and pregnancy outcome of routine Doppler ultrasound in unselected and low-risk pregnancies.

Search strategy
The Cochrane Pregnancy and Childbirth Group Specialised Register of Controlled Trials and the Cochrane Controlled Trials Register were searched. Date of last search: September 1999.

Selection criteria
Acceptably controlled trials of routine Doppler ultrasound (umbilical circulation and/or uterine circulation) in unselected or low-risk pregnancies.

Data collection and analysis
Both reviewers assessed trial quality and extracted data. Authors of two trials were contacted for additional information.

Main results
Five trials were included which recruited 14,338 women. The methodological quality of the trials was generally good. Based on existing evidence, routine Doppler ultrasound examination in low-risk or unselected populations did not result in increased antenatal, obstetric and neonatal interventions, and no overall differences were detected for substantive short-term clinical outcomes such as perinatal mortality. There is no available evidence to assess the effect on substantive long-term outcomes such as childhood neurodevelopment. There is no available evidence to assess maternal outcomes, particularly psychological effects. In two studies there were unexpected findings suggesting possible harmful effects but the explanation for these is not clear, and further evaluation regarding the safety of Doppler ultrasound is required.

Reviewers' conclusions
Based on existing evidence, routine Doppler ultrasound in low risk or unselected populations does not confer benefit on mother or baby. Future research should be powerful enough to address small changes in perinatal outcome and should include evaluation of maternal psychological effects, long-term outcomes such as neurodevelopment, and issues of safety.

Chapter 3

Detection of fetal abnormalities by routine ultrasound

Introduction

Two members of this review group were involved in the production of the RCOG Working Party report, *Ultrasound screening for fetal anomalies* (1997),[5] and were aware of the existence of a paper by Chitty (1995),[9] *Ultrasound screening for fetal abnormalities*. This paper is a well-structured, extensive literature review and, acknowledging the advances in ultrasound understanding and technology, it was decided not to review the literature predating it but rather to update it. There were a number of areas that it, and the RCOG report, did not address in detail. First, there was no mention of the methodology employed in assessing quality of studies for inclusion or exclusion in the reviews, that is, it is not clear if a systematic structured format was employed. Second, both publications concentrated on routine second trimester ultrasound screening for fetal abnormalities and, for the purposes of this project, data about first and third trimester routine ultrasound fetal anomaly detection performance was required. Third, there were few data at the time to assess the effect of detecting or reporting ultrasonographic 'soft' markers of chromosomal and structural abnormalities.

Methods

Inclusion/quality criteria

For a study to be included in the review, the following criteria had to be fulfilled.

1. The study should be population-based, using an unselected or low-risk population.
2. The aim(s) should be clearly stated.
3. The setting, participants and period covered should be specified.
4. The ultrasound intervention should be fully described, including gestation at the time of ultrasound, diagnostic approach, quality control, operator(s) and skills, and equipment used.
5. It should have an adequate description of the definition of anomalies sought.
6. The method of postnatal ascertainment, including reporting of false-positives and false-negatives, should be described and be comprehensive (including neonatal examination of all live-born babies; examination (preferably a formal post-mortem) of stillborn babies, babies who die in the neonatal period and fetuses aborted after the first trimester; and post-delivery follow-up of all abnormalities suspected at routine ultrasound examination and by other prenatal tests; whenever possible this should also include checking available fetal anomaly registers and databases of the genetics, neonatal, and paediatric departments).
7. Details of anomalies detected as per fetus/system should be reported.

Studies were identified using the search strategy presented in appendix 4. Material was managed using a reference manager database (Procite™).

Methodological evaluation and data extraction

Stage I – initial categorisation of studies

Each study was categorised on the basis of the title and abstract when available. The following initial criteria were used to determine the relevance of each study to the systematic review.

1. Primary study of routine ultrasound screening in pregnancy
   (a) randomised controlled trial (RCT)
   (b) prospective study
   (c) retrospective study
   (d) not clear whether RCT, prospective, retrospective.
2. Primary study which may be relevant, but not clear from the title or abstract.
3. Primary study which is not directly relevant but may have some relevant information.
4. Review, but not primary study.
5. Foreign language:
   (a) may be relevant
   (b) not relevant.
6. Document/letter/communication.
7. Not relevant.

E. Any study which might be relevant to the economic review was flagged as 'E' and passed on to the economic reviewers.

Stage II – further categorisation of studies

All studies in categories 1, 2 and 3 were considered relevant and were retrieved and reviewed in full.

No foreign language papers were retrieved – for reasons see results below. Retrieved studies were further categorised as follows:

A1 – relevant and acceptable quality, all data to be extracted
A2 – relevant and acceptable quality, some data to be excluded
B1 – relevant but does not meet criteria for data extraction
B2 – relevant but poor quality
C – not relevant.

This two-stage categorisation process was devised by and agreed between the two clinical reviewers.

Stage III – data extraction and manipulation

Data were extracted in three stages to fulfil the following aims.

1. To develop an overview of study characteristics including type of study, period, setting (population studied, type of service and country), intervention and overall performance, in order to identify factors which affect efficacy of routine ultrasound screening in pregnancy.
2. To determine detection rates for specific anomalies in anatomical systems and chromosomal abnormalities in each trimester of pregnancy.
3. To assign specific anomalies to pragmatic groups governed by the likely interventions and outcomes of affected pregnancies.
4. To provide clinical data based on available evidence to be incorporated by the economists involved in this project into refining a previously developed economic decision model of scanning policies in pregnancy.

As the overall aim was to assess the cost-effectiveness of routine ultrasound screening in pregnancy, the manner in which the data were managed and reported was largely governed by the structure of the decision model.

An example of the data extraction sheet is presented in appendix 5.

Results

Stage I

In all, 110 papers were identified by our search strategy, with a further eight from the Chitty paper, three from the RCOG Working Party report, and one published after the literature search had been performed. Thus the abstracts of 122 papers were reviewed in total.

A total of 37 papers were initially categorised 1 (25), 2 (11) or 3 (3). The remaining 85 fell into categories 4–7 and were not considered further. Seven papers flagged 'E' (i.e. possibly relevant to the economics review) were cross-referenced with the economic reviewers (TR and JH) and had been identified by them. Only five of the 25 foreign language papers were of possible relevance (category 5a). One would have been coded 1 and four coded 2; however, they were not pursued, mainly because, of the English language papers, all those coded 2 and more than half of those coded 1 were, when reviewed in full during stage III, not suitable for the review and, hence, it was unlikely that the 'possibly relevant' foreign language papers would have been.

Stage II

Of the 37 papers identified in stage I, 36 were reviewed in full. One paper in category 1 was not retrieved as the journal would have been difficult to obtain and, on rereading the abstract, seemed to refer to a subset of the population of babies who were born with anomalies and also referred for neonatal surgical treatment.

The study categorisations in stages I and II are summarised in *Table 1*, and details of all studies reviewed in stage II are summarised in *Table 2*,[10–46] together with the reasons given if they only qualified for partial data extraction (that is, categorised A2), or for exclusion if they failed on quality criteria (that is, categorised B1 or B2).

Of the 24 available studies in category 1, further categorisation was as follows: A1 (8), A2 (3), B1 (1), B2 (11), C (1). Of the 11 available studies in category 2, further categorisation was as follows: B2 (1), C (10). The one study in category 3 was further categorised as B2. Thus, 11 papers (classified A1 or A2) entered stage III.

TABLE 1 *Summary of categorisation of studies on the detection of fetal abnormalities by routine ultrasound*

Initial categorisation (stage I)	Number of papers	Subsequent categorisation after full review (stage II)					Not retrieved
		A1	A2	B1	B2	C	
1	25	8	3	1	11	1	1
2	11				1	10	
3	1				1		
4	12						
5	25						
6	7						
7	41						
Total	122	8	3	1	13	11	1

TABLE 2 *Summary of all studies reviewed in stage II – reasons for partial/total exclusion if relevant (i.e. categorised A2, B1 and B2)*

Study	Initial category	Country	Final category	Reasons for exclusion of all or some data
Studies identified by literature search				
Magriples & Copel, 1998[22]*	1c	USA (Connecticut)	A1	
Lee, et al., 1988[18]†	1c	Korea	A2	Only routine screening data extracted (data presented separately for routine and indicated screening).
Queisser, *et al.,* 1998[26]*	1d	Germany (Mainz)	B2	Gestation at anomaly detection not clear.
Grandjean, *et al.,* 1998[27]†	2	France (Toulouse)	C	Only reported detection of chromosomal abnormalities.
Van Dorsten, *et al.,* 1998[20]*	1b + E	USA (South Carolina)	A2	Only data for screened population extracted.
Zimmer, *et al.,* 1997[28]*	1d	Israel (Haifa)	B2	Gestation at which routine scan performed not reported. False-positives not reported. 30.6 % of population never scanned.
Dillon & Walton, 1997[29]‡	1c	UK (Stockton-on-Tees)	B2	False-positives not reported (cannot calculate specificity).
Skupski, *et al.,* 1996[21]*	1c	USA (Texas)	A1	
Ashe, *et al.,* 1996[30]†	1c	Northern Ireland (Belfast)	B2	False-positives not reported (cannot calculate specificity).
Geerts, *et al.,* 1996[31]*	1a + E	South Africa (Cape Town)	C	False-positives not reported. Detection of fetal anomalies not a primary aim of study.
Eurenius, *et al.,* 1996[32]‡	1b	Sweden (Uppsala)	B2	False-negatives not reported (cannot calculate sensitivity).
Nasrat, 1998[33] (not retrieved)	1c	–		Difficult to retrieve; on reading abstract again, referred to a subset of population in which babies born with fetal anomalies were referred for neonatal surgical treatment.
Boyd, *et al.,* 1998[19]*	1c	UK (Oxford)	A2	Only data independent of serum screening to be extracted.
Skari, *et al.,* 1998[25]‡	2	Norway (Oslo)	C	
D'Ottavio, *et al.,* 1998[24]†	3	Italy (Trieste)	B2	Mentions 15 with NT but only five of those abnormal karyotype; no postnatal ascertainment of the other ten but states 'no false positives' at TVS screening, therefore unclear.
Hernadi & Torocsik, 1997[23]*	1b	Hungary	B2	No reporting of false-positives.

† *Interlibrary loan* * *Liverpool Women's Hospital library* ‡ *Harold Cohen Library, University of Liverpool*
Final category: A1, relevant and acceptable quality; all data to be extracted
A2, relevant and acceptable quality; some data to be excluded
B1, relevant but does not meet criteria for data extraction
B2, relevant but poor quality
C, not relevant

continued

TABLE 2 contd *Summary of all studies reviewed in stage II – reasons for partial/total exclusion if relevant (i.e. categorised A2, B1 and B2)*

Study	Initial category	Country	Final category	Reasons for exclusion of all or some data
Romano & Waitzman, 1998[34†]	2 + E	USA (California)	C	
Waitzman & Romano, 1998[35†]	2 + E	USA (California)	C	
Dervaux, *et al.,* 1998[36†]	2 + E	France (Toulouse)	C	
Alexander, *et al.,* 1997[37*]	2	USA (Texas)	C	
Chew, *et al.,* 1996[38†]	2	Singapore	C	
Bernaschek, *et al.,* 1996[39*]	2	Austria (Vienna)	B2	114 (26 %) cases of abnormality excluded from analysis due to incomplete data.
Vintzileos, *et al.,* 1996[40*]	2	USA (Connecticut)	C	
Crombleholme, *et al.,* 1996[41†]	2	USA (Boston)	C	
De Vigan, *et al.,* 1997[42*]	2	France (Paris)	C	
Further studies identified				
Smith & Hau, 1999[43*]	1c	UK (Scotland)	B2	Gestation at scan changed over period but not stated when. No report of false-positives.
Carrera, *et al.,* 1995[44*]	1c	Spain (Barcelona)	B2	Data cover 22 years; equipment used pre-1980 irrelevant to present time. Percentage of population screened designated 'high risk' abnormally high (55%). No description of gestation when subjects scanned.
Goncalves, *et al.,* 1994[45*]	1c	USA (Nashville)	B2	Poor postnatal ascertainment: one matched control per case. Gestation at scan, information not clear.
Roberts, *et al.,* 1993[46†]	1c	New Zealand (Auckland)	B2	No reporting of false-positives.
Studies reviewed by Chitty[9]				
Chitty, *et al.,* 1991[12*]	1c	UK (Luton)	A1	
Shirley, *et al.,* 1992[14‡]	1d	UK (Hillingdon)	A1	

† *Interlibrary loan* * *Liverpool Women's Hospital library* ‡ *Harold Cohen Library, University of Liverpool*

Final category: A1, relevant and acceptable quality; all data to be extracted

A2, relevant and acceptable quality; some data to be excluded

B1, relevant but does not meet criteria for data extraction

B2, relevant but poor quality

C, not relevant

continued

TABLE 2 contd *Summary of all studies reviewed in stage II – reasons for partial/total exclusion if relevant (i.e. categorised A2, B1 and B2)*

Study	Initial category	Country	Final category	Reasons for exclusion of all or some data
Levi, *et al.,* 1991[13*]	Ib	Belgium (Brussels)	A1	
Luck, 1992[15*]	Ib	UK (Ascot)	A1	
Crane, *et al.,* 1994[16*]	Ia	USA (RADIUS)	A1	
Levi, *et al.,* 199517*	Ib	Belgium	A1	
Rosendhal & Kivinen, 1989[10*]	Id	Finland	B2	Two phases: phase 1: 18-week scan; phase 2: 18- and 34-week scan. However, not reported separately and gestation at diagnosis unclear.
Saari-Kempapainen, *et al.,* 1990[11*]	Ia	Finland (Helsinki)	B1	Anomalies detected not reported individually, so no available data to extract.

† *Interlibrary loan* * *Liverpool Women's Hospital library* ‡ *Harold Cohen Library, University of Liverpool*
Final category: A1, relevant and acceptable quality; all data to be extracted
A2, relevant and acceptable quality; some data to be excluded
B1, relevant but does not meet criteria for data extraction
B2, relevant but poor quality
C, not relevant

Stage III

The overall characteristics and overall results of the 11 included studies are presented in *Table 3*,[10,13–22] including type of study, period of study, country where performed, population studied, setting, personnel performing sonography, number of fetuses scanned, gestation at scanning, prevalence of anomalous fetuses and anomalies, number of false-positives, detection rates in each trimester including sensitivity and specificity, overall detection rates, termination of pregnancy rates and whether sonographic soft markers are reported.

Results of second trimester routine ultrasound for fetal anomalies were reported in all the included studies. In only four studies[13,16–18] were routine third trimester ultrasound results reported, and in none were the results of routine first trimester anomaly screening reported.

The detection rates at routine second trimester ultrasound of individual structural abnormalities reported in anatomical systems are shown in *Table 4*.

The detection rates at routine third trimester ultrasound of individual structural abnormalities reported in anatomical systems are shown in *Table 5*.

The prevalence and detection of congenital anomalies at second trimester ultrasound scan are summarised in *Table 6*, grouped according to their likely clinical consequences. These four pragmatic subgroups were proposed by the RCOG in 1997,[5] and include:

(i) lethal anomalies
(ii) anomalies associated with possible survival and long-term morbidity
(iii) anomalies which may be amenable to intra-uterine therapy
(iv) anomalies associated with possible immediate or short-term morbidity.

Included in this table is a column indicating the other interventions that may be offered on detection of the particular abnormality. These were listed for use in the cost-effectiveness section of this review, as previous models of cost-effectiveness assumed that all detected abnormalities would be offered interventions, and this in turn overestimates costs. These possible interventions were based on clinical practice at the Liverpool Women's Hospital and on knowledge of the association of some of the abnormalities with chromo-somal abnormalities and the long-term consequences to babies born alive with the listed

TABLE 3 *Overview of studies included in the literature review*

Study	Chitty, *et al.*, 1991[12]	Shirley, *et al.*, 1991[14]	Levi, *et al.*, 1991[13d]	Luck, 1992[15cf]	Crane, *et al.*, 1994[16d]	Levi, *et al.*, 1995[17d]	Skupski, *et al.*, 1996[21]	Magriples & Copel 1998[22]	Lee, *et al.*, 1998[18d]	Van Dorsten, *et al.*, 1998[20d]	Boyd, *et al.*, 1998[19ab]	Total
Type	Retrospective	Retrospective	Prospective	Prospective	RCT[e]	Prospective	Retrospective	Retrospective	Retrospective	Prospective	Retrospective	
Period	1988–89	1989–90	1984–89	1988–91	1987–91	1990–92	1990–1994	? 18 months	1990–94	1993–96	1991–96	
Country	UK (Luton)	UK (Hillingdon)	Belgium (Brussels)	UK (Ascot)	USA (RADIUS)	Belgium (Brussels)	USA (Texas)	USA (Connecticut)	Korea	USA (S. Carolina)	UK (Oxford)	
Population studied	Unselected	Unselected	Unselected	Unselected	Low risk	Unselected	Low risk	Low risk	Low risk	Unselected	Unselected	
Setting	District general hospital	District general hospital	5 hospitals	District general hospital	Primary + 28 laboratories	5 hospitals	Tertiary, single centre	Tertiary, single centre	Tertiary, single centre	Mixed, 2 sites	Tertiary, single centre	
Sonographer	Radiographers	Radiographers	Obstetricians; technicians; sonographers	Radiographers	Technicians; physician; sonologists radiologists	Obstetricians; technicians; sonographers	Experienced sonographers	Sonographers	Trained obstetric Fellow	Registered diagnostic medical sonographer	Not mentioned	
Number of fetuses (twins)	8785 (multiple pregancies not mentioned)	6412 (73 multiple pregnancies)	15,654 (?240 multiple pregnancies)	8844	7575 (?number multiple pregnancies)	9601 (?209 multiple pregnancies)	860 (6 twins)	911 (10 twins)	3004 (twins excluded)	1611 (twins excluded)	33,376 (? twins)	96,633
Number of scans (mean,SD)	?	?	?	?	?	?	?	1.8 ± 0.99	?	?	?	

[a] *Soft marker data excluded (will be presented separately)*

[b] *Includes some patients who had maternal serum alpha fetoprotein screening, but this is not provided routinely by the NHS*

[c] *Reported in systems, not per fetus*

[d] *Overall sensitivity calculated per fetus but individual anomalies reported per system not per fetus. Figures in parentheses refer to calculations based on number of anomalies, not number of anomalous fetuses*

[e] *Ultrasound-screened group only included*

[f] *Maternal serum alpha-fetoprotein screening in addition to ultrasound was undertaken in this population*

[g] *This figure calculated taking only those defects exposed to scan at 12–24 weeks (n = 259), i.e. not on intention-to-screen*

continued

TABLE 3 contd *Overview of studies included in the literature review*

Study	Chitty, *et al.*, 1991[12]	Shirley, *et al.*, 1991[14]	Levi, *et al.*, 1991[13d]	Luck, 1992[15cf]	Crane, *et al.*, 1994[16d]	Levi, *et al.*, 1995[17d]	Skupski, *et al.*, 1996[21]	Magriples & Copel 1998[22]	Lee, *et al.*, 1998[18d]	Van Dorsten, *et al.*, 1998[20d]	Boyd, *et al.*, 1998[19ab]	Total
Gestational age/s scanned	18–20 weeks	19 weeks	1st trimester 16–20 weeks 3rd trimester	12–14 weeks 19 weeks	15–22 weeks 31–35 weeks	1st trimester 16–20 weeks 3rd trimester	18–20 weeks	16–20 weeks 3rd trimester	18–20 weeks 32–34 weeks	15–22 weeks	18–22 weeks	
Prevalence of anomalous fetuses (%)	1.50 (130 fetuses)	1.40 (89 fetuses)	2.30 (381 fetuses)		2.30 (187 fetuses)	2.45 (235 fetuses)	1.16 (20 fetuses)	3.07 (28 fetuses)	0.76 (23 fetuses)	1.30 (21 fetuses)	2.17 (725 fetuses)	1839/ 97,789 + 2.09%
Prevalence of anomalies (%)			2.66 (417 anomalies)	1.90 (164 anomalies)	– (232 anomalies)	2.81 (270 anomalies)		– (40 anomalies)	– (37 anomalies)	– (29 anomalies)		
False-positives	2	1	8	3	7	9	1	5	0	1	15	52
Detection < 15 weeks*												
Detection < 24 weeks	93	61	(54)	(140)	31	(69)	3	20	3 (5)	10	298	509/1233
Sensitivity (%)	71.5	57.3	(21.0)[g]	(85.3)	16.6	(25.6)	15.0	71.4	13.5 (13.5)	47.6	41.1	41.3 %
Specificity (%)	99.98	99.97	(100.00)	99.90	99.90		99.90	99.40	100.00	99.90	99.90	99.94 %
Detection > 24 weeks			(135)		34	(109)			5 (6)			39/210
Sensitivity (%)			(37.2)		18.2	(40.4)			21.7 (16.2)			18.6%
Specificity (%)			?		?				100.00			

[a] *Soft marker data excluded (will be presented separately)*
[b] *Includes some patients who had maternal serum alpha fetoprotein screening, but this is not provided routinely by the NHS*
[c] *Reported in systems, not per fetus*
[d] *Overall sensitivity calculated per fetus but individual anomalies reported per system not per fetus. Figures in parentheses refer to calculations based on number of anomalies, not number of anomalous fetuses*
[e] *Ultrasound-screened group only included*
[f] *Maternal serum alpha-fetoprotein screening in addition to ultrasound was undertaken in this population*
[g] *This figure calculated taking only those defects exposed to scan at 12–24 weeks (n = 259), i.e. not on intention-to-screen*
[*] *None of the included studies reported detection of anomalies at < 15 weeks*

continued

TABLE 3 contd *Overview of studies included in the literature review*

Study	Chitty, *et al.*, 1991[12]	Shirley, *et al.*, 1991[14]	Levi, *et al.*, 1991[13d]	Luck, 1992[15cf]	Crane, *et al.*, 1994[16d]	Levi, *et al.*, 1995[17d]	Skupski, *et al.*, 1996[21]	Magriples & Copel 1998[22]	Lee, *et al.*, 1998[18d]	Van Dorsten, *et al.*, 1998[20d]	Boyd, *et al.*, 1998[19ab]	Total
Overall detection	93	51	154	(140)	65	120 (178)		20	8 (11)	10	298	822/1839
Sensitivity (%)	71.5	57.3	40.4	85.3	34.8	51.0 (65.9)	15.0	71.4	34.8 (29.7)	47.6	41.1	44.7 %
Specificity (%)	99.98	99.97	99.94	99.90	99.90	99.90	99.80	99.40	100.00	99.90	99.90	
Terminations of pregnancies	52	29	?	19	9	?	2`	6	3	4	169	293/71,378
Terminations of pregnancies (%)	0.6	0.45		0.21	0.12		0.23	0.67	0.09	0.25	0.51	0.41 %
Terminations of normal pregnancies	0	0	0	0	0		0	0	?	0	2 (1 soft marker)	
'Soft' markers	Yes	No	No	Yes	No	No	No	Yes	No	No	Yes	

[a] *Soft marker data excluded (will be presented separately)*

[b] *Includes some patients who had maternal serum alpha fetoprotein screening, but this is not provided routinely by the NHS*

[c] *Reported in systems, not per fetus*

[d] *Overall sensitivity calculated per fetus but individual anomalies reported per system not per fetus. Figures in parentheses refer to calculations based on number of anomalies, not number of anomalous fetuses*

[e] *Ultrasound-screened group only included*

[f] *Maternal serum alpha-fetoprotein screening in addition to ultrasound was undertaken in this population*

[g] *This figure calculated taking only those defects exposed to scan at 12–24 weeks (n = 259), i.e. not on intention-to-screen*

TABLE 4 *Detection of major abnormalities by routine second trimester ultrasound scan (presented in anatomical systems)*

Second trimester scan <24 weeks	**Chitty, *et al.*, 1991**[12]	**Shirley, *et al.*, 1991**[14]	**Levi, *et al.*, 1991**[13d]	**Luck, 1992**[15ad]	**Crane, *et al.*, 1994**[16d]	**Levi, *et al.*, 1995**[17bd]	**Skupski, *et al.* 1996**[21]	**Magriples & Copel 1998**[22]	**Lee, *et al.*, 1998**[18d]	**Van Dorsten, *et al.*, 1998**[20d]	**Boyd, *et al.*, 1998**[19a]	**Total (%)**
CNS	**20/21**	**15/16**	**17/35**	**11/11**	**9/10**	**17/35**		**3/4**	**2/3**	**7/9**	**45/47**[c]	**146/191 (76.4)**
Anencephaly	6/6	10/10	6/6	7/7	3/3	4/4		1/2				37/38 (97.4)
Spina bifida	5/5	3/3	2/5	2/2	4/5	4/11				2/2		22/33 (66.7)
Encephalocoele	2/2	1/1	2/2	1/1				1/1				7/7 (100)
Hydrocephaly	3/3	1/2	4/15			5/6			1/1	4/5		18/32 (56.3)
Holoprosencephaly	2/3		0/1	1/1				1/1	0/1			4/7 (57.1)
Other CNS abnormalities	2/2		3/6		2/2	4/14			0/1	1/2		12/27 44.4
Pulmonary	**7/9**	**4/5**	**2/7**	**3/6**	**2/5**	**0/2**	**1/1**	**0/1**	**0/2**	**1/2**	**5/10**	**25/50 (50)**
CDH	2/2	2/3	1/3	2/5	1/1	0/2			0/2	1/2		9/20 (45)
CAML	4/4	1/1		1/1								6/6 (100)
Pleural effusion	1/3											1/3 (33.3)
Other		1/1	1/4		1/4		1/1	0/1				4/11 (36.4)

[a] *Detected with maternal serum alpha-fetaprotein in some cases*
[b] *Detected < 22 weeks*
[c] *Includes only neural tube defects*
[d] *Reported per anomaly, not per anomalous fetus*

continued

TABLE 4 contd *Detection of major abnormalities by routine second trimester ultrasound scan (presented in anatomical systems)*

Second trimester scan <24 weeks	Chitty, et *al.*, 1991[12]	Shirley, et *al.*, 1991[14]	Levi, et *al.*, 1991[13d]	Luck, 1992[15ad]	Crane, et *al.*, 1994[16d]	Levi, et *al.*, 1995[17bd]	Skupski, *et al.* 1996[21]	Magriples & Copel 1998[22]	Lee, et *al.*, 1998[18d]	Van Dorsten, et *al.*, 1998[20d]	Boyd, et *al.*, 1998[19a]	Total (%)
Cardiac	**7/11**	**5/9**	**3/72**	**9/25**	**5/38**	**9/67**	**0/8**	**1/3**	**0/6**	**4/8**		**43/247 (17.4)**
Septal defects	1/1	1/1	0/26	0/1	0/19	0/25	0/6	0/1	0/4	0/3		2/87 (2.3)
– VSD			0/20	0/1	0/15		0/6	0/1	0/4	0/2		
– ASD		1/1	0/6		0/4					0/1		
Single ventricle	1/3		1/1	4/8		3/3			0/1			9/16 (56.3)
AVSD	0/1	0/1	2/2		2/7		1/1					5/12 (41.7)
Isolated valve abnormality			0/6			1/5	0/1		0/1			1/13 (7.7)
Complex abnormality	5/6	4/8	2/44	3/14	5/19	1/5	0/1	0/1		4/5		24/103 (23.3)
Gastrointestinal	**4/7**	**2/3**	**5/12**	**5/6**	**2/5**	**3/19**	**0/1**	**2/3**	**1/4**	**2/2**		**26/62 (41.9)**
Tracheo-oesophageal atresia	0/2		1/7	0/1	0/3				0/1	1/1		2/15 (13.3)
Anterior abdominal wall defect	4/4	2/2	4/4	4/4	1/1	3/6		1/1	1/1	1/1	9/10	30/34 (88.2)
– Exomphalos	3/3	1/1	2/2	2/2	1/1				1/1	1/1		11/11 (100)
– Gastroschisis	1/1	1/1	2/2	2/2				1/1				7/7 (100)
Small bowel obstruction /atresia	0/1	0/1	0/1	1/1	1/1	0/9			0/1			2/15 (13.3)
Other							0/1	1/2	0/1			1/4 (25)

[a] *Detected with maternal serum alpha-fetaprotein in some cases*
[b] *Detected < 22 weeks*
[c] *Includes only neural tube defects*
[d] *Reported per anomaly, not per anomalous fetus*

continued

TABLE 4 contd *Detection of major abnormalities by routine second trimester ultrasound scan (presented in anatomical systems)*

Second trimester scan <24 weeks	Chitty, *et al.*, 1991[12]	Shirley, *et al.*, 1991[14]	Levi, *et al.*, 1991[13d]	Luck, 1992[15ad]	Crane, *et al.*, 1994[16d]	Levi, *et al.*, 1995[17bd]	Skupski, *et al.* 1996[21]	Magriples & Copel 1998[22]	Lee, *et al.*, 1998[18d]	Van Dorsten, *et al.*, 1998[20d]	Boyd, *et al.*, 1998[19a]	Total (%)
Urinary tract abnormalities	**21/25**	**7/9**	**12/76**	**105/105**	**34/35**	**20/66**	**2/2**	**4/4**		**3/3**	**62/76**	**270/401 (67.3)**
Obstructive uropathy	10/10	7/8	2/47	99/99	28/29	7/36	1/1					154/230 (67)
Renal dysplasia	5/8	0/1	4/11	4/4		7/10	1/1	2/2		1/1		24/38 (63.2)
– [unilateral]	[3/5]			[4/4]			[1/1]	[1/1]		?		[9/11] (82)
– [bilateral]	[2/3]	[0/1]						[1/1]		?		[3/5] (60)
Renal agenesis	5/5		3/9	2/2		3/10						13/26 (50)
– [unilateral]	[1/1]											[1/1] (100)
– [bilateral]	[4/4]			[2/2]				1/1				[7/7] (100)
Prune belly syndrome			3/4									3/4 (75)
Other	1/2		0/5		6/6	3/10		1/1		2/2		13/26 (50)
Skeletal abnormalities	**17/27**	**2/8**	**5/53**	**6/8**	**4/30**	**4/32**	**0/3**	**2/3**	**0/4**			**40/168 (23.8)**
Limb reduction defect	2/5	1/1	0/6	1/2	2/5		0/1	0/1				6/21 (28.6)
Talipes	6/12	0/6	4/24	2/2	2/24	1/17	0/2		0/2		15/53	30/142 (22.5)
Spinal abnormality	3/3		0/2	1/1	0/1	1/1						5/8 (62.5)

[a] *Detected with maternal serum alpha-fetaprotein in some cases*
[b] *Detected < 22 weeks*
[c] *Includes only neural tube defects*
[d] *Reported per anomaly, not per anomalous fetus*

continued

TABLE 4 contd *Detection of major abnormalities by routine second trimester ultrasound scan (presented in anatomical systems)*

Second trimester scan <24 weeks	Chitty, et *al.*, 1991[12]	Shirley, et *al.*, 1991[14]	Levi, et *al.*, 1991[13d]	Luck, 1992[15ad]	Crane, et *al.*, 1994[16d]	Levi, et *al.*, 1995[17bd]	Skupski, *et al.* 1996[21]	Magriples & Copel 1998[22]	Lee, et *al.*, 1998[18d]	Van Dorsten, et *al.*, 1998[20d]	Boyd, et *al.*, 1998[19a]	Total (%)
Dwarfism	2/2	1/1	0/4	2/2		2/6						7/15 (46.7)
– [lethal]	`		[0/4]			[2/6]						– [non-lethal]
Other	4/5		1/17	0/1		0/8		2/2				7/33 (21.2)
Other												
Cystic hygroma	1/1	2/2		1/1	2/2			2/2	1/1	1/1		10/10 (100)
Facial cleft	2/9	3/9			3/10		0/2		0/6		12/25	20/61 (32.8)
Hydrops	2/2	0/1	3/18	1/1	0/2					1/1		7/25 (28)
Multiple abnormality/ syndrome	18/19	3/4		5/6			0/4	2/3	2/2			30/38 (78.9)
Chromosomal	3/21	6/13	3/25			3/16			0/5			15/80 (18.8)
Trisomy 21	1/14	3/10							0/3		11/70	15/97 (15.5)
Trisomy 18	1/1	3/3							0/2			4/6 (66.7)
Trisomy 13	1/2											1/2 (50)
Other	0/4											

[a] *Detected with maternal serum alpha-fetaprotein in some cases*
[b] *Detected < 22 weeks*
[c] *Includes only neural tube defects*
[d] *Reported per anomaly, not per anomalous fetus*

TABLE 5 *Detection of abnormalities by routine third trimester ultrasound scan (presented in anatomical systems)*

Third trimester scan > 24 weeks	**Levi, et *al.*, 1991**[13c]	**Crane, et *al.*, 1994**[16bc]	**Levi, et *al.*, 1995**[17ac]	**Lee, et *al.*, 1998**[18c]	**Total (%)**
CNS	**27/40**		**14/18**	**1/1**	**42/59 (71)**
Anencephaly					
Spina bifida	6/9		5/7		11/16 (69)
Encephalocoele					
Hydrocephaly	19/20		1/1		20/21 (95.2)
Holoprosencephaly				1/1	1/1 (100)
Other CNS abnormalities	2/11		8/10		10/21 (47.6)
Pulmonary	**1/5**		**2/2**	**1/2**	**4/9 (44.4)**
CDH	1/2		2/2	1/2	4/6 (66.7)
CAML					
Pleural effusion					
Other	0/3				0/3 (0)
Cardiac	**14/82**		**20/52**	**2/4**	**36/138 (26.1)**
Septal defects	2/35		6/25	2/4	10/64 (15.6)
– VSD					
– ASD					
Single ventricle	3/5				3/5 (60)
AVSD	1/2		4/5		5/7 (71.4)
Isolated valve abnormality	0/6		1/4		1/10 (10)
Complex abnormality	8/34		9/18		17/52 (32.7)
Gastrointestinal	**9/23**		**10/15**		**19/38 (50)**
Tracheo-oesophageal atresia					
Anterior abdominal wall defects	2/2		2/3		4/5 (80)
– Exomphalos					
– Gastroschisis					
Small bowel obstruction/atresia	7/21		8/9		15/30 (50)
Other			0/3		0/3 (0)
Urinary tract abnormalities	**42/64**	**2/2**	**32/46**		**76/112 (67.9)**
Obstructive uropathy	32/45		24/29		56/74 (75.7)
Renal dysplasia	5/7	1/1	2/3		8/11 (72.7)
– [unilateral]		[1/1]			[1/1]
– [bilateral]					
Renal agenesis	3/6		5/7		8/13 (61.5)
– [unilateral]					
– [bilateral]					
Prune belly syndrome	1/1				1/1 (100)
Other	1/5	1/1	1/7		3/13 (23.1)
Skeletal abnormalities	**5/26**		**7/20**		**12/46 (26.1)**
Limb reduction defect					
Talipes	1/20		3/16		4/36 (11.1)
Spinal abnormality	0/2				0/2 (0)
Dwarfism	4/4		4/4		8/8 (100)
– [lethal]	[4/4]		[4/4]		[8/8]
– [non-lethal]					
Other					

[a] *Detected > 22 weeks*

[b] *Unable to extract much data as only a few anomalies detected at routine 3rd trimester scan; most detected at indicated scans and, in some cases, it is unclear from text whether detected at routine or indicated scan*

[c] *Reported per anomaly, not per anomalous fetus*

Anomalies previously detected at second trimester anomaly scan were subtracted from the denominator.

continued

TABLE 5 contd *Detection of abnormalities by routine third trimester ultrasound scan (presented in anatomical systems)*

Third trimester scan > 24 weeks	**Levi, et *al.*, 1991**[13c]	**Crane, et *al.*, 1994**[16bc]	**Levi, et *al.*, 1995**[17ac]	**Lee, et *al.*, 1998**[18c]	**Total (%)**
Other					
Cystic hygroma					
Facial cleft					
Hydrops	7/15	1/2			8/17 (47.1)
Multiple abnormality/syndrome					
Chromosomal	**2/23**	**1/2**	**2/13**		**5/48 (10.4)**
Trisomy 21					
Trisomy 18		1/2			1/2 (50)
Trisomy 13					
Other					

[a] *Detected > 22 weeks*
[b] *Unable to extract much data as only a few anomalies detected at routine 3rd trimester scan; most detected at indicated scans and, in some cases, it is unclear from text whether detected at routine or indicated scan*
[c] *Reported per anomaly, not per anomalous fetus*
Anomalies previously detected at second trimester anomaly scan were subtracted from the denominator.

abnormalities. For example, in the presence of exomphalos, karyotyping would be offered as there is a known association with trisomies; however, the presence of gastroschisis is not an indicator of possible chromosomal abnormality and hence karyotyping would not be offered.

The detection of congenital anomalies at third trimester routine ultrasound scan in pregnancy are summarised in *Table 7* according to the aforementioned RCOG subgroups, and the table also includes a column indicating which interventions may be offered.

False-positive diagnoses at second trimester ultrasound scan are summarised in *Table 8*, including the RCOG subgroup with which they may be associated, and the false-positive rates in each RCOG subgroup are summarised in *Table 9*. A false-positive is defined as an anomaly suspected at any time prenatally which was not confirmed postnatally.

Details of ultrasonographic soft markers reported in some studies are summarised in *Table 10*.

Discussion

The prevalence of anomalous fetuses ranged from 0.76% to 2.45% with an overall prevalence of 2.09%. The study reporting a very low incidence of fetal anomalies[18] of 0.76% was undertaken in a low-risk population in Korea, and this may be due to poor postnatal ascertainment (although it fulfilled quality assessment for inclusion) or may reflect a real difference in the type of population studied.

Overall, the sensitivity for the detection of fetal anomalies was 44.7% but varied widely, 15–85.3%. The four UK studies included[12,14,15,19] showed slightly better overall sensitivity of 53% but still varied widely from 41.1% to 85.3%. It is difficult to determine why the sensitivity of routine ultrasound screening for fetal anomalies varies so extensively but it should be acknowledged that a number of factors contribute to successful detection of anomalies, including, the type of anomaly, gestational age at scanning, the skill of those performing the examination, the way in which the scan is conducted, and the quality of the equipment being used.

Differences in the manner in which the studies were conducted also affects the overall results. Of the included studies, one was an RCT, four were prospective observational studies and six were retrospective studies, but there was no obvious difference in incidence of abnormalities or detection rates according to type of study.

Studies that report data by number of anomalies rather than by number of fetuses overestimate sensitivity. The study reporting the highest sensitivity of 85.3% reported in this manner[15] and, in fact, there is no mention of the number of anomalous fetuses. Some studies report overall detection rates per fetus but per anomaly when presenting the anatomical system data.[13,16–18,20] With the exception of the study by Lee and colleagues,[18] the results of these studies demonstrate how

TABLE 6 *Prevalence and detection of congenital anomalies at second trimester routine ultrasound scan in pregnancy according to RCOG subgroup*

	Prevalence per 1000[c]	Possible intervention[*]	Chitty, *et al.*, 1991[12]	Shirley, *et al.*, 1991[14]	Levi, *et al.*, 1991[13b]	Luck 1992[15a]	Crane, *et al.*, 1994[16]	Levi, *et al.*, 1995[17b]	Skupski, *et al.*, 1996[21]	Margriples & Copel 1998[22]	Lee, *et al.*, 1998[18]	Van Dorsten, *et al.*, 1998[20]	Boyd, *et al.*, 1998[19]	Total (%)
Number of fetuses			8785	6412	15,654	8844	7575	9601	860	911	3004	1611	33,376	96,633
Lethal anomalies (totals)	**2.03**		**13/16**	**13/13**	**7/11**	**13/17**	**3/3**	**9/13**		**2/3**	**0/3**			**60/79 (76)**
Anencephaly	0.58	TOP	6/6	10/10	6/6	7/7	3/3	4/4		1/2				37/38 (97.4)
Trisomy 18	0.33	K, TOP	1/1	3/3							0/2			4/6 (66.7)
Trisomy 13		K, TOP	1/2											1/2 (50)
Hypoplastic left heart	0.35	TOP	1/3		1/1	4/8		3/3			0/1			9/16 (56.3)
Bilateral renal agenesis	0.38	TOP	4/4			2/2				1/1				7/7 (100)
Lethal musculoskeletal disorders	0.39	TOP			0/4			2/6						2/10 (20)
Possible survival and long-term morbidity (+/- surgery) (totals)	**8.84**		**48/68**	**20/36**	**16/88**	**20/36**	**12/30**	**11/38**	**0/6**	**6/8**	**4/13**	**13/16**	**11/70**	**161/409 (39.4)**
Spina bifida	0.56	TOP	5/5	3/3	2/5	2/2	4/5	4/11				2/2		22/33 (66.7)
Hydrocephalus	0.71	K, TOP	3/3	1/2	4/15			5/6			1/1	4/5		18/32 (56.3)
Encephalocoele	0.17	TOP	2/2	1/1	2/2	1/1				1/1				7/7 (100)
Holoprosencephaly	0.19	TOP	2/3		0/1	1/1				1/1	0/1			4/7 (57.1)
Down's syndrome	1.88	K, TOP	1/14	3/10							0/3		11/70	15/97 (15.5)
Complex cardiac malformations	1.71	K, TOP	5/6	4/8	2/44	3/14	5/19	1/5	0/1	0/1		4/5		24/103 (23.3)
AVSD	0.45	K, TOP			0/6			1/5	0/1		0/1			1/13 (7.7)
Non-lethal dwarfism		TOP												
Anterior abdominal wall defects														
– Gastroschisis	0.21		3/3	1/1	2/2	2/2	1/1				1/1	1/1		11/11 (100)
– Exomphalos	0.17	K	1/1	1/1	2/2	2/2				1/1				7/7 (100)
CDH	0.33	K, TOP	2/2	2/3	1/3	2/5	1/1	0/2			0/2	1/2		9/20 (45)
Tracheo-oesophageal atresia	0.33		0/2		1/7	0/1	0/3				0/1	1/1		2/15 (13.3)
Small bowel obstruction/atresia	0.25		0/1	0/1	0/1	1/1	1/1	0/9			0/1			2/15 (13.3)
CAML	0.25		4/4	1/1		1/1								6/6 (100)
Renal dysplasia (bilateral)	0.31		2/3	0/1						1/1		?		3/5 (60)
Multiple abnormality/syndrome	1.32	K, TOP	18/19	3/4		5/6			0/4	2/3	2/2			30/38 (78.9)

TOP, termination of pregnancy; K, karyotyping

[a] *Detected with maternal serum alpha-fetoprotein in some cases*

[b] *Detected < 22 weeks*

[c] *Calculated using number of cases per number of fetuses with anomaly, where denominator = total number of fetuses in screened population of particular studies in which prevalence of condition ascertained, e.g. for anencephaly, denominator = 8785 + 6412 + 15,654 + 8844 + 7575 + 9601 + 911 = 57,782, and numerator = 37*

continued

TABLE 6 contd *Prevalence and detection of congenital anomalies at second trimester routine ultrasound scan in pregnancy according to RCOG subgroup*

	Prevalence per 1000[c]	Possible intervention*	Chitty, *et al.*, 1991[12]	Shirley, *et al.*, 1991[14]	Levi, *et al.*, 1991[13b]	Luck 1992[15a]	Crane, *et al.*, 1994[16]	Levi, *et al.*, 1995[17b]	Skupski, *et al.*, 1996[21]	Margriples & Copel 1998[22]	Lee, *et al.*, 1998[18]	Van Dorsten, *et al.*, 1998[20]	Boyd, *et al.*, 1998[19]	Total (%)
Anomalies amenable to intra-uterine therapy[d]														
Obstructive uropathy/														
Pleural effusion/hydrothorax														
Anomalies associated with possible short-term/ immediate morbidity (totals)	**4.75**		**12/28**	**4/16**	**4/51**	**8/9**	**5/53**	**3/49**	**1/11**	**2/3**	**0/12**	**0/3**	**27/78**	**66/313 (21)**
Non-complex cardiac anomalies														
– ASD/VSD	1.38	K	1/1	1/1	0/26	0/1	0/19	0/25	0/6	0/1	0/4	0/3		2/87 (2.3)
– Isolated valve abnormality	0.27		0/1		0/1	2/2		2/7		1/1				5/12 (41.7)
Facial clefts	1.02		2/9	3/9			3/10		0/2		0/6		12/25	20/61 (32.8)
Talipes	1.51		6/12	0/6	4/24	2/2	2/24	1/17	0/2		0/2		15/53	30/142 (22.5)
Renal dysplasia (unilateral)	0.57		3/5			4/4			1/1	1/1		?		9/11 (82)

TOP, termination of pregnancy; K, karyotyping

[a] *Detected with maternal serum alpha-fetoprotein in some cases*

[b] *Detected < 22 weeks*

[c] *Calculated using number of cases per number of fetuses with anomaly, where denominator = total number of fetuses in screened population of particular studies in which prevalence of condition ascertained, e.g. for anencephaly, denominator = 8785 + 6412 + 15,654 + 8844 + 7575 + 9601 + 911 = 57,782, and numerator = 37*

[d] *No data available to extract in this category (see text)*

TABLE 7 *Prevalence and detection of congenital anomalies at third trimester routine ultrasound scan in pregnancy according to RCOG subgroup*

	Possible intervention	Levi, et *al.*, 1991[13a]	Crane, et *al.*, 1994[16]	Levi, et *al.*, 1995[17a]	Lee, et *al.*, 1998[18]	Total (%)
Number of fetuses		15,654	7575	9601	3004	35,834
Lethal anomalies		**10/15**	**1/2**	**9/11**		**20/28 (71.4)**
Anencephaly						
Trisomy 18	K		1/2			1/2 (50)
Trisomy 13						
Hypoplastic left heart		3/5				3/5 (60)
Bilateral renal agenesis		3/6		5/7		8/13 (61.5)
Lethal musculoskeletal disorders		4/4		4/4		8/8 (100)
Possible survival and long-term morbidity (+/– surgery)		**49/97**		**33/48**	**2/3**	**84/148 (56.8)**
Spina bifida		6/9		5/7		11/16 (69)
Hydrocephalus	K	19/20		1/1		20/21 (95.2)
Encephalocoele						
Holoprosencephaly					1/1	1/1 (100)
Down's syndrome						
Complex cardiac malformations	K	8/34		9/18		17/52 (32.7)
AVSD	K	1/2		4/5		5/7 (71.4)
Non-lethal dwarfism						
Anterior abdominal wall defects – Gastroschisis – Exomphalos	(K)	2/2		2/3		4/5 (80)
CDH	K	1/2		2/2	1/2	4/6 (66.7)
Tracheo-oesophageal atresia						
Small bowel obstruction/atresia		7/21		8/9		15/30 (50)
CAML						
Renal dysplasia (bilateral)		5/7		2/3		7/10 (70)
Multiple abnormality/syndrome						
Anomalies amenable to intra-uterine therapy[b]						
Obstructive uropathy						
Pleural effusion/hydrothorax						
Anomalies associated with possible short-term/ immediate morbidity (totals)		**3/61**	**1/1**	**10/45**	**2/4**	**16/111 (14.4)**
Non-complex cardiac anomalies						
– ASD/VSD	K	2/35		6/25	2/4	10/64 (15.6)
– Isolated valve abnormality		0/6		1/4		1/10 (10)
Facial clefts						
Talipes		1/20		3/16		4/36 (11.1)
Renal dysplasia (unilateral)			1/1			1/1 (100)

K, karyotyping
[a] *Detected > 22 weeks*
[b] *No data available to extract in this category (see explanation in text)*

sensitivity may be overestimated (see figures in parentheses in *Table 3*). The definition of anomalies included in the studies varies – some exclude minor anomalies,[12–14,17] or anomalies not detectable at ultrasound scan,[16] or both minor anomalies and anomalies not detectable by ultrasound scan.[20] Furthermore, there is a difference in the definition of major versus minor anomalies between some studies. Skupski and colleagues[21] define minor anomalies as those that are not serious or are chronic medical conditions, would not influence antenatal management, and are unlikely to result in termination of pregnancy if detected prenatally. In so doing, they include

TABLE 8 *False-positives at routine second trimester ultrasound scan: numbers, rates, descriptions and RCOG subgroup classification*

Author	Number of false-positives	False-positive rate	Description of false-positives	Outcome	RCOG subgroup[a]
Chitty, *et al.,* 1991[12]	2	0.02%	1 tracheo-oesophageal fistula – persistent polyhydramnios, small stomach bubble	Live birth	II
			1 CAML – echogenic lungs[b]	Live birth	II
Shirley, *et al.,* 1991[14]	1	0.02%	1 exomphalos	Live birth	II
Levi, *et al.,* 1991[13]	8	0.05%	3 microcephaly	Live births	II
			1 dolichocephaly[b]	Live birth	?
			1 clubhand	Live birth	IV
			1 intestinal mass	Live birth	II
			1 hydronephrosis (dilated renal pelvis)[b]	Live birth	IV
			1 cleft lip	Live birth	IV
Luck, 1992[15]	3	0.03%	1 oesophageal atresia	Live birth	II
			2 abnormal four-chamber view of heart	Live births	II/IV
Crane, *et al.,* 1994[16]	7	0.09%	1 unilateral multicystic renal dysplasia	Live birth	IV
			2 hydronephrosis[b]	Live births	IV
			3 cerebral ventriculomegaly	Live births	II
			1 sacrococcygeal tumour	Live birth	IV
Levi, *et al.,* 1995[17]	9	0.09%	3 microcephaly	Live births	II
			4 hydronephrosis (dilated renal pelvis)[b]	Live births	IV
			1 clubfoot	Live birth	IV
			1 megacystis	Live birth	III
Skupski, *et al.,* 1996[21]	1	0.12%	1 VSD	Live birth	IV
Magriples & Copel, 1998[22]	5	0.55%	1 hydronephrosis + clubfoot	Live birth	IV
			1 cleft lip	Live birth	IV
			1 small stomach + small bladder[b]	Live birth	II
			2 abnormal four-chamber view	Live births	II/IV
Lee, *et al.,* 1998[18]	0	0%			
Van Dorsten, *et al.,* 1998[20]	1	0.06%	1 hydrops (non-immune)[b]	Live birth	II/IV
Boyd, *et al.,* 1998[19]	15	0.04%	5 cystic hygromas[b]	Live births	II
			1 ascites[b]	Live birth	III
			3 clubfoot	Live births	IV
			1 intra-abdominal cyst	Live birth	II
			1 CAML[b]	Live birth	II
			1 VSD	Live birth	IV
			2 renal lesions (not defined in report)	Live births	?
			1 oesophageal atresia (absent stomach bubble)	Termination	II

[a] *RCOG subgroups: I, lethal anomalies; II, anomalies associated with possible survival and long-term morbidity (+/– surgery); III, anomalies amenable to intrauterine therapy; IV, anomalies associated with possible short-term/immediate morbidity*

[b] *These conditions fall into a group which may be present at anomaly scan but resolve spontaneously as pregnancy progresses, i.e. may not be true false-positives*

TABLE 9 *False-positive rates in RCOG subgroups*

RCOG subgroup	Number	False-positives (%)	False-positive rate[a]
Lethal anomalies	0	0	0
Possible survival and long-term morbidity (+/– surgery)	19/39	49	0.025%
Anomalies amenable to intrauterine therapy	2/39	5	0.002%
Anomalies associated with possible short-term/immediate morbidity	18/39	46	0.023%

[a] *Calculated by multiplying percentage in each pragmatic group by overall false-positive rate (0.05%; taken from Table 8)*

TABLE 10 *Studies reporting the detection of ultrasonographic soft markers*

	Chitty, et al., 1991[12]	Luck, et al., 1992[15]	Magriples & Copel, 1998[22]	Boyd, et al., 1998[19]	Total	Abnormality detection rates
Isolated soft markers (true-positives[a])	**20 (0)**	**96 (0)**	**39 (0)**	**163 (10)**	**318 (10)**	**3.14%**
Incidence	0.22%	1.09%	4.3%	0.49%	0.6%	
CPCs	8 (0)	2 (0)	15 (0)	64 (1)	89 (1)	1.12%
RPD	11 (0)	94 (0)	12 (0)		117 (0)	0
Echogenic bowel			10 (0)	21 (2)	31 (2)	6.5%
Nuchal translucency	1 (0)		2 (0)	78 (7)	81 (7)	8.6%
Two or more soft markers	**1 (0)**		**1 (0)**	**55 (6)**	**57 (6)**	**10.3%**

[a] *True-positive, anomaly confirmed by postnatal ascertainment, i.e. examination of aborted fetus, stillborn or liveborn baby*

anomalies in their minor anomaly list that would be considered major by other authors.

Reports of detection of fetal anomalies by routine ultrasound screening are dependent on the rate of postnatal ascertainment of anomalies, which may not always be complete, particularly if the anomalies are not externally visible, such as cardiac septal defects and renal abnormalities. If postnatal ascertainment is poor, performance of ultrasound in detecting anomalies could be overestimated. In an attempt to reduce this bias, only studies that report adequate methods of postnatal ascertain-ment are included. Crane and colleagues[16] suggest that assessing the prevalence of isolated cardiac septal defects in a reported population, with a known incidence of 1/200–1/400, may identify reports where poor postnatal ascertainment has occurred. The prevalence of cardiac septal defects in the included studies is shown in *Table 11*, apart from one in which this information was not available.[19]

TABLE 11 *Incidence of cardiac septal defects in the populations studied*

Study	Number of fetuses	Number of septal defects	Incidence
Chitty, *et al.,* 1991[12]	8785	1	1:8785
Shirley, *et al.,* 1991[14]	6412	1	1:6412
Levi, *et al.,* 1991[13]	15,654	26	1:602
Luck, 1992[15]	8844	1	1:8844
Crane, *et al.,* 1994[16]	7575	19	1:398
Levi, *et al.,* 1995[17]	9601	25	1:384
Skupski, *et al.,* 1996[21]	860	6	1:143
Margriples & Copel, 1998[22]	911	1	1:911
Lee, *et al.,* 1998[18]	3004	4	1:751
Van Dorsten, *et al.,* 1998[20]	1611	3	1:537
Total	63,257	87	1:727

Only three studies showed incidences of septal defects of < 1/400, two of which reported very poor overall detection rates.[16,21] This implies inadequate postnatal ascertainment in some studies and may explain the variance in overall detection rates.

An RCOG Study Group reporting in 1991 on *Antenatal diagnosis of fetal abnormalities*[4] recommended that anomaly scans should be performed at 18–20 weeks. This recommendation was based on the opinion of experts who considered that the widest range of anomalies could be detected at this time in pregnancy. In two of the included studies the gestational range at scanning was 15–22 weeks[16,20] and, in a further three studies, 16–20 weeks.[13,17,22] The overall sensitivity for detection of fetal anomalies at second trimester ultrasound in these studies was 21.5% (range 16.6–71.4%), lower than in studies in which the scan occurred after 18 weeks' gestation,[12,14,15,18,19,21] where the overall sensitivity of second trimester anomaly scanning was 51% (range 13.5–85.3%).

Only four trials included a routine third trimester ultrasound scan, comprising 35,834 screened fetuses (see *Table 5*). Very few data were usable from the Routine Antenatal Diagnostic Imaging Study (RADIUS),[16] as a number of the anomalies detected in the third trimester were the result of clinically indicated scans and not routine screening. These data must be interpreted with caution for three reasons. First, in all of these studies second trimester scans were performed and thus some anomalies were detected prior to the third trimester routine scan; hence, this does not reflect performance of the third trimester scan alone. Also, it should be noted that Levi and colleagues[13,17] reported detection at < 22 weeks and at > 22 weeks, whereas here 24 weeks is being used as the boundary. Second, Levi and colleagues

reported detection of individual anomalies in anatomical systems and not as anomalous fetuses; hence, those with multiple anomalies may be reported more than once, thus falsely increasing sensitivity. Third, the overall performance of these four studies in detection of fetal anomalies was not as good as in the UK studies reviewed, even though the UK studies reported routine scanning in the second trimester only. Thus this is the best available evidence but is not ideal. It is interesting to note, however, that the detection rates of routine third trimester ultrasound reported by the RCOG Working Party,[5] which were based on 'clinical hunch' (expert consensus) because of lack of available data, were similar to those found in this review.

No literature was available to address the clinical effectiveness of routine first trimester anomaly ultrasound scan in detecting fetal structural anomalies. Two studies identified in the search, which reported routine first trimester anomaly screening,[23,24] did not fulfil the quality requirements to be included in the review. First trimester routine ultrasound screening for fetal chromosomal and structural anomalies are discussed separately (in chapter 4).

It is of interest that the best UK performers were in district general hospital settings.[12,15] This is in contrast to the RADIUS study[16] conducted in the USA, for which a relative detection rate of 2.7 in tertiary versus non-tertiary ultrasound units was reported. In this study, however, there was wide variation in levels of skill and expertise among the sonographers, who included technicians, physician sonologists, obstetricians and radiologists.

Levi and colleagues[17] demonstrated that improvements in operator skill can result in better performance in the detection of abnormalities. Between 1984 and 1989 detection of anomalous fetuses by routine second and third trimester scans was 40.4%.[13] Following this, a programme of education and training was introduced, which resulted in an 11% improvement in detection to 51.1%. The RCOG Working Party on Ultrasound Screening for Fetal Anomalies[5] emphasised in its recommendations that ultrasound examinations should only be conducted by adequately trained personnel using equipment no more than 5 years old, and that a routine screening examination should be conducted using an agreed protocol or check list. The RCOG has recently published a document[223] detailing a suggested protocol for routine ultrasound scanning, including minimum standards required for provision of service and training.

In general, in this review, no patterns of performance could be identified according to the setting in which studies were undertaken, the expertise of the individual performing the scan or the equipment being used.

Overall detection rates for different anatomical systems varied considerably. At routine second trimester ultrasound, detection rates for different anatomical systems were: central nervous system (CNS) 76.4%, urinary tract 67.3%, pulmonary 50%, gastrointestinal 41.9%, skeletal 23.8% and cardiac 17.4% (see *Table 4*). At routine third trimester ultrasound, detection rates for different anatomical systems were: CNS 71%, urinary tract 67.9%, gastrointestinal 50%, pulmonary 44.4%, skeletal 26.1%, cardiac 26.1% (see *Table 5*). The variation of detection within anatomical systems is also wide. Factors which affect detection rates are complex but include: technical difficulties, such as maternal habitus and fetal position at the time of scanning; absence of or only subtle sonographic signs associated with the anomaly; and timing of the scan, as some anomalies are not visible ultrasonically in the first half of pregnancy.

The reasons for variable detection rates of individual anomalies within each anatomical system are discussed in detail in the review paper by Chitty.[9]

Detection of chromosomal abnormalities will depend on whether there are associated structural malformations, and, in this review, the overall detection rates for chromosomal abnormalities was 18.8% in the second trimester and 10.4% in the third trimester. The role of ultrasonographic soft markers in improving detection of chromosomal abnormalities is discussed in chapter 4.

It is important that both clinicians and women are aware of the limitations of routine ultrasound screening in detecting both structural anomalies and chromosomal anomalies.

The RCOG working party report on ultrasound screening for fetal anomalies[5] states that information about the clinical effectiveness of routine screening ultrasound in pregnancy is only of value if it can be placed in the context of clinical practice. In view of this the RCOG recommended the four pragmatic subgroups for fetal abnormalities (described above) that are governed by their likely consequences. Clearly, lethal congenital abnormalities if diagnosed prenatally are amenable to termination of pregnancy. Even if the woman does not wish to terminate the pregnancy, she may

be better prepared for the inevitable death of her baby after birth. Some argue that if congenital abnormalities associated with possible survival and long-term handicap are detected prenatally, the parents would have the option of considering termination of pregnancy in some cases but, if the pregnancy continues, knowledge of the abnormality may alter mode and place of delivery, which in turn may improve the outcome of these pregnancies. It is also argued that preparation of the parents may lessen the emotional trauma associated with the birth of a congenitally abnormal baby. Theoretically the detection of abnormalities that may be amenable to intra-uterine therapy may enable subspecialists in fetal medicine to alter the outcome of these conditions with *in-utero* interventions; however, this area of clinical practice is in its infancy and its advantages remain unproven. The same arguments are applicable to detection of abnormalities that may be associated with immediate/short-term morbidity but, conversely, this may have an adverse effect on the relationship between parent and child. The review of women's views (see chapter 5) seeks to answer some of these questions.

These RCOG subgroups are particularly useful when economic considerations are to be taken into account, as the birth of a congenitally malformed baby has implications for the use of healthcare resources. Hence, the data extracted from the included studies have been grouped to report detection rates in each of these subgroups (see *Tables 6* and *7*). The overall detection rate for lethal congenital malformations was 76% in the second trimester and 71.4% in the third trimester. The overall detection of anomalies associated with possible survival and long-term morbidity was 39.4% in the second trimester and 56.8% in the third trimester. The overall detection of anomalies associated with possible short-term or immediate morbidity was 21% in the second trimester and 14.4% in the third trimester. There were insufficient data available to calculate incidence of or detection rates for the group of anomalies amenable to intrauterine therapy. This was mainly because the studies did not report the obstructive uropathies in detail, and not all obstructive uropathies are associated with megacystis that may benefit from bladder drainage.

Of the lethal anomalies, detection of anencephaly and bilateral renal agenesis is good but trisomies 13 and 18, hypoplastic left heart and lethal musculoskeletal abnormalities, such as lethal dwarfism, less so. Both the latter abnormalities may only become apparent in later gestation, as is demonstrated by 100% detection of lethal musculoskeletal abnormalities in the third trimester. However, from a purely clinical and economic point of view, the birth of a baby with a lethal congenital abnormality will not place as large a burden on the health service as would the birth of a baby with a condition associated with possible survival and long-term handicap. The detection rates for these abnormalities are much lower, particularly complex cardiac malformations, atrioventricular septal defects, tracheo-oesophageal fistula, small bowel obstruction/atresia and Down's syndrome.

Prior knowledge of the presence of some abnormalities associated with possible survival and long-term handicap may alter the management of the pregnancy, with regard to mode of delivery or place of delivery, in an attempt to improve outcome. Evidence that the outcome of conditions, such as gastroschisis[47] and cardiac abnormalities,[48] may be improved by prenatal detection exists in the literature. However, Skari and colleagues[25] compared the effect of prenatal diagnosis on management of labour and neonatal outcome in neonates with congenital diaphragmatic hernia, abdominal wall defects, meningomyelocele and bladder exstrophy. They found that although all prenatally diagnosed fetuses were delivered by Caesarean section in the hospital attached to the neonatal surgical unit, there was no obvious difference in neonatal outcome. They also found a significantly lower gestational age at birth in the prenatally diagnosed group. They emphasised that there may be a difference in the severity of the condition among diagnosed versus non-diagnosed abnormalities, with the prenatally diagnosed cases being the more severe or serious, thus making comparisons difficult. Of concern is the fact that there may be more intervention, and hence risk of maternal morbidity, in pregnancies in which abnormalities are prenatally diagnosed, without a subsequent improvement in long-term outcome. The RADIUS study[16] found that ultrasonographic screening did not improve survival rates among infants with life-threatening anomalies in the screened versus the control group. To address this issue in full, a systematic review of the existing literature and primary studies reducing bias are needed.

Non-detection of anomalies associated with short-term or immediate morbidity, such as facial clefts and talipes may not be as important, as this is unlikely to alter prenatal management and outcome after delivery. Furthermore, these anomalies would be detected at the routine neonatal examination.

All studies had high specificity, confirming previously held beliefs that normal ultrasound

examinations may be reassuring. Of the 52 false-positives, none were suspected lethal anomalies, 19 were anomalies which may be associated with long-term handicap, two were suspected anomalies which may be amenable to intrauterine therapy, 18 were suspected anomalies which may be associated with short-term or immediate morbidity, and ten were suspected anomalies which may be associated with either long-term or short-term morbidity. Three of the false-positive diagnoses could not be classified. Thus false-positive rates for the pragmatic groups were calculated on the basis of the 39 cases which were classifiable (see *Table 9*). Termination of pregnancy was performed against the clinician's advice in one case reported by Boyd and colleagues.[19]

Recommendations for research

Further research is needed to assess the effect of detection of fetal abnormalities on substantive outcome in terms of short- and long-term morbidity and mortality for both mother and child. This is particularly important for conditions amenable to *in-utero* intervention and neonatal surgery.

Research into the efficacy of routine ultrasound screening for fetal abnormalities should ensure that comprehensive postnatal ascertainment is undertaken. This includes, in the case of fetuses aborted spontaneously or iatrogenically or in stillbirths, that an autopsy is undertaken, whenever possible, by a recognised perinatal pathologist; that all newborn babies are examined by a paediatrician before discharge, and that population-based fetal anomaly registers are established and methods of reporting to them are accessible.

Implications for policy and practice

This review of the effectiveness of anomaly detection has highlighted substantial variation in, and limits to, detection rates of certain structural abnormalities. It is important that both clinicians and women are made aware of this, and it may have relevance to proceedings in the medico-legal arena. Given these limits, the RCOG Working Party's recommendations seem appropriate – that ultrasound examinations should be conducted only by appropriately trained personnel, using equipment no more than 5 years old. Quality control mechanisms should be set in place to audit performance. The system of reporting suspected anomalies to regional fetal anomaly registers, should be encouraged where these exist.

Chapter 4

Other clinical aspects of routine ultrasound in pregnancy

Ultrasonographic soft markers

Introduction

Ultrasonographic soft markers are structural changes detected at ultrasound scan which may be transient and in themselves have little or no pathological significance, but are thought to be more commonly found in fetuses with congenital abnormalities, particularly karyotypic abnormalities. Markers that can be detected at second trimester ultrasound scan include CPCs, renal pelvic dilatation (RPD), mild cerebral ventriculomegaly, echogenic bowel, echogenic cardiac foci (golf balls), odd-shaped skull, short limbs, talipes and nuchal thickening. NT is a marker specifically screened for in the first trimester of pregnancy and is discussed on page 32. With improvements in ultrasound technology and greater awareness of the existence of these markers, the frequency of their detection is increasing.

There is disagreement about the definition of each soft marker, which soft markers may be clinically significant and for which to offer counselling and further tests, particularly invasive tests for fetal karyotyping. A questionnaire study of superintendent ultrasonographers in the UK North West Region to assess different policies regarding recognition, reporting and subsequent management after the detection of sonographic soft markers, highlighted the considerable variation in definition and management policies in different hospitals in the region.[49]

It was hoped that the review of primary studies in chapter 3 would provide enough general data about sonographic soft markers to construct the clinical pathways required for the cost-effectiveness analysis. However, only four studies (see *Table 10*) mentioned soft markers.[12,15,19,22] Three of these studies[12,15,22] only alluded to the presence of these markers and did not go into great detail about their significance in determining fetal congenital abnormalities. The overall incidence of soft markers in these studies was 0.6% but varied widely from 0.22–4.3%. Overall, in the presence of an isolated soft marker the abnormality rate was 3.14% but in the presence of two or more soft markers the abnormality rate was 10.3%. It has been shown that in the presence of more than one soft marker, or if a soft marker is associated with one or more major anomalies, there is more likely to be a chromosomal abnormality. It is also clear that the risks increase with advancing maternal age. Most of the controversy surrounds the presence of isolated soft markers in younger women.

The study by Boyd and colleagues[19] was the only one that assessed the effect of the detection of ultrasonographic soft markers on the efficacy of prenatal screening programmes. The authors reported that for a 4% increase in the detection rate of congenital abnormalities (from 51% to 55%), there was a 12-fold increase in false-positives and, hence, a decrease in the specificity of ultrasound screening. In the light of the relatively high false-positive rates associated with the detection of ultrasonograhic soft markers, concerns about the resource implications, risk of procedure-related normal pregnancy losses (i.e. as a result of invasive procedures for karyotyping), and the short- and long-term psychological sequelae arise. Chitty and colleagues[12] reported that 4/20 (20%) of pregnancies with isolated soft markers were karyotyped, and 3/3 (100%) of pregnancies with more than one soft marker or a soft marker associated with other structural abnormalities were karyotyped. The other studies did not mention whether karyotyping was offered or performed on detection of a soft marker. Only one normal pregnancy was terminated on the basis of the detection of a soft marker.[19]

Thus the review in chapter 3 did not provide enough information about the detection, subsequent management and outcome of sonographic soft markers. It was decided to conduct a sample search for studies reporting three known soft markers, namely CPCs, RPD and echogenic bowel, with the aim of assessing whether it would be viable to conduct a complete search and systematically review this topic in full.

Methods

Inclusion criteria

To be included in the review, studies had to fulfil the following criteria.

1. The study should be a population-based study of an unselected or low-risk population.
2. The study aim should be clearly stated.
3. The setting, participants and period of the study should be stated.
4. The ultrasound intervention should be fully described, including gestation at the time of ultrasound, diagnostic approach, quality control, operator/s and skills, and equipment used.
5. An adequate description should be given of the definition of the sonographic soft marker sought.
6. The method of postnatal ascertainment, including reporting of false-positives and false-negatives, should be described and comprehensive.

Studies were identified using the search strategy described in appendix 6. Material was managed using a Procite database.

Methodological evaluation

A similar approach to the methodological evaluation described in chapter 3 was applied.

Stage I – initial categorisation of studies Each study was categorised on the basis of its title and abstract, where available. The initial criteria listed below were used to determine the relevance of each study to the systematic review (agreed between clinical reviewers).

1. Primary study of the detection and clinical significance of the three chosen sonographic soft markers at routine ultrasound screening in pregnancy.
2. Primary study which may be relevant but this is not clear from the title or abstract.
3. Primary study which is not directly relevant but may have some relevant information.
4. Review but not a primary study.
5. Foreign language:
   (a) may be relevant
   (b) not relevant.
6. Document/letter/communication.
7. Not relevant.

E Any study which might be relevant to the economic review was flagged 'E' and passed on to the economic reviewers.

Stage II – further categorisation of studies All studies in categories 1, 2 and 3 were considered relevant and were retrieved and reviewed in full. Retrieved studies were further categorised as follows:

A, relevant and acceptable quality
B, relevant/may be relevant but does not meet quality criteria
C, not relevant.

Stage III – data extraction Data were to have been extracted in a manner similar to that described in chapter 3, However, for the reasons discussed below, this was not done.

Results

Stage I

A total of 56 papers were identified. One paper was duplicated and three had been identified in the search described in chapter 3, one of which was included in the review. In addition, one study published after the literature search had been performed was reviewed. Hence, the abstracts of 53 papers were reviewed.

Of the 53 papers, 21 were initially categorised 1 (16), 2 (3) or 3 (2). The remaining 32 were put into categories 4–7 and not considered further. No foreign language papers were considered relevant.

Stage II

All 21 papers identified in stage I were reviewed in full.

The study categorisations in stages I and II are summarised in *Table 12*, and details of all studies reviewed in stage II are summarised in *Table 13*,[50–70] together with the reasons given for exclusion if they failed on quality criteria (i.e. categorised B1), or were not relevant (i.e. categorised C).

Of the 16 papers in category 1, further categorisation was as follows: A (4), B (3), C (9). Of the three available studies in category 2, further categorisation was as follows: B (1), C (2). Both papers in category 3 were further categorised B. Thus, four papers (classified A) would have been suitable for review.

At this stage, this part of the systematic review was abandoned, as few of the identified studies were suitable for the review. Of the 53 papers identified in the sample search, only four were studies of low-risk/unselected populations. This was not surprising as it is generally accepted that many of the assumptions about the clinical significance of sonographic soft markers are based on studies of high-risk or selected populations. In order to address the clinical effectiveness of the detection and management of sonographic soft markers comprehensively, it was considered that a more extensive search was required using more terms for papers reporting all soft markers, including other search strategies such as handsearching and searching of grey literature. This would be a large undertaking, and beyond the scope of this project.

TABLE 12 *Summary of categorisation of studies relating to ultrasonographic soft markers*

Initial categorisation (stage I)	Number of papers	Subsequent categorisation after full review (stage II)		
		A	B	C
1	16	4	3	9
2	3		1	2
3	2		2	
4	7			
5	3			
6	5			
7	17			
Total	53	4	6	11

Discussion

Even though a systematic review of sonographic soft markers of chromosomal and other structural abnormalities was not undertaken, there are a number of issues worth mentioning, which present a real dilemma in prenatal screening for a number of reasons.

There is limited understanding of the biology and natural history of soft markers. While some described markers are indeed transient findings and may resolve spontaneously, for example, CPCs, the distinction between a 'marker' and structural pathology is not always simple. For example, echogenic bowel may signify prior concealed bleeding and risk of further placental accident leading to insufficiency and intrauterine growth restriction, and some others may represent the early stages of more severe disease, for example renal pelviectatsis progressing to full-blown urinary tract obstruction, and ventriculomegaly progressing to severe hydrocephaly. RPD may also identify a fetus at higher risk of urinary tract abnormalities in extra-uterine life, but whether identification of these fetuses at risk of neonatal or childhood illness translates into a decrease in morbidity and improved outcome remains unclear. This lack of distinction is exhibited in some studies reviewed in chapter 3, in which some markers were included as actual anomalies; Luck included hydronephrosis (RPD) < 10 mm in the section of renal system abnormalities.[15]

TABLE 13 *Summary of all studies reviewed in stage II and reasons for exclusion (categories B and C)*

Study	Initial category	Country	Final category	Reasons for exclusion
Morcos, *et al.,* 1998[50] *	1	USA (California)	C	High-risk population.
Leonardi, *et al.,* 1998[51] *	1	USA (Detroit)	C	Not population based: reviewed outcome of a subgroup of fetuses with CPCs, who were karyotyped.
Deren, *et al.,* 1998[52] *	1	USA (Connecticut)	C	High-risk population: study of fetuses at genetic amniocentesis.
Geary, *et al.,* 1997[53] *	1	UK (London)	A	
Digiovanni, *et al.,* 1997[54] *	3	USA (Chicago)	B	Population not defined.
Reinsch, 1997[55] *	1	USA (San Diego)	A	
Gratton, *et al.,* 1996[56] *	2	USA (Pittsburgh)	C	Not a primary study.
Slotnick & Abuhamad, 1996[57] *	2	USA (Norfolk)	B	Population not defined.
Sepulveda, *et al.,* 1996[58]	1	UK (London)	B	Screened population not described.
Donnenfield, 1995[59] *	2	USA (Philadelphia)	C	Not a primary study.
Gonen, *et al.,* 1995[60] *	3	Israel (Haifa)	B	Screened population not described.
Hill, *et al.,* 1994[61] *	1	USA (Pittsburgh)	C	Not population-based screening: most scans performed for clinical indications.
Kupferminc, *et al.,* 1994[62] *	1	USA (Chicago)	C	Selected population.
Bromley, *et al.,* 1994[63] *	1	USA (Boston)	B	Population not defined.
Porto, *et al.,* 1993[64] ‡	1	USA (California)	B	Population not defined.
Nyberg, *et al.,* 1993[65] ‡	1	USA (Seattle)	C	High-risk population.
Scioscia, *et al.,* 1992[66] *	1	USA (San Diego)	C	High-risk population.
Perpignano, *et al.,* 1992[67] ‡	1	USA (New York)	C	High-risk population.
Chinn, *et al.,* 1991[68] †	1	USA (California)	A	
Platt, *et al.,* 1991[69] *	1	USA (California)	C	High-risk population.
Chitty, *et al.,* 1998[70] †	1	UK (London)	A	

† *Interlibrary loan*
* *Liverpool Women's Hospital library*
‡ *Harold Cohen Library, University of Liverpool*
Final category:
A, relevant and acceptable quality; B, relevant/may be relevant but does not meet quality criteria; C, not relevant

As mentioned before, most of the studies on which the original assumptions about the clinical significance of soft markers report data collected from high-risk or selected populations, or do not describe the population studied, and are therefore biased. This was highlighted in the group of 21 studies identified in our sample search, where seven of the studies were of high-risk or selected populations, six did not define the populations, two were not population-based, and only four were studies of unselected or low-risk populations.

One of the studies identified,[70] reported the results of a large prospective observational multicentre study of the significance of CPCs in an unselected population comprising 101,600 births, included a review of the literature related to CPCs, and highlights a number of the issues mentioned above. *Table 14* illustrates the difference in incidence of CPCs, abnormal karyotype associated with the detection of isolated CPCs, and abnormal karyotype associated with the detection of CPCs in the presence of other abnormalities, according to the populations studied. The lowest incidence and associated karyotypic abnormalities occur in the unselected populations but there is a significant association between CPCs with other abnormalities and abnormal karyotype. This pooling of data also confirmed that the most common karyotypic abnormality associated with CPCs is trisomy 18. We are unable to comment on the quality of literature reviewed by the authors of this publication but the primary study did fulfil the quality criteria for our systematic review. The primary study confirmed the findings of their literature review. The incidence of CPCs was 0.65% and the overall incidence of aneuploidy in fetuses with CPCs was 2.1% (0.5% if isolated CPCs and 20% with other sonographic abnormalities). In all, 12/14 (85.7%) aneuploid fetuses had trisomy 18. When taking maternal age into account, the risk of aneuploidy in the presence of isolated CPCs was 0.36% if < 36 years of age and 2.4% if ≥ 36 years of age; and, in the presence of CPCs and other sonographic abnormalities, 16% if < 36 years of age and 50% if ≥ 36 years of age. The authors concluded that in the presence of isolated CPCs and with maternal age < 36 years one should be cautiously optimistic as the risk remains small; however, with increasing maternal age and identification of other sonographic abnormalities the risks increase. The authors cautioned, however, that counselling is important and that parents should be allowed to decide for themselves about whether to undergo karyotyping. They also concluded that in fetuses with isolated CPCs and no other risk factor, the risk of trisomy 21 is very small. Unfortunately this study did not report on the number of invasive procedures offered for karyotype determination and the uptake of these procedures, making it difficult to evaluate the cost implications of such screening.

Recommendations for research

The issues surrounding the detection, clinical significance, resource implications, and psychological sequelae of sonographic soft markers remain complex. There should be ongoing clinical research into the significance and implications of detection of all sonographic soft markers in unselected and low-risk populations. These findings should be interpreted in the light of other screening programmes for chromosomal abnormalities (e.g. biochemical screening).

First trimester ultrasound screening for fetal chromosomal and structural abnormalities

In recent years there has been a move to take prenatal screening into the first trimester. The known advantages of booking first trimester ultrasound screening are earlier detection of the non-viable fetus, detection of multiple pregnancies and determination of chorionicity, and accurate gestational dating which increases the efficiency of serum screening and is associated with reduced rate of induction of labour for post-dates pregnancies.[71] This is a simple examination focussing on measurement to establish gestational

TABLE 14 *Summary of the literature relating to CPCs (adapted from Chitty,* et al., *1998[70])*

	Number of studies (total population)	Incidence of CPCs (%)	Abnormal karyotype if isolated CPCs (%)	Abnormal karyotype if CPCs plus another abnormality (%)	Abnormal karyotype = trisomy 18 (%)
Unselected populations	13 (247,406)	0.59	0.52	23	77
Selected/mixed populations	14 (48,977)	1.1	1.07	44	82.3
Undefined populations	6 (7016)	2.1	2.1	38	76.5

age, confirmation of viability by detection of fetal heart activity, and detection of multiple pregnancy. Fortuitous detection of gross fetal abnormalities, such as anencephaly and cystic hygroma, may also occur but this simple examination does not include a systematic assessment of fetal anatomy.

The aim of routine first trimester anomaly screening is to assess fetal anatomy in order to detect fetal anomalies early enough to allow earlier termination of pregnancy when abnormalities are detected. Such screening could include both ultrasound and biochemical screening. These examinations are often time-consuming (with consequent cost implications), and may be difficult and require transvaginal scanning to clarify the features that are not clear from transabdominal ultrasound examination.

Detailed first trimester screening would include measurement of fetal NT – an area of subcutaneous fluid behind the fetal neck that may, when excessive, indicate an increased likelihood of Down's syndrome and other chromosomal and structural abnormalities. The group that has most enthusiastically advocated this screening programme is based in King's College Hospital, London. The most recent publication[6] on NT screening from this group has described the outcome of over 96,000 pregnancies screened in 22 centres by one of 306 sonographers. Of women with normal pregnancies, 8.3% were adjudged at high risk of having a fetus with Down's syndrome (≥ 1:300), based on an algorithm that includes maternal age, gestational-age related prevalence of Down's syndrome, and NT thickness compared with fetal crown–rump length. In all, 82% of Down's syndrome pregnancies were identified by this technique, as were 78% of other chromosomal abnormalities. However, a number-needed-to-treat calculation showed that 30 women underwent invasive diagnostic procedures to detect one chromosomally abnormal fetus. Furthermore, there were no data on the total number and type of invasive tests performed, and the resultant procedure-related pregnancy losses. Nor were there data reported about the number of normal pregnancies terminated as a result of anxiety related to testing. It is likely that such screening will, in the future, include biochemical measurements to further refine risk calculations for Down's syndrome. NT measurements may also help identify fetuses with cardiac defects.[7] Some other groups[72,73] have not found such a strong association between NT screening and Down's syndrome detection; whether this is due to lesser technical expertise or to some other methodological or population difference is not clear. The HTA study, SURUSS, being undertaken at 17 centres in the UK, will provide insights into the generalisability of this technique. Its aims are: (i) to quantify the performance of first trimester screening (10–12 weeks) based on biochemical and ultrasound markers, and to compare this with screening at 16 weeks of pregnancy; (ii) to develop a new integrated method for Down's syndrome screening in the first trimester; and (iii) to specify the components of the new screening method.

It is worth stressing that the majority of anomalous fetuses that are detected by routine first trimester ultrasound have structural defects rather than chromosomal abnormalities such as Down's syndrome. The questions about the potential value of routine first trimester ultrasound are therefore substantially broader than arguments about the advantages[74] and disadvantages[75,76] of implementing NT scanning as a routine service provision.

There are, however, disadvantages in routine first trimester anomaly screening. A number of abnormal fetuses will die *in utero* in the late first or early second trimester. First trimester screening may pre-empt this and, in pregnancies where the fetus is destined to die *in utero*, the parents may be unecessarily exposed to the psychological burden and long-term consequences of having to consciously decide whether to terminate the pregnancy. Chorionic villus sampling (CVS) is the invasive procedure employed to karyotype fetuses with suspected chromosomal abnormalities but, in 1–2% of cases, mosaicism may present a diagnostic dilemma and it has a higher procedure-related pregnancy loss rate than amniocentesis, which is employed for karyotyping in the second trimester.[77] Unfortunately first trimester amniocentesis does not perform as well as second trimester amniocentesis in terms of procedure-related loss rate, 0.5–1% versus 1.5–2.5%.[78] CVS is also more expensive than amniocentesis in terms of laboratory processing.

Chitty and Pandya[79] reviewed the published literature on first trimester ultrasound screening programmes for both aneuploidy and fetal structural abnormalities. They noted that there are relatively few data on screening unselected or low-risk populations, as most papers report results of screening in high-risk populations. *Table 15* is a summary of studies reporting the use of NT measurement in screening for aneuploidy in unselected or low-risk populations modified from this paper.[80–85] Some of the studies reporting screening of unselected low-risk populations

exhibit high failure to measure NT rates, thus questioning the feasibility and reproducibility of this examination. The overall detection rate of all abnormal karyotypes in these studies is 70% but this varies widely from 40% to 100%, with the overall detection rate of trisomy 21 being 62% but varying widely from 33% to 100%. The overall false-positive rate is 4% but this varies widely from 0.9% to 6.3%. We did not review these papers, so cannot comment on the methodological quality.

A few authors have reported other sonographic features that may be associated with chromosomal abnormalities, including variations in fetal heart rate patterns, smaller than expected crown–rump length and the detection of structural anomalies such as exomphalos and urinary tract obstruction. The studies reporting sonographic features other than NT are small and the findings preliminary.

Chitty and Pandya[79] identified five studies of first trimester anomaly screening. Having reviewed these studies, mentioning some of the methodological weaknesses, they concluded that "the natural history of abnormalities (some of which may be physiological variants) needs to be more accurately defined before this technique can be considered for widespread application to the low-risk population, and care must be taken in interpretation of findings". Furthermore, first trimester anomaly screening may be affected by the same factors which are problematic in second trimester anomaly screening, such as technical difficulties, subtle or no sonographic signs for some anomalies, and features not evident at the particular gestation of scanning.

In view of the paucity of data on routine first trimester screening for fetal structural and chromosomal anomalies in low-risk or unselected populations, it was not possible to provide data that could be used in the cost-effectiveness analysis.

Recommendations for research

Before the widespread introduction of first trimester ultrasound screening for fetal anomalies, both structural and chromosomal, its efficacy in detecting anomalies and the implications for health service resources need to be established. Furthermore, the issue of clinical harm which can result from such a screening programme needs to be addressed, in terms of pregnancy losses related to invasive karyotyping procedures, termination of normal pregnancies and psychological sequelae.

Implications for policy and practice

If first trimester anomaly and NT screening were to be introduced, extensive training would be required and hence significant costs incurred.

TABLE 15 *Summary of studies reporting the use of NT measurement in screening for aneuploidy in unselected or low risk populations (modified from Chitty & Pandya, 1997[79])*

Study	Gestation (weeks)	NT (mm)	Number screened	↑NT (%)	All aneuploidies (% detected)	Trisomy 21 (% detected)	False-positive rate	Failure to measure NT
Bewley, *et al.,* 1995[80]	8–14	≥ 3	1368	70 (5.1)	2 (40)	1 (33)	6.0	18 %
Szabo, *et al.,* 1995[81]	9–12	≥ 3	2100	27 (1.3)	9 (100)	4 (100)	0.9	?
Hafner, *et al.,* 1995[82]	10–13	≥ 2.5	1972	26 (1.3)	8 (73)	2 (50)	0.9	?
Kornman, *et al.,* 1996[83]	≥ 13	≥ 3	439	23 (5.2)	2 (67)	2 (67)	4.8	42%
Pandya, *et al.,* 1995[84]	10–13	≥ 2.5	1763	63 (3.6)	4 (76)	3 (75)	3.4	?
Bower, *et al.,* 1995[85] [a]	8–13	≥ 3	2566	169 (6.6)	8 (53)	5 (45)	6.3	?
Total			8840	308 (3.5)	31 (70)	16 (62)	4.0	

[a] *Includes Bewley,* et al., *1995*

Chapter 5

Consequences of routine ultrasound: Liverpool Women's Hospital

Introduction

It was expected that in the systematic review of the literature to assess the clinical effectiveness of routine ultrasound, there would be a paucity of data relating to the actual clinical pathways associated with and resulting from routine ultrasound screening. Papers usually report numbers of women and fetuses scanned, numbers of abnormalities detected and missed, and outcomes. However, details of the efficiency of the screening programme in relation to technical problems, and the effect of individual clinicians' and women's decisions need to be taken into account. These factors are essential to assess the true costs of routine ultrasound as no screening system can be 100% efficient. While it is possible that local factors, such as women's cultural beliefs, ultrasonographers' skill and equipment, play a part in the efficiency of a system, it was decided that a primary study at Liverpool Women's Hospital might elucidate some of the hidden events in the routine screening programme, which in turn may have a significant impact on costs and cost-effectiveness. For the purposes of the primary costing study reported later in this report, details were also needed of the obstetric ultrasound workload of the Imaging Department at the Liverpool Women's Hospital.

Objectives

1. To elucidate the 'hidden events' and clinical pathways that develop as a result of routine ultrasound screening in pregnancy, particularly those that are not reported in the literature.
2. To assess what proportion of obstetric ultrasound scanning workload is attributable to routine screening.

Methods

The routine ultrasound screening in pregnancy programme at the Liverpool Women's Hospital includes a booking scan to assess fetal viability, gestational dating and identify multiple pregnancies, and a second trimester anomaly scan at 19–20 weeks to detect fetal structural anomalies and markers for chromosomal abnormalities. The Imaging Department ultrasound records of a sample of women who attended for routine ultrasound examination in 1997 were examined. A list of all those with an antenatal booking in 1997 was obtained from the antenatal clinic records, and surnames, hospital numbers and dates of first booking appointments were entered on a database. This comprised data for 6261 women. All scan reports are filed in alphabetical order at the hospital and hence the database was in alphabetical order. The first 1281 women's records were perused. The following information was added to the database: routine booking scan; booking scan gestation; correlation with menstrual dating (if recorded); repeat booking scans and indication; clinically indicated scans performed at < 20 weeks' gestation and indication; anomaly scan and abnormal findings; repeat anomaly scan and indication; further scans and procedures performed as a result of findings at routine scan and indication; and clinically indicated scans performed at > 20 weeks' gestation and indication. If information in the records was incomplete, other sources were accessed for further information. Missing details were obtained by accessing the hospital computer records and case-note review in some cases. The Fetal Centre database was accessed for details of further scans and procedures performed when a scan report indicated that a woman had been referred to the fetal centre or when an abnormality was detected. The cytogenetics laboratory records were checked to cross-reference cytogenetic analysis requests on specimens from any of the analysed pregnancies; and the regional anomaly register (Unit of Perinatal and Paediatric Epidemiology, Department of Public Health, Liverpool) was checked for all abnormalities notified from 1 January 1997 to the end of September 1998.

Results

In all, 1281 women with antenatal appointments were included (surnames beginning with A–C);

TABLE 16 *Number of antenatal bookers analysed per month in 1997*

Month	Jan	Feb	Mar	Apr	May	Jun	July	Aug	Sept	Oct	Nov	Dec	Total
Number booked	491	512	501	530	547	516	571	478	509	562	528	516	6261
Number analysed	85	100	116	112	117	112	120	97	115	112	93	102	1281
Percentage analysed	17.3	19.5	23.2	21.1	19.6	21.7	21.0	20.2	22.6	19.9	17.6	19.8	20.5

this comprised 20.5% of all those in 1997. Although this was only a sample of all those appointments booked in 1997, they were fairly evenly spread across the 12 months covered (17.3–23.2%; see *Table 16*).

For 26 women, data were incomplete and for 68 no data could be found. Thus complete data were available for 1187 pregnancies.

A total of 1075 women had booked at less than 20 weeks' gestation, 74 (6.2%) at 20–24 weeks' gestation and 38 (3.2%) at > 24 weeks' gestation. One woman declined all routine ultrasound screening. Those who booked at 20–24 weeks' gestation had a combined anomaly and dating scan.

Booking scans

In the 1074 women who had booking scans, 27 (2.5%) were repeated (24 singletons and 3 twins).

The median gestation at booking was 12 weeks (range 5–19); 120 booking scans occurred at > 14 weeks' gestation. Last menstrual period information was available for 846 (81%) of the 1046 viable pregnancies. In 480 women (57%), the scan gestation was within 5 days of the gestation by last menstrual period; 134 (16%) were unsure of their last menstrual period and were dated by scan, and 232 pregnancies (27%) were redated as the last menstrual period gestation was > 5 days different to scan gestation. Hence, 43% of the pregnancies were dated by ultrasound scan.

Three women were not pregnant, 24 had non-viable pregnancies and one a molar pregnancy. In three instances, increased NT was noted and these women were referred for further assessment at the Fetal Centre. Of these, one woman had a detailed scan and CVS biopsy which confirmed Down's syndrome and the pregnancy was terminated, and two had early and 20-week detailed scans at the Fetal Centre and no further tests. One women was referred to the Fetal Centre for a detailed scan as placental lakes were noted, no abnormality was detected and she returned to the routine programme. There were 23 twin pregnancies and one triplet pregnancy, but five of the twin pregnancies were 'vanishing twins' and therefore analysed as singletons.

Between the booking scan and intended anomaly scan, eight further pregnancies ended in miscarriage (one twin pregnancy), one woman had a social termination of pregnancy and four transferred care to another region; 28 women left the routine screening programme as they had clinical indications for ultrasound scan (one twin). There were thus 1002 ongoing pregnancies which remained in the routine screening programme (985 singletons, 16 twins, one triplet).

Anomaly scans

Anomaly scans were attended by 981 women with singleton pregnancies and 17 with multiple pregnancies (16 twin, one triplet). Four women who had had booking scans did not attend. Furthermore, 74 women booked at 20–24 weeks' gestation, 73 of whom had had routine anomaly scans (one had a clinical indication for ultrasound scan), one of which was a twin pregnancy. Thus 1071 routine anomaly scans were performed (1053 singletons and 18 multiple pregnancies). A total of 81 anomaly scans (7.6%) were repeated (80 singletons, one twin), mainly because of technical difficulties such as poor visualisation generally, and inability to see the four-chamber view of the heart, intracranial anatomy or fetal spine in at least two planes.

There were 27 fetuses with a suspected abnormality (25 singletons, two twins), of which 25 were referred to the Fetal Centre. The abnormalities comprised 19 isolated soft markers (prevalence 1.8%), one with two soft markers, and seven possible major anomalies.

A total of 16 fetuses with isolated soft markers, plus the one with two soft markers, were referred to the Fetal Centre for further evaluation. In two cases

the soft markers were not confirmed (may have resolved at the time they were rescanned). Five with isolated soft markers and the one with two soft markers underwent fetal karyotyping (amniocentesis (4) and CVS (1)). It was not clear from the notes or the Fetal Centre database as to why some were offered karyotyping and others not. One fetus with ventriculomegaly had trisomy 21 but was a twin (the couple elected to continue with the pregnancy and this fetus died *in utero*). One amniotic fluid cell culture failed and fetal blood sampling, which was undertaken in the third trimester, was reported to be normal. Some cases of RPD and CPCs had further detailed scans; however, it is not clear why some did and some did not. Both fetuses with ventriculomegaly (one trisomy 21) had further detailed scans, presumably to assess disease progression in the singleton pregnancy and the well-being of the normal twin in the twin pregnancy. The fetus with two soft markers and normal karyotype had a further detailed scan, presumably to assess fetal well-being and to search for further abnormalities.

Of seven women with possible major anomalies, three were found to be normal at detailed scanning. Four major abnormalities were confirmed, one lethal (anencephaly) for which termination of pregnancy ensued. All of the remaining three major anomalies had further detailed scans. Unfortunately we have no details of the neonatal outcome of these cases.

Details of fetal abnormalities, further tests and immediate outcomes are presented in *Table 17*.

Third trimester scans

One woman was scanned in the third trimester as a result of an anomaly scan finding of slightly increased liquor volume, and this scan was normal. Two women were scanned again in the third trimester to assess fetal growth since their anomaly scans were performed slightly late at 24 weeks' gestation.

In 60 individuals (5.6%), low placentas were noted at anomaly scan. Of these, two were twin pregnancies and therefore placental assessment took place at the time of planned regular growth scans. It was intended that the remaining 58 would have placental site scans at 34 weeks' gestation. Of these, one delivered preterm and prior to 34 weeks' gestation, seven had indicated scans for antepartum haemorrhage, and five had indicated scans for other reasons but the placental site was assessed at the same time. Two were not scanned at 34 weeks for unknown reasons. Thus 43 women had placental site scans at 34 weeks' gestation, of which four were repeated and placenta praevia diagnosed in three cases. However, none of these three experienced antepartum haemorrhage. Two women had elective Caesarean sections at 38–39 weeks' gestation, one of whom had a history of previous Caesarean section, which was cited as the primary reason for it. Both of these pregnancies were characterised by high presenting parts (five-fifths palpable above the pelvic brim) and this alone would have been a clinical indication for ultrasound scan, at which time the placenta praevia would have been identified. The other case of placenta praevia at 34 weeks' gestation presented in established labour and subsequently had a normal vaginal delivery without complication.

Late booking scans were performed on 38 women who booked after 24 weeks' gestation. One was a twin pregnancy. One fetus at 27 weeks' gestation was thought to have a major anomaly and was referred to the Fetal Centre where infantile polycystic kidney disease was diagnosed, and the couple elected to terminate the pregnancy a week later. Six women were rescanned (three once, one twice, and two four times) for concerns about fetal size or liquor volume at the late booking scan.

In total, there were 31 women with suspected fetal abnormalities (three at booking, 27 at anomaly scan, and one at late booking scan), 29 of whom were referred to the Fetal Centre; 23 were soft markers and, of these, seven had fetal karyotyping, resulting in the detection of two chromosomal abnormalities. There were eight suspected major anomalies, of which five were confirmed abnormalities; none had fetal karyotyping. There were three terminations of pregnancy, one in each trimester, for trisomy 21, anencephaly and infantile polycystic disease. In total, there were 3276 scans performed in these pregnancies, of which 2300 (70%) were routine ultrasound scans (primary) or directly as a result of findings at routine ultrasound scan (secondary). In singleton pregnancies, the median number of routine primary/secondary scans was 2 (range 0–7) and the mean was 2 (standard deviation (SD) 0.61). In twin pregnancies, the median number of routine primary/secondary scans was 2 (range 1–6) and the mean was 2.4 (SD 1.01).

Discussion

The clinical effectiveness of the two-scan regimen of routine ultrasound screening at the Liverpool Women's Hospital cannot be commented on

TABLE 17 *Cases of fetal abnormality detected at second trimester anomaly scan, referral, further tests and immediate outcome*

Case number	Suspected abnormality	Referred to Fetal Centre	Confirmed abnormality	Karyotyping procedure	Further detailed scan	Outcome
Soft markers						
1	Isolated RPD	Yes	Yes		1	Normal
2	Isolated RPD	Yes	Yes		1	Normal
3	Isolated RPD	Yes	No		0	Normal
4	Isolated RPD	Yes	Yes		0	Normal
5	Isolated RPD	Yes	Yes		2	Normal
6	Isolated RPD	No				Normal
7	Isolated RPD	Yes	Yes		0	Normal
8	Isolated RPD	Yes	Yes	Amniocentesis – failed culture; fetal blood sampling in 3rd trimester	2	Normal
9	Isolated RPD	Yes	Yes		1	Normal
10	Isolated CPC	Yes	Yes	Amniocentesis	0	Normal
11	Isolated CPC	Yes	Yes	Amniocentesis	0	Normal
12	Isolated CPC	Yes	No		0	Normal
13	Isolated CPC	Yes	Yes		1	Normal
14	Isolated CPC	Yes	Yes		0	Normal
15	Isolated CPC	No (twin)				
16	Echogenic bowel	Yes	Yes, but low grade			Normal
17	Ventriculomegaly	Yes	Yes	CVS	1	Normal karyotype, hydrocephalus
18	Ventriculomegaly	Yes (twin)	Yes	Amniocentesis	4	Trisomy 21; fetal death *in utero*
19	Short limbs	Yes	No		0	Normal
20	NT and CPC	Yes	Yes	Amniocentesis	1	Normal
Suspected major anomaly						
21	Unilateral renal dysplasia	Yes	Yes		2	Postnatal follow-up
22	Anencephaly	Yes	Yes		0	Termination of pregnancy
23	Calcified liver cyst	Yes	Yes		1	
24	Irregular heartbeat	Yes	No		0	Normal
25	Oligohydramnios	Yes	No		0	Normal
26	Abnormal heart	Yes	No		0	Normal
27	Cardiac anomaly	Yes	Yes		4	

following this work, for several reasons. First, it was not the primary intention of this study. Second, the numbers are small and some data is missing. Third, there was not adequate postnatal ascertainment of abnormal fetuses to report sensitivity and false-negatives, hence specificity.

The authors recognise that looking at records for patients with surnames beginning with A, B or C may have introduced bias, for example, in relation to ethnic mix. However, this is unlikely to have modified the conclusions.

One interesting factor that was highlighted is the poor reporting of suspected abnormalities to the Unit of Perinatal and Paediatric Epidemiology, Department of Public Health, Liverpool, as only four of the eight suspected major anomalies, and 12 of the 23 soft markers were on the register. This information was conveyed to the Unit.

Ultrasound scanning was required for accurate gestational dating in 43% of cases and this has implications for serum screening programmes, as well as for the management of post-term pregnancies.

Although three cases of increased NT were reported at booking scans, this does not reflect the prevalence of increased NT in our population

as NT screening is not the intention of the booking scan at Liverpool Women's Hospital. The fact that one of the three reported cases was a chromosomal abnormality may overestimate the efficiency of NT screening, as it can be argued that if the intention of the booking scan at Liverpool Women's Hospital is not to measure NT, then only obvious or severe cases will be noted opportunistically.

It was of interest that 2.5% of booking scans and 7.6% of anomaly scans were repeated, as this implies that for every 100 women included in a two-scan regimen routine ultrasound screening programme, ten extra scans are performed. Not only does this have cost implications but it may also be associated with maternal psychological consequences.

It is also of note that a number of women book late, either at 20–24 weeks' gestation (6.2%) or > 24 weeks' gestation (3.2%). This has implications with regard to accurate gestational dating and the feasibility of the introduction of routine first trimester anomaly screening programmes. In this study, 232 (19.5%) women booked at > 14 weeks and would not be eligible for NT screening if it were part of the programme.

Of this population, 1.8% exhibited soft markers at second trimester anomaly scan, of which six were karyotyped (30%) and only two had confirmed abnormalities, one chromosomal and one structural. Although postnatal ascertainment is not complete for this series, there seems to be a significant number of false-positive scans. Fortunately no pregnancies were terminated as a result of this.

The presence of a low placenta at second trimester anomaly scan triggered 47 third trimester scans for placental site, only three of which were abnormal, but it is questionable as to whether prior knowledge of placenta praevia improved or changed the outcome of these pregnancies. Seven women with low placentas at anomaly scan had antepartum haemorrhages and, therefore, clinical indication for repeat scanning. It may be that routinely checking placental site at 34 weeks' gestation is not necessary as a low placenta/placenta praevia will reveal itself if there is to be associated morbidity.

Of the 38 women who booked at > 24 weeks' gestation, six (15.8%) had further scans as dating and hence fetal size was of clinical concern. This emphasises the value of knowing gestational dates from early scans. One major fetal anomaly incompatible with long-term survival was detected.

Recommendations for research

This primary study identified a number of inefficiencies in the routine ultrasound screening programme at Liverpool Women's Hospital, including the need for 10% of routine scans to be repeated and that women present for antenatal booking at varying gestations. Some of this is unavoidable but it has implications for both its clinical and cost-effectiveness. These findings need to be validated prospectively in other settings.

The implications and management of the finding of a low placenta at second trimester scan needs to be addressed in prospective research (none of the studies reviewed in chapters 2 or 3 addressed this issue either.).

Implications for practice

As there are some women who book after 14 weeks or even after 24 weeks, the likely coverage of first trimester and second trimester scan regimens should be taken into account when planning or auditing routine screening programmes. This and the scan repeat rate should be taken into account when costs and cost-effectiveness of routine ultrasound screening are assessed.

Systems of reporting suspected anomalies to the population-based fetal anomaly registers need to be audited and reviewed to ensure that they accurately reflect existing clinical findings and anomaly prevalence.

Chapter 6

Women's views of antenatal ultrasound: a structured review

Introduction

This topic presents some challenges for the reviewer. Ultrasound is one of many methods used in pregnancy for screening and diagnosis. Some features of ultrasound may be special – the chance to see the baby and the immediacy of the knowledge gained – but it is not unique, and many of the questions that can be asked about ultrasound can also be asked about other screening and diagnostic tests. The impact of antenatal ultrasound on a woman (and her partner) is likely to depend on a number of factors:

- the purpose of the scan
- what women know about the purpose and likely outcomes
- how it is carried out
- what follows from it.

Because the subject is potentially so wide, a decision was made to limit the review to studies that included direct data from women (and, in a few cases, partners) about antenatal ultrasound (used for any purpose). Studies and reviews about prenatal screening and diagnosis were not covered systematically but some key papers are referred to as background and to put the ultrasound material in its proper context.

Two recent reviews about ultrasound were identified. One was a structured review of the psychological impact of antenatal ultrasound, which was identified towards the end of the process.[86] This review sets out to answer a number of key questions, which will be referred to in the results. The second review[87] is listed in the main results table because it includes some data from a large study of antenatal care. It posed some of the same questions as that by Baillie and colleagues[86] and also has a useful section on the role of care-givers. We are grateful to the authors of these reviews for the detailed work that went into them and for the different questions that they posed. Both took a mainly psychological perspective. The present review covers some of the same issues but puts more emphasis on questions about the social context of ultrasound and on women's views.

There is another challenge in carrying out a review in an area like this. The essence of systematic reviewing is to build on past work so that research can move on. Social and psychological studies of ultrasound are very context-specific. The way in which the technology is used has changed over time and varies between and within countries. Many studies do not give much contextual information so, for example, it is not always possible to work out when the research was done. It is necessary to be very cautious about putting together the results of studies in a review like this and, also, to be aware that review findings may not be relevant in all settings or over time. It would be possible for two thorough, well-conducted structured reviews in this field to appear to be very different because the authors had asked different questions of the data, or given different weight to the contextual factors. This is not wrong but it means that a lot more work and discussion are needed when reviewing studies using non-experimental or mixed methods.

Methods

The initial search strategy was designed to find material on the views and experiences of women relating to antenatal screening and diagnosis of all types. The search of databases was carried out by Marie-Anne Martin; it involved combining the terms shown in appendix 7 and searching for material from 1981 onwards on MEDLINE, CINAHL, EMBASE and BIDS–SSCI. About 200 publications were picked up, many of them providing general background. Studies that were likely to be about ultrasound were then identified from the abstracts.

All the papers about ultrasound, and the wider reviews identified, were combed for additional relevant publications about women's views and experiences of ultrasound. Many more were found this way, perhaps because literature about ultrasound has been published in such a wide range of journals. Material was also found by contacting UK and French researchers for information on new or key articles. This helped

to identify some forthcoming papers and work in progress. A few publications were still being identified when the tabulation of studies was closed for this report. Unpublished work and studies published in languages other than English are more likely to have been missed.

Publications obtained were read by one author and sorted into three categories:

(i) relevant – including direct research about views on pregnancy ultrasound and about its social or psychological impact
(ii) background – not falling into (i) but relevant to understanding the findings of reports in (i) (e.g. reviews, work on prenatal diagnosis more generally and the history of use of ultrasound)
(iii) not relevant – usually comments or studies outside maternity care.

Out of 102 reports that reached this stage, 76 were classified as relevant but a number of these were reporting data from the same study. In all, 59 studies were represented in the 76 reports. A further six papers, covering five studies, were found after the first version of the report was written; these have been added to the table. Papers were initially tabulated and categorised according to their relevance to the questions listed below. They were not graded in terms of research quality, or removed from the review for reasons of poor quality, although many had problems of design and reporting. This was because even where the methods were unsuitable to answer the question posed by the researcher, a study had often generated useful information with which to address one or more of the questions posed in the review. One paper was rejected because the methods were too poorly described for it to be used.

Results

The studies included in this review are shown in *Table 18* (see page 49). Other material is cited and listed in the references. The data have been used to address a series of questions.

A. What do women know about reasons for using ultrasound and what a scan can do?
B. What do women like or value about scans?
C. What are women's views about the way in which the scan is performed?
D. What is the impact of the results?
E. What is the psychological impact of ultrasound?
F. What might be the wider impact of ultrasound on society?

The studies identified ranged widely in terms of the questions addressed and the methods used (see *Table 18*) and also in terms of when and where they were undertaken (summarised in the box below). Some studies did not specify where they were done and so we have guessed. Many did not give the date when the work was carried out, so we have used any information available to give a likely date. This may mean that some of the dates given are later than they should have been because of delays in publication.

Ideally, each study should have been categorised in terms of the way in which ultrasound was being used, but this information was only available in a clear way in a handful of studies (see comments column in *Table 18*).

What do women know about the reasons for using ultrasound and what a scan can do?

A recent short article in the *BMJ*[88] told of the experience of a British general practitioner (GP) who received an NT scan without being aware of its purpose. The GP was angry because she did not want to know if her fetus was likely to have Down's syndrome. The rapid changes in the way that ultrasound is being used and the fact that policies differ between hospitals in the UK mean that a woman may well not know what is scan is intended to do unless she has been told. This can leave her vulnerable to a painful shock if the scan shows a problem when she was not aware that anomalies were being looked for. On the other hand, lack of information about what the scan can do may mean that she believes that the absence of anomalies detected means that all is well.

BOX 1 *Studies by country and estimated dates*

Scandinavia and Finland	UK	USA	The Netherlands	France	Canada	Israel	Other
10	20	16	2	4	3	2	7

Not later than 1980	1981–85	198–90	1991–95	1996 or later
3	13	22	21	6

Researchers have addressed these issues from several angles. Almost all the studies show some deficit in women's knowledge of the purpose of their scan, which tallies with studies of other aspects of prenatal screening and diagnosis reviewed by Marteau.[89] A commendably clearly reported study of women attending for routine scanning at the UK hospital[90] found that few women were aware that one aim of the scan was to look for markers associated with Down's syndrome. This paper describes in detail what the scans were intended for but many other papers do not make his clear. This makes it hard to judge how well women have understood the purpose of the scan. A recent local study in England[91] found that two-thirds of women who had recently had a scan, which included measurement of NT, considered that they had not been adequately prepared for the scan.

Two Swedish studies carried out in the 1990s of women coming for routine mid-trimester scans, asked in different ways about their knowledge of the purpose of the scan.[92–94] The women (and their partners) in Uppsala[93,94] selected purposes for the scan that seemed to match well those described by the authors, although the parents put more emphasis on the detection of malformations than the authors thought was appropriate, given the way in which the aims of scanning had been described in the hospital information leaflet. In Lund[92] women seemed less well informed, with 62% thinking that the scan was compulsory, and one-third claiming that they had not been given information that the scan could detect malformations.

A French study carried out in 1990[95] addresses a reported concern about women's unrealistic expectations of ultrasound. Women were interviewed by phone after the birth. Most were well informed about the purposes of mid-trimester scans. Only 9% thought that if no anomaly was found on ultrasound they could be sure that the fetus was normal. This view was more common, though, in women with the fewest years of education. In Santalahti and colleagues' study in Finland,[96] education levels were also linked to knowledge about what the scan is for and what it can detect.

Gaps in the provision of information have been highlighted in some UK studies. An observation study of routine antenatal consultations in six UK hospitals[97] found that information about fetal anomaly scanning was very limited, with about two-thirds of women receiving no information in the consultation about the purposes of scans. A survey of midwives and obstetricians carried out by the same team[98] found gaps in staff knowledge about antenatal screening. A survey of UK hospital practice[99] found that just under half of the maternity units surveyed routinely gave women information about the potential of a scan to detect anomalies.

Researchers have tried to improve the information provided to women, although only one randomised trial has been identified. In a quasi-experimental study in Sweden,[100] women at seven clinics were given extra information about antenatal screening and their take-up of tests was compared with that of women at ten control clinics. None of the women in either group declined ultrasound but 1% (11 women) attending the clinics giving extra information chose to have only an early ultrasound and to avoid the mid-trimester scan for detecting malformations. In a British study with historical controls,[90] two surveys were carried out. In the second, women had been given extra written information about ultrasound. Some aspects of knowledge were better in the group given the extra information. In a trial of the offer of additional information (individually, or in a group) about antenatal screening,[101] the uptake of ultrasound was not affected by the intervention and was very high in all three groups (99%). Uptake of screening for cystic fibrosis was lowered in the two intervention groups when compared with the control group. The groups who were offered extra information reported increased satisfaction with information received and improved knowledge when compared with the control group. Take-up of extra information was relatively low – 61% for those offered individual sessions and 42% for classes.

Further work could be done to improve our understanding of staff attitudes to information-giving relating to ultrasound (and other prenatal tests). Good communication about these complex issues takes time and requires considerable knowledge and confidence on the part of staff. Procedures that are seen as routine or no longer novel may not be perceived by staff to need as much explanation as newer techniques. Explaining about ultrasound may be seen as less important because it is viewed as non-invasive. Women, too, may put up barriers to detailed information about the possible outcome of a scan, because of the strong attraction exerted by ultrasound, as discussed below.

What do women like or value about ultrasound scans?

"At the first scan I was only 11 weeks and didn't feel very pregnant, but it was a marvellous sight

seeing this **tiny** thing moving about and its heart beating. I felt pregnant then."[102]

"The face, and heart beating. The closest you can imagine to seeing or meeting your baby before you have him. You can 'wave' to him. I would have them weekly if I could, and take friends to meet baby."[103]

The studies that were found show that most women react very positively to ultrasound. Some are unhappy about the way in which the scan is done (see the next question below). Some women get bad news as a result of the scan and may regret having had it; again this is discussed below. A very small number of women choose not to be scanned at all, or avoid scans that are intended to detect anomalies. One or two women quoted in the studies that have been reviewed feel uncomfortable seeing the image of the fetus during the scan because they feel it intrusive, or because they are worried that they may feel too much for the fetus and then find it hard to cope if something goes wrong.[103–105]

Concerns about ultrasound are reported relatively rarely in research studies. In one early study from the USA,[106] some women were afraid (before the scan) that it would be painful for them; in addition, half expressed the fear that it might harm the baby. A British study from the early 1980s[102] found that over 85% of women reported the things they enjoyed about the scan, while 15% reported worries. Altogether, 77% mentioned only enjoyable aspects and 4% only worries. The types of worries included fears of harm to the fetus and concerns about what the scan might show. The enjoyable aspects related to seeing the baby or details of the baby and seeing movements. Women enjoyed the reassurance brought by the scan and feeling that their pregnancy had become more real to them. They also mentioned their partner's presence and increased involvement with the baby. Ten women in this study (from 107) said that they would like more scans, and this is mentioned in some other studies.[87,107–109] In a Swedish study carried out in 1991,[93,94] women interviewed before a scan had anxieties about what the scan might reveal but only 2% feared that it might harm the baby. In Crang Svalenius and colleagues' study,[92] 4% of women were apprehensive that the scan might harm the baby.

A number of studies have asked women to describe how they felt about a scan, using a list of adjectives from which they must pick one or more. Positive adjectives were far more likely to be chosen.[92–94,107–109] Several trials have compared the reactions of women to scans when explanations are offered and the women can see the screen (high feedback) with scans when only the operator can see the screen and the women are told at the end of the scan that all is normal (low feedback). These trials are discussed further below but they do show that women in the high feedback groups are more likely to choose very positive adjectives to describe their feelings after the scan.[110,111]

What women like about the scan has been summed up by Clement and colleagues[87] as having three main elements: meeting the baby, sometimes with other family members; having a visual confirmation of the reality of pregnancy; and gaining reassurance about the well-being of the fetus. Ultrasound is different from other kinds of test because it provides the first two of these alongside the third.

What are women's views about the way in which the scan is performed?

Before looking at some of the issues that women raised about the scan procedure itself, it is worth mentioning the small number of studies that report direct observation of ultrasound clinics and scans. These, again, are very time and context specific. Several authors emphasise the extent to which a mother's experience is mediated through the person carrying out the scan. Because the image is difficult to recognise, the doctor or ultrasonographer needs to explain what is being seen. For example, in an early French study,[112] the following exchange was observed:

"Doctor: 'A single fetus, head down.'
Woman: 'Oh, I can't see anything.'
Doctor: 'Yes, there. It's the head.'
Woman: 'Which side? I can't see.'
Doctor: 'Good, OK. BIP 4.4, cardiac activity noted, placenta in posterior position ...'
Woman: 'Is that the heart I can see?'
Doctor: 'What? It's the baby. Good, there is the stomach, umbilical vein...'
Woman: 'It's a shame. I saw nothing'."

In another early study,[106] the women's reactions are described in detail. At first most were very tense (one thought she was going to be 'opened-up' for the procedure). The technician doing the scan reassured them with general phrases about the baby looking fine. During the phase of the scan when the dynamic image was shown, women's attention became fixed on the screen. When they recognised some part of the baby, their reactions were strong. 'Oh, I see it!' The contribution of the technician was crucial to this recognition.

In a study carried out in Greece in 1990/91,[113,114] the authors observed more than 80 scans at a large teaching hospital in Athens and at a smaller hospital away from capital. In general, the doctor did not speak during the scan except to say if the fetus was male or female and to read-off the gestation from a chart. If the doctor did not say that the baby was all right, the woman usually asked (no malformations were detected in the scans they observed). One of the authors, Mitchell,[114] who had observed scans in Canada in 1995, put more emphasis on the social assumptions revealed in the ways that the sonographers talked about the fetus. One, for example, told a father not to say fetus: "Your fetus? Ugh! Don't say that. It's your baby."

There is a lack of more recent observation studies of the way in which ultrasound is being used. It would be helpful, for example, to know what explanations of the purposes of the scan are given by the person performing it. This would complement the evidence referred to earlier about the lack of information given in antenatal clinics about the purposes of ultrasound.[97] It would also be useful to know more about how much women are told before the scan by the person performing it, and how any problems detected during the scan are talked about. This is mentioned in Baillie's interview study[115] of women with potential problems detected at a scan. Some women in that study reported that they picked up a worried or serious reaction from the ultrasonographer before anything had been said about a problem.

Women need to know what to expect during the scan itself, although few women now would expect the scan to be painful.[106] Barton and colleagues[116] did a study of women referred for fetal echocardiography because of concerns or risk factors. Some women found the long silent period at the start of the scan very unsettling and the authors recommended that women be told that this does not mean that an anomaly has been found. In other studies women have commented about the discomfort of a full bladder[117] or uncomfortable couches.[103] Women need to know about such practical aspects and also to be told who can accompany them.[102]

The key issue for most women, though, is the part played by the person doing the scan. Women respond badly to unspoken tensions, muttered comments, to lack of explanation, or dismissive answers.[102,115,118–120] In this, as in other aspects of care, women appreciate being treated kindly and respectfully.[121] Ultrasound creates extra tensions because of the immediate knowledge gained and the possibility of worrying news. It is likely that practice has changed over time, so that women are given more feedback now during the scan and sonographers are more aware of how women feel. We have no evidence about this, however.

In the early days of ultrasound, some user group representatives commented on the problem of having to wait for the scan results to be given by a doctor.[122] This issue was also raised in a survey of a volunteer sample of National Childbirth Trust members.[119,120] Other studies have tended not to mention this, which may be because scans were performed by obstetricians in many studies, or because ultrasonographers now provide information about the outcome of the scan directly to women.

What is the impact of the results?

From a woman's point of view a scan can have the following outcomes.

- No adverse findings.
- News – for example twins, or finding out the sex of the baby.
- Failure to see or measure what was intended, leading to further tests or scans.
- A worrying finding leading to further tests or scans.
- A clear-cut bad outcome, such as death or serious malformation.

What is the likely impact of each of these possible outcomes?

No adverse findings

Some women who are told that nothing bad has been found may still be worried by something they heard or saw during the scan.[102,123] In addition, a proportion of women will experience a poor outcome of pregnancy and may feel that the scan should have picked it up. A small number of genuine false-negatives will also happen, so that a baby with an anomaly may be born after a negative test result. A recent general review of the impact of false-negatives in screening programmes[124] suggested that better information about the limitations of screening programmes should be provided so that participation in screening is more fully informed. The authors point to evidence of gaps in public understanding of screening and limited perceptions of risk, and recommend the development and testing of better approaches to information-giving. A recent study of false-negative results following antenatal screening for Down's syndrome[125] showed a limited adverse impact on parental adjustment detected between 2 and

6 years after the birth. These authors also emphasise the need for better information for parents about the limitations of screening tests.

News – for example twins, or finding out the sex of the baby

Examples of individual women's responses to news from scans, such as the presence of twins or learning the baby's gender, have been quoted in some studies. Some women may be upset if their baby's gender is revealed to them when they did not want to know it.[87]

Failure to see or measure what was intended

Scans that fail to get the necessary information can be quite difficult for women.[87,103] They miss the hoped-for reassurance and have to spend time on another visit. They may also be very anxious in case something that is wrong with the baby was the cause of the failed scan. For example:

"They could not see all the spine. It was not fully developed. We had to go back in two weeks to be checked. I was quite worried. It would have been shattering without my husband."[103]

The findings in chapter 5 about the use of ultrasound at the Liverpool Women's Hospital provide a figure of 7.6% of women having a repeat anomaly scan, mostly because some aspect of the scan could not be completed.

A worrying finding leading to further tests or scans

If the ultrasound finding indicates a possible problem, the woman is likely to find herself involved in extra tests and scans. For example, if a woman's placenta appears low she will be scanned again regularly. Some low placentas will resolve spontaneously, although the woman may still be anxious about her labour.[103] An early paper reporting a short case series of false-positive results from ultrasound warned of the potential costs to the service and stress on women.[126] A woman in Oakley's study in New Zealand[103] had a routine scan at 18 weeks that indicated a kidney problem in the fetus. The woman commented after the scan:

"I regret having a scan. I preferred my baby the way things were."

The woman went on to have further scans which did not confirm that there was an anomaly and the baby showed no kidney problems at 6 weeks.

A recent British study looked at the experiences of women who had had a false-positive result from serum or NT screening.[115] Women in this study who had soft markers found on ultrasound had been unprepared for adverse findings. Ultrasound was, for them, a high spot in pregnancy. One said:

"We were thinking – brilliant. We'll be able to know if it's a boy or a girl and all things like that, not that anything would be wrong."[115]

Parents in this study[115] found it difficult to understand the idea that the scan finding indicated an increased risk rather than a definite finding, and also reported their confusion and difficulty in asking further questions. Some women were not fully reassured by the later test findings that ruled out the abnormality. They also experienced a more generalised anxiety – now that something had gone wrong with the pregnancy other disasters might follow.

A clear-cut bad outcome

For a small number of women the scan leads to a clear-cut bad outcome. Findings of fetal death in early scans must be quite common but little has been written about the impact on women, or the way the news is conveyed.[127] Later in pregnancy, ultrasound may detect serious malformations. The impact on women is likely to be similar whether ultrasound is involved or some other screening technique. Women may, however, be less prepared for untoward findings when having a routine scan.

The issues facing women in these situations have been considered in reviews about prenatal testing.[89,128] Parents often rely on care-givers for information about the conditions diagnosed, although those at increased risk or with inherited conditions may be well-informed from their own experience. As Marteau[89] points out, we have little knowledge of the social and family context within which decisions about termination are made. Information and counselling is crucial for parents considering termination. For those who would not consider termination, the option of avoiding screening tests altogether must be available, which returns to the discussion of information needs at the start of this review.[60,92]

Only three of the identified studies were about women's experiences after the detection of malformations.[129–131] They deal mainly with the pain and grief experienced by parents and the decision to have a termination, and not with the process of ultrasound diagnosis. Some anomalies may be treatable after birth and it is possible that parents may find it helpful to know in advance so that they can be prepared. This specific issue was not

addressed in the three relevant papers just mentioned. A study that analysed termination decisions after ultrasound diagnosis of anomalies found that that terminations were less likely when the anomaly was classified as 'mild' or 'uncertain'.[132] Those in the 'uncertain' category included abnormalities that have a variable natural history or cases when there were worrying but inconclusive signs on ultrasound. This study did not involve any direct data collection from parents (and so is not included in *Table 18*). The authors speculated in their discussion that parents with an 'uncertain' scan result may feel increasingly confident in the abilities of care-givers to intervene to treat the abnormality.

What is the psychological impact of ultrasound? Two recent reviews[86,87] have explored the impact of ultrasound on a range of psychological variables using many of the studies summarised in *Table 18*. Rather than repeat this process, their key findings are summarised here.

Ultrasound and anxiety

It is likely that the reductions in anxiety following a scan reported in some studies are mainly caused by increased anxiety just before the scan, rather than a real benefit of ultrasound. Much of the research, however, covers very small samples and no trials of routine ultrasound (compared with no routine scans) have measured psychological outcomes.

Ultrasound and attachment

Evidence about this is inconclusive. Early suggestions of improved attachment to the baby following ultrasound and women's comments in qualitative studies led to an assumption in much of the literature that this was a real effect. Prospective studies, however, show a trend to increased attachment over the course of pregnancy. The only randomised trial to consider it showed no impact of high feedback ultrasound on attachment.[133] This outcome has not been assessed in trials comparing ultrasound with no ultrasound. Studies of pregnancy loss do raise the issue of whether the experience of having seen an ultrasound image has an impact on subsequent bereavement.[134–136]

Ultrasound and health behaviour

There is no evidence from trials of any impact of ultrasound on smoking, or of high feedback on smoking and other aspects of health behaviour.

What might be the wider impact of ultrasound on society?

Writers and researchers have raised a number of issues relating to the potential impact of antenatal ultrasound more widely.

A psychoanalytic approach

The French language literature refers to a concern arising from psychoanalytic theory about the possible adverse effect of ultrasound on a woman's own image of the fetus. The ultrasound image, seen by the woman, is thought to interfere with the 'child of the imagination' that she needs to develop in the course of her pregnancy.[137,138] A study in Quebec,[139] referred to these anxieties but the authors did not feel that their evidence, from interviews and self-completion questionnaire, supported the psychoanalytic viewpoint. Well-designed comparisons of ultrasound with no ultrasound have not looked for an impact on the relationship between the parents and the baby, or at other aspects of psychological or psychoanalytic well-being in the short or long term.

Bonding and the pro-life agenda

A survey of 50 sonographers working in an American city[140] suggested that their experience with ultrasound had made them less favourable to abortion, and all but four believed that ultrasound with feedback 'strengthened maternal–fetal bonding'. In Europe the possibility that ultrasound increases attachment to the fetus has been raised either as a general benefit or as a potential problem for parents who may have an anomaly diagnosed and then find it difficult to consider termination. The emphasis has tended to be different in the USA, and some writers have expressed concern that ultrasound is being used as part of an anti-abortion agenda.[141] The use of ultrasound pictures in the anti-abortion film, *The Silent Scream*, was also discussed by Petchesky,[141] who suggested that visual images of the fetus can strengthen the emphasis on the rights of the fetus as an individual. This theme was also discussed by Mitchell and Georges,[114] who contrasted the North American individualisation of the fetus with the very different Greek perspective in which the emphasis is on the community or nation.

Other feminist concerns

Feminist writers and researchers have raised a number of interlocking issues about the impact of ultrasound. Mitchell, in her paper with Georges,[114] described her impression of the scan as an opportunity for messages to be given to pregnant women about appropriate behaviour and language. This fits in with the work cited earlier, which showed how dependent the woman is on the interpretation of the person doing the scan. Ann Oakley[142] expressed the concern that ultrasound was a further way of reducing the importance of women's own knowledge about their bodies in favour of 'objective' measures and this is echoed by examples in Mitchell

and Georges' study. This 'direct' access to the fetus and the use of images of the fetus detached from the mother's body is linked back to the individualisation of the fetus and the political conflicts that have arisen when the rights of the fetus and the woman come into conflict.[141] All these concerns have to be viewed in the light of the general popularity of ultrasound and the lack of evidence of widespread unhappiness among those who experience it. Petchesky[141] discusses these apparent dissonances in the concluding section of her article.

Conclusions

Ultrasound is very attractive to women and their partners and this may be because, unlike other forms of prenatal screening, it provides them with early visual confirmation of pregnancy and contact with their babies, in addition to reassurance about fetal well-being. These features, though, may augment the potential for feelings of anxiety, shock and disappointment when the scan shows a problem. Recent changes in the use of ultrasound may lead to more findings of uncertain clinical significance and this is likely to have important psychological and social consequences for women.

Early studies reported that some women feared that ultrasound might harm the fetus. Concerns of this type are not a feature of later research, although this may be partly because researchers have not asked about fears.

Reports of a reduction in anxiety after ultrasound examination are likely to reflect increased anxiety before the scan rather than a real benefit.

There is no reliable evidence of reduced smoking or any other positive health behaviour as a consequence of routine ultrasound.

Trials comparing ultrasound with no ultrasound have not looked at its psychological or social impact on parents and babies.

Recommendations for research

New or extended uses for pregnancy ultrasound should be evaluated in psychological and social, as well as clinical terms.

Ways of improving women's understanding of the information gained from ultrasound should be developed and evaluated.

Comparative research on the ways in which pregnancy ultrasound is carried out and experienced in different counties and cultures would be valuable.

Studies of women's views about ultrasound should report the date and place of the research and should describe the clinical contexts and purposes for which ultrasound was used for those research participants.

Implication for practice

Rapid changes in care may leave maternity staff and women behind. Better information is needed for both.

TABLE 18 *Studies included in the structured review of women's views of ultrasound*

Study	Year carried out	Methods	Country Setting Participants/sample size	Results	Comments
Allen, 1996[143]	1995	Self-administered questionnaire - no details of how or when. Women asked to select, from a list, reasons for use of ultrasound and rank them in order of importance.	UK Hospital clinics in Trent region Pregnant women, *n* = 44.	95% of women selected 'to see if the baby has any abnormality' as one of their four reasons. Half these ranked this as most important reason.	Very little detail given of methods or findings, and sample very small.
Anderson, 1995[144]	1994	Aim was to find out about women's views and knowledge in order to improve the information provided. Short self-completion questionnaire given at the clinic.	UK, West Midlands Maternity unit 50 consecutive pregnant women attending for antenatal care.	Women's answers about reasons for scan tallied fairly well with information leaflet sent out to them. They tended to underestimate ability of scan to detect problems.	Very small sample.
Baillie, 1997[115]	1995–96	Study of impact of being 'false-positive' using psychometric tests at three points in time (after amniocentesis but before result; after result; at about 34 weeks) and qualitative interview at same time as second questionnaire.	UK, Leeds Fetal assessment unit Pregnant women referred for amniocentesis because of triple test results or suspicious ultrasound scan; those with no problem detected on further testing (false-positives) formed study sample (36 after triple test and 24 after ultrasound).	Women unprepared for adverse findings from scan. Many continued to be anxious even after amniocentesis found no anomaly.	One of few studies of impact of false-positives.
Barton, *et al.,* 1989[116]	Not later than 1988	Prospective interview study with cases and controls. All scanned, with immediate feedback. All interviewed before and after scan. Topics: knowledge, views, anxiety, experience of scan.	UK Specialist centre, probably London (not stated) Cases: 24 women referred for fetal echocardiography because identified as at increased risk; controls: 26 women selected at random from antenatal clinics.	No abnormalities detected. 'High-risk' group more anxious before scan. State of anxiety lower in both groups after scan, with 'high-risk' score falling further, to same level as controls. Similar finding for attitude to baby and baby's health.	Early use of scanning to detect fetal abnormality.
Barton, *et al.,* 1989[116]	Not later than 1988	Prospective interview study, cases only. Pre-scan interview: psychological and social issues and attitudes; post-scan: experience of scan, level of information anxiety. Follow-up questionnaire at 2 weeks (by post): satisfaction.	UK Specialist centre, probably London (not stated) 48 women referred for fetal echocardiography (as above); no controls.	No abnormalities detected. State of anxiety lower after scan. Anxiety and changes in anxiety varied a great deal within this sample. Aspects of scan procedure commented on.	

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TABLE 18 contd *Studies included in the structured review of women's views of ultrasound*

Study	Year carried out	Methods	Country Setting Participants/sample size	Results	Comments
Berwick & Weinstein, 1985[145]	Not later than 1984	Focus groups with eight pregnant women who had ultrasound to discuss valued aspects of information from it. Questionnaire then developed to assess 'willingness-to-pay'. Administered by interview; analysed quantitatively.	USA, Harvard Community Health Plan 43 women currently pregnant, all 'considered normal'; 37 had ultrasound.	Authors emphasise value attached to non-decisional information. Information on health and normality of baby was valued most highly.	Method used for economic analyses. How do findings relate to real choices? Ultrasound not named in questionnaire. Scenarios describe information from unnamed test.
Black, 1992[134]	1985–88	Women approached 1 month and 6 months after pregnancy loss. Partly structured telephone interviews carried out and tape-recorded.	USA Women enrolled in national study of CVS and amniocentesis, who then had miscarriage or termination for abnormality (about half and half); 121 women took part in one or both interviews; participants relatively well-educated and affluent; gestation at pregnancy loss, 7–27 weeks; all had had scan at 7–10 weeks at entry to main study and many had had further scans.	Results presented from first interviews with 105 women. For nearly half (44%), seeing fetus at scan had made loss more difficult to cope with. Author discusses impact of scan, positive and negative, in women's own words. One woman reports her thoughts about scan image during termination. Other women also found ultrasound images helpful; e.g. in providing confirmation that fetus had died or in giving the woman something more real to grieve for.	
Boyer & Porret, 1991[138]	Not later than 1987	Semi-structured interview study carried out before women's second ultrasound at 20 weeks.	France, Grenoble Pregnant women in the course of antenatal care; *n* = 630.	77% of women said that scan had helped them to imagine baby. 43% said that they had dreamed more since scan.	Focus on psychoanalytic concerns about parents' image of fetus/baby.
Braithwaite & Economides 1997[117]	Not later than 1996	Comparison of transvaginal and transabdominal ultrasound. Women first had transabdominal scan and were then asked if they would have transvaginal scan. Then asked to complete questionnaire. Mainly looking at discomfort. Women asked to empty bladders before transvaginal scan.	UK Probably London teaching hospital (but not specified) 160 unselected 'low-risk' women attending for routine dating scan (12–13 weeks gestation).	160 had transabdominal scan, 141 had transvaginal. Women who had filled bladders reported most discomfort with transabdominal scan. Transvaginal scan associated with more reported mild discomfort than transabdominal. Women less anxious about transvaginal scan if they had had one before.	-

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TABLE 18 contd *Studies included in the structured review of women's views of ultrasound*

Study	Year carried out	Methods	Country Setting Participants/sample size	Results	Comments
Brown, 1988[146]	Not later than 1987	Quasi-experimental study. Some fathers saw image of baby, others attended visit but did not see scan. Completed range of psychological tests before and after woman's scan on anxiety, stress and attitudes to pregnancy. For those who witnessed scan, some questions on what they had seen. No information on level of feedback during scan.	USA, Los Angeles Couples attending antenatal appointment at office of three doctors in private obstetric practice 35 men saw scan; 32 did not.	Slightly greater reduction in stress scores after procedure for fathers who saw scan.	No mention of why some fathers saw scan and not others but implication is that it was the father's choice.
Brown, *et al.,* 1994[147]	1989	Questionnaire study of all aspects of maternity care. Postal survey sent out 6 months after birth.	Australia, Victoria All women giving birth in the state over fixed period; *n* = 790/1107.	Over 70% of women rated ultrasound as one of best aspects of their antenatal care.	
Cappa, *et al.,* 1987[148]	Not later than 1987	Interview study of two groups of pregnant women, one 'normal', other with 'pathological events' in first 3 months of pregnancy; studied at about first (10–16 weeks) and second (25–30 weeks) scans. All primigravida. Focus mainly qualitative.	Italy ?location ?sample size.	This was preliminary paper and suggested (authors' abstract) that women in higher-risk group needed reassurance about health of fetus. Those with normal pregnancies more interested in description of their child.	No main report found
Clement, *et al.,* 1998[87]	1993–95	Part of trial of different schedules of antenatal visits. Data came from analysis of free-text written answers to questions about best and worst aspects of antenatal care in a postal questionnaire completed at about 34 weeks of pregnancy.	UK, South-east London Three hospitals taking part in trial Analysis of data from sub-sample of 700 women who returned question-naires between December 1993 and June 1994 and who wrote something in response to at least one of the open questions.	Among best things mentioned by women about their antenatal care, ultrasound came second. Women liked seeing baby, liked confirmation that they were pregnant and were reassured that baby was well. They like involving partner and family, and having a picture.	This chapter mainly a review, with data from trial and women's comments to illustrate themes.
Colluciello, 1998[149]	Not later than 1998	Self-completion questionnaire given to women before and after ultrasound scan, during routine antenatal visit. Aim was to discover their perception of the fetus.	USA, midwest Maternal/fetal health clinics 50 pregnant women aged 19 years or younger.	Differences in perception scores before and after scan reported but no tables shown and directions of any differences not given, except that the young women had more accurate perception of babies' lie after scan.	Numbers small; data not fully presented, and significance of any changes in perceptions not discussed. Did scan have any impact on how young women relate to their babies later?

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TABLE 18 contd *Studies included in the structured review of women's views of ultrasound*

Study	Year carried out	Methods	Country Setting Participants/sample size	Results	Comments
Cox, *et al.,* 1987[110]	Not later than 1986	Women randomly assigned to high or low information during scan. Tests before and after scan to look at anxiety, etc.	Canada, Vancouver 100 women with 'low- and high-risk' pregnancies (50 in each group) 8–16 weeks.	High information groups much more likely to say they felt 'wonderful' during scan. Anxiety fell further in high information group, post scan, but only for low-risk women.	
Crang Svalenius, *et al.,* 1996[92]	Not later than 1995	Semi-structured interview just after scan, to ask about information, knowledge and choices. Every fourth woman booked for appointment asked to take part, unless fetal diagnosis carried out or previous malformed fetus/baby. Interview by one person, midwife/ultrasonographer.	Sweden Lund University Hospital 50 nulliparous; 50 parous; interviewed after routine scan (17–18 weeks gestation). Not clear whether scan for dating and/or for anomaly detection.	One-third could not recall having been told that scan could detect some types of malformation; 62% thought scan was compulsory; 95% satisfied with infomation during and after scan. 90% reported feeling better after scan than before.	Discussion raises links between prior information and reactions in women who have a problem diagnosed.
Crang-Svalenius, *et al.,* 1996[100]	1992–93	Quasi-experimental study comparing women's decisions in clinics where extra information on antenatal screening had been given to those attending control clinics. No data collected from women but their choices recorded about antenatal screening.	Sweden Antenatal clinics in catchment area of Lund University Hospital Seven clinics gave extra information to 1004 women; ten clinics (controls) had 1408 women during study period; women had to book before 10 weeks and agree to take part in intervention clinics.	No woman declined offer of an ultrasound scan but small number (1%) opted to avoid mid-trimester scan that would detect malformations and have only early, dating scan.	
Dixon, 1994[90]	Not later than 1994	Two surveys: 200 women interviewed briefly before scan by ultrasonographer to assess knowledge of purpose of scan. 100 women given information sheet at booking then interviewed before scan in same way as first group.	UK, Leeds St James's Hospital 200 consecutive pregnant women attending routine 18-week scan performed for dating placental site, soft markers, structural abnormalities; 100 women attending scan who had been given an information sheet at booking.	Emphasises how few women aware of possibility that scan would show pregnancies with increased risk of Down's syndrome.	Highlights need for women to be aware of purpose of scan. One of few papers that state explicitly what scan is for in that setting.
Draper, *et al.,* 1984[102]	1983	Questionnaire and interview prospective study of antenatal care. Questionnaires at 24 weeks, 37 weeks and after birth. Different aspects of ultrasound covered in questionnaires.	UK, Cambridge Hospital and community antenatal clinic Unselected pregnant women, *n* = 170.	Over 2/3 of women reported only enjoyable aspects of scan and only 4% reported only worrying aspects. Enjoyable aspects were about seeing and feeling baby and reassurance. Worries were about effect on baby, and on concerns that followed from scan.	Comments on way scan was done useful.

continued

TABLE 18 contd *Studies included in the structured review of women's views of ultrasound*

Study	Year carried out	Methods	Country Setting Participants/sample size	Results	Comments
Eurenius, *et al.*, 1996;[93] 1997[94]	1991	Questionnaires given to each woman and her partner. One before scan (while waiting) and one to be filled in after (at home) and sent back. Questions included knowledge of purpose of scan, desire for information, smoking plans.	Sweden Uppsala University 393 unselected, consecutive women and their partners coming for mid-trimester scan; exclusion, no Swedish language; part 1 completed by 299 women and 255 men; part 2 by 271 women and 228 men.	1996 paper deals with smoking and ultrasound; found that scan did not seem to have effect on proportion of men or women who thought that their ability to stop smoking was better than 50%. 1997 paper gives details of views about purpose of scan and their expectations, including some differences between women's and men's views. Anxieties before scan related to baby's health and possible malformations. Only 2% of women feared that scan might harm baby. Feelings about scan far more positive than negative for both women and men, when series of adjectives offered.	
Field, *et al.*, 1985[150]	Not later than 1984	Women randomly assigned to low or high feedback group (n = 20 per group). Ultrasound took place on three occasions in pregnancy. Assessed after each scan with psychological tests, a fetal activity schedule to complete at home for a half-hour period for 5 nights, and a record of sleep and dreams. Follow-up within 2 days of birth to look at infant behaviour.	USA (presumed but not specified) 40 pregnant women referred for ultrasound assessment of gestational age.	All results are presented as means, split between first-time mothers and others. Authors conclude that birthweight and Brazelton scores better for babies of first-time mothers in high feedback group, but very small numbers and large standard deviations make this less than convincing.	
Fleeman & Dawson, 1995[151]	1994	Postal questionnaire study of all aspects of maternity care 7–8 weeks after birth.	UK Liverpool Health Authority Women resident in area who had given birth during a fixed period; n = 526/701 sent out.	In response to questions about information needs, 35–40% of women said they had wanted more information either before, during or after scan; 96% reported that scan had been pleasant experience.	
Garel & Franc, 1980[112]	1978–79	Ultrasound examinations observed and then women interviewed. Results of analysis of observation data reported.	France, Paris Large maternity hospital 75 women; data used here refer only to 54 first-time mothers; scans routine at third and sixth month of pregnancy.	Woman experiences scan 'through' doctor, who explains and interprets image. Reactions are varied and complex.	

continued

TABLE 18 contd *Studies included in the structured review of women's views of ultrasound*

Study	Year carried out	Methods	Country Setting Participants/sample size	Results	Comments
Georges, 1996[113]	1990–91	Observation and interview study of antenatal care including ultrasound examinations.	Greece Public hospital in a small city Formal interviews with 26 women in 3 days after delivery; additional observation in a teaching hospital in Athens.	Results of this descriptive study are difficult to summarise but it illustrates way that ultrasound is used in different contexts and role it plays in doctor–woman relationship.	
Harrington, *et al.*, 1996[152]	Not later than 1996	Questionnaire study, completed by sonographer just before scan, to find out whether woman wanted to know fetal gender.	UK One (or more?) London hospitals Women attending for routine 20-week anomaly scan; 472 took part.	75% of women wanted to know fetal gender. It was determined in 89% of fetuses. In 3%, gender was incorrectly determined.	
Heidrich & Cranley, 1989[153]	Not later than 1988	Assessment of maternal–fetal attachment before and after a scan or amniocentesis. Control group had no intervention. Data collection at (mean) 16 weeks and (mean) 20 weeks, using two psychometric scales.	USA, place and setting not specified 91 pregnant, mid-trimester women; 2/3 multiple pregnancies; 19 had amniocentesis, 37 had ultrasound, 35 neither.	Women who reported feeling fetal movements scored higher on attachment scale but direction of causation, if any, is not clear. No suggestion that attachment increased more between two assessments in ultrasound group.	Small numbers in subgroups. Not a trial so findings difficult to interpret.
Huffman & Sandalowski1 997[154]	Not later than 1996	Observation and interview study of staff approaches to ultrasound. Ethnographic study with very small sample.	USA (presumed, not specified) Obstetric department of large teaching hospital; three nurses, one doctor, two technicians.	Describes different styles of individual care given during scan.	
Hunfeld, *et al.*, 1993[131]	1990–91	Reactions to severe malformations diagnosed by ultrasound. In-depth study with interviews 2–6 weeks after diagnosis and then 3 months after birth.	The Netherlands, Rotterdam Dijkzigt University Hospital 46 women with diagnosis of severe/lethal malformation; by second interview all but five babies had died.	Results are about grief and not about use of ultrasound to diagnose malformation.	
Hyde, 1986[118]	1984	Interviews carried out in hospital while women waiting for scan (Hospital R) or for antenatal check (Hospital S).	UK, Manchester Two hospitals, 'R' and 'S' At R, scan at 16 weeks routine, at S, scan only for clinical indications R, 97 women; S, 307 women; all pregnant, no indication of gestation; 78% had had a scan already either in this or previous pregnancy.	Women's views about ultrasound varied between two hospitals and seemed to reflect way that ultrasound had been presented to them. Some women unhappy about level of feedback during scan.	Discussion raises issue of how findings should be explained to women and by whom.

continued

TABLE 18 contd *Studies included in the structured review of women's views of ultrasound*

Study	Year carried out	Methods	Country Setting Participants/sample size	Results	Comments
Janus & Janus, 1980[155]	1979	Individuals given questionnaires before and after ultrasound.	USA, NY, Mount Sinai Hospital All patients having pelvic/abdominal ultrasound (important: not just pregnant women); *n* = 204 (134 female), number pregnant not given.	Generally, patients poorly informed about purpose of scan and way that ultrasound works. 90% of pregnant women commented favourably on experience.	Includes non-obstetric ultrasound.
Jörgensen, *et al.,* 1985[129]	1984	Interviews carried out either at home or in department of obstetrics. Semi-structured. Exploring diagnosis of severe malformation, decision to have abortion and feelings since.	Sweden University Hospital Lund Women who had had termination following diagnosis of major fetal malformation following routine scan at 17 weeks; 10 women, 6–34 months after termination.	Discussion of difficult decision to have termination and reactions felt afterwards, including fears that women had in some way caused malformation. Five women had some reason to suspect problem in pregnancy and five did not. Study did not find any difference in reported reactions to diagnosis.	Findings relating to specific features of ultrasound not given. For example, it would have been useful (for this review) to have details of women's experiences of scan and being told about the malformation.
Jörgensen, *et al.,* 1985[130]	1984	Semi-structured interviews either at home or in department of obstetrics about pregnancy after having a malformation seen on ultrasound.	Sweden University Hospital Lund Women who had had fetal malformation diagnosed late in pregnancy at routine 32-week scan; 14 women, 7–39 months after birth of baby; all babies alive and half judged to be healthy at time of follow-up.	Three women were not told about malformation during pregnancy and who suspected that something was wrong were upset at time of interview about not being told. Women reported that remainder of pregnancy was great strain. Some had imagined very severe malformation and experienced some relief after birth.	Study deals with type of consequences that can also arise from other methods of identifying fetal anomalies.
Jørgensen, 1995[156]	1988–89	Self-completion questionnaires handed out to be filled in then or returned by post either at 30 weeks (those accepting alpha-fetoprotein screening) or approx. 16–18 weeks (those, approximately 10%, who declined it. Questions about routine offer of amnio-centesis/CVS and ultra-sound.	Denmark, Sønderjylland Catchment area of Hvidovre Hospital All pregnant women over 18 years; *n* = 4553; 3667 analysed (81%)	Women who had declined alpha fetoprotein test less favourable towards routine offer of ultrasound for detecting malformation. Where ultrasound already routine, more women supported routine use. Women more likely to say that they would accept screening than to recommend its routine offer.	
Julien-Reynier, *et al.,* 1994[95]	1990	Telephone interviews, mainly closed questions, ?in first few days/weeks after birth, to ask reasons for use of ultrasound and what it can do.	France, Bouches-du-Rhone Representative sample of French-speaking women who had normal live-born baby; 644 approached, 514 interviewed.	93% said that mid-trimester ultrasound was to see if baby was normal. Only a small proportion (9%) thought that one could be sure that baby would be normal if no abnorm-alities seen with ultrasound. These women more likely to have lower education level.	

continued

TABLE 18 contd *Studies included in the structured review of women's views of ultrasound*

Study	Year carried out	Methods	Country Setting Participants/sample size	Results	Comments
Kohn, *et al.*, 1980[157]	1978	Self-completion questionnaires pre- and post scan about views of baby. Scan was seen by the women and explained with opportunity for discussion. Includes comments from authors about women's questions during scan and reactions of a few women in longer term.	USA Pennsylvania Hospital. Women referred for obstetric ultrasound who had never seen scan or X-ray image in this or any earlier pregnancy. Possible fetal death was reason for exclusion from study.	Questionnaires reprinted with numbers of responses for each item. Some changes are apparent after scan, e.g. in descriptions of fetus as active and perception of space for fetus. Women particularly interested in seeing movement and reported that seeing heart beating was important to them. A few said that they were worried in case seeing fetus made it more difficult if something went wrong. Authors report on three women who they considered showed better attachment to baby after scan. All but four women said that they enjoyed seeing baby.	This early study responded to new technology that provided real-time images. It recorded only immediate reactions to scan. Though authors careful in their conclusions, work has been taken to show an impact of scanning on attachment more generally.
Kovacevik, 1993[158]	Not later than 1992	Quasi-random? 146 high feedback, 150 low feedback; gave a 4-way split by risk status and feedback. Psychological test pre- and post-scan. Fathers also included.	Croatia, Zagreb Primigravid, referred for ultrasound; *n* = 296; at-risk, *n* = 150; no risk, *n* = 146.	Anxiety and stress fell after scan, as in other studies. Not clear whether high feedback associated with sharper falls in anxiety, etc.	
Krubel, 1996[159]	Not later than 1996	Comparison of women having and not having transvaginal ultrasound. Telephone interviews to assess views and satisfaction.	USA, San Diego Large health maintenance organisation Pregnant women attending emergency room with vaginal bleeding: 44 had trans-vaginal ultrasound, 52 did not; respondents 33/44 and 26/52.	Women who had transvaginal ultrasound more satisfied with their care than those who did not.	What care did controls get? When did phone interviews take place? What was subsequent management?
Langer, *et al.*, 1988;[160] Ringler, *et al.*, 1985;[161] Fischl, *et al.*, 1983[162]	Not later than 1985	Given questionnaires before and after scan to assess views of fetus and pregnancy.	Austria University of Vienna Women at 12–20 weeks gestation, scanned for first time this pregnancy and before fetal movements felt; *n* = 60.	There were changes in some of ways in which the fetus described. After scan, fetus more likely to be described as active.	
Layng, 1998[91]	Not later than 1998	Postal questionnaire to ask about preparation for ultrasound test and knowledge of Down's syndrome.	UK, Berkshire 96 women within (?) one general practice who had recently had ultrasound scan to look at NT; 68 replied.	42/68 women replied that they felt they had not been adequately prepared for test. 24/62 rated their knowledge of Down's syndrome as 3 or less on scale of 1–10.	Small local study, but little work available so far on use of ultrasound for Down's screening. Report is brief.

continued

TABLE 18 contd *Studies included in the structured review of women's views of ultrasound*

Study	Year carried out	Methods	Country Setting Participants/sample size	Results	Comments
Lydon & Dunkel-Schetter, 1994[163]	Not later than 1991	Interviews on commitment to baby at four time points: 1 and 2, immediately before and after ultra-sound and amnio-centesis; 3, by telephone 7–10 days later; 4, by telephone 2–7 days after result.	Place not specified but probably North America 41 women, all having an amniocentesis on grounds of maternal age; 14–20 weeks; amniocentesis preceded by scan, no abnormalities detected.	Number of fetal body parts reported by woman as having been seen at ultrasound is said to be predictive of woman's expressed commitment at first telephone interview.	
Michaelacci, *et al.,* 1988[164]	Not later than 1988	Series of psychological tests before and after each scan.	Italy, Bologna 20 'low-risk' pregnant women having three scans, one in each trimester, same obstetrician.	Anxiety fell after each scan. Pre-scan anxiety rather similar for each trimester.	
Milne & Rich, 1981[106]	Not later than 1981	Study using observation and interview. Women were accompanied by researcher from period before scan, during and after. 16/20 were inter-viewed afterwards.	USA, north-east Large university hospital 20 women, 20–35 weeks pregnant; first experience of real-time scanning; aim of scan was dating.	Detailed and illuminating data about how scans done and how women reacted. Women concerned that this novel procedure could harm their baby and might be painful. Women's pleasure at recognition of baby's shape or movement described.	An early study (probably carried out before 1981).
Mitchell & Georges, 1998[114]	Not later than 1993	Observation of scans, 'conversations' with care-givers and interviews with 49 women (and some partners).	Canada Place not specified Pregnant women expecting first baby and labelled as 'low risk'. *n* = 49.	Results of this qualitative study difficult to summarise but touch on views of sonographers about women from different ethnic backgrounds. Descriptions given of way scan is 'interpreted' for parents, and way staff could be said to use scan to put across messages about appropriate behaviour.	This chapter also compares Mitchell's findings with those of Georges (see entry in this table).
Oakley, 1997[103]	1994–95	Semi-structured interviews mainly at home, following scan.	New Zealand, Dunedin 41 pregnant women, 15–42 weeks; all had received scan but unclear as to main purpose; volunteer sample.	Most thought they had had scan because it was routine. Information given during scan varied a lot. Confusion over post-scan 'results' for some women. Impact of uncertain or 'worrying' scan results, and 'false-positives'.	Some of the verbatim accounts and detailed comments in this thesis are very useful.

continued

TABLE 18 contd *Studies included in the structured review of women's views of ultrasound*

Study	Year carried out	Methods	Country Setting Participants/sample size	Results	Comments
Puddifoot & Johnson, 1999[135] Johnson & Puddifoot, 1998[136]	Not later than 1998	Study of male partners of women who had miscarried, using self-completion questionnaires and psychological scales, within 8 weeks of miscarriage. Two reports of same study.	England Men referred through health services in NE England and West Midlands All partners of women who had miscarried before 25 weeks of pregnancy *n* = 323;[135] *n* = 158[136]	Men reported levels of grief comparable with those in studies of women. First paper reports higher grief scores in men who had seen fetus at scan. Second paper reports that vividness of men's reported imagery about fetus positively associated with whether they had seen scan and, to lesser extent, whether they had planned to see scan. Those who had neither seen one nor planned to had lowest scores.	Taken together, two reports could suggest that seeing scan images may affect way that fetus is imagined and may influence grief after loss. Alternatively, it may be that men's pre-disposition towards baby affects both choice to go to scan and grief. All these must be very tentative because of effect of collecting data retrospectively.
Reading, 1983;[169] Reading & Cox, 1982;[166] Reading, *et al.,* 1981;[133] 1982;[165,168] 1984;[167] 1988;[170] Campbell, *et al.,* 1982[111]	Not later than 1981	Women randomly allocated to either 'high feedback' (*n* = 67) or 'low feedback' (*n* = 62) group. Anxiety and other measures pre- and post-scan. Then again with further scans at 16, 32 weeks, just after birth and at 3 months post birth. High feedback meant seeing screen and having image explained.	UK, London King's College Hospital 'Obstetrically normal' first-time mothers, 10–14 weeks pregnant at entry to study: *n* = 129.	High feedback group more positive about scan immediately afterwards. No differential impact found on anxiety. No longer-term effects found except that women in high feedback group were most likely to rate that first scan as most important for them.	Longitudinal element of study has also been used to look at change over time regardless of allocated group.
Reading & Platt, 1985[171]	Not later than 1984	Women randomly allocated to one of four groups: high feedback ultrasound (*n* = 11); low feedback ultrasound (*n* = 8); fetal heart rate monitoring (*n* = 11); control group who viewed video of an ultrasound of a fetus that they knew was not their own (*n* = 7). Psychological assessment before and after procedure.	USA, Los Angeles Women at 'high risk' in third trimester.	Very small numbers, and lack of detail about trial procedures and comparability, make it difficult to know what to make of this study. Anxiety fell for all women after test but appeared to fall more sharply for women in high feedback ultrasound group.	
Roberts, 1986[119,120]	1983–84	Women wrote in response to a short questionnaire published in magazine asking basic questions about experience of ultrasound.	UK Readers of *New Generation*, magazine of National Childbirth Trust. Volunteer sample, *n* = 142.	Importance of how, when, and by whom, results were discussed. Also discomfort and lack of reassurance during scan.	

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TABLE 18 contd *Studies included in the structured review of women's views of ultrasound*

Study	Year carried out	Methods	Country Setting Participants/sample size	Results	Comments
Sandelowski 1994[104,105]	1987–93	Interviews at several points during pregnancy. Study designed to look at transition to parenthood, with focus on infertility.	USA (place not specified) 62 childbearing couples, 42 of whom had been infertile. All had had at least one ultrasound scan.	Contrasting reactions to ultrasound and amniocentesis (experienced by a subset). Men's views about ultrasound and women's views about their partner's reactions. Photos and videos: ultrasound as a 'first meeting with the baby'.	Data about use of ultrasound not gathered deliberately.
Santalahti, *et al.*, 1996;[172] 1998;[96]	1993–94	Self-completion questionnaire on knowledge and views of prenatal screening, including ultrasound, handed out at clinic visits. Two separate surveys (a) and (b). Not clear whether identical questionnaire used for each survey.	Finland (a) Ultrasound survey Pregnant women from town of Turku attending for antenatal care; 497 offered questionnaires; 424 returned. Almost all between 15 and 22 weeks pregnancy; all but five had had scan. (b) Serum screening survey 1035 pregnant women from towns of Jyvaskyla and Kuopio attending antenatal care offered questionnaire; 909 returned.	Findings cover knowledge of tests and views about what they can detect. Education level linked to knowledge. Women less aware of potential for ultrasound to detect abnormalities.	
Skov, 1991[173]	1988	Survey of whether ultrasound should be available routinely in Denmark.	Denmark, Kolding Hospital 220 pregnant women.	93% of respondents supported routine offer of ultrasound to all pregnant women (from author's abstract).	
Smith & Marteau, 1995[97]	Not later than 1994	Observation study of routine antenatal visits to look at how serum screening and fetal anomaly scanning are mentioned/explained to women.	UK 6 hospitals 215 women, 28 midwives, 9 obstetricians; women either seeing midwife at booking (10–12 weeks) or an obstetrician at 16 weeks.	Information about serum screening given more often than information about fetal anomaly scanning. Purpose of anomaly scanning less likely to be mentioned. Information about meaning of results and possible errors very rarely given.	An important part of picture of women's knowledge and choices.
Sommerseth, 1993[174]	1990	Questionnaire survey about information given to women in relation to routine scan at about 17 weeks of pregnancy.	Norway National representative sample of pregnant women; *n* = 891.	Just over half the respondents said that they had been given no information about scan. Substantial number thought that scan compulsory. Author argues for better information for women (from abstract).	

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TABLE 18 contd *Studies included in the structured review of women's views of ultrasound*

Study	Year carried out	Methods	Country Setting Participants/sample size	Results	Comments
Sparling, *et al.,* 1988[175]	Not later than 1988	Women approached when attending for ultrasound between 20 and 32 weeks. Psychological and other questionnaires completed. Ultrasound session observed. Further contacts with women in later pregnancy, just after birth and 3 months after. Interviews and observation of parent/child interaction carried out.	USA, North Carolina 108 pregnant women referred for ultrasound (? 'high-risk'); final sample was 80 in three-risk strata, on basis of first ultra-sound (impaired, 16, questionable, 31, normal, 33).	Differences between three 'risk' groups not detected in scores on anxiety, depression and hostility (but numbers are very small). No differences in mother–child interaction detected.	
Teichman, *et al.,* 1991[176]	Not later than 1990	Intervention appears to involve giving or withholding information on gender of fetus. Not clear how randomisation worked since it appears that there were three groups; 100 given information on fetal gender; 41 not given information; 56 who said in advance they would not want it. Anxiety and depression assessed 10–14 days before scan, just after scan and after birth.	Israel Primigravid 'low risk'; no previous ultrasound; (25–27 weeks); *n* = 197; all had a scan.	Anxiety (for all 197 women) higher after scan than before, and higher still just after birth.	
Thornton, *et al.,* 1995[101]	1991–94	RCT assessing impact of extra information on prenatal tests, uptake of tests, and anxiety, satisfaction and understanding. Three groups: (i) control; (ii) extra information given individually; (iii) extra information given in a class. Postal question-naires at 16–18 weeks, 20 weeks, 34 weeks and 6 weeks post birth.	UK, Leeds and Bradford 1691 women booking for antenatal care before 15 weeks.	Intervention did not affect uptake of ultrasound or serum screening for Down's syndrome, but lower uptake of screening for cystic fibrosis. Anxiety lower in group offered individual information (at 20 and 34 weeks). 99% of women took up offer of ultrasound.	
Thorpe, *et al.,* 1993[177]	Not later than 1993	Qualitative interview study exploring women's reactions to pregnancy ultrasound and to cerebral ultrasound for their newborn	UK (assumed Bristol) 42 mothers, approached for consent for cerebral ultrasound scan on their new baby (not because of any risk factor or indication); 30/42 agreed to baby having scan; all but three mothers had had pregnancy ultrasound.	Many women voiced concern about safety of cerebral ultra-sound for their new baby. Pregnancy ultrasound categorised by some women as being about reassurance and confirmation of normality. Women's comments also highlighted emotional appeal of pregnancy ultrasound.	

continued

TABLE 18 contd *Studies included in the structured review of women's views of ultrasound*

Study	Year carried out	Methods	Country Setting Participants/sample size	Results	Comments
Tourette & Bouhard, 1986[137]	Not later than 1985	Questionnaire administrator not clear. Covered experience of ultrasound, knowledge of purpose, reactions to scan, information, was partner there, etc.	France (place unspecified) 85 women at different gestations, 25 before ultrasound, 60 after; 31 locations, hospital, private clinic of woman's obstetrician, at a radiologist's clinic.	Women generally well-informed about purposes of ultrasound. Some aspects of scan and communication with staff caused concern.	
Tsoi & Hunter, 1987;[109] Tsoi, *et al.,* 1987;[108] Hunter, *et al.,* 1987[107]	Not later than 1985	Pre- and post scan interviews: anxiety; attitude to pregnancy. Then postal questionnaire 4 weeks after scan.	UK, London King's College Hospital 30 pregnant women with raised alpha-fetoprotein for ultrasound 30 pregnant women 'controls' for routine ultrasound.	Alpha-fetoprotein group more anxious before scan. Anxiety fell for both groups after scan (no differences then, or at follow-up). Women in both groups reacted very positively to scan. Some wanted more information during and after scan.	One-third of women dropped out between post-scan and follow-up assessments, so this may undermine reported finding of rise in anxiety in both groups at follow-up.
Tymstra, *et al.,* 1991[178]	Not later than 1985	Women offered four scenarios in postal questionnaire. These covered: amniocentesis and CVS; ultrasound for treatable abnormalities; ultrasound for untreatable abnormalities; serum alpha-fetoprotein. Asked whether screening options should be offered to all women in The Netherlands and whether they would take up such an offer.	The Netherlands University Hospital Groningen 185 women, 'a few months' post delivery; all had had first baby; 127 returned questionnaires.	Women most positive about use of ultrasound for detecting treatable abnormalities but even for CVS/amniocentesis 36% said they would definitely wish for it during their next pregnancy, if offered.	
Valbo & Blaas, 1991[179]	1989	Alternate allocation trial of extra information on routine ultrasound. Women completed questionnaire after scan.	Norway, place not clear 655 pregnant women.	Results difficult to interpret because some women excluded from analysis. Women who received extra written information seemed more satisfied with information than those who did not. Women very positive about scan and about information received during it.	
Villeneuve, *et al.,* 1988[139]	Not later than 1987	Direct observation (not reported here). Interviews with pregnant women and partners. Some seen more than once. Questionnaire distributed to women and men in clinic on selected days over 3-week period and returned by post.	Canada, Montreal Women and partners attending for antenatal care. Questionnaires returned by: 154/207 women and 64/90 men	Problems with seeing image of baby reported. Women said what they liked best about seeing image of baby. Fathers as positive as mothers about scan.	

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TABLE 18 contd *Studies included in the structured review of women's views of ultrasound*

Study	Year carried out	Methods	Country Setting Participants/sample size	Results	Comments
Wu & Eichmann, 1988[180]	Not later than 1988	Questionnaires at 18 weeks and again at 37 weeks. Self-completion, attachment scales. Also (?) telephone interview at about same time (37 weeks).	USA (assumed) No place specifies 57 couples, recruited at 18-week ultrasound clinic; then 34-week scan where those who asked were told fetal gender.	Attachment scores lower (but what counts as low?) in parents who knew fetal gender, compared with those who did not, but their scores already lower before being told fetal gender.	
Zlotogorski*et al.*, 1995;[181] 1996[182]	Not later than 1994	Women completed psychological questionnaire and then randomly assigned to either high (*n* = ?) or low feedback (*n* = ?); 182/211 reported in results but not clear if missing 29 allocated or not.	Israel Shaare Zedek Medical Centre *n* = 211; (4–41 weeks pregnant).	Authors conclude that feedback level did not affect anxiety. Women in both areas less anxious after the scan. Conclusions about effect of feedback limited by lack of information on randomisation and likelihood that some women were excluded after randomisation.	

Chapter 7

Introduction to costs and cost-effectiveness of ultrasound in pregnancy

The RCOG Working Party on Ultrasound Screening for Fetal Abnormalities (1997)[5] was set up in 1995, in response to concerns raised by purchasers, professionals in the speciality and, occasionally, patients about the justification for routine ultra-sound screening for fetal anomalies and the number of scans. Little real evidence exists but anecdotal evidence suggests that the package of antenatal screening varies widely depending on the area of the country, health authority or antenatal clinic providing the care. For most women, the antenatal package will consist of at least one ultrasound scan.[1] However, there is no consistent policy in hospitals or among clinicians regarding either the optimal number of scans or when during pregnancy the scans should be carried out.

A preliminary review of the economic evidence for routine ultrasound screening,[183] was used to construct a decision analytical model. This presented the possible permutations and clinical pathways for screening programmes to illustrate the wide range of uncertainty surrounding the comparative cost-effectiveness of various ultra-sound screening options for the detection of fetal anomalies. It was not possible to select any single programme as a clear choice for NHS purchasers, because of the uncertainty illustrated by the wide overlapping ranges and the unknown factors that had to be excluded in the initial model. However, it was demonstrated by the analysis that a large amount of resources are used in routine ultra-sound screening and it was recommended that more robust evidence should be sought, which would allow areas of uncertainty in the model to be resolved.

In this report, the current evidence relating to the cost-effectiveness of different strategies for routine ultrasound in pregnancy in the NHS is presented in three parts.

1. The evidence available from existing research and systematic reviews is assessed and estimates of costs and cost-effectiveness of different aspects of ultrasound are described in chapter 8.
2. A primary study of costs of routine ultrasound scanning and its immediate cost consequences in one NHS Trust is presented in chapter 9.
3. A decision model of the cost-effectiveness of scanning for fetal anomalies in pregnancy is refined and updated, using data from the previous two chapters. Ranges of cost-effectiveness of alternative policies based on this model and existing data and the associated incremental cost-effectiveness ratios are assessed in chapter 10.
4. Finally, the evidence for cost-effectiveness of other aspects of ultrasound considered in chapters 8–10 is discussed in chapter 11.

Chapter 8

Systematic review of cost and cost-effectiveness studies

Introduction

Systematic reviewing and meta-analysis of clinical studies, particularly of RCTs, is a well-established research method. However, economic and cost studies are only beginning to be considered in this way.[184] In her thesis, Mugford[185] reviewed costs and economic studies of neonatal care and care in labour. A systematic review of costs and economic studies of antenatal care has also been carried out using the same methodology.[186]

Previous work also carried out by members of the project team includes a preliminary review of the economic evidence relating to ultrasound in pregnancy, from which it was concluded that there was very little good data on costs or effectiveness.[183]

The objective of this section of the project was to review the costs and cost-effectiveness of routine ultrasound screening in pregnancy based on systematic review of the literature. The aim was to include all information relating to costs of all aspects of routine ultrasound in pregnancy.

Methods

Inclusion criteria

To be included in this study, reports had to meet the following criteria.

Participants: pregnant women undergoing routine antenatal care.
Interventions: primary ultrasound, secondary screening as appropriate.
Studies: formal economic evaluations, cost studies. Cost studies include studies reporting primary research on the costs and utilisation of care, and studies that discuss economic aspects of care and contain useful primary or secondary cost or utilisation data.

The 'cost-generating' events or knock-on costs influenced by ultrasound screening were also considered. These include: further tests/outpatient visits/other changes in management of pregnancy/delivery/changes in neonatal management/post-natal care for women.

Studies were identified using the search strategy described in appendix 8. Material was managed using a Procite database and covered 1984–98.

Selection of papers for review

Stage 1 – initial categorisation of studies

Each study was categorised independently by two investigators (JH, TR) on the basis of its title, Medical Subject Heading (MeSH) and abstract, when available. Each reviewer was blind to the categorising decision of the other throughout the study. Discussion and consensus resolved any differences.

The following initial criteria were used to determine the relevance of each study to the systematic review.

A. Primary research is reported on the costs or utilisation of care and formal economic evaluation included.
B. Economic aspects of care discussed and useful primary or secondary cost or utilisation data included.
C. Contains useful information but does not obviously fall into categories A or B.
D. Economic aspects of policies for care are discussed but study is in neither category A nor B.
E. Study does not have any relevance to the economic evaluation of ultrasound.

Studies in categories A, B and C were considered relevant to the systematic review. Those in categories D and E were not considered further.

Studies were coded as C when there was insufficient information in the title, MeSH or abstract to be certain of its relevance to the review. For pragmatic reasons, a decision rule was designed to approach this issue. A random sample of 25% of category C documents were retrieved and reviewed in full. If 20% of these were considered useful, the remaining 75% were to be retrieved, reviewed in full and included in

the review. However, if less than 20% were subsequently deemed useful then the remaining 75% would be rejected from the review.

Studies that were considered to relate to other sections of this review, such as the clinical section (chapters 2–5), or the women's views section (chapter 6) were passed to the appropriate reviewers. Similarly, the reviewers of the clinical and women's views sections passed on any papers of potential relevance to the economics reviewers.

Stage II–further categorisation of studies

All studies in categories A, B (or C) were further classified after reading the full paper into the categories below by type of study.

1. Economic evaluation (cost-minimisation analysis, cost-effectiveness analysis, cost–utility analysis, cost–benefit analysis)
2. Other cost study
3. Effectiveness study with some assessment of implications for cost or quantity of resources used
4. Description of methods used in aspects of economic evaluation of ultrasound screening
5. Review of economic aspects of care
6. Other, such as, survey of resources and facilities, survey of utilisation, estimate of economic burden of disease, discussion of health finance or policy
7. Not relevant to the economic evaluation of antenatal ultrasound screening
8. Foreign language: to be reviewed by relevant linguist

All studies classified as A(1), A(2), B(1), B(2), C(1), or C(2) were included in the quality assessment section of the review. Some studies classified as A(3) and B(3) were also included. Foreign language papers were included if relevant. All other papers and studies that did not fall into one of the above categories were rejected.

Stage III – quality criteria

The quality of the economic evaluations was assessed according to the criteria used in a review of economic studies of antenatal care.[186] The criteria listed below were short-listed from 35 criteria in the *BMJ* checklist for economic evaluations.[187]

The eight criteria shortlisted from the *BMJ* check list of 35 were decided by discussion and consensus between the three economists in the review group (TR, JH, MM). These criteria were agreed by the group to be 'hanging offences' on the basis that, if any of these eight criteria were not fulfilled, the data available for extraction would be useless for this review. For example, if a paper under review did not present currency and price information then it risked misrepresentation and might dilute the quality of the other collected data when pooled. Other *BMJ* criteria not included in the shortlist were, for example, questions regarding sensitivity analysis. While the authors regard sensitivity analysis as an extremely important aspect of economic evaluation, it was considered that the baseline data presented in a reviewed study would be appropriate for extraction since it would be pooled and subjected to our own sensitivity analysis.

Economic evaluation quality criteria for papers coded A(1), B(1), or C(1) were as follows:

- the research question is stated/implied or apparent (provision of comparative options)
- the viewpoints(s) of the analysis are stated/implied
- the source(s) of effectiveness estimates used are stated/implied or apparent
- the primary outcome measure(s) are stated/implied or apparent
- quantities of resources are reported separately from their unit costs or can be derived
- both currency and price data are recorded
- details of currency or price adjustments for inflation or currency conversion are given (if appropriate)
- the discount rate is stated/apparent and justified (if relevant).

Cost study quality criteria for papers classified A(2), B(2), C(2) and, in certain cases, A(3) or B(3), were:

- methods for the estimation of quantities and unit costs are described (or cited)
- sources of cost data are stated/apparent
- indirect costs (if included) are reported separately from direct costs
- both currency and price data are recorded
- details of currency or price adjustments for inflation or currency conversion are given (if appropriate)
- the discount rate is stated/apparent and justified (if relevant).

If the studies fulfilled all the necessary criteria they were considered for data extraction in Stage IV. Some studies that just missed fulfilling all the quality criteria, but which, nevertheless, contained information that might be relevant and might be the only such available data, were not rejected but were marked with a query (?).

Stage IV – data extraction

An example of a data extraction sheet is presented in appendix 9. Data were extracted then converted from their respective currencies to £ (sterling) using purchasing power parities published by the Organization for Economic Cooperation and Development.[188] Once converted to £ (sterling), the cost data were inflated to 1997 prices using the NHS Executive Hospital and Community Health Services Pay and Prices inflation index.

Results

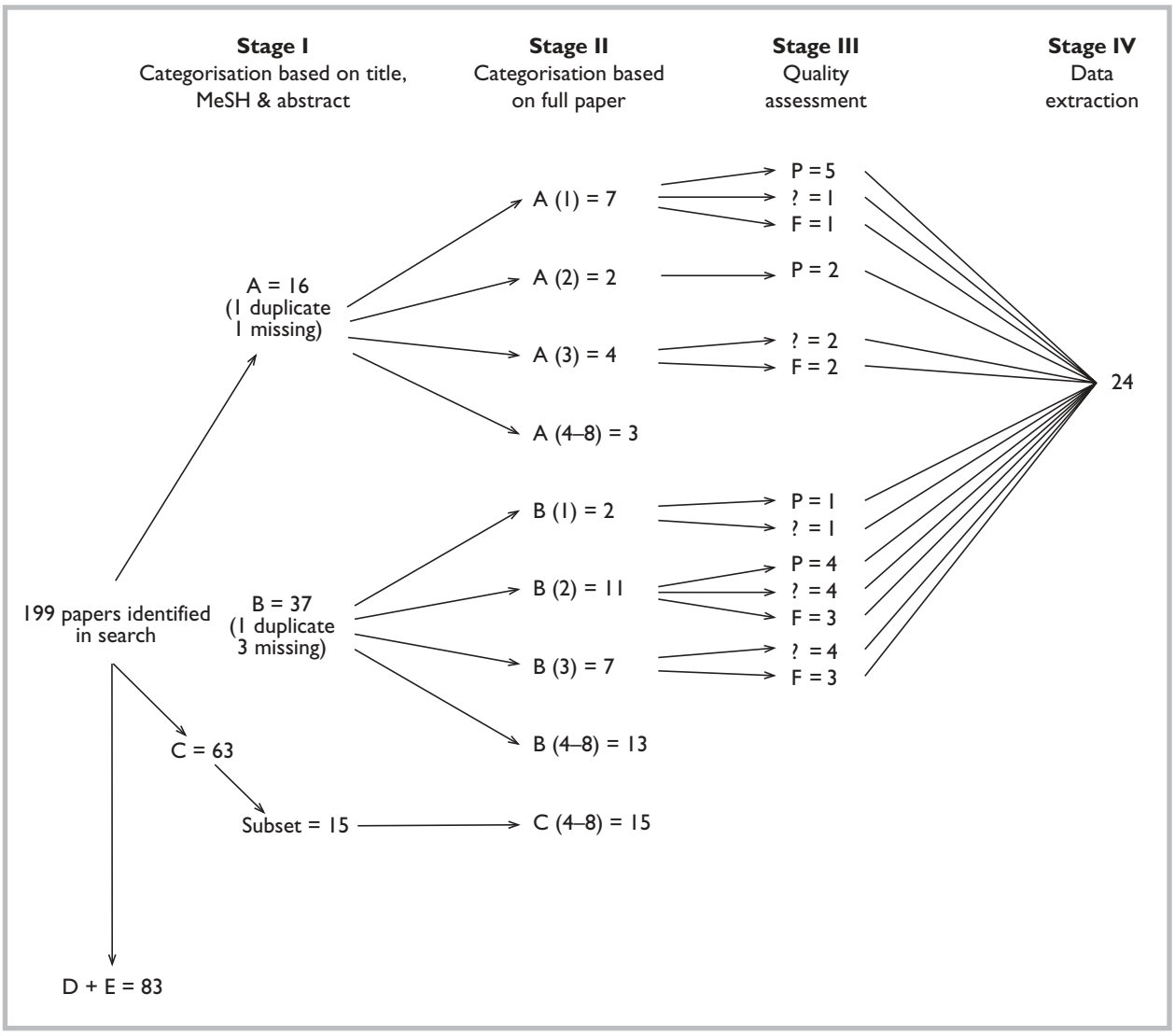
Stages I, II and III

A total of 188 papers were identified by the literature search. Two economic reviewers (TR, JH) reviewed their titles, MeSH and abstracts independently. The initial and subsequent classifications of these studies, together with the result of the quality assessment, are shown in *Figure 1*. Four papers could not be retrieved and two that were reviewed in full turned out to be duplicate publications. A random sample (25%; $n = 15$) of those in category C were retrieved according to the decision rule and reviewed in full. None of these studies were subsequently classified as C(1) or C(2). Consequently, no studies classified as category C were considered further in the review. An additional 11 papers were retrieved as a result of following-up relevant references in reviewed papers.

The two reviewers agreed on the quality of 77% of the papers. The final categorisation of the 23% of papers on which the reviewers disagreed was reached by consensus. Agreement was tested using the kappa statistic; this was 0.68, which has a z value of 3.62, showing highly statistically significant agreement between reviewers ($p < 0.01$).

At the end of stage III, 24 papers were considered for data extraction (stage IV). Nine of these were

Figure 1 *Flow chart of various stages in review showing numbers of papers at each stage (P = pass; F = fail)*



economic evaluations (two of which had initially been coded as cost studies); the other 15 papers reported cost studies or effectiveness studies with some assessment of costs. Of the 24 papers, 12 passed the quality checklist and 12 were of slightly dubious quality, but were included when they reported the only data available on a particular topic. Details of the nine economic evaluations are presented in *Table 19*.[183,189–196] Data were extracted from six papers but the data from the other three proved to be too poor for inclusion. Data were also extracted from six of the 15 cost or effectiveness studies, as shown in *Tables 20*[31,35,197–203] and *21*,[204–209] respectively. Resource use data were not extracted because of their generally poor quality.

The reported costs of various procedures converted to £UK at 1997 values are shown in *Table 22*. The range of costs and charges for scans, amniocentesis and CVS was very great. Costs for routine scans ranged from £18 to £204; costs for non-routine scans were reported less frequently and ranged from £32 to £113. All the studies from the USA and Canada quoted charges (which the authors acknowledged were not the same as costs) and these were generally higher than costs estimated in the four UK or Scandinavian studies, all of which reported primary costing research. The mean of the estimates reported (see bottom line of table) is a summary measure of different studies reporting different techniques on different populations and this should therefore be treated with considerable caution.

TABLE 19 *Economic evaluations in stage IV of the review (i.e. coded A(1) and B(1))*

Study Country	Final classification and quality assessment	Primary focus	Viewpoint	Study design	Data sources	Year and type of currency	Data extracted
DeVore, 1994[189] USA	A(1) (?)	Routine ultrasound re: RADIUS	Health service	Cost-effectiveness analysis	RADIUS and other secondary data (California maternal serum alpha-fetoprotein study)	1994 US$	No
DeVore, 1998[190] USA	B(1) (?)	Routine ultrasound re: RADIUS	Health service	Cost-effectiveness analysis	RADIUS and other secondary data	1994 US$	No
Ganiats, *et al.,* 1994[191] USA	B(1) Pass	Serum	Health service	Cost-effectiveness analysis	Published sources	1990 US$	Yes
Leivo, *et al.,* 1996[192] Finland	A(1) Pass	Routine ultrasound in 2nd trimester (16–20 weeks' gestation)	National economy	Cost-effectiveness analysis: alongside Helsinki ultrasound trial (RCT)	Primary data alongside trial	1990 US$ & FIM	Yes
Long & Sprigg, 1998[193] UK	A(1) Pass	Routine ultrasound in 2nd trimester (18–20 weeks' gestation)	Health service	Cost–benefit analysis based on before and after study	Primary data collection on site	1993 £ UK	Yes
Nadel, *et al.,* 1997[194] USA	A(1) (?)	Maternal serum	Health service	Cost-effectiveness analysis	Secondary sources	? US$	Yes
Roberts, *et al.,*1998[183] UK	A(1) Pass	Routine ultrasound: compared 12 different options	Health service	Cost-effectiveness analysis: based on modelling using decision analysis	Published literature	1996 £ UK	No
Vintzileos, *et al.,* 1998[195] USA	A(1) Pass	Non-routine ultrasound (1st trimester; advanced maternal age)	Societal	Cost-effectiveness analysis	Effectiveness data from the literature. Cost data from Medirisk tables (US medical reimbursement cost estimates	1997 US$	Yes
Wald, *et al.,* 1998[196] USA	A(1) Pass	Serum screening for Down's syndrome	Health service	Cost-effectiveness analysis	Published literature	1995 £ UK	Yes

Estimates of costs of various tests and measures of benefit reported in economic evaluations are shown in *Table 23*. Summary measures of economic benefit (such as cost per perinatal death avoided) are clearly dependent on the quality of the effectiveness data. Only one study[192] was based on a RCT; one other study[193] was based on a before–after comparison. All the other studies cited effectiveness data from the literature and modelled their economic evaluation on them.

In *Tables 24* and *25*, estimates are presented of other health service costs associated with ultrasound scans and other antenatal tests. Some are presented as full costs (e.g. of equipment) others are average costs per woman tested. In two studies,[192,197] the woman's travel costs were also considered. At 1997 prices, these amounted to between £1.43 and £16.65, depending on the distance travelled.

Detailed comments on economic evaluations

Four of the economic evaluations entering stage IV had routine ultrasound as the primary focus of the study (see *Table 19*).[182,189,190,192,193] One economic evaluation[195] had non-routine ultrasound screening for Down's syndrome for women of advanced maternal age as the primary focus. The primary focus of the remaining three studies[191,194,196] was maternal serum screening. However, it was considered important to evaluate and extract data from these because of their potential relevance to routine ultrasound screening programmes in the UK, and the implications for the cost-effectiveness of any combined programme.

An earlier study by two of the project team[183] presented 12 possible routine screening options using different permutations of ultrasound scans at different stages in pregnancy. Ranges of relative cost-effectiveness in terms of cost per target anomaly detected were presented for each screening programme in terms of best and worst scenarios for costs. The study referred to the UK and the costs, which were derived from national and international literature, were presented in £UK at 1996 prices. However, the ranges of uncertainty in the costs presented did not allow selection of any one programme as a clear choice for NHS purchasers. The authors emphasised that the data on both costs and effectiveness were poor. They were also explicit that the cost data, in particular, had been selected from a very inclusive search of the international health evaluation literature and a low threshold for criteria of quality had been used in the review of the studies identified. Thus no data were extracted from this study but it forms the basis of chapter 10 later.

Only one other economic evaluation of routine ultrasound referred specifically to the UK.[193] Initially this study did not pass all the quality criteria and was marked with a query, but clarification was obtained from the authors. The objective of the study was to carry out an economic evaluation of a change in policy from selective (high-risk) ultrasound scanning to routine ultrasound scanning for fetal anomalies. The study covered 24 months of data collection, from July 1992 to July 1994 at one centre in Sheffield. Selective screening was monitored in the first 12 months until July 1993, when routine second trimester ultrasound for fetal anomalies was introduced and offered to all women at 18–20 weeks' gestation after appropriate counselling. All congenital abnormalities, mode of detection and outcome were recorded, and each cohort of women was followed-up until 24 months after delivery. The authors conducted their own cost analysis. The total cost, including all staff, equipment, disposables and capital costs, for the department for each year was calculated from the hospital finance data. The net increase in costs of routine fetal anomaly ultrasound scans was estimated and apportioned by the increased workload of resulting from the routine scans. Additional staff were employed in the second year of the study to take on the additional workload, and additional disposables, for example, were purchased. No additional equipment needed to be purchased as it was relatively underused in the previous year. The proportion of the departmental workload represented by routine fetal anomaly scans was 49%. The final cost of introducing routine second trimester scanning was estimated to be equivalent to £16 per pregnancy at 1993 prices. The additional cost of additional tests, such as amniocentesis, carried out as a result of the routine scans was included in this figure. The specificity and sensitivity of the tests involved are not explicit in this study because the outcome data in terms of fetal anomalies detected is measured before and after the introduction of routine screening.

The authors concluded that the total cost saving of introducing the routine second trimester screening programme was £957,973 in 1 year (1993 prices). This saving to the health service is based on the averted lifetime costs of the anomalies detected by the introduction of routine screening in the first year, for which the pregnancies were subsequently terminated, minus the cost of the routine ultra-

sound screening programme in the first year. The final result should be treated with caution as there may be many confounding factors and the population included in the study for the year before and after the introduction of routine screening may not be homogenous or representative of a typical year. However, the authors point out that, despite its small numbers, this study has the advantage of representing comparative data for patients scanned in the same unit by the same experienced sonographers. A multicentre study may have the advantage of

TABLE 20 *Cost studies entering stage IV of the review (i.e. coded A(2) and B(2))*

Study Country	Final classification and status	Primary focus	Data sources for costs	Year and type of currency	Data extracted	Comment
Backe & Buhaug, 1994[197] Norway	B(2) Pass	General antenatal care	Primary	1988 NOK Swedish kroner	Yes	Good cost study from broad clinical and economic perspective. Detail provided on cost of scan, antenatal visits, travel and lost work time.
Bolling, *et al.*, 1998[198] USA	B(2) ?	Routine maternal serum screening for NTD	Secondary	Not stated ? US$ but not explicit	No	Provides cost data on different tests: ultrasound scans, amniocentesis, maternal serum alpha-fetoprotein. These appear to be quite old but not clear to which year they refer.
Geerts, 1996[31] S. Africa	B(2) ?	Routine ultrasound	Secondary	Not stated ? £ UK but not explicit	No	RCT appears comprehensively carried out. Costs given but detail on them poor.
Hahn,*et al.*, 1988[199] USA	B(2) ?	Routine ultrasound	Primary resource use and charges	1985 implied US$	Yes	Study estimates cost saving of GPs performing and reading own ultrasound scans, as opposed to referring patients to hospital and paying laboratory fee. Contains cost data on cost of machine. Scan performed by GP ($95) and scan performed in hospital ($185).
Kay, *et al.*, 1991[200] USA	B(2) Pass	Community-based antenatal care for adolescents	Primary resource use and charges	1987 US$	Yes	Not directly relevant to routine ultrasound but provides some useful cost data. Provides dollar ranges for two sites in study. Range extracted includes lowest and highest of two sites combined. Data provided on cost of scan, laboratory tests, initial and later antenatal visits and inpatient stay.
Rosenblatt, *et al.*, 1995[201] UK and USA	B(2) Pass	Routine and non-routine ultrasound	Primary	1993 US$	Yes	Gives costs for range of different ultrasound machines. In increasing sophistication: old poor resolution, mid-range basic, high-resolution basic, high-resolution Doppler and state-of-the-art colour Doppler.
Rouse, *et al.*, 1996[202] USA	B(2) ?	Non-routine ultrasound	Secondary – charges	1995 US$	Yes	Authors state that charges are typically substantially greater than costs. So, to be conservative, charges adjusted. Charges reimbursement rates (0.59 of charges).
Sadovnick & Baird, 1982[203] Canada	B(2) Pass	Non-routine ultrasound (Down's syndrome and NTD)	Primary resource use and charges	1980 Can $	Yes	Some useful cost information but very old.
Waitzman & Romano, 1998[35] USA	A(2) Pass	Routine ultrasound	Secondary	1992 US$	No	Provided cost range for scan but this later found to be sourced from another study (ref 9: Pitkin, 1991) which had failed our quality check and was not included in this review.

Note: A(2), initially classified as economic evaluation, subsequently coded as costs study; NTD, neural tube defect; NOK, Norwegian krone

increased numbers but the disadvantage of variability in equipment and sonographer expertise between departments.

Two papers, both by De Vore,[189,190] refer at least in part to the RADIUS study.[210] RADIUS was an RCT in which ultrasound screening was compared with clinically indicated ultrasonography only, and was designed to test the hypothesis that routine screening ultrasonography would improve perinatal outcome. In a related paper,[211] the same authors claimed, in the penultimate paragaraph, that "...the routine use of ultrasound screening as presented in the RADIUS study added on average 1.6 scans per pregnancy. Thus screening more than 4 million pregnant women annually in the USA at $200 per scan would increase the costs by more than $1 billion." No explanation of the source of the cost for the ultrasound scan was provided, nor were there any details of what the cost of a scan included (such as counselling, staff, overheads and consequential costs) or to what year the cost referred. Consequently, neither study reached any stage of our review. Both studies by De Vore[189,190] used these data in subsequent economic analyses, which served to undermine their quality, leading us to mark both studies by De Vore with a query in regard to quality. In spite of this use of poorly explained data, both studies otherwise appear to have been well conducted. They provide evidence for an important message about the relationship between the skill of the sonographer carrying out the scans, the time taken to perform a scan and the effect these can have on the relative cost-effectiveness of screening programmes. De Vore[189] also compared routine second trimester ultrasound in low risk women (as in the RADIUS study) with maternal serum alpha-fetoprotein for low risk women (taken from the California maternal serum alpha-fetoprotein programme). The absolute cost results provided by De Vore in terms of cost per case detected for each programme in the comparison are considered unreliable and have not been extracted. However, the conclusion drawn by De Vore, based on the relative cost-effectiveness between screening programmes, shows that sonographers who are not properly trained to undertake routine screening for anomalies will

TABLE 21 *Effectiveness studies with some assessment of costs or resource use (coded A(3) or B(3))*

Study Country	Final classification and status	Primary focus	Data collection period	Primary or secondary data	Year and type of currency	Data extracted	Comment
Bakketieg, *et al.*, 1984[204] Norway	B(3) ?	Routine ultrasound	1979–80	Not available	Not given US$	No	Cost of screening programme, $250 per pregnancy. Includes two scans; increased use of hospital resources, loss of time and income for attending women and cost of travel to and from hospital for ultrasound. Price year not specified.
Copel, *et al.*, 1997[205] USA	B(3) ?	Non-routine ultrasound for CHD	Not available	Not available	Not available	No	Resource use only; relevant to neonatal stay but not routine ultrasound.
Haley, *et al.*, 1997[206] UK	B(3) ?	Non-routine ultrasound	Not available	Not available	Not available	No	Resource use only. Non-routine ultrasound. Small-for-gestational-age babies: days in hospital, 2.5 (cardiotocograph) vs. 1.1 (Doppler).
Nienhuis, *et al.*, 1991[207] The Netherlands	A(3) ?	Non-routine Doppler ultrasound	Not available	Not available	Not available	No	Resource use only. Non-routine ultrasound. No cost data.
Omtzigt, *et al.*, 1994[208] The Netherlands	B(3) ?	Non-routine Doppler ultrasound	Not available	Not available	Not available	No	Non-routine. Resource use only:– antenatal admissions 3.26 days (Doppler group) vs. 3.03 days (control group). Neonatal admissions, 37.4% vs. 39.3%.
Rustico, *et al.*, 1995[209] Italy	A(3) ?	Non-routine ultrasound	1986-92	Primary	Not given US$	No	Cost of scan = $40. Takes 30 minutes to perform and includes 2-dimensional ECG. But no price year.

Note: A(3), initally coded as economic evaluation, subsequently coded as effectiveness study with some assessment of costs; B(3), initially coded as cost study, subsequently coded as effectiveness study with some assessment of costs; B(2), coded as cost study at both stages. CHD, congenital heart disease

TABLE 22 *Extracted data on unit costs of procedures at 1997 UK prices*

Study Country	Patient group	Primary or secondary data	Routine scan (£)	Other scan (£)	Double test (£)	Serum alpha-fetoprotein (£)	Termination of pregnancy (£)	Amniocentesis (£)	CVS (£)
Backe & Buhaug, 1994[197] Norway	Pregnant women	Primary	44.96						
Ganiats, *et al.,* 1994[189] USA	Hypothetical cohort	Secondary			95.70		416.73	870.00	
Hahn, *et al.,* 1988[199] USA	Family practice	Secondary (charges)	103.32 201.21						
Kay, *et al.,* 1991[200] USA	Teenagers	Secondary (charges)	185.66						
Leivo, *et al.,* 1996[192] Finland	Pregnant women	Primary	33.00 45.66	32.23 39.90			625.14	380.05	
Long & Sprigg, 1998[193] UK	Pregnant women	Primary	18.08						
Nadal, *et al.,* 1997[194] USA	Hypothetical cohort	Secondary	118.48					239.66	
Rouse, *et al.,* 1996[202] USA	Diabetic and non-diabetic women with fetal macrosomia	Secondary (charges)	143.38 204.32 53.77						
Sadovnick & Baird, 1982[203] Canada	Hypothetical cohort	Secondary (charges)	77.04	112.67		28.34 37.46			
Vintzileos, *et al.,* 1998[195] USA	Hypothetical cohort	Secondary	198.00						792.00
Wald, *et al.,* 19981[96] UK	Serum screening population	Primary					508.25	160.50	267.50
Mean of estimates reported			109.76	61.60	95.70	32.90	516.70	412.55	529.75

Note: some studies cite different costs for an item; this may be for a variety of reasons, e.g. different sites, or equipment used, or sources for secondary charges

TABLE 23 *Summary of economic evaluation results at 1997 UK prices*

Study	Comparison	Cost per woman screened (£)	Incremental cost of test (£)	Average cost per case detected (£)	Cost per perinatal death avoided (£)	Net benefit of providing screening (£)
Ganiats, *et al.*, 1994[191] USA	Serum screening		103,617			
Leivo, *et al.*, 1996[192] Finland	Routine ultrasound			6300	8093	14,856
Long & Sprigg, 1998[193] UK	Routine ultrasound					1,082,509
Nadal, *et al.*, 1997[194] USA	Serum screening			2625 10,434		
Vintzileos, *et al.*,1998[195] USA	Genetic ultrasound vs. CVS			34,320		
Wald, *et al.*, 1998[196] UK	Serum screening	3.75		29,464		

Note: some studies cite different costs for an item; this may be for a variety of reasons, e.g. different sites, or equipment used, or sources for secondary charges

have a detrimental effect on the cost-effectiveness of any screening programme.

Only one economic evaluation considered in stage IV of the review was based entirely on an RCT. A cost-effectiveness study was carried out alongside the Helsinki Ultrasound Trial.[192] In this trial, routine practice of normal antenatal care was compared with a policy of normal antenatal care that included one routine ultrasound scan between 16 and 20 weeks' gestation. Apart from the addition of the ultrasound, the control group received the same antenatal care as the experimental group. The principal outcome measured was perinatal mortality in the screened group compared with the control group. This was the only economic evaluation to clearly pass all the quality criteria at the outset. The results of the evaluation estimated that the net overall cost of introducing routine screening was actually a cost saving of US$17,077 (1990 prices). The difference was mainly due to better early detection of major malformations (detection rate 47%) and subsequent induced abortions. The study concluded that one-stage second trimester ultrasound screening is cost-effective when all significant costs and effects were taken into account. The study also noted that the malformation detection rate was better at one of the centres (a university hospital) than at another (a city hospital) (75% versus 35%). Thus it was also concluded that ultrasound screening performed by specially trained nurses keeps the cost significantly lower, and further improves the cost-effectiveness ratio via the high malformation detection rate.

One economic evaluation of non-routine ultrasound reached stage IV of the review.[195] This was an economic evaluation of first trimester genetic sonography for prenatal detection of Down's syndrome for women over 35 years of age. The study compared a strategy of providing CVS for all women over 35 years of age with a strategy of first trimester ultrasound for all women over 35 years of age, with CVS reserved only for those women with abnormal ultrasound results, in particular, NT. The study found that an overall cost saving arose with the latter policy because there were fewer fetal losses since fewer women were exposed to the risks of miscarriage associated with CVS. However, more cases of Down's syndrome were likely to have been missed. The authors concluded that first trimester

TABLE 24 *Reported unit costs specific to ultrasound scanning at 1997 UK prices*

Study Country	Patient group	Ultrasound machine		Consumables	Staff	Counselling	Laboratory tests
		Per machine (£)	Per scan (£)	Per scan (£)			
Hahn, *et al.*, 1988[199] USA	Hypothetical cohort	28,278					
Kay, *et al.*, 1991[200] USA	Teenagers						20.63
Leivo, *et al.*, 1996[192] Finland	Pregnant women		6.04	0.67	7.39		121.71
Long & Sprigg, 1998[193] UK	Pregnant women	27,572					
Nadal, *et al.*, 1997[194] USA	Hypothetical cohort					26.93	
Rosenblatt, *et al.*, 1995[201] USA & UK	Comparison of machines used in Washington State, USA and Wales, UK	5424 31,820 47,731 101,971 151,148					
Sadovnick & Baird, 1982[203] Canada						155.91	319.25

Note: some studies cite different costs for an item; this may be for a variety of reasons, e.g. different sites, or equipment used, or sources for secondary charges

TABLE 25 *Other health service costs incurred in ultrasound screening programmes at 1997 UK prices*

Study Country	Patient group	Outpatient visit (£)	Outpatient visit without referral (£)	Outpatient visit after referral (£)	First antenatal visit (£)	Later antenatal visit (£)	Inpatient visit (£)	Over-heads (£)	Floor space per m^2 (£)
Backe & Buhaug, 1994[197] Norway			38.83	126.70	50.78	14.61			
Kay, *et al.*, 1991[200] USA	Control group Teenagers		30.94	115.52	76.33	326.97	18.57	110.37	470.35
Leivo, *et al.*, 1996[192] Finland	Routine ultrasound No routine ultrasound	39.90 16.88			195.78	5.47	1.73		

ultrasound cannot be economically beneficial unless the overall sensitivity in detecting Down's syndrome is greater than 70%. Although not strictly evaluating routine ultrasound in the first trimester, the implications of the results of this study for first trimester routine ultrasound screening for anomalies may be of potential importance.

Three other economic evaluations reached stage IV of the review[191,194,196] but none of these were relevant to routine ultrasound directly as all were evaluating different strategies of maternal serum screening. However, the results may have implications for any strategy of routine ultrasound screening which includes routine serum screening as part of the package. Cost data and some economic evaluation data were extracted from all these studies.

Discussion

The main focus of economic evaluation has been on the specific question of screening for fetal anomalies, rather than the general issue of the role of ultrasound in improving fetal or maternal outcomes (with one exception).

This review has clearly shown the dearth of good quality primary cost studies of ultrasound scanning in pregnancy. The majority of data came from the USA and used secondary charge data that do not accurately reflect costs. It had been hoped that estimates of the costs of various different scan types could be obtained but these were not available. Even less has been reported on women's costs for attending ultrasound scans, indeed little has been written about women's costs for attending antenatal care generally. When cost-effectiveness was reported, the quality of the effectiveness evidence was often dubious; only one economic evaluation was based on a RCT.[192] Longer-term cost consequences have not been explored at all.

In other areas, where more and better cost data are reported, it may be possible to quantitatively aggregate the results of different studies, as is commonly done with systematic reviews of RCTs. In the area of ultrasound in pregnancy it has not been possible to do this.

However, some important messages did emerge as a result of the literature review. The skill of the sonographer and the time taken for a scan may both have an effect on the cost-effectiveness of any ultrasound screening programme. Sonographers who are not properly trained to perform routine anomaly screening may have a detrimental effect on the efficiency, in terms of cost-effectiveness, of any screening programme. This result was reiterated by two studies.[189,192] In addition, the only economic evaluation conducted alongside a trial concluded that one-stage second trimester ultrasound is cost-effective.[192]

Recommendations for research

There is a need for more published data on the costs and cost-effectiveness of policies for use of routine ultrasound screening both for fetal anomalies and for other purposes, such as dating, and also of longer-term consequences of scanning for anomalies. Routine scanning in the second trimester alone is worthy of further examination.

Implications for policy and practice

There are some implications for policy and practice relating to the provision of adequate training for ultrasonographers who choose to specialise in anomaly screening. These skills may need to be assessed at frequent intervals to ensure the maintenance of required standards.

Chapter 9

Primary studies of costs

Resource use and costs of procedures associated with routine antenatal ultrasound screening carried out at the Liverpool Women's Hospital

Background

The preliminary, unsystematic, review of the literature that was undertaken for the RCOG Working Party report on cost-effectiveness of ultrasound screening for fetal anomalies[183] emphasised the lack of good cost data. In particular, the authors reported that little explanation was provided on the methods used to estimate costs or the types of costs reported. For instance, when the cost of a scan was reported it was not clear who had carried out the scan, the exact purpose of the scan, for example, whether for dating or anomaly, or whether or not counselling or other additional care was included in the basic cost provided.

Although the authors were aware that the current systematic review might prove more successful in gaining information with the required detail, there was concern that this might prove misleading and unhelpful in the UK context if obtained from international studies alone, since different routine procedures might prevail.

UK hospital finance departments often have their own estimates of resource use and costs for different procedures, and can provide an estimate of a cost of a routine antenatal ultrasound scan. However, they typically have insufficiently detailed data on scans carried out for different purposes by different personnel, which may make such data unrepresentative. Thus a primary study was under-taken to estimate resource use and costs of procedures directly involved and associated with routine antenatal ultrasound screening at Liverpool Women's Hospital. This centre was chosen primarily for convenience, as the centre of study for two authors of this review (JN, LB). It is also one of the largest European centres providing antenatal care.

Objective

The objective of the primary research was to provide a contextual, NHS-based comparison for data collected from the systematic literature review of economic studies reported in chapter 8. This primary research also has the advantage of completing gaps in information not filled by the review but needed for confident estimation of cost-effectiveness. In particular, it would provide the necessary resource components with a range of costs for scans that are carried out for different purposes. The authors acknowledge that these costs are representative of only one UK centre, and the size and throughput of this hospital is likely to present resulting cost data that will not necessarily be representative of the costs and resource use of other UK centres. These methods could, however, be applied in other centres willing to repeat the exercise.

Definition of different scans/procedures

Booking scan: a scan undertaken at first antenatal visit, preferably before 16 weeks' gestation, to measure the fetus for gestational dating, identify multiple pregnancies and associated chorionicity, and assess viability.

Anomaly scan: a scan undertaken at 18–20 weeks' gestation to perform a fetal structural survey and detect structural anomalies, fetal biometry to confirm appropriate size for gestational age, and assess the placental site and liquor volume.

Growth scan: a scan performed for fetal biometry to assess fetal size and growth.

Fetal wellbeing scan: this represents a number of alternatives used to assess the condition of the fetus, and which may include fetal biometry, fetal weight estimation, liquor volume assessment subjectively or by measuring the amniotic fluid index, umbilical artery Doppler velocimetry, and biophysical profile assessment (fetal tone, fetal movements, fetal breathing movements and amniotic fluid volume). As all, some or one of the above factors may be assessed in different combinations, they have been 'lumped together' because few data were collected by staff for the various combinations, the time spent was not dissimilar and it was considered too complicated to present them separately.

Detailed scan: a scan performed by a consultant (sub-specialist in feto–maternal medicine, special interest in feto–maternal medicine, radiologist) to assess all or some of the fetal structural anatomy, or other aspects of the pregnancy, such as suspected pelvic abnormalities. Such a scan may occur as a result of an abnormality suspected at routine ultrasound scan, a family or personal or obstetric history of congenital abnormality, a maternal condition associated with a higher risk of congenital abnormality (e.g. diabetes, advanced maternal age), or an abnormal antenatal test other than ultrasound (e.g. serum screening).

Amniocentesis: an invasive procedure performed transabdominally under ultrasound guidance whereby amniotic fluid is tapped and sent for cytogenetic or, in some cases, other analysis.

CVS: an invasive procedure performed transabdominally or transvaginally whereby placental tissue is aspirated and sent for cytogenetic analysis.

Methods

Setting

This study was undertaken at the Liverpool Women's Hospital, a university teaching hospital that provides maternity care for the local population and serves as a tertiary referral centre for hospitals in Merseyside, North Wales and the Northwest region of the UK. At their first antenatal visit women are offered a routine booking scan (usually at about 12 weeks' gestation). This takes place at the antenatal clinic, the scan being carried out by Imaging Department staff who are also responsible for gynaecological and neonatal scanning. Various other routine antenatal tests, including biochemical tests, are offered and performed at about 16 weeks' gestation. At 18–20 weeks, women routinely attend the Imaging Department for an anomaly scan. If a problem is suspected, a woman may go on to have other scans and/or invasive prenatal tests (amniocentesis or CVS) in the Fetal Centre. In the Imaging Department and antenatal clinic, scans are performed by one of nine full-time or four part-time ultrasonographers. At the Fetal Centre, scans or invasive procedures are performed by one of five consultants (two feto-maternal medicine sub-specialists, two obstetricians and one radiologist).

For each type of scan (booking, anomaly, growth, placental site and fetal well being) performed in the Imaging Department, and for scans and procedures performed by specialist staff at the Fetal Centre (detailed scans with or without fetal echocardiography, amniocentesis, CVS), costs were estimated in consultation with the finance department at the Liverpool Women's Hospital, and the administrative staff of the Imaging Department, the Fetal Centre and the Cytogenetics Department.

Staff costs

Hourly rates of pay For non-medical staff (radiographers, midwives, healthcare assistants and clerical staff), hourly rates were calculated by adding annual salaries and dividing by the total number of hours of expected work per annum, taking annual leave and bank holidays into account. Two radiographers had both administrative and clinical duties, and thus, in determining their hourly rates, only that percentage of their salary apportioned to clinical work was included. The remaining portion of their salary for administrative work was included in the administrative cost calculations.

Hourly consultant rates were calculated using information from the finance department that stated the number of sessions each consultant dedicated to work in the Fetal Centre and the portion of their salary attributed to these sessions. Annual leave and bank holidays were taken into account.

All salaries were taken from 1998/99 pay budgets and included employer's contributions for national insurance and superannuation.

Time For each type of scan performed by radiographers in the Imaging Department, staff time was recorded using diaries designed for this purpose over a period of 1 week in November 1998 (see appendix 10). The week represented a typical week of work in the Imaging Department, and no member of staff was on annual or sick leave at the time. If staff training was involved, this was indicated in the diaries.

For each type of scan or procedure performed in the Fetal Centre over 5 weeks in November and the beginning of December 1998, details of the procedure, staff time and other staff assisting or present were recorded using datasheets (see appendix 11). Training during scans or procedures was also documented. Because of the wide range of procedures and scans undertaken at the Fetal Centre, as well as the fact that they are customised to suit the individual clinical situation, the times calculated for scans and procedures at the Fetal Centre were supplemented by observation of events and discussions with staff.

All these calculations included time spent counselling, documenting and arranging follow-up for the scan or procedure. Clerical time related to each scan was estimated to be 5 minutes in each case.

Consumables

Consumable costs were calculated using different methods. For the cost of gel and tissue paper used per scan, the radiographers reported how much was used in a particular day and the cost was then apportioned to the number of scans performed in that day using those consumables (i.e. costed up). Costs of other consumables were obtained by listing those used in an average scan/procedure and then calculating the costs from the purchasing documents in the Imaging Department and the Fetal Centre.

Laboratory costs

Laboratory costs for processing and reporting on samples for karyotyping were obtained from the Cytogenetics Department who had undertaken an independent costing exercise.

Administrative costs

Administrative staff costs for the two departments were calculated by adding together the administrative salary portion of the two radiographers with administrative duties, the Imaging Department office manager's salary and, in the case of the two clinical directors, the extra payment received for their work related to clinical directorship; the total was then divided by the number of tests/procedures performed in each department (Imaging or Fetal Centre) in the year 1997. In the case of the Imaging Department, the calculations included non-obstetric tests/procedures, including those performed in other areas of the hospital (e.g. gynaecology urgency room, neonatal unit) as the department also provides gynaecological and neonatal services, and if these were not accounted for the costs would have been overestimated.

Other departmental costs

Other departmental costs (i.e. costs not included in the other calculations and overheads), such as postage, computer consumables and furniture replacement, were obtained from the finance department. These used 1998/99 costing based on year-end expenditure documents for each of the two departments, apportioned by dividing the total by the number of tests/procedures performed in each department in the year 1997. Some of the costs were shared between departments and some were specific to individual departments; hence the unit costs are slightly different.

Overheads

Hospital overhead costs were estimated, by the finance department, to be 11% of recurrent costs; they include the cost of management and administration, IT services, cleaning, electricity and water.

Capital charges

Annual equipment costs were estimated based on the net present value of the equipment used, using straight line depreciation at 7% per annum, using the discount factor recommended by HM Treasury, and length of life of equipment as recorded in the departmental inventory. Cost of equipment per test was estimated by dividing the annual cost by the number of scans performed in either the Imaging Department or Fetal Centre. Equipment costs for each department were calculated separately; Fetal Centre equipment costs were higher as relatively fewer tests/procedures were performed in this department per annum, and the equipment itself is technologically more complex. Maintenance costs were estimated from the maintenance contracts for each machine and then added to the annual equipment cost.

Building costs were calculated by apportioning annuatised building costs for the year end 1997/98 (from the finance department) according to floor space of each department, and dividing by the number of scans/procedures performed in each department separately.

All capital charges had 6% added for return on capital employed, which is an external charge imposed by the government.

It was assumed that all the different scans had the same costs for consumables; also that administrative staff, buildings, other departmental costs and equipment costs differed between the Imaging Department and the Fetal Centre but not within these departments. Administrative, other departmental, equipment and building costs were apportioned per scan/procedure. This assumes that non-obstetric scans did not consume disproportionately more or less of these resources. All costs are presented in £ sterling at 1998/99 price levels.

Results

During one week in November 1998, 317 obstetric scans were performed and noted in the diary by Imaging Department staff, of which only five (1.6%) were excluded from analysis because of incomplete data. In the Fetal Centre, over the 5 weeks in November and December 1998, 200 datasheets were completed, of which 12 (6%) were

excluded from analysis because of incomplete data. These datasheets varied greatly in terms of indication for the scan/procedure, time spent on the scan/procedure and staff involved.

Details of the staff present and the average duration of each different type of scan or procedure are presented in *Table 26*; this is based on the staff diaries and datasheets, with the maximum and minimum recorded times being given in parentheses. The table also shows the increase in duration of scans when a sonographer was being trained. No booking scans involved training in the period studied but training increased procedure time for growth and anomaly scans by 36–44%.

For each procedure presented, the variation in time was reflected only in the key person(s) carrying out the scan, but typically 5 minutes of clerical time were associated with each procedure, for such tasks as filing and arranging appointments. At the Fetal Centre, detailed scans were performed by a consultant. During other secondary procedures, such as amniocentesis, or transabdominal or transvaginal CVS, a midwife was usually present also. In the Fetal Centre, a healthcare assistant usually prepared the room for the next consultation and cleared away and, for invasive procedures, set up and cleared the trolley.

All elements of the costs for the different scans and procedures are presented in *Table 27*. Booking, anomaly, growth and fetal wellbeing scans typically cost between £14 and £16. This contrasts with detailed scans, for which the estimated cost was £51, and with amniocentesis, transabdominal and transvaginal CVS, for which the costs were £189, £239 and £264, respectively.

Sensitivity analysis

The key variables in this analysis were:

(i) the staff present
(ii) the duration of the different scans and procedures
(iii) the effect of training
(iv) equipment costs
(v) on-site cytogenetics.

(i) The status and grade of staff present has the potential to influence the results. The baseline analysis used data from the hospital finance department relating to the staff employed. If staff of a lower grade were employed, the costs would be proportionately lower. Similarly, at the Liverpool Women's Hospital, consultants carried out the detailed scans, amniocenteses and CVS. Registrars typically get paid about half the salary of consultants[212] and, thus, costs would be commensurately lower. However, registrars are not generally trained in scanning, amniocentesis or CVS, so the vast majority are undertaken or supervised by consultants.

(ii) The range of durations of different scans and procedures is shown in *Table 26*. For dating, anomaly, growth and fetal wellbeing scans, the range was quite small and only made a difference of £3–£4. For detailed scans, however, the range was large, from 17 to 70 minutes, representing a range in cost for this procedure of £12–£45.

TABLE 26 *Staff time for each scan or procedure*

Staff	Cost per hour (£)	Mean time (range) (minutes)							
		Dating/ booking scan	Anomaly scan	Growth scan	Fetal wellbeing scan	Detailed scan	Amnio-centesis	Trans-abdominal CVS	Trans-vaginal CVS
Sonographer	16.46	16 (9.4–23.4)	20.2 (17–30)	21 (14–28)	20.2 (17–30)	N/A	N/A	N/A	N/A
Training			29.1 (22.5–35.7)	28.6 (21.6–35.6)					
Counsultant	37.88	N/A	N/A	N/A	N/A	34 (17–70)	40 (30–50)	45 (30–60)	45 (30-60)
Midwife	12.87	N/A	N/A	N/A	N/A	N/A	30 (20–40)	45 (30–60)	45 (30–60)
Healthcare assistant	3.73	N/A	N/A	N/A	N/A	5	5 (5–10)	5 (5–10)	5 (5–10)
Clerical	6.20	5	5	5	5	5	5	5	5

TABLE 27 *Cost of each scan or procedure at Liverpool Women's Hospital at 1998/99 UK prices*

	Dating/ booking scan (£)	Anomaly scan (£)	Growth scan (£)	Fetal wellbeing scan (£)	Detailed scan (£)	Amnio-centesis (£)	Trans-abdominal CVS (£)	Trans-vaginal CVS (£)
	Imaging Department				Fetal Centre			
Consumables	0.15	0.15	0.15	0.15	0.15	8.91	26.78	49.11
Laboratory costs	N/A	N/A	N/A	N/A	N/A	105.00	126.00	126.00
Administrative staff	1.17	1.17	1.17	1.17	1.89	1.89	1.89	1.89
Building	1.01	1.01	1.01	1.01	3.86	3.86	3.86	3.86
Other departmental costs	0.50	0.50	0.50	0.50	0.51	0.51	0.51	0.51
Equipment[a]	5.71	5.71	5.71	5.71	20.03	20.03	20.03	20.03
Staff	5.02	6.06	6.28	7.68	22.29	32.52	38.89	38.89
(range)	(3.10–6.94)	(4.22–7.90)	(4.36–8.20)	(3.13–12.62)	(11.56–45.02)	(26.04–41.29)	(26.21–51.89)	(26.21–51.89)
Hospital overheads[b]	0.74	0.86	0.86	0.86	2.73	16.37	21.35	23.80
Total costs	**14.19 (12.18–16.44)**	**15.46 (13.42–17.51)**	**15.71 (13.58–17.84)**	**15.46 (11.67–21.16)**	**51.47 (39.55–76.69)**	**189.09 (182.61–197.86)**	**239.31 (226.63–252.31)**	**264.09 (251.41–277.09)**
Total including training		18.17 (16.17–20.18)	18.02 (15.89–20.15)					

[a] *Includes maintenance costs* [b] *Implies 11% added to all costs except buildings and equipment*

(iii) The effect of sonographer training is shown in *Table 26*, in which the duration of anomaly and growth scans was increased by 36–44%. Data relating to other scans and procedures or about training of other staff are unavailable, but the effect is likely to be the same. It is, however, worth noting that the costs associated with medical teaching, including training of registrars, is met centrally in resource allocation.

(iv) Equipment costs are based on a number of assumptions, including the interest rate used and the estimated lifetime of the equipment. In the sensitivity analyses, interest rates were varied between 3% and 10%, and length of life of equipment, based on the departmental inventory, was extended by 25%. These together produced a range of equipment costs of £4.67–6.32 for the Imaging Department, and £13.79–18.45 for the Fetal Centre. Maintenance costs were additional to these figures.

(v) At the Liverpool Womens' Hospital the cytogenetics laboratory is on site. Smaller hospitals may not have these facilities and samples would then have to be taken to another hospital, which may be more costly.

Discussion

The costs reported here are consistent with other primary costing studies in this area but differ substantially from much of the literature in which reported costs (or charges) for ultrasound are substantially higher.

In the next chapter, the final total costs for each procedure are compared with the costs found in the review of the economic literature. These costs are used to refine the original decision model for cost-effectiveness of options for ultrasound screening for fetal anomalies. The results of this exercise are compared with the results of the model, estimated using the costs from the economic literature review.

Implications for research and practice

This detailed costing study will need to be repeated in one or more other hospitals to validate the methodology and to examine the extent of variation between centres.

Primary study of the costs for women of attending for ultrasound scans at Liverpool Women's Hospital

Introduction

Most economic evaluations of healthcare interventions do not look beyond the perspective or viewpoint of the health service. However, many health service interventions have implications for

the users of the service and for society as a whole. It is therefore recommended that a societal viewpoint be adopted when there is doubt about the extent of the impact of a policy beyond the health sector.[213] From previous work undertaken at the National Perinatal Epidemiology Unit, the authors were aware that little work had been done on women's costs of attending for care in pregnancy and childbirth.[186] This primary study was thus undertaken with the aim of estimating costs to women, their friends and family and costs to society of attending for ultrasound in pregnancy.

Methods

Women attending the Liverpool Women's Hospital for ultrasound scans in one week in January 1999 were asked to complete a short questionnaire, in which they were asked about costs incurred by themselves or their friends and family to attend for their scan. The questionnaire was adapted from one used in a WHO trial of antenatal care.[214] The local ethics committee approved the patient information leaflet and questionnaire (see appendix 12). Women were asked about lost pay for themselves or anyone accompanying them, the length of time they spent at the hospital and in travelling, what their travel costs were and whether they had any additional costs for childcare or care of other dependents. Separate, slightly different, questionnaires were used for women attending the Imaging Department or Fetal Centre and for women having a scan in the course of their antenatal booking appointment (i.e. first antenatal visit). This was to accurately estimate the time spent on ultrasound, without confusing it with time spent in other departments; it was assessed differently purely for logistical reasons. Scans done in the course of a booking appointment were to determine dates, fetal viability and multiple pregnancies. These were all performed at the antenatal clinic. All other scans (anomaly, growth, fetal wellbeing) were performed at the Imaging Department or Fetal Centre.

The opportunity cost of time lost from work was estimated from the mean gross weekly wage rate for women in Great Britain at April 1998 (£309.60).[215] Minus tax, pension and national insurance contributions (estimated at 35% of gross salary), the mean hourly rate (assuming a 37.5-hour week) was £5.37. This rate was used when a woman lost pay to attend for care. If she took part of her annual holiday allowance or her appointment was outside working time, her time was valued at 40% of the mean female wage rate (i.e. £2.15 per hour). This valuation of leisure time is somewhat arbitrary and was varied in the sensitivity analysis. Women who were not in paid employment were considered in the base case scenario to have an opportunity cost approximating to that of cleaning work or informal care (£4 per hour). This also was varied in the sensitivity analysis. When women were accompanied for the duration of their visit, the **female** wage rate could not be assumed and the mean adult wage rate was used for those who would otherwise have been working (i.e. £384.50 gross[215] or £6.66 net per hour using the same assumptions as above). It was also assumed that all accompanying persons who would have otherwise been working had taken unpaid leave and that they experienced the mean travel time. If a woman was accompanied by someone who would not have been working otherwise, their time was costed at the informal wage rate (£4 per hour).

Although, in general, women attending hospital for a booking appointment had an obstetric history taken and various tests as well as their scan, these could equally well have been carried out in the community. Thus the full travel costs are attributed to ultrasound in this analysis. Liverpool health authority reimburses travel expenses to women on income support at the rate of £0.10 per mile or their bus or train fare (not taxis), and this same rate was used for cost of travel. All costs are expressed in £UK at 1998/99 prices.

Results

The response rate for questionnaires from women attending the Imaging Department or Fetal Centre was 72 out of 89 (81%). For women being scanned at the antenatal booking clinic, the response rate was 35/36 (97%). The total number of women who completed a questionnaire was 107. Response rates to individual questions (or sets of questions) was > 99% with one exception; only 42% of women attending the Imaging Department or Fetal Centre responded to the question on the duration of their appointment. The results are summarised in *Table 28.*

Lost pay

If not attending for a scan, 41 women (38%) would have been in paid employment. Of these, 25 took paid absence, the cost being borne by the employer, six took unpaid absence or intended to make the time up – the cost therefore being borne by themselves, and four took holiday. The other six came outside work time.

The mean duration of an appointment at the Imaging Department/Fetal Centre was 29 minutes, which included approximately 10 minutes waiting

TABLE 28 *Costs to women or their family and friends of attending for ultrasound scans at Liverpool Women's Hospital*

	Number (%)	Mean cost per woman affected (£)	Cost averaged over all women responding (£)
Lost pay	6 (5.7)	6.76	0.38
Lost leisure	4 (3.8)	2.70	0.15
Accompanying adults off work	45 (42.8)	8.38	3.59
Accompanying adults not in paid employment	40 (37.4)	5.03	1.88
Travel[a]			
Car	79 (74.5)	1.40	1.04
Public transport	16 (15.1)	5.48	0.83
Taxi	9 (8.5)	8.46	0.72
Parking fees	23 (21.9)	0.53	0.12
Childcare			
Paid	3 (2.8)	17	0.48
Time off work	3 (2.8)	8.38	0.23
Total	107 (100)	–	12.42

[a] *Does not include women eligible to have their travel cost reimbursed by health authority*

time; in antenatal booking clinics, appointments were of approximately 33 minutes duration, of which waiting time averaged 17 minutes. As these estimates were so close, the analyses are presented for all women together. The mean journey time to the hospital for all women was 22 minutes. It was assumed that the return journey involved the same time and expense. Thus women who forfeited pay to attend for ultrasound scans lost, on average, £6.76. However, as this only related to six women, the impact averaged over all women responding was small, only £0.38.

Four women took paid holiday to attend for ultrasound. At 40% of the mean wage rate, their time can be valued at £2.70 (40% of £6.76). At the time of their scan, 59% of women were not in paid employment. Even at a comparatively low wage rate (£4 per hour), this amounted to £5.03 per affected woman or £2.96 averaged over all women.

The vast majority (92%) of women said they were not losing income through attending for ultrasound. The other responses ranged from £5 to £200. A total of 85 women (79%) were accompanied by at least one other person, of whom 53% had taken time off work (the costs are summarised in *Table 28*).

Travel

The majority of women (74%) travelled by private car. Of these, 23 women paid parking fees, ranging from £0.20 to £5.50, mean £0.53. The mean distance travelled (each way) was 7.0 miles. The average fare (each way) paid by the 16 women who travelled by public transport was £1.99 (each way). Nine women travelled by taxi, at an average cost of £4.23 each way.

A total of 30 women were on income support, and thus eligible to have their travel costs reimbursed by the health authority. Assuming that they all claimed reimbursement, the travel costs for these 30 women cost the health authority £27.80 in total. Technically, this may represent a transfer payment and, as such, should not be counted when a societal perspective is being taken. However, it is included here to enable hospital trusts to look at costs from their own perspective.

Childcare/care of dependants

Only three women paid for childcare while they attended for ultrasound. Three women indicated that someone had taken time off work to care for other children or dependents. Assuming average travel and ultrasound time, this may have cost the carer £8.15 in lost pay. It is, however, also possible that a half-day may have been taken off work (costing more) or that the time off may have been taken as holiday (leisure time) and thus costed at other than the full working rate.

Costs to employers

Additional costs to society through employers are incurred through paid absence for women to attend for ultrasound when they would otherwise be working. Of the 41 women in paid employment, 25 had paid absence to attend for their scan. Using average gross female weekly wage rates of £309.60 (as above) and a mean time away from work of 76 minutes, the estimated cost to employers was £10.46. Averaged over all women responding (including those not in paid employment), this amounts to £2.45 per woman.

Sensitivity analyses

The key assumptions made in valuation of women's costs were that:

(i) women not in paid employment had an opportunity cost equivalent to unskilled work or informal care
(ii) leisure time should be valued at 40% of work time
(iii) the mean female wage rate was appropriate for this population

(iv) all women entitled to reimbursement of travel costs claimed them
(v) there were seasonal effects on costs.

(i) Of the women in the sample, 59% were not in paid employment. If their time were costed at zero, it would decrease the costs to women by £5.03 per woman affected or £2.96 averaged over all women responding.

(ii) Leisure time can be valued at anything from 0% to 150% of the usual wage rate.[213] This was only applicable to four women but, for them, 150% would amount to £10.14. However, averaged over all women responding this amounted to only £0.38.

(iii) The detailed occupational information required to accurately estimate costs to employers and employees of time off work were not collected. Therefore, average female wage rates were used. However, wages have a skewed distribution and the mean may be a poor measure of central tendency. If the median female wage rate was used instead (i.e. £270.00 instead of £309.60 per week), minus tax, national insurance and pension contributions (estimated at 35% of gross salary), and an average working week of 37.5 hours was assumed (i.e. £4.68 per hour), the lost pay per woman affected declined by £0.87 to £5.89. However, because so few women actually lost pay to attend for a scan, the effect is very small, less than £0.50 averaged over all women. Costs to employers declined by £1.40 through using the median female wage instead of the mean but, again, averaged over all women, this was a difference of only £0.33.

(iv) In many cases people entitled to benefits do not claim them. If none of the women entitled to reimbursement of travel costs claimed them then these women would be, on average, £0.93 worse off.

(v) This survey was undertaken in January and it is possible that some factors, such as travel costs, may be greater at this time of year. For example, women may choose to travel by car or bus when in summer they might walk or cycle.

Discussion

For women to attend for ultrasound scans costs them about £12.42 (95% CI, £11.58 to £13.26). The majority of the women sampled were not in paid employment. This finding may not be generalisable to other cities because Liverpool has relatively high rates of unemployment. The majority of the women in paid employment took paid absence from work, and their employers and society therefore bore the cost of these absences. A small proportion of women took unpaid leave, intended to make the time up or took annual holiday to attend for their scan; however, averaged over all women attending, the impact of this was small. Of the women attending for a scan, 81% were accompanied by at least one other adult and approximately half of these accompanying adults took time off work to do so. These costs made up a substantial proportion of the total costs incurred by the women and their friends and family. Women's costs were sensitive to assumptions about the valuation of unpaid work. Otherwise the findings were robust.

Because of employment rights for pregnant women, for employed women most of the cost of lost working time is met by their employer. The employers' costs estimated for a scan are only a small part of the much larger cost to them of providing for maternity rights, part of which are repaid by the Department of Social Security through the Statutory Maternity Pay scheme.

Most women welcome the opportunity to 'see' their baby via an ultrasound scan[92,94] and would not perceive time spent in this way as a 'cost'. Nevertheless, such costs may be an important proportion of household resources in low-income households. The impact of changes in health-care practice may therefore influence either the family economy or clinic attendance as a result, but this requires further evaluation. The similarity between women's costs and NHS costs is consistent with that found by Meldrum in Aberdeen in 1989.[216] Costs to families are sensitive to assumptions about the value of women's time given to this activity. There is scope for further investigation of the values women attach to their own time and to attending for a scan in different circumstances.

Implications for research and practice

Costs to the NHS are not as great as suggested in the majority of the literature. Further costing of ultrasound services in other settings is, however, necessary to validate this study.

Women's costs associated with attendance for ultrasound scans can clearly be substantial. Economic evaluations should attempt to include users' costs, particularly where cost shifting may occur.

Chapter 10

Modelling cost-effectiveness of ultrasound screening for fetal anomalies

Introduction

One of the principle objectives of the current project was to refine and extend the RCOG Working Party's original decision analytic model of routine ultrasound screening[183] using new data from the systematic review of the economic literature, the primary costing research at the Liverpool Women's Hospital and effectiveness estimates from the systematic clinical reviews.

The original model

Scope of the model

The decision model was designed to assess the relative cost-effectiveness of different ultrasound scanning options. The outcome, detection of anomaly, was chosen for pragmatic reasons. The model does not, therefore, include costs arising prior to a woman presenting for her first scan or subsequent to the confirmation of an anomaly; that is, termination of pregnancy, delivery and postnatal costs have not been included. Scanning may well result in outcomes other than detection of an anomaly. Some, such as psychological outcomes, have been discussed earlier in the report (see chapter 6). Reduced induction rates resulting from accurate gestational dating have not been included; similarly, hospital admission for low-lying placenta is not included in the model.

TABLE 29 *Options for routine ultrasound scanning policies*

Option	Trimester			
	1		2	3
	Dating	Anomaly		
1				
2	✓			
3			✓	
4				✓
5	✓		✓	
6	✓			✓
7			✓	✓
8	✓		✓	✓
2a		✓		
5a		✓	✓	
6a		✓		✓
8a		✓	✓	✓

Source: RCOG, 1997[5]

Structure of the model

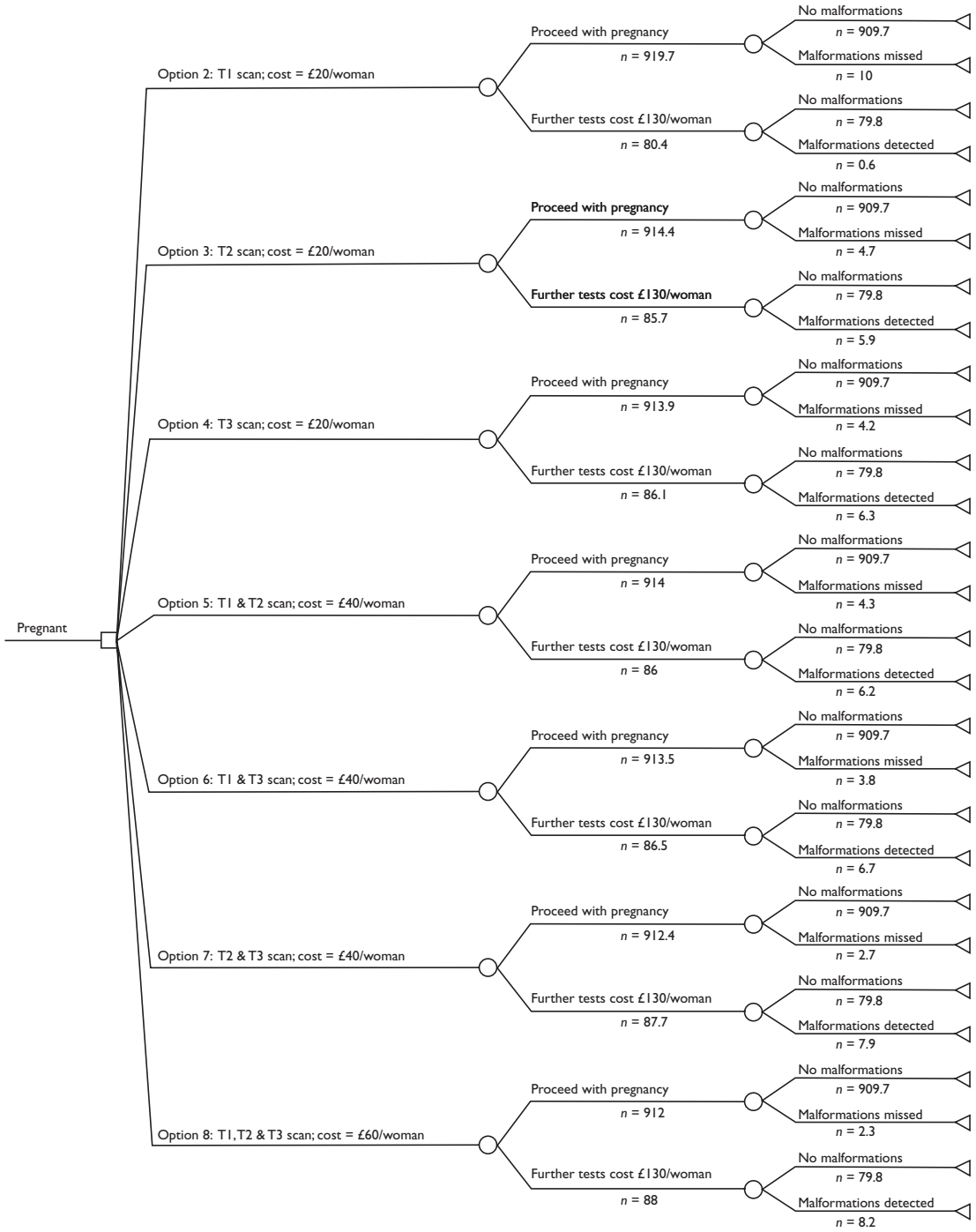
It is necessary to recap in some detail the structure of and analysis carried out in the original model.[183]

A decision tree was constructed to link together alternative scanning options with their intermediate clinical outcomes. The 12 options for routine ultrasound scanning used in the original model are shown in *Table 29*. They include the different permutations and combinations of known types of routine scans that can be used in screening programmes, including first trimester dating scan, first trimester anomaly scan, second trimester anomaly scans and third trimester scan.

These original results are presented graphically in *Figure 2*. The chance of following any particular path was determined by a node preceding the choice of paths. Decision nodes (square) reflect where women and their carers would make choices. Chance nodes (round) represent the uncertainty of an outcome after a clinical intervention, determined by the population incidence of anomalies and the assumed effectiveness of the ultrasound scan or scans. Terminal nodes (triangles) represent the outcome for a patient whose uncertainty is resolved in the manner indicated by the probabilities leading to the node.

The main clinical outcome measure used was the estimated number of women with a 'target' malformation detected antenatally. The target malformations included were two specific anomalies (Down's syndrome and spina bifida) and two groups of anomalies (congenital cardiac defects and lethal anomalies). The analysis looked only at outcomes in terms of diagnostic success in the short term and did not consider longer-term survival and quality-of-life issues. Because of the uncertainty of the data quality, it was decided to consider 'best' and 'worst' scenarios, from an economic viewpoint, for clinical effectiveness.

FIGURE 2 *Number of anomalies detected for 1000 women, taking each option's best scenario from original model*



□ Decision node

○ Chance node

◁ Terminal node

n = number of women following each path

T = trimester

Clinical effectiveness data used in the original model (i.e. the prevalence of the target anomalies, and ultrasound sensitivity and specificity) was based on the work of the RCOG Working Party on ultrasound screening for fetal abnormalities[5] and is documented in their report. They combined both a non-systematic literature review and expert consensus to provide these data.

Combined sensitivities were used to estimate the number of positive diagnoses in an option that included more than one routine scan (i.e. options 5, 6, 7, 8, 5a, 6a and 8a from *Table 29*). Combined sensitivities were used rather than simply the highest detection rate of the scans performed because each scan has a detection rate additional to the previous one (see appendix 13 for a fuller explanation and an illustrated example of the calculation).

Obviously, for each option, a proportion of women would have been given a false-negative diagnosis, because the combined sensitivity of the test for any option was not 100%. These women were assumed to continue with their pregnancy unaware that they had a malformed fetus. The specificity of the test was used to estimate the number of women who would be given a 'false-positive' diagnosis (i.e. 1 minus the specificity).

The **best scenario** was that with highest prevalence for the target anomalies, highest likely sensitivity of the test for each anomaly and highest specificity (lowest false-positive rate) for each anomaly. The **worst scenario** was that with lowest prevalence for the target anomalies, lowest sensitivity of the tests and lowest specificity (highest false-positive rate) for the detection of anomalies.

For each of the four target anomalies, the outcomes of each of the screening options were estimated for both scenarios using the upper and lower limits of the data as appropriate. For each of the target anomalies the prevalence was used to estimate how many true fetal anomalies there would be in a population of 1000 women.

Cost data used in the original model were derived from sources found in a very inclusive search of international health evaluation literature, and a low threshold for criteria of quality of cost evidence was adopted. A generic cost of a scan was used for each different option. For example, option 2, which consisted of a first trimester dating scan, was given the same cost as option 3, which consisted of a second trimester anomaly scan. This was because it was not possible to ascribe a particular cost to a particular scan due to a paucity of good data.

In the initial study, it was also assumed that all woman for whom an anomaly was detected would undergo a package of further tests, including a serum test, a detailed scan and amniocentesis. It was assumed that these tests would conclusively determine an anomaly and rule out any false-positives. In the initial study, the generic cost of a scan was also used in this package of further tests.

Cost-effectiveness for the best and worst scenarios was estimated by attaching the lower limit of available costs to the best scenario and the upper limit of available costs to the worst scenario. The cost of the initial package of scans, which defined each option path, was multiplied by 1000 (women) to give the initial cost of that programme. The cost of the further non-routine tests encountered by women who would have fetal anomalies detected, including the false-positives, was added to the initial cost of the programme to give the total cost of that programme.

The results of this original model are shown in *Table 30* and *Figure 2*. Costs per case detected varied widely between the scenarios and the different options.

Methods

Refining the model

There were three stages to assessing the impact of different cost sources. All three stages included new clinical data from chapter 3 on detection of fetal abnormalities by routine ultrasound.

1. Using costs from the systematic review of the economic literature (chapter 8).
2. Using costs from the primary costing study at Liverpool Women's Hospital (chapter 9).
3. Extending the viewpoint of the model resulting from Stage 2, from that of the health service, which considers only direct health service costs, to a wider, societal perspective to include costs to women, their families, friends and employers. Data for this were from chapter 9 (page 81).

New clinical effectiveness data

The model was also extended to include almost all anomalies which may be detectable by ultrasound, grouped pragmatically into RCOG subgroups as described in chapter 3 and shown in *Tables 6* and *7*. Anomalies that were not reported consistently in

TABLE 30 *Preliminary estimates of costs and effects of ultrasound screening options per 1000 women screened based on original model looking at four specific anomalies (Down's syndrome, spina bifida, congenital cardiac defects and lethal anomalies)*

Option	Best scenario				Worst scenario			
	Cost (£ 1996)	Target defects detected	Cost per case detected (£)	Target defects missed	Cost (£ 1996)	Target defects detected	Cost per case detected (£)	Target defects missed
2: 1st trimester dating scan	30,450	0.6	50,750	10	216,971	0.6	361,618	5.0
3: 2nd trimester scan	31,139	5.9	5278	4.7	217,565	2.0	108,782	3.6
4: 3rd trimester scan)	31,198	6.3	4952	4.2	217,798	2.5	87,119	3.0
5: 1st (dating) & 2nd trimester scans	51,187	6.2	8256	4.3	366,745	2.4	152,810	3.1
6: 1st (dating) & 3rd trimester scans	51,244	6.7	7648	3.8	366,998	3.0	122,333	2.5
7: 2nd & 3rd trimester scans	51,399	7.9	6506	2.7	367,074	3.2	114,711	2.4
8: 1st (dating), 2nd & 3rd trimester scans	71,442	8.2	8710	2.3	516,246	3.6	143,402	1.9
2a: 1st trimester anomaly scan)	30,583	1.6	19,114	8.5	217,099	0.9	241,221	4.7
5a: 1st (anomaly) & 2nd trimester scans	51,274	6.9	7431	3.6	366,860	2.6	141,100	2.9
6a: 1st (anomaly) & 3rd trimester scans	51,350	7.5	6847	3.0	367,125	3.3	111,250	2.2
8a: 1st (anomaly), 2nd & 3rd trimester scans	71,518	8.8	8127	1.7	516,360	3.8	135,884	1.7

the clinical systematic literature review were excluded, including very rare anomalies, anomalies that did not fit into any specific subgroup and those amenable to intrauterine therapy. The detection rates for each subgroup of anomalies, derived from the systematic review of the literature, refer only to available data for second and third trimester routine ultrasound scan (see *Tables 6* and *7*). The detection of anomalies at first trimester ultrasound, performed for dating, identifying multiple pregnancies and confirming viability, were based on consensus of expert opinion, in the same manner as in the original model. This refers to fortuitous detection of major abnormalities at early ultrasound scan performed for reasons other than fetal structural survey. There were no usable data for determining detection rates of fetal structural and chromosomal anomalies at first trimester anomaly scan (see page 32); hence, scanning options including first trimester anomaly scans were not included in the refined model. These data and combined detection rates (calculated as shown in appendix 13) are presented in *Table 31*. Specificity was calculated by subtracting the false-positive rates for each RCOG subgroup (presented in *Table 9*) from one. This was held constant throughout, as were prevalence and sensitivity.

For each of the subgroups, the prevalence was used to estimate how many true fetal anomalies there would be in a population of 1000 women. This was based on the prevalence of the anomalies in the populations studied and reported in the studies included in the systematic review of literature (see *Tables 6* and *7*). The combined detection rates were used to estimate the number of positive diagnoses.

Unlike in the original model, it was assumed that all women who were positively diagnosed would receive a detailed scan and counselling, and that only 25% would have karyotyping by amniocentesis or CVS. The assumption that only 25%, and not all women would have karyotyping was based on knowledge of clinical practice and the known association of some, but not all, abnormalities with chromosomal abnormalities. It was also assumed that all false-positive diagnoses were corrected with further tests and that all true positive cases of lethal anomaly and half the anomalies associated with long-term problems were terminated. The assumptions about termination of pregnancy were also based on clinical practice, and on the knowledge that termination of pregnancy would be offered and accepted in some of these cases as a management option. In the review of the clinical literature, only one woman had a

TABLE 31 *Prevalence, detection rates and combined detection rates for grouped anomalies*

	Prevalence (per 1000)[b]	False-positive rate (%)[b]	Sensitivity (detection rates)[b] (%)			Combined detection rate[a] (%)
			1st trimester	2nd trimester	3rd trimester	
Lethal anomalies	2.03	0	10	76	71	1st + 2nd = 78 1st + 3rd = 74 2nd + 3rd = 93 1st + 2nd + 3rd = 94
Possible survival and long-term morbidity	8.84	0.033	10	39	57	1st + 2nd = 45 1st + 3rd = 61 2nd + 3rd = 74 1st + 2nd + 3rd = 76
Possible immediate/short term morbidity	4.75	0.032	0	21	14	1st + 2nd = 21 1st + 3rd = 14 2nd + 3rd = 32 1st + 2nd + 3rd = 32

[a] *Method for combining detection rates illustrated in appendix 13*
[b] *Based on data derived from review described in chapter 2*

termination of a normal pregnancy (i.e. termination resulting from a false-positive diagnosis). Women given a negative diagnosis were assumed to continue with their pregnancy.

This new clinical effectiveness data from the systematic review of the clinical literature was used for all the stages of refining the model. When not available, consensus of expert opinion was used. This was reached by the RCOG Working Party members, who undertook at least two rounds of repeated estimation with different people present.

New cost data

Comparison of cost estimates from the original model, the literature review (see chapter 8) and the primary costing research (see chapter 9) are presented in *Table 32*. All costs are presented in £ sterling (1997 prices). Other currencies were converted to sterling using the Organization for Economic Coordination and Development conversion rates,[188] inflated to 1997 prices using NHS pay and prices indices. The range of cost estimates from the literature review is wide – wider than the range initially used by Roberts and colleagues.[183] However, to reach this stage of the review, all the data had been through quality checks unlike the data used in the initial study. Furthermore, there is no evidence to suggest that any cost presented is more accurate than another, as it will depend on the context in which the routine screening is carried out. The mean of the estimates reported for the cost of a routine scan based on the literature search was £109.76. This is much higher than the cost of any of the routine scans estimated in the costing study carried out at the Liverpool Women's Hospital; these averaged between £14 and £16, depending on the exact purpose of the scan. However, only three studies presented primary data on the cost of ultrasound;[192,193,197] the average cost of a scan based on these three studies alone was £35.42. Furthermore, primary costing was based on UK data in only one study,[193] and it is noteworthy that their cost of a routine scan (£18.08) is closest to our own estimates. The estimated cost reported by Long and Sprigg[193] refers to that of a second trimester scan (carried out at 18–20 weeks). This corresponds to the Liverpool routine anomaly scan that was estimated to cost £15.46. Long and Sprigg estimated that this scan would take between 15 and 20 minutes, which falls within the range of timings for this scan estimated in Liverpool. The mean reported estimate based on secondary data was £142.

The average cost of the 'other scans' extracted from the literature was £61.60. Only two studies presented a cost for this procedure.[197,203] Leivo and colleagues[192] presented the costs based on primary data, while Sadovnick and Baird's[203] cost is based on charges from 1982. It is not clear from the literature, although it is implied, that this 'other scan' refers to a specialised, non-routine scan carried out to confirm diagnosis of an anomaly or other complications. If this is correct, then it corresponds most closely to the 'detailed scan' in the Liverpool estimates, carried out by a consultant. The primary cost estimates presented by Leivo

TABLE 32 *Comparison of average costs of procedures (£ sterling, 1997 prices)*

	Costs used by Roberts and colleagues[183]	Economic literature review	Primary costing from Liverpool
	Best – worst scenario (£)	**Combined average (range) (£)**	**Average (range) (£)**
Routine scan	21.00 – 156.00	109.76 (18.08–204.30) 35.42[P] 142.79[S]	N/A
Dating scan	N/A	N/A	14.19 (12.18–16.44)
Growth scan	N/A	N/A	15.71 (13.58–17.84)
Anomaly scan	N/A	N/A	15.46 (13.42–17.51)
Detailed scan/other scan	N/A	61.60 36.06[P] 112.67[S]	51.47 (39.55–76.69)
Fetal well-being scan	N/A	N/A	15.46 (11.67–21.16)
Amniocentesis	99.00 – 261.00	412.55 (160.50–870.00) 270.28[P] 554.83[S]	189.09 (182.61–197.86)
CVS	N/A	529.75 267.50[P] 792.00[S]	239.31 (226.63–252.31) (transabdominal) 264.09 (251.41–277.09) (transvaginal)
Serum alpha-fetoprotein	16.00 – 26.00	32.90 (28.34–37.46)[S]	N/A
Double test	N/A	95.70[S]	N/A
Termination of pregnancy	N/A	516.70 (416.76–625.14)	

[P] *Average based on primary data*
[S] *Average based on secondary data (charges)*

and colleagues, and the average for this procedure, are all within the range for this procedure estimated at the Liverpool Women's Hospital.

A cost for amniocentesis was presented in four studies.[191,192,194,196] Only the costs presented by Leivo and colleagues[192] and Wald and colleagues[196] were based on primary costing. The study by Wald and colleagues was the only one presenting UK primary data and their estimate of £160.50 is very close to the estimate of £189.09 calculated at the Liverpool Women's Hospital.

Two studies presented cost estimates for CVS. In the study by Wald and colleagues,[196] primary costs were based on UK data and, once again, this estimate is close to the cost estimated in the primary costing study at Liverpool.

Cost-effectiveness calculation

Because of the wide variation in costs reported, two scenarios were used: a 'best' scenario using low costs and a 'worst' scenario using high costs. All other factors remained constant. The average cost per case detected was estimated by taking the cost of the scan or scans, which defined each option path, multiplied by 1000 (women) to give the initial cost of that programme. The cost of the further non-routine tests encountered by women who had fetal anomalies detected, including the false-positives, were added to the initial cost of the programme. Costs of terminations of pregnancy were not included nor were the costs associated with delivery.

Incremental cost-effectiveness ratios (ICERs) were estimated for each RCOG subgroup, both separately and for the aggregated results, using the costs collected at each stage of the review. The ICER is important because it makes explicit the extra cost that would have to be paid for detecting the additional anomalies, over and above what would be achieved from current practice or some other reference programme. ICERs are estimated by comparing the difference in costs (C) with the difference in effects (E) for the programmes (a and b) being compared; that is:

$$ICER = (C_a - C_b) / (E_a - E_b)$$

For each subgroup and the aggregated group, a reference option was chosen and used as the benchmark with which to compare other competing options. Typically the reference option

was one of the least costly options but also one that detected a significant number of anomalies per thousand women, and so some degree of discretion was necessary. In some cases an alternative option proved slightly cheaper but detected too few anomalies to be a serious competitor. ICERs were calculated for all those options which were both more costly and detected more anomalies than the reference case. They were also calculated for options which proved less costly and detected slightly fewer anomalies than the reference case. Options were considered 'dominated' if they were more costly and detected fewer anomalies than a competing option. However, in some cases, an option was also described as 'dominated' if it was £10,000 more costly, and detected fewer than 0.5 anomalies per thousand women, than the next best option, to avoid over-precision of the estimate for the detection and insignificant differences providing misleading results with regard to relative cost-effectiveness.

Results

Stage 1

Costs from the systematic review of the literature failed to provide separate costs for routine scans performed at different times in pregnancy. Hence, a low primary cost and a high charge from secondary sources were used in the two scenarios described above. The review of the literature did reveal a separate cost for a detailed scan and this was included in follow-up costs of positive diagnoses. The number of options was reduced to eight because data of a satisfactory quality were not retrievable on the detection rates of first trimester anomaly scanning.

The estimated costs per case detected are presented for each RCOG subgroup in *Table 33*. This shows substantially higher costs than the original model, reflecting the greater unit costs of scans and other tests on which they are based. For all anomaly groups, average cost per case detected was highest with a first trimester dating scan reflecting the poor sensitivity of this type of scan. Lowest cost per case detected for lethal and short/medium-term anomalies was associated with the second trimester anomaly scan but for the long-term morbidity group and all anomalies combined a third trimester scan was associated with lowest costs per case detected.

The ICERs for the relevant options are presented in *Table 34*, using the costs from the review of the economic literature for each of the RCOG subgroups and the aggregated detection rates for anomalies. The results for the individual subgroups do show some variation compared with the aggregated group.

Stage 2

The data collected from the primary cost study carried out at the Liverpool Women's Hospital (see chapter 7) provided substantially more detailed information with which to refine the model. Thus different levels of costs were applied for options incorporating different types of scans. For example, for option 8, the cost of a dating scan was applied to a first trimester scan, the cost of an anomaly scan to a second trimester scan and the cost of a growth/fetal well-being scan to a third trimester scan. In addition, a separate cost was applied for a detailed scan required in the package of consequential tests for confirmation of diagnosis. The cost of counselling was included in the scan cost.

The results of this model are presented in *Tables 35* and *36*. The total costs and cost per case detected (*Table 35*) are substantially lower than for either those based on the literature review or the original model. As before, the highest cost per case detected was associated with a first trimester scan and the lowest with either a second or third trimester scan. Detection rates, missed cases and false-positive diagnoses were the same as for stage 1.

The ICERs for the relevant options are presented in *Table 36*, using the costs from the primary costing survey for each of the RCOG subgroups and using the aggregated detection rates for anomalies. Compared with stage 1, the costs from the primary study lead to more consistent results throughout each of the subgroups and for the aggregated results, and the reference case was always one second trimester scan (option 3). However, when the results were aggregated, one third trimester scan (option 4) was relatively cost-effective for the best but not for the worst scenario. Option 7, which comprises one second trimester scan and one third trimester scan, detected more anomalies in any 1000 women at an additional cost of between £23,426 and £42,466 per additional anomaly detected.

Stage 3

The results of the primary research at the Liverpool Women's Hospital into cost for women and their families and employers of attending for ultrasound (see page 81) were included at this stage. The results are shown in *Tables 37* and *38*. The unit cost of an ultrasound scan was substantially

TABLE 33 *Estimates of cost-effectiveness based on prevalence, sensitivity and specificity from clinical review of literature and costs from economic review of literature (costs per 1000 women screened, 1997 prices)*

Option	Best scenario		Worst scenario	
	Cost (£)	Cost per case detected (£)	Cost (£)	Cost per case detected (£)
Lethal anomalies				
2: 1st trimester dating scan	35,012	172,473	142,055	699,776
3: 2nd trimester scan	35,042	22,713	142,415	92,309
4: 3rd trimester scan	35,039	24,311	142,388	98,791
5: 1st & 2nd trimester scans	70,043	44,236	284,426	179,630
6: 1st & 3rd trimester scans	70,041	46,625	284,404	189,325
7: 2nd & 3rd trimester scans	70,051	37,105	284,508	150,701
8: 1st, 2nd & 3rd trimester scans	105,052	55,053	426,513	223,516
Anomalies associated with possible survival and long-term morbidity				
2: 1st trimester dating scan	35,182	39,798	142,553	161,260
3: 2nd trimester scan	35,572	10,213	143,741	41,270
4: 3rd trimester scan	35,805	7,106	144,452	28,668
5: 1st & 2nd trimester scans	70,646	17,759	285,968	71,887
6: 1st & 3rd trimester scans	70,858	13,140	286,614	53,151
7: 2nd & 3rd trimester scans	71,031	10,858	287,139	43,894
8: 1st, 2nd & 3rd trimester scans	106,057	15,786	429,220	63,887
Anomalies associated with possible short-term/immediate morbidity				
2: 1st trimester dating scan	35,048	–[a]	142,146	–[a]
3: 2nd trimester scan	35,197	35,286	142,601	142,959
4: 3rd trimester scan	35,148	52,853	142,449	214,210
5: 1st & 2nd trimester scans	70,197	70,373	284,601	285,315
6: 1st & 3rd trimester scans	70,148	105,485	284,449	427,744
7: 2nd & 3rd trimester scans	70,276	46,234	284,840	187,395
8: 1st, 2nd & 3rd trimester scans	105,276	69,260	426,840	280,816
All above anomalies				
2: 1st trimester dating scan	35,172	32,357	143,844	132,331
3: 2nd trimester scan	35,660	5920	146,248	24,280
4: 3rd trimester scan	35,771	5006	146,794	20,545
5: 1st & 2nd trimester scans	70,713	10,781	289,509	44,140
6: 1st & 3rd trimester scans	70,812	9367	289,996	38,361
7: 2nd & 3rd trimester scans	71,049	7141	291,160	29,264
8: 1st, 2nd & 3rd trimester scans	106,068	10,454	434,256	42,798

[a] *This option detected no anomalies*

increased with the inclusion of societal costs, which is reflected in the costs shown in *Table 37*. Relative costs per case detected were the same as for previous iterations of the model. *Figure 3* shows the number of malformations correctly diagnosed, cases missed (false-negatives) and false-positive diagnoses. Compared with *Figure 2* (based on 'expert opinion'), *Figure 3* shows fewer malformations detected with each option. *Figure 3* also shows fewer false-positives than *Figure 2*. The clinical outcomes of the model are summarised in *Table 39*. The high specificity of all the scans led to very few false-positive diagnoses. Iatrogenic loss (miscarriage resulting from invasive testing) was also very low.

The ICERs for the relevant options are presented in *Table 38* for the societal perspective for each of the RCOG subgroups and based on the aggregated group. Option 3 (second trimester scan) and option 4 (third trimester scan) appear to be the most potentially cost-effective options. The additional cost per additional case detected per 1000 women is in the range of just £271–477 for option 4, which comprises one third trimester scan compared with one second trimester scan (option 3). Option 7 (one second trimester and one third trimester scan) also appears to be relatively competitive, costing approximately £7369–8509 more per additional anomaly detected than option 3.

TABLE 34 *Incremental cost-effectiveness ratios calculated using cost data from the systematic review of the literature (1997 prices)*

	Defects detected	Cost (£)		Comment	ICER: additional cost per additional case detected (£)	
		Best scenario	Worst scenario		Best scenario	Worst scenario
Lethal anomalies						
2: 1st trimester dating scan	0.20	35,012	142,055	Dominated by option 3		
3: 2nd trimester scan	1.54	35,042	142,415	Compare with option 4	30	270
4: 3rd trimester scan	1.44	35,039	142,388	Reference case		
5: 1st & 2nd trimester scans	1.58	70,043	284,426	Dominated by option 3		
6: 1st & 3rd trimester scans	1.50	70,041	284,404	Dominated by option 3		
7: 2nd & 3rd trimester scans	1.89	70,051	284,508	Compare with option 4	77,804	315,822
8: 1st, 2nd & 3rd trimester scans	1.91	105,052	426,513	Compare with option 4	148,964	368,993
Anomalies associated with possible survival and long-term morbidity						
2: 1st trimester dating scan	0.9	35,182	142,553	Dominated by option 3		
3: 2nd trimester scan	3.5	35,572	143,741	Reference case		
4: 3rd trimester scan	5.0	35,805	144,452	Compare with option 3	155	474
5: 1st & 2nd trimester scans	4.0	70,646	285,968	Dominated by option 4		
6: 1st & 3rd trimester scans	5.4	70,858	286,614	Compare with option 3	18,581	75,196
7: 2nd & 3rd trimester scans	6.5	71,031	287,139	Compare with option 3	22,026	47,799
8: 1st, 2nd & 3rd trimester scans	6.7	106,057	429,220	Dominated by option 7		
Anomalies associated with possible short-term/immediate morbidity						
2: 1st trimester dating scan	0	35,048	142,146	Not a viable option		
3: 2nd trimester scan	1.0	35,197	142,601	Compare with option 4	163	507
4: 3rd trimester scan	0.7	35,148	142,449	Reference case		
5: 1st & 2nd trimester scans	1.0	70,197	284,601	Dominated by option 3		
6: 1st & 3rd trimester scans	0.7	70,148	284,449	Dominated by option 3		
7: 2nd & 3rd trimester scans	1.5	70,276	284,840	Compare with option 4	43,910	177,989
8: 1st, 2nd & 3rd trimester scans	1.5	105,276	426,840	Dominated by option 7		
All above anomalies						
2: 1st trimester dating scan	1.09	35,172	143,844	Dominated by option 3		
3: 2nd trimester scan	6.02	35,660	146,248	Reference case		
4: 3rd trimester scan	7.15	35,771	146,794	Compare with option 3	98	483
5: 1st & 2nd trimester scans	6.56	70,713	289,509	Dominated by option 4		
6: 1st & 3rd trimester scans	7.56	70,812	289,996	Dominated by option 4		
7: 2nd & 3rd trimester scans	9.95	71,049	291,160	Compare with option 3	9004	36,873
8: 1st, 2nd & 3rd trimester scans	10.15	106,068	434,526	Compare with option 7	175,095	716,830

The cost per case detected in the three iterations of the model, using costs from the review of the economic literature, costs from the primary costing research at the Liverpool Women's Hospital and, lastly, extending the perspective to include women's, families' and employers' costs, are summarised in *Table 40*.

Sensitivity analyses

All variables presenting a range of possible values were varied in the sensitivity analyses to test the effect on the results. The key assumptions tested in the sensitivity analyses were:

(i) the unit cost inputs to the model

(ii) the prevalence, sensitivity and specificity of scans

(iii) that 25% of detected anomalies would be karyotyped

(iv) the importance of serum screening.

(i) Unit costs

It was demonstrated in chapters 6 and 7 that a wide range of cost estimates for routine scans and other tests could be used in the model. An attempt has been made to show the effects of this by going through several stages in the model and using 'best' and 'worst' scenarios. The results are clearly highly sensitive to this factor.

TABLE 35 *Estimates of cost-effectiveness based on prevalence, sensitivity and specificity from clinical review of literature and costs from primary costing study (costs per 1000 women screened, 1997 prices)*

Option	Best scenario		Worst scenario	
	Cost (£)	Cost per case detected (£)	Cost (£)	Cost per case detected (£)
Lethal anomalies				
2: 1st trimester dating scan	12,197	60,084	16,468	81,124
3: 2nd trimester scan	35,550	8782	17,724	11,488
4: 3rd trimester scan	11,791	8181	21,360	14,820
5: 1st & 2nd trimester scans	25,733	16,252	34,170	21,580
6: 1st & 3rd trimester scans	23,976	15,961	37,809	25,169
7: 2nd & 3rd trimester scans	25,249	13,374	38,932	20,622
8: 1st, 2nd & 3rd trimester scans	37,430	19,615	55,375	29,020
Anomalies associated with possible survival and long-term morbidity				
2: 1st trimester dating scan	12,282	13,893	16,608	18,788
3: 2nd trimester scan	13,740	3945	18,040	5179
4: 3rd trimester scan	12,121	2405	21,906	4347
5: 1st & 2nd trimester scans	25,962	6526	34,548	8685
6: 1st & 3rd trimester scans	24,330	4512	38,395	7120
7: 2nd & 3rd trimester scans	25,667	3924	39,625	6057
8: 1st, 2nd & 3rd trimester scans	37,862	5636	56,089	8349
Anomalies associated with possible short-term/immediate morbidity				
2: 1st trimester dating scan	12,207	–[a]	16,484	–[a]
3: 2nd trimester scan	13,531	13,564	17,693	17,737
4: 3rd trimester scan	11,753	17,673	21,297	32,025
5: 1st & 2nd trimester scans	25,711	25,775	34,133	34,218
6: 1st & 3rd trimester scans	23,933	35,989	37,737	56,747
7: 2nd & 3rd trimester scans	25,244	16,608	38,926	25,609
8: 1st, 2nd & 3rd trimester scans	37,424	24,621	55,366	36,425
All above anomalies				
2: 1st trimester dating scan	12,326	11,339	16,681	15,346
3: 2nd trimester scan	13,980	2321	18,437	3061
4: 3rd trimester scan	12,324	1725	22,243	3113
5: 1st & 2nd trimester scans	26,205	3995	34,951	5329
6: 1st & 3rd trimester scans	24,539	3246	38,741	5125
7: 2nd & 3rd trimester scans	25,980	2611	40,143	4035
8: 1st, 2nd & 3rd trimester scans	38,177	3762	56,610	5579

[a] *This option detected no anomalies*

(ii) ***Prevalence, sensitivity and specificity***
Prevalence, sensitivity and specificity were derived from the clinical studies that passed a stringent quality threshold defined in chapter 2. However, if the studies did not have complete postnatal ascertainment of the anomalies detected, prevalence may be higher than reported. It is also possible that these clinical studies are not representative of the quality of scanning generally, which may have lower sensitivity and specificity. The effect was tested on average cost per case detected of using extremes of prevalence, sensitivity and specificity from the studies included. The values used are shown in *Table 41*. The results of this sensitivity analysis are summarised in *Table 42*. With high prevalence, high sensitivity and high specificity and baseline costs, a second trimester scan produced the lowest cost per case detected for all anomalies combined (£2353). With low prevalence, low sensitivity and low specificity the highest cost per case detected for all anomalies was associated with one second trimester plus one third trimester scan (£263,117). It is worth noting that, although there was a narrow range of prevalence and specificity in the different studies, the range of sensitivity was very wide – from 0% to 100% in some cases, as shown

TABLE 36 *Incremental cost-effectiveness ratios calculated using cost data from the primary costing study (1997 prices)*

	Defects detected	Cost (£)		Comment	ICER: additional cost per additional case detected (£)	
		Best scenario	Worst scenario		Best scenario	Worst scenario
Lethal anomalies						
2: 1st trimester dating scan	0.20	12,197	16,468	Dominated by option 3		
3: 2nd trimester scan	1.54	13,550	17,724	Reference case		
4: 3rd trimester scan	1.44	11,791	21,360	Dominated by option 3		
5: 1st & 2nd trimester scans	1.58	25,733	34,170	Dominated by option 3		
6: 1st & 3rd trimester scans	1.50	23,976	37,809	Dominated by option 3		
7: 2nd & 3rd trimester scans	1.89	25,249	38,932	Compare with option 3	33,426	60,594
8: 1st, 2nd & 3rd trimester scans	1.91	37,430	55,375	Compare with option 3	64,540	101,759
Anomalies associated with possible survival and long-term morbidity						
2: 1st trimester dating scan	0.9	12,282	16,608	Dominated by option 3 ?		
3: 2nd trimester scan	3.5	13,740	18,040	Reference case		
4: 3rd trimester scan	5.0	12,121	21,906	Compare with option 3	−1079	2577
5: 1st & 2nd trimester scans	4.0	25,962	34,548	Dominated by option 4		
6: 1st & 3rd trimester scans	5.4	24,330	38,395	Dominated by option 4		
7: 2nd & 3rd trimester scans	6.5	25,667	39,625	Compare with option 3	3975	7195
8: 1st, 2nd & 3rd trimester scans	6.7	37,862	56,089	Dominated by option 7		
Anomalies associated with possible short-term/immediate morbidity						
2: 1st trimester dating scan	0	12,207	16,484	Not a viable option		
3: 2nd trimester scan	1.0	13,531	17,693	Reference case		
4: 3rd trimester scan	0.7	11,753	21,297	Dominated by option 3		
5: 1st & 2nd trimester scans	1.0	25,711	34,133	Dominated by option 3		
6: 1st & 3rd trimester scans	0.7	23,933	37,737	Dominated by option 3		
7: 2nd & 3rd trimester scans	1.5	25,244	38,926	Compare with option 3	23,426	42,466
8: 1st, 2nd & 3rd trimester scans	1.5	37,424	55,366	Dominated by option 7		
All above anomalies						
2: 1st trimester dating scan	1.09	35,172	143,844	Dominated by option 3		
3: 2nd trimester scan	6.02	13,980	18,437	Reference case		
4: 3rd trimester scan	7.15	12,324	22,243	Compare with option 3	−1465	3368
5: 1st & 2nd trimester scans	6.56	26,205	34,951	Dominated by option 4		
6: 1st & 3rd trimester scans	7.56	24,539	38,741	Dominated by option 4		
7: 2nd & 3rd trimester scans	9.95	25,980	40,143	Compare with option 3	3053	5523
8: 1st, 2nd & 3rd trimester scans	10.15	38,177	56,610	Compare with option 7	60,985	82,335

**NB: In some cases, an option was also described as 'dominated' if it cost more than £10,000 and detected fewer than 0.5 anomalies per 1000 women more than the next best option*

in *Table 42*. In the low sensitivity scenario, this led to cost per case detected being even higher than those resulting from the worst scenario of stage 1, which used high costs from the literature.

(iii) ***Percentage karyotyped***

The proportion of those anomalies detected that are karyotyped depends on what anomalies are detected and on local practice. The effect of karyotyping all suspected anomalies only increased costs by about 2%.

(iv) ***The importance of serum screening***

The original project was designed to compare different ultrasound screening regimes. It was not proposed to include serum screening in the comparison. Moreover, a study (SURUSS) is currently underway to quantify the performance of first trimester screening based on biochemical (serum and urine) and ultrasound markers (NT), and to compare this with second trimester serum screening, in detecting babies with Down's syndrome. Nevertheless, second trimester serum screening is routinely offered to pregnant

TABLE 37 *Estimates of cost-effectiveness from a societal perspective based on prevalence, sensitivity and specificity from clinical review of literature and costs from primary costing study (costs per 1000 women screened, 1997 prices)*

Option	Best scenario		Worst scenario	
	Cost (£)	Cost per case detected (£)	Cost (£)	Cost per case detected (£)
Lethal anomalies				
2: 1st trimester dating scan	27,077	133,382	31,348	154,422
3: 2nd trimester scan	28,492	18,468	32,667	21,174
4: 3rd trimester scan	28,639	19,870	32,978	22,881
5: 1st & 2nd trimester scans	55,547	35,081	63,985	40,410
6: 1st & 3rd trimester scans	55,697	37,077	64,299	42,803
7: 2nd & 3rd trimester scans	56,987	30,186	65,441	34,663
8: 1st, 2nd & 3rd trimester scans	84,040	44,041	96,755	50,705
Anomalies associated with possible survival and long-term morbidity				
2: 1st trimester dating scan	27,209	30,779	31,535	35,673
3: 2nd trimester scan	28,789	8266	33,089	9500
4: 3rd trimester scan	29,153	5786	33,708	6690
5: 1st & 2nd trimester scans	55,904	14,053	64,491	16,212
6: 1st & 3rd trimester scans	56,249	10,431	65,084	12,070
7: 2nd & 3rd trimester scans	57,640	8811	66,368	10,145
8: 1st, 2nd & 3rd trimester scans	84,713	12,609	97,710	14,544
Anomalies associated with possible short-term/immediate morbidity				
2: 1st trimester dating scan	27,092	–[a]	31,369	–[a]
3: 2nd trimester scan	28,462	28,534	32,625	32,707
4: 3rd trimester scan	28,579	42,976	32,893	49,463
5: 1st & 2nd trimester scans	55,512	55,652	63,935	64,095
6: 1st & 3rd trimester scans	55,629	83,652	64,203	96,546
7: 2nd & 3rd trimester scans	56,981	37,487	65,432	43,047
8: 1st, 2nd & 3rd trimester scans	84,031	55,283	96,742	63,646
All above anomalies				
2: 1st trimester dating scan	27,277	25,094	31,632	29,101
3: 2nd trimester scan	29,164	4842	33,620	5582
4: 3rd trimester scan	29,471	4125	34,159	4781
5: 1st & 2nd trimester scans	56,284	8581	65,030	9915
6: 1st & 3rd trimester scans	56,575	7484	65,546	8671
7: 2nd & 3rd trimester scans	58,128	5842	67,061	6740
8: 1st, 2nd & 3rd trimester scans	85,204	8397	98,407	9699

[a] *This option detected no anomalies*

women in many hospitals in the UK, and so an attempt has been made to incorporate this into the model. It should be noted, however, that serum screening is used to detect only Down's syndrome, albeit one of the commonest congenital abnormalities. While routine ultrasound in the second and third trimester is not clinically effective for detecting chromosomal abnormalities, it may be employed to detect a multitude of structural abnormalities (in chromosomally normal and abnormal fetuses). In an HTA report on antenatal screening for Down's syndrome,[196] the authors showed that second trimester screening performance varies according to the choice of markers used and whether ultrasound is used to estimate gestational age. When ultrasound is used to date the pregnancy, the second trimester serum screening detection rate is 59%, 69%, and 76% for the double, triple and quadruple tests, respectively, for a 5% false-positive rate.[196] Therefore if the package of antenatal care includes serum screening a dating scan will be desirable to optimise the efficiency of serum screening. Costs for serum screening were taken from the review of the economic literature (see *Table 22*). Sensitivity and specificity for serum screening were taken from the earlier HTA report.[196] Costs per case detected appeared to be lower for serum

TABLE 38 *Incremental cost-effectiveness ratios calculated using cost data that includes the societal perspective (1997 prices)*

	Defects detected	Cost (£)		Comment	ICER: additional cost per additional case detected (£)	
		Best scenario	Worst scenario		Best scenario	Worst scenario
Lethal anomalies						
2: 1st trimester dating scan	0.20	27,077	31,348	Dominated by option 3		
3: 2nd trimester scan	1.54	28,492	32,667	Reference case		
4: 3rd trimester scan	1.44	28,639	32,978	Dominated by option 3		
5: 1st & 2nd trimester scans	1.58	55,547	63,985	Dominated by option 3		
6: 1st & 3rd trimester scans	1.50	55,697	64,299	Dominated by option 3		
7: 2nd & 3rd trimester scans	1.89	56,987	65,441	Compare with option 3	81,414	93,640
8: 1st, 2nd & 3rd trimester scans	1.91	84,040	96,755	Compare with option 3	150,129	173,211
Anomalies associated with possible survival and long-term morbidity						
2: 1st trimester dating scan	0.9	27,209	31,535	Dominated by option 3		
3: 2nd trimester scan	3.5	28,789	33,089	Reference case		
4: 3rd trimester scan	5.0	29,153	33,708	Compare with option 3	242	412
5: 1st & 2nd trimester scans	4.0	55,904	64,491	Dominated by option 4		
6: 1st & 3rd trimester scans	5.4	56,249	65,084	Dominated by option 4		
7: 2nd & 3rd trimester scans	6.5	57,640	66,368	Compare with option 3	9617	11,093
8: 1st, 2nd & 3rd trimester scans	6.7	84,713	97,710	Dominated by option 7		
Anomalies associated with possible short-term/immediate morbidity						
2: 1st trimester dating scan	0	27,092	31,369	Not a viable option		
3: 2nd trimester scan	1.0	28,462	32,625	Reference case		
4: 3rd trimester scan	0.7	28,579	32,893	Dominated by option 3		
5: 1st & 2nd trimester scans	1.0	55,512	63,935	Dominated by option 3		
6: 1st & 3rd trimester scans	0.7	55,629	64,203	Dominated by option 3		
7: 2nd & 3rd trimester scans	1.5	56,981	65,432	Compare with option 3	57,038	65,614
8: 1st, 2nd & 3rd trimester scans	1.5	84,031	96,742	Dominated by option 7		
All above anomalies						
2: 1st trimester dating scan	1.09	27,277	31,632	Dominated by option 3		
3: 2nd trimester scan	6.02	29,164	33,620	Reference case		
4: 3rd trimester scan	7.15	29,471	34,159	Compare with option 3	271	477
5: 1st & 2nd trimester scans	6.56	56,284	65,030	Dominated by option 4		
6: 1st & 3rd trimester scans	7.56	56,575	65,546	Dominated by option 4		
7: 2nd & 3rd trimester scans	9.95	58,128	67,061	Compare with option 3	7369	8509
8: 1st, 2nd & 3rd trimester scans	10.15	85,204	98,407	Compare with option 7	135,380	156,730

**NB: In some cases, an option was also described as 'dominated' if it cost more than £10,000 and detected fewer than 0.5 anomalies per 1000 women more than the next best option*

screening without a dating scan (£53,333) than for serum screening with a dating scan (£69,773). These appear to compare favourably with a first trimester ultrasound scan for Down's syndrome (£103,139 per case detected) based on data from the RCOG report.[5] There is clearly a need for further more rigorous evaluation of the cost-effectiveness of the various options and combination of options. Furthermore, Wald and colleagues[196] emphasise that multiple stepwise uncoordinated screening of Down's syndrome (i.e. more than one method of screening of the same women at different stages of pregnancy) should be avoided, and methods of screening should not be introduced into clinical practice before they have been fully evaluated.

Discussion

Decision analysis is an approach to modelling that has the advantage of transparency. Each stage is set

FIGURE 3 *Number of anomalies detected for 1000 women taking each option's best scenario, cost data from primary cost study, societal perspective and clinical data from clinical review*

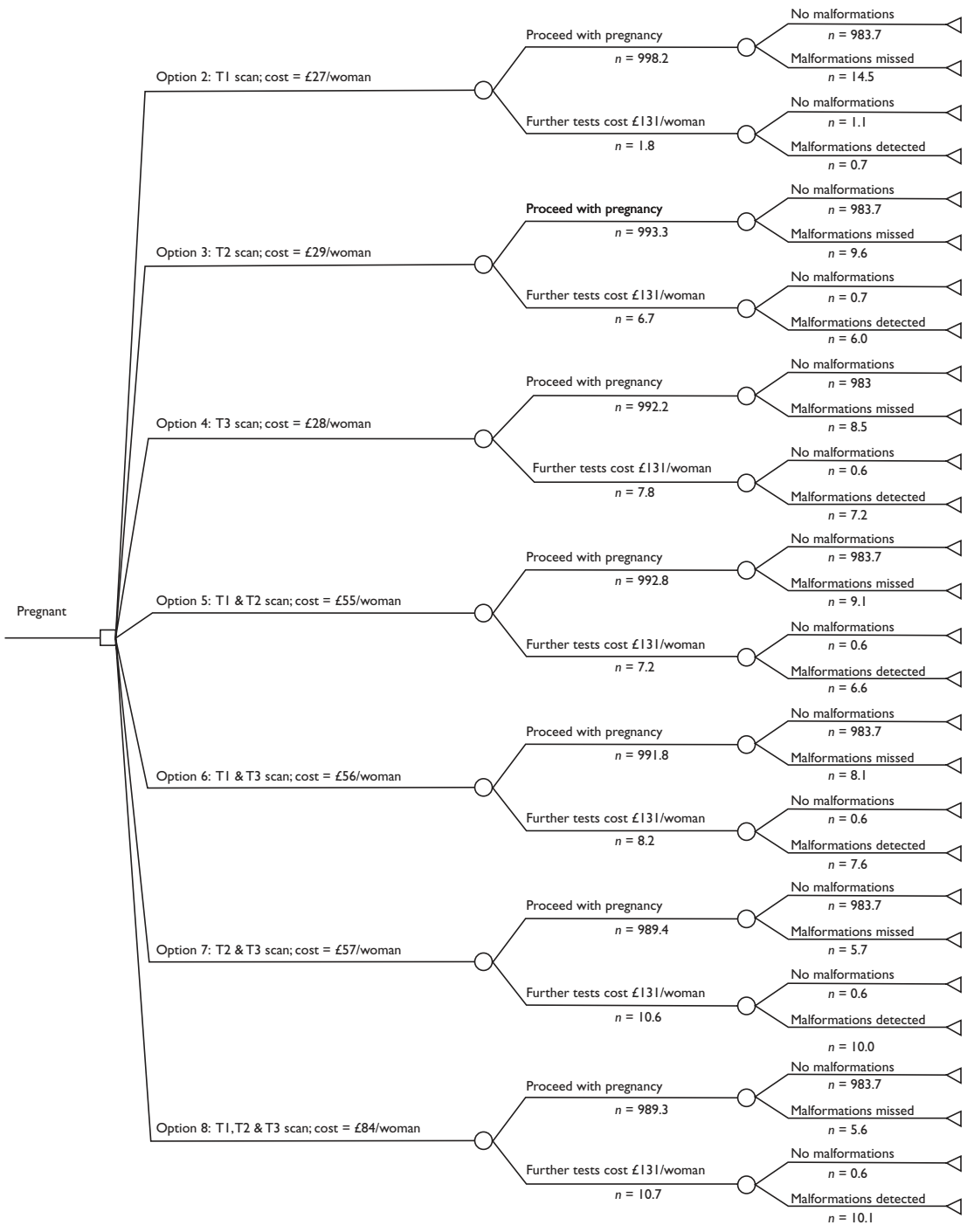


TABLE 39 *Clinical outcomes of the model (per 1000 women)*

Options	Target defects detected (true-positives)	Target defects missed (false-negatives)	Target defects incorrectly diagnosed (false-positives)	Iatrogenic loss
Lethal anomalies				
2: 1st trimester dating scan	0.2	1.8	0	0
3: 2nd trimester scan	1.5	0.5	0	0
4: 3rd trimester scan	1.4	0.6	0	0
5: 1st & 2nd trimester scans	1.6	0.4	0	0
6: 1st & 3rd trimester scans	1.5	0.5	0	0
7: 2nd & 3rd trimester scans	1.9	0.1	0	0
8: 1st, 2nd & 3rd trimester scans	1.9	0.1	0	0
Anomalies associated with possible survival and long-term morbidity				
2: 1st trimester dating scan	0.9	8.0	0.3	0
3: 2nd trimester scan	3.5	5.4	0.3	0
4: 3rd trimester scan	5.0	3.8	0.3	0.1
5: 1st & 2nd trimester scans	4.0	4.9	0.3	0
6: 1st & 3rd trimester scans	5.4	3.4	0.3	0.1
7: 2nd & 3rd trimester scans	6.5	2.3	0.3	0.1
8: 1st, 2nd & 3rd trimester scans	6.7	2.1	0.3	0.1
Anomalies associated with possible short-term/immediate morbidity				
2: 1st trimester dating scan	0	4.7	0.3	0
3: 2nd trimester scan	1.0	3.7	0.3	0
4: 3rd trimester scan	0.7	4.1	0.3	0
5: 1st & 2nd trimester scans	1.0	3.7	0.3	0
6: 1st & 3rd trimester scans	0.7	4.1	0.3	0
7: 2nd & 3rd trimester scans	1.5	3.2	0.3	0
8: 1st, 2nd & 3rd trimester scans	1.5	3.2	0.3	0

out and the assumptions and data used are made explicit. This decision model, originally developed by Roberts and colleagues,[183] has been refined using effectiveness evidence from the clinical review of the literature and costs from the systematic review of the economic literature and from the primary costing research carried out at the Liverpool Women's Hospital. The results show large variation in costs, especially when the costs were from the economic literature. The clinical literature produced detection rates that were somewhat lower than those of the RCOG Working Party[2] that formed the basis for the original model. The model using new clinical data shows fewer malformations detected with each option than in the original model, which was based on a mixture of 'expert opinion' and a non-systematic literature review. It is worth noting that anomaly detection rates for first trimester scans performed for reasons other than anomaly detection are not available from the literature, so this figure was still based on consensus of expert opinion. This new model also showed fewer false-positives than the original, which reflects the higher specificity reported in the clinical studies reviewed. This difference may also be due to differences in definition and timing. A false-positive may not be considered as such if it is subsequently corrected in a detailed scan and only considered a false-positive if checked at a post-mortem. The effects of ultrasonographic soft markers were discussed in chapter 4. They have the potential to increase sensitivity by up to 4% but, also, to increase the number of false-positives generated. Thus, on both counts, costs would be expected to increase.

Miscarriages are a potentially important factor not included in the model. However, the vast majority of miscarriages occur prior to the date at which most women would present for their first scan and thus fall outside the scope of the model. Iatrogenic loss resulting from amniocentesis or CVS was included (see *Table 40*). Reassuringly, numbers were very low. Psychological effects cannot, however, be quantified.

At the Liverpool Women's Hospital, the routine option used is first trimester dating scan followed by second trimester anomaly scan (option 5). It was noted that 2.5% of dating scans and 7.6% of anomaly scans had to be repeated because of uncertainty in findings, also that a small

TABLE 40 *Summary of estimates of cost per case detected according to each stage of refining the original decision model (1997 prices)*

Option	Best scenario: cost per case detected			Worst scenario: cost per case detected		
	Stage of refining the original model					
	1 Literature review costs (£)	2 Primary costing (£)	3 Women's costs included (£)	1 Literature review costs (£)	2 Primary costing (£)	3 Women's costs included (£)
Lethal anomalies						
2: 1st trimester dating scan	17,2473	60,084	133,382	699,776	81,124	154,422
3: 2nd trimester scan	22,713	8782	18,468	92,309	11,488	21,174
4: 3rd trimester scan	24,311	8181	19,870	98,791	14,820	22,881
5: 1st & 2nd trimester scans	44,236	16,252	35,081	179,630	21,580	40,410
6: 1st & 3rd trimester scans	46,625	15,961	37,077	189,325	25,169	42,803
7: 2nd & 3rd trimester scans	37,105	13,374	30,186	150,701	20,622	34,663
8: 1st, 2nd & 3rd trimester scans	55,053	19,615	44,041	223,516	29,020	50,705
Anomalies associated with possible survival and long-term morbidity						
2: 1st trimester dating scan	39,798	13,893	30,779	161,260	18,788	35,673
3: 2nd trimester scan	10,213	3945	8266	41,270	5179	9500
4: 3rd trimester scan	7106	2405	5786	28,668	4347	6690
5: 1st & 2nd trimester scans	17,759	6526	14,053	71,887	8685	16,212
6: 1st & 3rd trimester scans	13,140	4512	10,431	53,151	7120	12,070
7: 2nd & 3rd trimester scans	10,858	3924	8811	43,894	6057	10,145
8: 1st, 2nd & 3rd trimester scans	15,786	5636	12,609	63,887	8349	14,544
Anomalies associated with possible short-term/immediate morbidity						
2: 1st trimester dating scan[a]	–	–	–	–	–	–
3: 2nd trimester scan	35,286	13,564	28,534	142,959	17,737	32,707
4: 3rd trimester scan	52,853	17,673	42,976	214,210	32,025	49,463
5: 1st & 2nd trimester scans	70,373	25,775	55,652	285,315	34,218	64,095
6: 1st & 3rd trimester scans	105,485	35,989	83,652	427,744	56,747	96,546
7: 2nd & 3rd trimester scans	46,234	16,608	37,487	187,395	25,609	43,047
8: 1st, 2nd & 3rd trimester scans	69,260	24,621	55,283	280,816	36,425	63,646
All above anomalies						
2: 1st trimester dating scan	32,357	11,339	25,094	132,331	15,346	29,101
3: 2nd trimester scan	5920	2321	4842	24,280	3061	5582
4: 3rd trimester scan	5006	1725	4125	20,545	3113	4781
5: 1st & 2nd trimester scans	10,781	3995	8581	44,140	5329	9915
6: 1st & 3rd trimester scans	9367	3246	7484	38,361	5125	8671
7: 2nd & 3rd trimester scans	7141	2611	5842	29,264	4035	6740
8: 1st, 2nd & 3rd trimester scans	10,454	3762	8397	42,798	5579	9699

[a] *No anomalies were detected with this option*

proportion of the karyotyping failed. This suggests that costs may be 5–10% higher than documented, and points to areas of inefficiency in the system that are probably not limited to the Liverpool Women's Hospital.

The sensitivity analyses confirmed that the costs of the various options are highly sensitive to variations in unit costs and to variations in scan sensitivity. Other factors had less of an impact but the findings cannot be considered robust.

ICERs, which present results in terms of additional cost per additional case detected, made explicit the additional resources that would be required to detect additional anomalies in 1000 women. Whether a competing option is considered cost-effective is a subjective judgement, and will depend on whether a decision maker has a certain limit on additional funds, or a notional limit on the extra resources that can be afforded to detect the additional anomalies. Alternatively, benchmark figures from other areas of screening

TABLE 41 *Clinical outcomes of the model (per 1000 women)*

	Lethal anomalies	Anomalies associated with possible survival and long-term morbidity	Anomalies associated with possible short-term/ immediate morbidity
Prevalence (per 1000)			
Baseline	2.03	8.84	4.75
Low	0.40	2.10	1.02
High	3.29	8.79	12.78
Detection rates: 1st trimester (%)			
Baseline	10	10	0
Low	10	10	0
High	10	10	0
Detection rates: 2nd trimester (%)			
Baseline	76	39	21
Low	0	0	0
High	100	75	89
Detection rates: 3rd trimester (%)			
Baseline	71	57	14
Low	50	50	5
High	82	69	100
Specificity (%)			
Baseline	100	99.97	99.97
Low	100	99.45	99.45
High	100	99.98	99.98

or antenatal care may be available to help the decision maker.

The results of this analysis show that, overall, option 3, which comprises one second trimester scan, is a clear reference case being both one of the cheapest options, while still detecting a significant number of anomalies. It can also be used for accurate dating purposes. One third trimester scan (option 4) also appears to be a cost-effective alternative in detecting anomalies; however, this option is unlikely to be practical because of the difficult issues and complexity of procedures associated with late terminations. In addition, the detection rates of third trimester ultrasound need to be interpreted with caution because in all studies reporting third trimester routine scans, second trimester scans were also performed; hence, this does not reflect the performance of third trimester scans alone (see chapter 3). Furthermore, routine third trimester scans for reasons other than anomaly detection do not confer any benefits to the mother or baby (see appendix 2). Option 7, a combination of a second trimester scan and a third trimester scan, may also be considered relatively cost-effective.

Finally, it is worth emphasising that the model is limited to examining the efficiency of ultrasound screening in detecting anomalies and that the cost consequences or the benefits of detection, which are complex and multidimensional, are

TABLE 42 *Sensitivity analyses: costs per case detected (1997 prices)*

Option	Lethal anomalies (£)	Long-term morbidity (£)	Short-term morbidity (£)	All anomalies (£)
High prevalence, sensitivity and specificity				
2: 1st trimester dating scan	82,350	30,934	–[a]	22,567
3: 2nd trimester scan	8730	4426	9981	2353
4: 3rd trimester scan	10,677	4826	8947	2508
5: 1st & 2nd trimester scans	16,952	8311	19,391	4414
6: 1st & 3rd trimester scans	20,214	8905	17,322	4639
7: 2nd & 3rd trimester scans	17,377	7151	17,706	4019
8: 1st, 2nd & 3rd trimester scans	25,599	10,384	26,080	5837
Low prevalence, sensitivity and specificity				
2: 1st trimester dating scan	782,936	154,142	–[a]	133,597
3: 2nd trimester scan	–[a]	–[a]	–[a]	–[a]
4: 3rd trimester scan	163,736	32,311	661,597	26,898
5: 1st & 2nd trimester scans	1,592,436	308,333	–[a]	263,117
6: 1st & 3rd trimester scans	291,186	56,498	1,275,518	46,513
7: 2nd & 3rd trimester scans	325,636	63,149	1,296,499	51,787
8: 1st, 2nd & 3rd trimester scans	438,368	84,533	1,910,420	69,220

[a] *No cases were detected with this option*

not considered. Also, other screening methods, such as serum screening, have not been evaluated except in a very limited manner. NT screening has not been evaluated, for the reasons highlighted in the introduction. Furthermore, first trimester scans have been included in the model but they have not been evaluated in terms of their assistance in confirming and dating a pregnancy, which is most often their main purpose.

Recommendations for research

Improvement of the model requires data about the proportions of women having different types of scans at different times. This data is not collected nationally and would require a nationally representative survey.

To improve the model would also require more representative cost data, as well as data on the effects of first trimester anomaly scanning which were not included here.

Many of the options analysed were shown to be dominated by option 3 (one second trimester scan), option 4 (one third trimester scan), and option 7 (one second trimester and one third trimester scan). It may be appropriate for future research, if based on the outcome of cost per case detected, to concentrate on further assessment of this smaller number of options. The interaction of these options with a first trimester dating scan carried out specifically for dating purposes, also requires further analysis.

It must be emphasised, however, that if future economic evaluations are carried out based on other outcomes, that take the cost of treatment and/or other longer-term costs into account, then this restricted number of options will be inappropriate.

Chapter 11

Evidence for the cost-effectiveness of ultrasound in pregnancy

Decision makers seek economic evidence, sometimes before good evidence about costs and effectiveness is available. It has been illustrated how the simple question of the cost of using ultrasound screening for detecting specific fetal anomalies has a relatively different answer based on different sources of evidence. Although to some extent the review of evidence of both costs and effectiveness actually broadened the range of uncertainty about cost-effectiveness, a consistent message about which options were likely to be most cost-effective did emerge. The primary study of costs provides a point estimate but is applicable in fewer settings. The literature review of costs also illustrates that very little is known about the costs to women of routine ultrasound examinations. The primary research suggests that including women's costs might substantially increase the cost of a scan. However, in all three analyses, the range was narrowed to three principal options, namely one second trimester scan (option 3), one third trimester scan (option 4) or a combination of both (option 7). Almost all other options are dominated by one or more of these three options.

The authors of the Helsinki Ultrasound trial[192] also recommended a second trimester routine scan as being the most cost-effective option.

However, the results from this review, which has narrowed the model to three principal options, should be considered with caution. It is not simply the aim of ultrasound screening to detect fetal anomalies. Furthermore, the model is limited to the antenatal period. Ultrasound is also used to confirm fetal viability, the dates of the pregnancy, identify multiple pregnancies (and chorionicity thereof) and to check fetal growth, placental position and assess liquor volume. It may have beneficial effects but it may also lead to higher intervention rates in labour and generate anxiety, even if the results of the scan are reassuring. The information presented in chapter 6 suggests that women themselves may not be entirely aware of the reason for a scan, and may not have the same objectives as caregivers. It is likely that women might make different choices, depending on the nature of the anomaly or problem sought, the possible options if a problem should be found at different stages of pregnancy, the length of time they may be faced with uncertainty, what they understand about the risks and performance of subsequent tests and investigations, and many other factors. Women may have different views about their experience at different stages in pregnancy and postnatally. Thus, to identify the optimal programme will require a great deal more data about women's experiences in general and with respect to specific anomalies, or types of anomaly, as well as more evidence about clinical options, costs and outcomes at and after the end of pregnancy.

Chapter 12

Authors' synthesis and comments on the review

Introduction

The evidence relating to the clinical effectiveness, cost-effectiveness and women's views of ultrasound screening in pregnancy has been reviewed. The review has been conducted by a multidisciplinary team and has considered different decision-makers' viewpoints. In this chapter, the relationship between the findings from the different areas and the overall implications for the NHS and for further research are considered. The methods of the review are also discussed and the possible implications for methodological research.

Overview of findings

The evidence that has been reviewed suggests several general findings for specific decision makers. From the clinical point of view, the research highlights the wide variation in the performance of scans, whenever they are done, and it is important that both clinicians and women are aware of this and the resultant limitations of routine ultrasound screening. It is also clear that the scanning procedure cannot be expected to significantly reduce perinatal mortality, particularly with less than optimum service provision.

From the point of view of users of the service, the review confirms that ultrasound is very attractive to women but that this very fact may make the shock of unexpected results of a scan greater. There is evidence that women's views of ultrasound have changed over time, as the technology has become more widespread, from earlier fear to current enthusiasm. However, the rapid change in the technology is difficult to assimilate and there is evidence from this review that women, and their healthcare providers, may not be fully aware of the potential and limitations of different scanning modalities.

Costs to women have been found to be important and these should be taken into account when decisions are made about incorporation of scanning into antenatal care. The number of cost-effective options has been reduced, with the specific objective of detecting anomalies using routine ultrasound, subject to the limitations of the model discussed in chapter 10, and the data discussed in chapters 2–4. The decision analysis for the cost-effectiveness of detecting anomalies with ultrasound has ruled out options for a first trimester scan only, and a first trimester scan in combination with one or more of second or third trimester scans. These options are always dominated by the second trimester and third trimester scans, alone or together.

Although these seem the most cost-effective options for routine scanning for fetal anomalies in terms of detection rates, the analysis does not determine what would be acceptable to women and also does not take account of the other benefits of routine ultrasound, for example, accurate dating of pregnancy. This is particularly important to note, since, as has been shown for the RCOG groupings of anomalies, it is clear that scanning has different performance for different types of anomaly at different trimesters. Each broad grouping of anomalies is likely to have widely differing consequences for healthcare and social costs and benefits in the longer term.

Several issues emerged which were common to the reviews from the different viewpoints. Firstly, newly emerging applications and rapid diffusion of ultrasound in pregnancy mean that information for decision makers, care providers and users does not keep up with what is available. This raises the question of whether such changes can be restrained and introduced in the context of evaluations. A further common finding from all the reviews was that the level of training and skill, and the type of equipment used, is important, and investment in higher levels of training would improve cost-effectiveness. A general observation was that, with few exceptions, the quality of reporting was not adequate to derive evidence about the nature and context of the scanning conducted.

The original intention of this review was to consider optimum frequency and timing of scanning in pregnancy. Adopting an ultrasound screening strategy relies on the fundamental belief that screening rather than selective scanning is the

only reliable way to identify fetal abnormalities and date pregnancies accurately. The provision of screening depends on the availability of resources, screening objectives, the planned package of antenatal care and acceptability to women, including that of termination of pregnancy. The optimal performance of the screening programme relies on appropriate training and technical expertise and use of the best available technology. In their 1997 report,[5] the RCOG Working Party recommended a two-stage regimen of booking ultrasound, principally to date the pregnancy, followed by a second ultrasound anomaly scan at 18–20 weeks. This is the regimen offered at the Liverpool Women's Hospital, where the primary cost studies were carried out.

The advantages of accurate dating are reduced induction for presumed post-term pregnancy, increased efficacy of serum screening programmes[196] (4–10% increased efficacy) and optimal timing of second trimester anomaly scan.

The primary study at the Liverpool Women's Hospital (chapter 5) has shown that care provided in 43% of pregnancies relied on accurate dating by ultrasound scan. At the time of the initial drafting of this report, no comparative information was available on the clinical impact of different regimens. Since then, an RCT comparing the two-stage regimen with a 20-week scan alone has been reported.[217] This showed less need for re-adjustment of dates at the mid-pregnancy scan in the two-stage group (with possible consequences for timing serum screening if available) and less anxiety among women. Accurate dating could be undertaken at the time of the second trimester (18–20 weeks) anomaly scan but, if serum screening is part of the antenatal care package, the requirement for accurate dates to calculate the reliable risk estimates would not be fulfilled.

Other presumed advantages of a first trimester dating scan include earlier detection of non-viable pregnancies and multiple pregnancies. The primary study at the Liverpool Women's Hospital (see chapter 5) has shown that 2.2% of women have non-viable pregnancies at booking scan. However, in the Australian trial,[217] ultrasound scan at first visit did not result in significantly earlier diagnosis of non-viable pregnancies (8 versus 9.4 weeks, $p = 0.91$). Earlier detection of twin pregnancies does not appear to result in improvement in substantive outcomes such as perinatal mortality. However, the earlier the scan, the easier and more accurate the assessment of chorionicity.[218] This has implications for practice if complications requiring intervention arise at a later stage in pregnancy.

On current evidence, a scan undertaken between 18 weeks' and 20 weeks' gestation is the most effective method available to detect a wide range of fetal abnormalities and, at this stage in pregnancy, there remains time to perform invasive diagnostic tests and offer termination of pregnancy if indicated. Even at this stage in pregnancy, the sensitivity of detection of fetal anomalies varies widely according to the anatomical system affected and the type of anomaly. There is some evidence (from one RCT)[11] that if termination of pregnancy is widely accepted by the population screened, anomaly screening in the second trimester will result in a reduction in perinatal mortality.

The potential advantages and disadvantages of first trimester NT and anomaly screening were discussed in chapter 4. It is clear that further research is required before this option is introduced into routine practice. Preliminary reports suggest that even if this option were introduced, an additional second trimester scan to detect fetal abnormalities would be required.[219]

No convincing evidence was found of clinical benefit from routine examination in late pregnancy (> 24 weeks) whether imaging or Doppler ultrasound was used. Assessment of placental appearances may, as an adjunct to fetal measurement, help reduce perinatal mortality, but this needs to be evaluated in a large trial.

Timing and frequency were considered in the economic model, to the extent that the options compared consisted of combinations of one or more scan in different trimesters performed to detect fetal structural and chromosomal abnormalities. This model did not address the potential advantage of accurate dating. Although the options have been narrowed down to second and third trimester scanning options, there is not enough evidence from the review, and a need for more research, about the relative preferences women have in the choices between timing of detection and subsequent decisions about diagnosis and possible termination.

This review relates to the UK at present, and will be relevant in many parts of the world where similar forms of ultrasound are being included in antenatal care programmes. The question of ultrasound versus no ultrasound has not been considered explicitly in this review, because nearly all centres in the UK will offer at least one scan per

woman and the RCOG guidelines propose two scans (first trimester dating scan and second trimester anomaly scan).

Because this review covers a rapidly changing technology, it inevitably has a 'shelf life'. Already there is new information about earlier screening,[217] and there will be published data from SURUSS by early 2001. Data from controlled trials on effectiveness of scanning options will continue to be updated regularly in the Cochrane Database of Systematic Reviews.[220]

Methods of the review

Health technology assessment asks 'does the technology work, for whom, at what cost, and how does it compare with the alternatives?' The emphasis is on a comprehensive approach, considering users' views, clinical effectiveness and cost, taking into consideration relevance and efficiency within specific economic and social contexts. Very few studies of the studies reviewed met this demanding brief. Instead, good studies of clinical effectiveness were more likely than not to exclude questions of psychological outcome or cost. Economic studies did not use the best evidence of effectiveness or women's preferences. Studies of women's views were not focussed on specific uses of ultrasound in pregnancy. One study[11,192] was included in both the clinical effectiveness and economics reviews, and none of the others were included in more than one review.

Although the approach to systematic review was the same in each of our reviews, different criteria were set for the inclusion of studies in each review. For example, systematic reviews of clinical effectiveness that were based on the criteria for Cochrane reviews, sought and included adequately controlled studies. This criterion was not applicable to the reviews designed to inform other issues such as test efficacy, cost, or women's views.

Methods for the review of clinical effectiveness

The review of clinical effectiveness used the well-established methods of the Cochrane Pregnancy and Childbirth Group to assess RCTs. Explicit criteria for inclusion of studies and pre-specified outcome measures were stated. When there was not enough evidence from RCTs, primary studies fulfilling pre-stated quality criteria were reviewed (as in chapter 3 – detection of fetal abnormalities by routine ultrasound). The NHS Executive has endorsed a scheme whereby, in the absence of evidence from RCTs, other research may be used provided that the methodology of the research has been robust. The main aim of reviewing primary studies in chapter 3 was to report detection rates of abnormalities in anatomical systems, and randomised trials are not necessarily the most appropriate study design to assess in detail the performance of diagnostic or screening tests. For the review of primary studies, foreign language studies were excluded as there were time constraints but, more importantly, the quality of most of the English language studies that were reviewed in full was poor and it was judged unlikely that any of the foreign language papers, if reviewed in full, would have been suitable for inclusion.

In addition, a primary study was undertaken (chapter 5 – consequences of routine ultrasound: Liverpool Women's Hospital) to identify any inefficiencies or hidden events in the ultrasound screening programme, as it was anticipated that this information would not be available in the literature reviewed. The primary study of pathways achieved this purpose, and informed the economic modelling exercise, and can thus be seen as an essential part of the methodology of this review.

Methods for the review of women's views

The review of women's views necessarily had differences in method from what is commonly understood in a systematic review. It differed in three main ways, which arose from the exploratory nature of this review.

First, the structure of the review was different. Unlike some quantitative reviews, this one did not start out with a clear question. The questions to be asked of the material were developed by a process of reading and re-reading. The questions chosen were to some extent idiosyncratic, and other reviewers might well come to this material with a different agenda. On the other hand, the work is of value at least in so far as it tabulates the studies covered and allows another team to build on what has been done.

Second, no quality criterion was used for the review but there are often comments on the extent to which the study was able to answer the questions posed by the researchers. Studies of poor methodological quality in terms of the aims of the researchers often still had valuable information within them. It was noted that conclusions from earlier studies were quite often repeated in later work by other authors but without any check on whether the conclusions were supported by the

evidence. In many cases, the studies lacked key information about time, place and type of ultrasound scan being performed.

Third, this review used quite wide boundaries. It was taken as far back in time as possible and caught some interesting studies from the early days of obstetric ultrasound. There was no language criterion but probably some studies in languages other than English were missed. Some studies of miscarriage were on the borderline, and some have been included in the review, perhaps not in a fully systematic way. Studies on screening that did not refer to ultrasound were not tabulated but some key studies and reviews were used in the writing.

Methods for the review of economic studies and modelling

Economic studies were included if they evaluated currently-used prenatal screening technologies, including use of ultrasound. *BMJ* criteria[187] were used for inclusion of the chosen papers. The way in which these criteria were applied was discussed earlier (see chapter 8). There have now been several studies using these criteria for this purpose, although it is not what they were originally intended for. The authors will contribute the experience from this exercise for analysis in an empirical review of the use of *BMJ* criteria to be undertaken within the Cochrane Economics Methods Group.

Primary research on costs in Liverpool was conducted jointly between the clinical and economics researchers. The use of this source gave weight to the interpretation of the literature on costs and allowed cost-effectiveness to be modelled in a local setting.

Interdisciplinary issues

Interdisciplinary issues arose in comparing the results of the reviews and in conducting the reviews. It is clear from the results of the reviews that different disciplines ask different questions about technologies. This was illustrated in the reviews. Studies of clinical effectiveness and of women's views considered different uses of the technology, were concerned with different outcomes and used different research methods. The authors do not, therefore, have a clear idea whether the best clinical options would suit women best, or whether women were concerned about the clinical effectiveness of ultrasound. Clinical effectiveness results are used in economic studies but only one economic study was based on evidence from an RCT.

The research group represented clinical researchers, social scientist, economists, and an information specialist. All had worked previously in a multidisciplinary environment. Nevertheless, all learned from each other during the review and found challenges in framing key questions and terminology. For example, the interpretation and implications of false-positive results has different meaning for each discipline. Clinicians are concerned about making the correct diagnosis but avoiding unnecessary intervention; hence, if an initial scan shows a possible abnormality, and this is not confirmed at a subsequent detailed scan, the clinical problem is solved. If the significance of a finding is unclear, the clinician is faced with management dilemmas. However, for the women concerned this may cause considerable distress and, for the economist, this has resulted in the use of further resources.

It was essential to meet and communicate with the whole group regularly and, because the team was dispersed geographically, this was facilitated by good e-mail links. The exercise developed the potential for closer linkage between disciplines in future reviews and has informed the process that will be followed in the Cochrane Pregnancy and Childbirth Review Group, to ensure reviewers consider wider issues in their reviews. Lessons for other such reviews include the need for team meetings to allow time for interpretation of and reflection on the findings from each other's perspectives. This in turn has costs in terms of time and travel of reviewers.

Policy relevance and further research

The objectives of this review were inevitably limited. The review was not a comparison between ultrasound and other antenatal diagnostic methods. This remains a question: although the review has narrowed down the cost-effective options for anomaly screening with ultrasound, there are some more complex questions and decisions to be made by women and healthcare providers about the interactions between ultrasound and serum screening. Our findings provide a necessary building block for those decisions.

Setting the review in context within the NHS is difficult, because there are few national data about the use of ultrasound in the UK. There is a need for a more up-to-date picture of the use of ultrasound. The most recent national survey, done

under the aegis of the RCOG and the RCR, was undertaken in 1995.[2] Given the speed of change in ultrasound technology and its application, much may be different already. Diagnostic tests are not recorded routinely in NHS data systems, such as the Hospital Episode System.[221,222]

The economic model was necessarily limited in scope to consider technologies and options, which had been defined and were in use in 1996. Although comprehensive data are not available about the current provision of services, it is known that the nature and uses of ultrasound are changing fast but the published (and available unpublished) evidence does not keep up. In order to define options for future models, a horizon scanning approach to defining the emerging uses of ultrasound could be used.

Although it was not the aim of this review, the efficiency of ultrasound departments is an important question for radiography/radiology managers, and needs further examination. This would be relevant to our review, as the cost of a scan in any setting is not only determined by the time it takes but is likely to be dependent on the distribution of fixed costs between uses, and the volume of activity. Our review found very little information about the types of equipment in use and the protocols for screening.

The study of pathways has illustrated the practical issues facing service providers attempting to implement an evidence-based programme. This work resulted in the conclusion (page 39) that "As there are some women who book after 14 weeks or even after 24 weeks, the likely coverage of first trimester and second trimester scan regimes should be taken into account when planning or auditing routine screening programmes. This and the scan repeat rate should be taken into account when costs and cost-effectiveness of routine ultrasound screening are assessed."

Conclusions about further research

In each part of this study, there were questions about ultrasound in pregnancy which could not be answered, and for which further research would be needed. Clinical effectiveness of fetal NT and anomaly screening in the first trimester has not been evaluated in RCTs and, although becoming widespread, still could feasibly be evaluated in this way. If this were done, cost-effectiveness and women's views should be considered, as well as clinical outcomes. The lack of clarity about what 'soft markers' predict needs further epidemiological investigation. Further research is also needed to assess the effect of detection of fetal abnormalities on substantive outcome in terms of short- and long-term morbidity and mortality for both mother and child. Placental grading in the third trimester may be valuable but whether reported results are reproducible remains to be seen. Future research into routine Doppler ultrasound needs to be powerful enough to address small changes in perinatal outcome and continued vigilance with regard to its safety is required.

Whether it is a research question or not, the clear evidence that quality of ultrasound scanning is less good in non-specialist centres needs to be addressed. Given the lack of national data about ultrasound, there is a place for a study of a representative sample of departments to document current provision and use, and to test hypotheses about variations in performance of scans. The interaction between use of ultrasound for gestational age assessment and for screening for anomalies needs to be further considered from the clinical and economic points of view. Such a study might also consider the role of staff training and qualifications in the provision of routine scans.

The lack of awareness of many women, and possibly some caregivers, of the clinical purposes of ultrasound, and the strong effects it may have on women and their partners, should be also be further investigated. This would provide a better basis for communication at the time of the scan, and also would inform development of outcome measures for trials of ultrasound. A better understanding of how decisions are made by women who are having ultrasound would help improve care, and would also advance understanding of how to measure utility of healthcare, especially the relationship between anticipated and experienced benefits. Given the emerging uses of ultrasound with enhanced imaging this seems a current and relevant research priority.

Other gaps in knowledge were found about women's views, including potential differences between different cultures, the role of ultrasound scans in women's experience of miscarriage, and the effect on women of the need for repeat scans.

Further research on the economics of scanning would include the need for long-term data on pathways, costs, effects and quality of life, following detection of anomalies up to delivery and in the

following years for the child and parents. In addition, representative national data on costs of scanning would need replication of our primary costing study in a sample of centres. Both of these would inform the extension of the models of cost-effectiveness described in chapter 10.

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Appendix 1

Ultrasound for routine fetal assessment in early pregnancy (< 24 weeks' gestation): updated Cochrane review

This review has undergone the Cochrane Collaboration peer review process.

Cover sheet

Title: Ultrasound for routine fetal assessment in early pregnancy
Reviewer: Neilson JP
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Date of last substantive update: 11/07/98
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Intramural sources of support University of Liverpool, UK.

Extramural sources of support None.

Acknowledgements Professor SH Eik-Nes, Drs KA Salvesen, LJ Vatten, O Okland have provided unpublished results from the Alesund trial. The review was modified following the publication of a critique by the British Columbia Office of Health Technology Assessment, Canada.

Potential conflict of interest None known.

Abstract

Background Advantages of early pregnancy ultrasound screening are considered to be more accurate calculation of gestational age, earlier identification of multiple pregnancies, and diagnosis of non-viable pregnancies and certain fetal malformations.

Objective The objective of this review was to assess the use of routine (screening) ultrasound compared with the selective use of ultrasound in early pregnancy (i.e. before 24 weeks).

Search strategy The Cochrane Pregnancy and Childbirth Group trials register and the Cochrane Controlled Trials Register (up to July 1998) were searched.

Selection criteria Adequately controlled trials of routine ultrasound imaging in early pregnancy.

Data collection and analysis One reviewer assessed trial quality and extracted data. Study authors were contacted for additional information.

Main results Nine trials were included. The quality of the trials was generally good. Routine ultrasound examination was associated with earlier detection of multiple pregnancies (twins undiagnosed at 26 weeks, OR 0.08; 95% CI, 0.04 to 0.16) and reduced rates of induction of labour for post-term pregnancy (OR 0.61; 95% CI, 0.52 to 0.72). There were no differences detected for substantive clinical outcomes such as perinatal mortality (OR 0.86; 95% CI, 0.67 to 1.12). When detection of fetal abnormality was a specific aim of the examination, the number of terminations of pregnancy for fetal anomaly increased.

Reviewers' conclusions Routine ultrasound in early pregnancy appears to enable better gestational age assessment, earlier detection of multiple pregnancies and earlier detection of clinically unsuspected fetal malformation at a time when termination of pregnancy is possible. However, the benefits for other substantive outcomes are less clear.

Background

Diagnostic ultrasound examination may be employed in a number of specific circumstances during pregnancy, such as after clinical complica-

tions (e.g. bleeding) or when the fetus is perceived to be at a particularly high risk of malformation or of being inappropriately grown. Because adverse outcome may also occur in pregnancies without clear risk features, assumptions have been made that the routine use of ultrasound in all pregnancies would prove beneficial. Such screening examinations may be planned for early pregnancy, or for late gestation, or for both. The focus of this review is on routine early pregnancy ultrasound and will not discuss late pregnancy screening. The main theoretical advantages of early pregnancy screening are more accurate calculation of gestational age, earlier identification of multiple pregnancies, and diagnosis of non-viable pregnancies and certain fetal malformations. However, the quality of ultrasound imaging is dependent not only on the technical capabilities of the ultrasound equipment but also on the experience and expertise of the operator, and standards are variable. Mistakes certainly occur in the prenatal diagnosis of fetal structural abnormalities (both false-positive and false-negative) and it is essential that a rigorous assessment of routine ultrasound is achieved before any confident recommendation that, in practice, it does more good than harm.

Objectives

To assess whether routine early pregnancy ultrasound (i.e. its use as a screening technique) influences the diagnosis of fetal malformations and of multiple pregnancies, the rate of clinical interventions, and the incidence of adverse fetal outcome (including perinatal death) compared with its selective use (for specific indications).

Criteria for considering studies for this review

Types of studies

All acceptably controlled trials of routine ultrasound in early pregnancy were considered. In light of the shortage of information, studies that employed quasi-random allocation (e.g. date of birth or hospital number) have been included. Trials have either compared routine versus selective performance of ultrasound, or routine versus selective reporting of ultrasound findings.

Types of participants

All participants were women with early pregnancies (usually less than 20 weeks). Their group characteristics varied between trials as some trialists attempted to recruit all women (e.g. Trondheim trial), while others excluded the recruitment of women with risk features, previous complications, medical problems, and any clinical uncertainty about gestational age (e.g. RADIUS trial).

Types of interventions

Ultrasound examination. Only two trials (Helsinki; RADIUS) included, as an important priority, a detailed examination to detect anatomical malformations in the fetus.

Types of outcome measures

See 'Outcomes' under 'Characteristics of included studies'.

Search strategy for identification of studies

This review has drawn on the search strategy developed for the Pregnancy and Childbirth Group as a whole.

Relevant trials were identified in the Group's Specialised Register of Controlled Trials. See Review Group's details for more information.

The CENTRAL/CCTR database was searched in July 1998 (CCTR 1998).

Methods of the review

See 'Search strategy'.

Description of studies

See 'Characteristics of included studies' below.

In only two trials (Helsinki; RADIUS) was the stated aim a detailed study of fetal anatomy to allow detection of fetal structural malformations.

Methodological quality of included studies

The methodological quality was, on the whole, good. The London trial was 'quasi-randomized' with allocation effected by hospital case record number, with a consequent risk of biased allocation; this study was further weakened by the revelation of 30% of results in the 'blind' control group, because of clinical concern in later pregnancy.

Results

See meta-analysis table (*Table 43*) and metaview (*Figure 4*).

TABLE 43 *Meta-analysis: routine versus selective ultrasound for fetal assessment in early pregnancy*

Outcome	Number of studies	Number of participants	Statistical method	Effect size	Significant effect (see *Figure 4*)
Termination of pregnancy for fetal abnormality	4	27,377	Peto OR (95% CI)	**3.19 (1.54 to 6.60)**	✓
Twins undiagnosed at 20 weeks	1	74	Peto OR (95% CI)	**0.12 (0.02 to 0.56)**	✓
Twins undiagnosed at 26 weeks	6	220	Peto OR (95% CI)	**0.08 (0.42 to 0.16)**	✓
Antenatal hospital admission	5	9044	Peto OR (95% CI)	1.01 (0.90 to 1.13)	
Induction for 'post-term' pregnancy	6	24,195	Peto OR (95% CI)	**0.61 (0.52 to 0.72)**	✓
Apgar score ≤ 7 at 1 minute	4	8136	Peto OR (95% CI)	1.11 (0.95 to 1.29)	
Apgar score ≤ 7 at 5 minutes	4	8143	Peto OR (95% CI)	0.94 (0.69 to 1.29)	
Low birthweight (< 2.5 kg) in singletons	6	17,517	Peto OR (95% CI)	0.96 (0.82 to 1.12)	
Birthweight			No numerical data		
Admission special care (singletons)	5	8927	Peto OR (95% CI)	0.86 (0.74 to 1.00)	
Perinatal mortality	8	34,245	Peto OR (95% CI)	0.86 (0.67 to 1.12)	
Perinatal mortality excluding lethal malformations	8	34,251	Peto OR (95% CI)	0.96 (0.72 to 1.28)	
Perinatal mortality (twins)	5	550	Peto OR (95% CI)	0.81 (0.36 to 1.80)	
Poor oral reading at school	1	1993	Peto OR (95% CI)	1.02 (0.72 to 1.45)	
Poor reading comprehension at school	1	1984	Peto OR (95% CI)	0.82 (0.54 to 1.23)	
Poor spelling at school	1	1982	Peto OR (95% CI)	0.73 (0.53 to 1.00)	
Poor arithmetic at school	1	1993	Peto OR (95% CI)	0.90 (0.59 to 1.36)	
Poor overall performance at school	1	1993	Peto OR (95% CI)	0.95 (0.61 to 1.49)	
Dyslexia	1	603	Peto OR (95% CI)	0.75 (0.41 to 1.36)	
Reduced hearing in childhood	2	5418	Peto OR (95% CI)	0.90 (0.67 to 1.20)	
Reduced vision in childhood	2	5417	Peto OR (95% CI)	0.82 (0.66 to 1.01)	
Use of spectacles	2	5331	Peto OR (95% CI)	0.87 (0.72 to 1.05)	
Non right-handedness	2	4715	Peto OR (95% CI)	1.13 (0.97 to 1.32)	
Left-handedness	1	1663	Peto OR (95% CI)	1.33 (0.90 to 1.97)	
Ambidexterity	1	1663	Peto OR (95% CI)	1.25 (0.92 to 1.71)	

When compared with selective examinations, routine ultrasound examination in early pregnancy results in earlier diagnosis of twin pregnancies and a reduced incidence of induction of labour for apparent post-term pregnancy. Previous publications of this review have also reported an unexplained decrease in the incidence of babies born with low birth-weight, and the perceived need for special neonatal care. With the addition of new data, particularly from the Tygerberg trial, no such effect on the incidence of low birth-weight babies can be demonstrated and, although fewer babies from the routinely screened pregnancies were admitted for special care, the 95% CIs now reach 1.00.

When the detection of fetal abnormality is a specific aim, the number of planned terminations of pregnancy increases. In the trial in which this policy was pursued with greatest commitment (Helsinki), this resulted in fewer perinatal deaths. Overall, however, no clear benefit in terms of a substantive outcome measure like perinatal mortality can yet be discerned to result from the routine use of ultrasound. There was also no evidence of reduced perinatal mortality among twin babies, despite generally earlier diagnosis in the ultrasound-screened pregnancies.

Long-term follow-up of children in Norway, who, as fetuses, were entered into the Alesund and Trondheim trials, has shown no adverse influence on school performance or neurobehavioural function as a consequence of prenatal exposure to ultrasound; however, fewer of the ultrasound-exposed children are right-handed. Similar follow-up of a subset of children from the trial in Sweden also showed no evidence of an adverse effect on vision or hearing; this study failed to demonstrate any overall effect on non-right-handedness, although there may have been an effect if male children who were exposed to early ultrasound (regardless of group of assignment in the trial) are considered separately.

Discussion

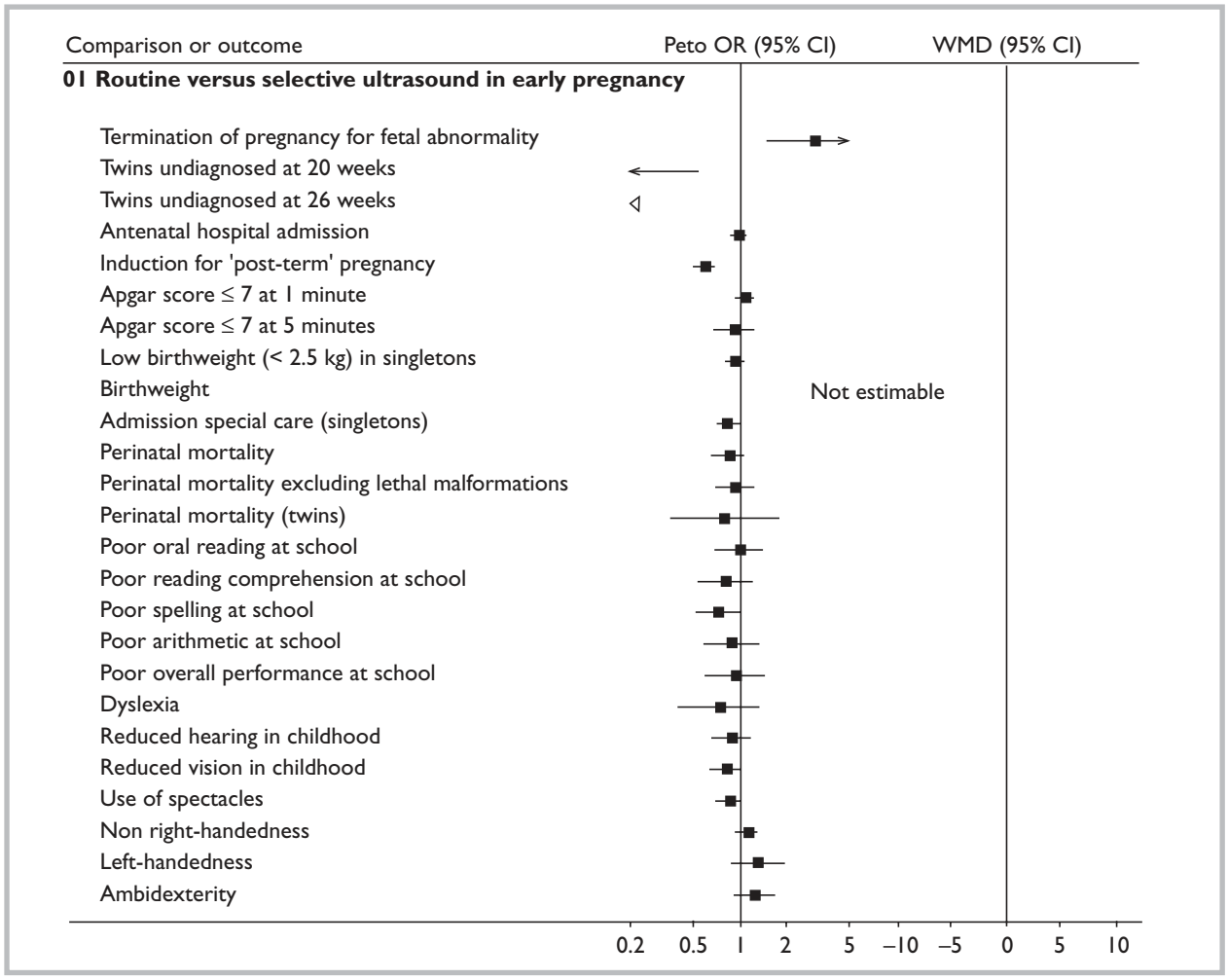
See 'Author's implications'.

Reviewers' conclusions

Implications for practice

Assumed benefits of routine ultrasonography in early pregnancy have been: (1) better gestational age assessment; (2) earlier detection of multiple

FIGURE 4 *Metaview: ultrasound for fetal assessment in early pregnancy*
(See Table 43 for statistical values, Peto ORs and 95% CIs)



pregnancies; (3) detection of clinically unsuspected fetal malformation at a time when termination of pregnancy is possible.

These assumptions appear to have been justified by analysis of data from the controlled studies. The reduced incidence of induction of labour for apparent post-term pregnancy in the routinely scanned groups presumably results from better gestational 'dating', and twin pregnancies are detected earlier. Neither of these effects has been shown to improve fetal outcome but much larger numbers of participants would be required to demonstrate this if such an effect were to be real. The detection of fetal malformation has been addressed in detail in only two trials. The Helsinki trial showed improved detection with a resultant increase in the termination of pregnancy rate and a drop in perinatal mortality; there were, however, large differences in the detection rates between the two hospitals involved in this study, which reinforces the need for expert ultrasonography in such a programme. This point is further emphasised by the low detection rate of major fetal malformations in the large RADIUS trial – only 17% of such babies were identified in the ultrasound-screened group before 24 weeks of pregnancy. Based on the Helsinki trial results and other reports of observational data, this implies unsatisfactory diagnostic expertise. A combination of low detection rates of malformation together with a gestational age limit of 24 weeks for legal termination of pregnancy in the RADIUS trial produced minimal impact on perinatal mortality, unlike the Helsinki experience.

Many obstetric units already practise routine early pregnancy ultrasonography. For those considering its introduction, the benefit of the demonstrated advantages would need to be considered against the theoretical possibility that the use of ultrasound during pregnancy could be hazardous and the need for additional resources. At present, there is no clear evidence that ultrasound examination

during pregnancy is harmful. The findings from the follow-up of schoolchildren, exposed as fetuses to ultrasound in the Norwegian and Swedish trials (Norway; Sweden) are generally reassuring; the finding that fewer children in the Norwegian ultrasound groups were right-handed was not confirmed by intention-to-treat analysis of long-term follow-up data from the Swedish trial. The Norwegian finding is difficult to interpret. This may have been a chance observation that emanated from the large number of outcome measures assessed, or from the method of ascer-tainment; alternatively, if it was a real consequence of ultra-sound exposure, then it could imply that the effect of diagnostic ultrasound on the developing brain may alter developmental pathways. No firm conclusion can be reached from available data and there is a need to study these children formally rather than to rely on a limited number of questionnaire responses obtained from the parents (Paneth, 1998).

The financial costs also need to be considered. Calculations by the authors of the RADIUS report indicate that screening 4 million pregnant women in the USA at $200 per scan would increase costs by $1 billion per year. While costs might be less in other countries, economic issues will still be relevant. Clinicians, health planners and pregnant women need to decide if these results justify the expense of providing routine ultrasound examination in early pregnancy.

Ultrasound scans are, however, popular – the potential enjoyment that parents can receive from seeing the image of their baby *in utero* is discussed elsewhere (Neilson, 1995).

Implications for research

1. Other benefits which could result from better gestational age assessment, e.g. better management of pregnancies complicated by fetal growth retardation, need to be assessed in much larger studies than have been reported so far.
2. Earlier detection of twin pregnancies has not been translated into an improvement in fetal outcome. The continuing high perinatal mortality rate from multiple pregnancies is a legitimate cause for concern and requires to be studied on a number of fronts; at least, early detection improves the potential for the proper scientific study of other, potentially useful, interventions in multiple pregnancies.
3. There is a lack of useful data about the value of detection of fetal malformations as part of routine ultrasound examination programmes. Most information comes from 'centres of excellence'. That these results may not be representative of those obtained in primary level obstetric units has been confirmed by Rosendahl and Kivinen (1989) and indeed by the RADIUS trial.
4. The optimal timing of the examination, if adopted, could be addressed by an RCT. Earlier examination provides (theoretically) more accurate assessment of gestational age; later examination (e.g. between 18 and 22 weeks) allows more full inspection of fetal anatomy but is more complex and time-consuming.
5. The desirability, or not, of implementing a programme of routine ultrasound screening will be influenced by whether or not a screening programme for fetal Down's syndrome (e.g. by biochemical testing) is in operation. Analysis of such test results relies strongly on accurate knowledge of gestational age.

Characteristics of included studies

See *Table 44* for details of all included studies.

References to studies

Included studies

Alesund (published and unpublished data)
Eik-Nes SH, Okland O, Aure JC, Ulstein M. Ultrasound screening in pregnancy: a randomised controlled trial. *Lancet* 1984;**i**:1347.

Eik-Nes SH, Salvesen KA, Okland O, Vatten LJ. Routine ultrasound fetal examination in pregnancy: the 'Alesund' randomized controlled trial. *Ultrasound Obstet Gynecol.* In press.

Salvesen KA. Routine ultrasonography in utero and development in childhood – a randomized control-led follow-up study [thesis]. Trondheim: University of Trondheim, Faculty of Medicine; 1993.

Helsinki (published data only)
Saari-Kemppainen A, Karjalainen O, Ylostalo P, Heinonen OP. Ultrasound screening and perinatal mortality: controlled trial of systematic one-stage screening in pregnancy. *Lancet* 1990;**336**:387–91.

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Saari-Kemppainen A. Use of antenatal care services in a controlled ultrasound screening trial. *Acta Obstet Gynecol Scand* 1995;**74**:12–14.

London (published data only)
Bennett MJ, Little G, Dewhurst J, Chamberlain GVP. Predictive value of ultra-sound measurement in early pregnancy: a randomized controlled trial. *Br J Obstet Gynaecol* 1982;**89**:338–41.

Missouri (published data only)
Ewigman B, LeFevre M, Hesser J. A randomized trial of routine prenatal ultrasound. *Obstet Gynecol* 1990;**76**:189–94.

Norway (published data only)
Salvesen KA, Bakketeig LS, Eik-Nes SH, Undheim JO, Okland O. Routine ultrasonography in utero and school performance at age 8–9 years. *Lancet* 1992;**339**:85–9.

Salvesen KA, Jacobsen G, Vatten LJ, Eik-Nes SH, Bakketeig LS. Routine ultrasonography in utero and subsequent growth during childhood. *Ultrasound Obstet Gynecol* 1993;**3**:6–10.

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Salvesen KA, Vatten LJ, Eik-Nes SH, Hugdahl K, Bakketeig LS. Routine ultrasonography in utero and subsequent handedness and neurological development. *BMJ* 1993;**307**:159–64.

RADIUS (published data only)
Ewigman BG, Crane JP, Frigoletto FD, LeFevre ML, Bain RP, McNellis D,*et al.* Effect of prenatal ultrasound screening on perinatal outcome. *N Engl J Med* 1993;**329**:821–7.

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LeFevre ML, Evans JK, Ewigman B, and the RADIUS study group. Is smoking an indication for prenatal ultrasonography? *Arch Fam Med* 1995;**4**:120–3.

Sweden (published and unpublished data)
Kieler H, Axelsson O, Haglund B, Nilsson S, Salvesen KA. Routine ultrasound screening in pregnancy and the children's subsequent handedness. *Early Hum Dev* 1998;**50**:233–45.

Kieler H, Haglund B, Waldenstrom U, Axelsson O. Routine ultrasound screening in pregnancy and the children's subsequent growth, vision and hearing. *Br J Obstet Gynaecol* 1997;**104**:1267–72.

Waldenstrom U, Axelsson O, Nilsson S, Eklund G, Fall O, Lindeberg S, *et al.* Effects of routine one-stage ultrasound screening in pregnancy: a randomised controlled trial. *Lancet* 1988;**ii**:585–8.

Trondheim (published data only)
Bakketeig LS, Jacobsen G, Brodtkorb CJ, Eriksen BC, Eik-Nes SH, Ulstein MK, *et al.* Randomised controlled trial of ultrasonographic screening in pregnancy. *Lancet* 1984;**ii**:207–10.

Tygerberg (published data only)
Geerts LTGM, Brand EJ, Theron GB. Routine ultrasound examinations in South Africa: cost and effect on perinatal outcome – a prospective randomised controlled trial. *Br J Obstet Gynaecol* 1996; **103**:501–7.

Excluded studies
None

Studies awaiting assessment
Oxford (unpublished data sought but not used)
Wald N. Randomized controlled trial of routine dating ultrasound in pregnancy. Oxford: personal communication, 21 March, 1988.

Ongoing studies
Adelaide
Crowther CA. Trial to assess whether ultrasound examination at the booking antenatal visit reduces the number of repeat screenings and results in earlier diagnosis of non-viable pregnancy/congenital abnormality. Adelaide, Australia: personal communication, 1999.

Other references
Additional references
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Paneth N. Prenatal sonography – safe or sinister? *Lancet* 1998;**352**:5–6.

Rosendahl H, Kivinen S. Antenatal detection of congenital malformations by routine ultrasonography. *Obstet Gynecol* 1989;**73**:947–51.

TABLE 44 *Characteristics of included studies*

Study	Method	Participants	Interventions	Outcomes	Notes
Alesund	Randomisation by sealed envelopes	Nearly all women in that geographical area, including those with 'high-risk pregnancies. Recruitment 1979–81, 1628 women.	Routine ultrasound examinations at 18 (biparietal diameter measured) and 32 weeks (biparietal diameter and mean abdominal diameter) with additional examination at 36 weeks if fetus small for gestational age or presenting by the breech – versus selective examination for specific clinical indications only. In the control group 77% of women did not have ultrasound examination. Ultrasound examinations performed by one of two experienced doctors.	Primary outcome: induction of labour for 'post-term' pregnancy; secondary outcomes: indices of perinatal mortality and morbidity.	Trial first reported in letter form only in 1984. It subsequently became clear that there were inconsistencies in results and it was therefore temporarily withdrawn from this review. Data have now been re-analysed by authors. Data entered into this version of review are derived from only those pregnancies that were singleton, except for perinatal mortality rates which are calculated from all pregnancies.
Helsinki	Randomisation by sealed envelopes	All women attending one of 64 health centres. Recruitment 1986–87.	Routine ultrasound examination at 16–20 weeks, versus selective scanning for specific reasons; 77% of women in the control group underwent at least one ultrasound scan during pregnancy. Mean scans per pregnancy: 2.1 (study group), 1.8 (control group).	Fetal outcome and clinical interventions.	
London	Allocation by last digit of hospital number	All women attending one of three consultant antenatal clinics.	Ultrasound on all at approximately 16 weeks: results revealed (study group) or concealed (controls). Recruitment started 1977.	Perinatal mortality; birthweight for gestational age; Apgar score (1 minute).	Value of this study weakened by revelation of 30% of results in 'blind' concealed group, because of clinical concern in later pregnancy.
Missouri	Randomisation by sequentially numbered sealed opaque envelopes: 'double consent' randomisation	Women who did not have 'an indication for ultrasonography' based on medical disorder, uncertain gestational age, previous or current pregnancy complication, i.e. those eligible for inclusion were at low risk of adverse pregnancy outcome. They also had to be < 18 weeks gestation. Only 42% of women fulfilled criteria and were eligible for recruitment (1984–86).	Routine ultrasound - optimally at 10–12 weeks but permissible up to 18 weeks in the study group. Ultrasound for specific indications allowed at any time in either group.	Major outcomes: induction of labour for post-term pregnancy; early detection of multiple pregnancy (< 24 weeks); adverse perinatal outcome (perinatal death, admission to neonatal ICU; 5 minutes Apgar < 6).	

continued

TABLE 44 contd *Characteristics of included studies*

Study	Method	Participants	Interventions	Outcomes	Notes
Norway	See Alesund and Trondheim trials	See Alesund and Trondheim trials	See Alesund and Trondheim trials	Educational, neurological, and other behavioural outcomes.	All traced children who, as fetuses, were included in Alesund and Trondheim trials were followed-up. Results from these trials not analysed separately so pooled outcome data have been designated 'Norway'.
RADIUS	Randomisation by micro-computer after stratification by practice site; intention-to-treat	Women who did not have 'an indication for ultrasonography' based on medical disorder, uncertain gestational age, previous or current pregnancy complication, i.e. those eligible for inclusion were at low risk of adverse pregnancy outcome (and comprised 40% of the total population).	Intended ultrasound screens at 18–20 and at 31–33 weeks' gestation, versus selective ultrasonography for specific reasons only. 97% of women in screened group had at least two ultrasound examinations; 55% of women in control group had no scan at all. Mean number of scans was 2.2 (screened group) and 0.6 (control group). Ultrasound to include detailed study of fetal anatomy. Recruitment 1987–91.	Fetal outcome and indices of care/intervention during pregnancy. Primary outcomes: fetal and neonatal mortality; 'moderate or severe' neonatal morbidity.	
Sweden	Randomisation by opaque sealed envelopes	All consenting women at <19 weeks who had not already had ultrasound scan and who did not have one of number of pre-specified indications for ultrasound (mainly uncertainties about gestational age, medical disorder, previous complications). Recruitment 1985–87.	Planned that women allocated to screening group would have ultrasound scan at about 15 weeks (range 13–19 weeks); 98.7% did. Planned that women in control group would not have scan before 19 weeks, although 4.1% did; 31% of control group women had scan after 19 weeks.	Major outcome: 'neonatal morbidity' defined by admission to (and duration of stay) neonatal ward. Follow-up data on neuro-developmental outcome available for about 70% of sample at ages 8–9 years; data obtained by postal questionnaire. Data also available on growth characteristics during childhood but not in form that allows inclusion in data tables; there was little difference between groups.	
Trondheim	Randomisation by sealed envelopes	Nearly all women in Trondheim attending for antenatal care, 1979–80.	Ultrasound group offered ultrasound examinations at both 19 and 32 weeks of gestation.	Antenatal hospital admission; induction of labour; birthweight; length gain; head circumference gain; small for gestational age; large for gestational age; Apgar score (1 & 5 minutes); resuscitation; admission to neonatal ICU; death of baby.	

continued

TABLE 44 contd *Characteristics of included studies*

Study	Method	Participants	Interventions	Outcomes	Notes
Tygerberg	Randomisation by sealed, opaque envelopes	Women at less than 24 weeks of pregnancy. Exclusions: already had ultrasound examination, diabetes, rhesus sensitisation, increased risk of fetal malformation. Recruitment 1991–92.	Study group: 'level 1' ultrasound examination by obstetric registrar or medical officer. Control group: ultrasound examination only for specific clinical indication (25% of women did undergo ultrasound examination at some time).	Sample size estimated from 'overall adverse outcome', a composite index that includes perinatal mortality, admission to neonatal ICU and prolonged admission to neonatal ward. Economic implications also explored.	Analysis by intention-to-treat.

Appendix 2

Routine ultrasound in late pregnancy (> 24 weeks gestation): Cochrane review

This review has undergone the Cochrane Collaboration peer review process.

Cover sheet

Title: Routine ultrasound in late pregnancy (> 24 weeks' gestation)
Reviewer(s): Bricker L, Neilson JP
Date edited: 07/02/00
Date of last substantive update: 01/10/99
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Review first published: Issue 1, 2000
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Extramural sources of support None.

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Potential conflict of interest JP Neilson was principal investigator in a trial that was considered for inclusion.

Synopsis

Routine screening with ultrasound in late pregnancy (24 weeks onwards) does not appear to have any major impact on physical outcomes or care.

Ultrasound can be used in late pregnancy to find the cause of complications such as bleeding. However, screening all women for possible problems late in pregnancy is controversial. Routine late ultrasound aims to detect growth or other problems in the baby, abnormalities in the amount of fluid around the baby, problems with the placenta, and the baby's position. Potential problems with such screening include increasing major interventions (such as caesarean sections) without benefit. The review found that there is as yet no evidence that routine late ultrasound improves outcome or increases interventions. There is no evidence about the psychological impact.

Abstract

Background Diagnostic ultrasound is used selectively in late pregnancy where there are specific clinical indications. However, the value of routine late pregnancy ultrasound screening in unselected populations is controversial. The rationale for such screening would be the detection of clinical conditions that place the fetus or mother at high risk, which would not necessarily have been detected by other means such as clinical examination, and for which subsequent management would improve perinatal outcome.

Objectives To assess the effects on obstetric practice and pregnancy outcome of routine late pregnancy ultrasound, defined as greater than 24 weeks' gestation, in women with either unselected or low-risk pregnancies.

Search strategy The Cochrane Pregnancy and Childbirth Group Specialised Register of Controlled Trials and the Cochrane Controlled Trials Register were searched.

Selection criteria All acceptably controlled trials of routine ultrasound in late pregnancy (defined as after 24 weeks).

Data collection and analysis The principal reviewer assessed trial quality and extracted data, under supervision of the co-reviewer.

Main results Seven trials recruiting 25,036 women were included. The quality of trials overall was satisfactory. There was no difference in antenatal, obstetric and neonatal intervention or morbidity in screened versus control groups. Routine late pregnancy ultrasound was not associated with improvements in overall perinatal mortality. Placental grading as an adjunct to a third trimester examination scan was associated with a significant reduction in the stillbirth rate in the one trial that assessed it. There are few data relating to long-term substantive outcomes such as neuro-development. There are few data on maternal psychological effects.

Reviewers' conclusions Based on existing evidence, routine late pregnancy ultrasound in low-risk or unselected populations does not confer benefit on mother or baby. There are few data about the potential psychological effects of routine ultrasound in late pregnancy, and the effects on both short- and long-term neonatal and childhood outcome. Placental grading in the third trimester may be valuable but whether reported results are reproducible remains to be seen, and future research of late pregnancy ultrasound should include evaluation of placental textural assessment.

Background

Diagnostic ultrasound is a sophisticated electronic technology, which utilises pulses of high frequency sound. The transducer that is moved across the area to be examined emits the pulses of ultrasound that propagate through the tissues and some are reflected back to the transducer, which converts these returning echoes into electronic signals. Tissue interface characteristics determine the strength of the returning echo. Signals are processed by a computer, which displays each echo in both strength and position as an image on a screen.

Diagnostic ultrasound is used selectively in late pregnancy when there are specific clinical indications, such as antepartum haemorrhage or clinical concern that the fetus may be poorly grown. However, the value of routine late pregnancy ultrasound screening in unselected populations is controversial. The rationale for such screening would be the detection of clinical conditions that place the fetus or mother at high risk, which would not necessarily have been detected by other means such as clinical examination, and for which subsequent management would improve perinatal outcome.

Fetal growth/size

Small-for-gestational-age fetuses are at greater risk of stillbirth, birth hypoxia, neonatal complications in the perinatal period, impaired neuro-development and cerebral palsy in childhood, and non-insulin dependent diabetes and hypertension in adult life (Barker, *et al.,* 1993). The majority of these small infants are not diagnosed until delivery (Leeson & Aziz, 1997), and detecting these fetuses prenatally remains a priority of antenatal care. Methods of detecting such fetuses include antenatal clinical examination, measurement of symphysis–fundal height, fetal anthropometry and ultrasound-estimated fetal weight. Harding and colleagues (1995) demonstrated that symphysis–fundal height measurements perform relatively poorly compared with ultrasound abdominal circumference measurements. A combined approach of screening with symphysis–fundal height measurement, complemented by ultrasound derived fetal abdominal circumference if failing growth is suspected has been advocated. Holmes and Soothill (1996) caution that small size should be viewed as a clinical sign and not as a diagnosis, as a number of small fetuses are not at risk of adverse outcome. Furthermore, the use of ultrasound to detect the small-for-gestational-age fetus is dogged by a number of complicating factors, including the lack of defined thresholds for normality versus abnormality, its dependence on accurate gestational dating, the fact that the assessment of growth velocity (serial measurements) may be more valuable clinically than a single estimate of size, and differences due to other factors, namely, maternal ethnicity and parity, fetal gender and environmental factors (Altman & Hytten, 1989). A previous systematic review of routine late pregnancy anthropometry concluded that despite increased intervention (admission to hospital and induction of labour), there was no identifiable benefit in fetal outcome (Neilson, 1995).

Another clinical concern is with the large-for-gestational-age fetus. These babies are at increased risk of perinatal morbidity and mortality, which arises mainly from birth injury and asphyxia; their mothers are at increased risk of cephalo-pelvic disproportion and its sequelae, and operative delivery and the associated morbidity. Our ability to detect fetal macrosomia antenatally by clinical examination remains limited (Lurie, *et al.,* 1995), and the antenatal prediction of fetal macrosomia is associated with a marked increase in Caesarean births without a significant reduction in the incidence of shoulder dystocia or fetal injury (Weeks, *et al.,* 1995). This is because most cases of shoulder dystocia and birth trauma occur in non-

macrosomic infants (Gonen, et al., 1996). Hence, the value of detecting these fetuses by routine ultrasound in late pregnancy is questionable.

Amniotic fluid

Fetal urine is the major source of amniotic fluid in the latter half of pregnancy (Brace & Wolf, 1989). Decreased amniotic fluid volume (oligohydramnios) in the absence of ruptured membranes or fetal anomalies is considered to be associated with chronic fetal compromise and redistribution of regional blood flow leading to reduction in fetal renal blood flow, fetal oliguria and, thus, less amniotic fluid. Increased amniotic fluid volume (polyhydramnios) occurs as a result of overproduction (polyuria in fetuses of diabetic mothers, rare placental tumours), decreased turnover (congenital anomalies affecting fetal swallowing), or unknown aetiology. Both oligohydramnios and polyhydramnios can be diagnosed by ultrasound measurement of maximum pool depth, two-diameter amniotic fluid pocket or amniotic fluid index (the sum of the vertical maximum pool depths in four quadrants), and applying the result to normal reference ranges. While in high-risk pregnancies, such as post-dates pregnancies, the measurement of amniotic fluid volume may have bearing on management decisions, there is some debate about the best measurement method and the clinical significance of the available reference ranges, which compounds the uncertainty about the effect on perinatal outcome of detecting amniotic fluid abnormalities.

Placenta

Placenta praevia occurs in 0.5% of pregnancies and is associated with considerable risk to both mother and fetus. Ultrasound is the best available method of locating the placental position (Neilson & Grant, 1989). Only 10% of low placentas at second trimester scan remain low at term (Rizos, *et al.,* 1979). However, in most pregnancies with placenta praevia, a clinical indication for diagnostic ultrasound, such as antepartum haemorrhage and fetal malpresentation, will arise and hence the role of screening for placenta praevia is debatable.

Grannum and colleagues (1979) described a classification system to grade the placental texture appearances on ultrasound imaging and suggested a correlation between maturational changes of the placenta as seen on ultrasound and fetal pulmonic maturity. This was not confirmed in further study but an association between 'mature' appearances at earlier gestations with maternal smoking and placental dysfunction was postulated. Thus, the knowledge of placental appearances in late pregnancy could, in theory, result in care leading to improved perinatal outcome.

Structural fetal abnormalities

A number of structural fetal abnormalities may manifest later in pregnancy. These include craniospinal abnormalities (microcephaly and hydrocephaly), gastrointestinal abnormalities (intestinal obstruction and atresia), urinary tract abnormalities and some skeletal abnormalities (Chitty, 1995). It has been suggested that the value of detecting fetal structural abnormalities before birth allows for the optimal timing and mode of delivery, leading to improved management and outcome. However, a report of a Working Party of the RCOG on Ultrasound Screening for Fetal Abnormalities (RCOG, 1997) stated that further research is required to evaluate whether prior identification of an abnormality before birth, particularly those amenable to intrauterine procedures and neonatal surgery, is advantageous in both the short and long term.

Fetal presentation

Some fetal malpresentations (e.g. breech) go undetected during routine antenatal care but would be identified by routine ultrasound in late pregnancy. In a retrospective case review, Nwosu and colleagues (1993) showed that babies undiagnosed as a breech were not subject to increased morbidity and mortality compared with a breech diagnosed prior to labour. This highlights the uncertainty about the clinical value of routine ultrasound screening for fetal malpresentations.

Safety

The use of routine pregnancy ultrasound needs to be considered in the context of potential hazards. Theoretically, some ultrasonic energy propagated through tissue is converted to heat, and biological effects of ultrasound have been observed in laboratory experiments. However, these effects have been produced using continuous wave ultrasound with long 'dwell' time (time insonating one area) and high power output. Diagnostic ultrasound is pulsed wave (short pulses of sound propagation) and most modern machines have inbuilt safety features so that safe power output limits cannot be exceeded. Operators are advised to apply the ALARA principle (As Low As Reasonably Achievable) to the ultrasound power output used (EFSUMB, 1995) and to ensure time taken for an examination, including the 'dwell' time over a specific target, is kept to a minimum. At present, there is no clear epidemiological evidence that ultrasound examination during

pregnancy is harmful but no firm conclusion has been reached from available data (see Neilson, 1999); hence, continual vigilance is necessary.

Objectives

To assess the effects on obstetric practice and pregnancy outcome of routine late pregnancy ultrasound, defined as greater than 24 weeks' gestation, in women with either unselected or low-risk pregnancies.

Criteria for considering studies for this review

Types of studies

All acceptably controlled trials of routine ultrasound in late pregnancy (after 24 weeks). Because of an anticipated paucity of RCTs, quasi-randomised trials were considered for inclusion. Routine ultrasound in early pregnancy (Neilson, 1999) was considered in a previous Cochrane review. Routine Doppler ultrasound in pregnancy will be considered in a separate review.

Types of participants

Women in late pregnancy (after 24 weeks' gestation) in both unselected populations and designated low-risk populations.

Types of interventions

Routine ultrasound examination in late pregnancy (after 24 weeks' gestation) to assess one/some/all of the following: fetal size; amniotic fluid volume; placental site; placental grading; fetal structural anatomy; fetal presentation.

Types of outcome measures

Pre-specified outcome measure

Interventions

– antenatal admission to hospital
– antenatal fetal monitoring
  Kick Count Chart
  cardiotocography
  biophysical profile
  Doppler ultrasound
  further ultrasound
– intention to deliver
– induction of labour
– operative delivery
  elective Caesarean section
  emergency Caesarean section
  instrumental vaginal delivery
  Caesarean section for distress
  Caesarean section for distress antepartum
  Caesarean section for distress intrapartum

Perinatal outcome

– gestational age at birth
– birthweight (mean and standard deviation)
– birthweight < tenth percentile
– birthweight < third percentile
– preterm delivery < 37 weeks
– preterm delivery < 34 weeks
– low birth weight (< 2.5 kg)
– very low birth weight (< 1.5 kg)
– need for resuscitation
– need for ventilation
– admission to special care baby unit and average length of stay
– low Apgar score (< 7 at 5 minutes)
– perinatal death

Neonatal outcome

– acute neonatal problems
  hypoxic ischaemic encephalopathy
  necrotising enterocolitis
  intraventricular haemorrhage
  intraventricular haemorrhage with cystic periventricular leukomalacia
  pulmonary haemorrhage
– early neonatal death (in first week of life)
– late neonatal death (from 1 to 4 weeks)
– infant death (1 month to 1 year)
– neurodevelopment at age 2 years

Maternal outcome

– psychological effects
  (including stress, anxiety, depression, quality of life, satisfaction)

Detection of

– major anomaly before birth
– malpresentation before labour.

Primary outcome measures

Only six of the above outcome measures will be used for subgroup analysis, as follows:

– induction of labour
– Caesarean section
– all deaths (perinatal, neonatal and infant)
– preterm delivery < 34 weeks
– neurodevelopment at age 2 years
– maternal psychological effects.

Furthermore, the following **non-prespecified outcome measures** were used:

– post-term delivery > 42 weeks
– birthweight < fifth percentile
– moderate neonatal morbidity (includes any of the following: presumed neonatal sepsis, oxygen required > 48 hours, necrotising enterocolitis without perforation, grade I or II intraventricular haemorrhage, fracture of clavicle or other bones,

facial nerve injury, brachial plexus injury, stay > 5 days in the special care nursery)
– severe neonatal morbidity (includes any of the following: grade IV retinopathy of prematurity, bronchopulmonary dysplasia, mechanical ventilation > 48 hours, intestinal perforation due to necrotising enterocolitis, grade III or IV intraventricular haemorrhage, subdural or cerebral haemorrhage, spinal cord injury, neonatal seizures, placement of chest tube, documented neonatal sepsis, stay > 30 days in the special care nursery)
– perinatal mortality of twins.

Search strategy for identification of studies

This review drew on the search strategy developed for the Pregnancy and Childbirth Group as a whole.

Relevant trials were identified in the Group's Specialised Register of Controlled Trials. See Review Group's details for more information. In addition, the Cochrane Controlled Trials Register was searched. Date of last search: Issue 3, 1999.

Methods of the review

All potential studies were identified as outlined in the search strategy. The two reviewers independently assessed the trials for methodological quality and appropriateness for inclusion. The reason for exclusion of any trial was clearly stated. The trials were not assessed blinded and the reviewers knew the author's name, institution, source of the publication and results when applying inclusion criteria. Disagreements were resolved by discussion until consensus was reached. Additional information was sought from some trialists by personal contact.

Data extraction was performed by the principal reviewer and double-checked for discrepancies with the co-reviewer. Statistical analysis was performed using Review Manager (RevMan) software.

If appropriate, stratified analyses for all outcome measures were performed as follows.

Routine ultrasound after 24 weeks gestation versus no routine ultrasound/concealed routine ultrasound (caregivers not aware of results) in the following categories:

(i) all participants
(ii) unselected populations
(iii) designated low risk populations
(iv) single ultrasound examination after 24 weeks' gestation
(v) serial ultrasound examinations (2 or more) after 24 weeks' gestation.

If appropriate, subgroup analyses for the primary outcome measures were performed for each of the above categories according to the type of ultrasound performed, as follows:

(i) to detect small-for-gestational-age or intrauterine growth retardation
(ii) to detect large-for-gestational-age
(iii) to detect amniotic fluid abnormalities
(iv) to detect fetal malpresentation
(v) to assess placental site
(vi) for placental grading/maturity.

If the findings of any of the above subgroup analyses for the primary outcome measures were significant, the analysis was extended to include all outcome measures.

It was conceivable that some studies would have incorporated a combination of the above diagnostic approaches.

If appropriate, sensitivity analyses were performed on the basis of quality of randomisation.

Description of studies

See 'Characteristics of included studies' below.

Seven trials comprising 25,036 women were included (Alesund 1999; Glasgow 1984; New Zealand 1993; Perth 1996; Peterborough 1987; RADIUS 1993; Trondheim 1984).

Ultrasound examination options differed between trials, with some offering no routine scans at any time in pregnancy to the control group, some offering routine scans to all participants earlier in pregnancy (before 24 weeks' gestation), and some offering routine scans at all stages of the trial but only revealing results of late pregnancy ultrasound (after 24 weeks' gestation) for the study groups. Three trials (Alesund 1999 (Norway); RADIUS 1993 (USA); Trondheim 1984 (Norway)) offered routine ultrasound in the second and third trimesters versus selective ultrasound. In the New Zealand 1993 trial, all women had second trimester ultrasound scans and only the study group underwent further third trimester ultrasound. In the Glasgow 1984 trial, all women were offered second

and third trimester ultrasound but the results of third trimester ultrasound were revealed only for the study group. In the Peterborough 1987 trial, all women had routine second and third trimester ultrasound but placental grading at third trimester ultrasound was revealed only for the study group. In the Perth (Australia) 1996 trial, all women had routine second trimester ultrasound scans and only the study group were offered serial ultrasound screening thereafter.

The trials evaluated different aspects of third trimester ultrasound. Two trials (Glasgow 1984; New Zealand 1993) addressed ultrasound screening for small-for-dates. The Peterborough 1987 trial addressed the value of placental grading as an adjunct to routine third trimester ultrasound scan. The RADIUS 1993 trial in the USA was the only study which reported in detail the detection of fetal abnormalities at routine third trimester ultrasound scan. The Perth (Australia) 1996 trial combined repeated ultrasound scan for fetal biometry and amniotic fluid assessment with Doppler ultrasound; the data were therefore analysed in a separate comparison (serial ultrasound and Doppler ultrasound versus selective ultrasound) and were also included in another Cochrane review, *Routine Doppler ultrasound in pregnancy*.

The results of the review should be considered in the light of these different factors, as the specific nature of the ultrasound regimens may have had some effect on the outcome measures.

Methodological quality of included studies

The methodological quality in general was good. The Glasgow 1984 study was 'quasi-randomised' with allocation according to hospital number, and this had the potential to introduce bias.

Results

See meta-analysis table (*Table 45*) and metaview (*Figure 5*).

There were no or few data available for some of the prespecified outcome measures, particularly maternal outcomes, neonatal outcomes and long-term neurodevelopmental outcome.

Five outcome measures that were not pre-specified were included, namely post-term delivery, birth weight < 5th centile (< 3rd centile was pre-specified but there were no data), moderate neonatal morbidity, severe neonatal morbidity and perinatal mortality specifically of twin babies.

Stratified and subgroup analyses were not performed due to the small number of included studies and, hence, limited data.

Routine ultrasound after 24 weeks gestation versus no/concealed/selective ultrasound after 24 weeks' gestation

The screened group were less likely to have further ultrasound scans (Peto OR, 0.70; 95% CI, 0.57 to 0.85). There were no differences in antenatal admissions or other tests of fetal well-being, nor were there significant differences in obstetric interventions, such as induction of labour, instrumental deliveries and Caesarean section.

Screened groups were less likely to deliver post-term (after 42 weeks' gestation) (Peto OR, 0.69; 95% CI, 0.58 to 0.81). Pre-term delivery rates and birth-weight data were similar in study and control groups. Overall, perinatal mortality, including or not including, congenital abnormalities was no different. There was also no difference in perinatal mortality of twins. Only two studies reported separate data for stillbirths and neonatal deaths in congenitally normal fetuses/neonates (Glasgow 1984; Peterborough 1987). The Peterborough 1987 data suggested a reduction in the stillbirth rate if placental grading is incorporated into routine third trimester ultrasound scan (Peto OR, 0.13; 95% CI, 0.04 to 0.50).

Neonatal interventions such as resuscitation, ventilation, admission to special care, were no different in screened/revealed versus control groups; nor was there a difference in 5-minute Apgar scores. The only study in which moderate and severe neonatal morbidity was reported (RADIUS 1993) showed no differences between study groups.

Psychological and other maternal outcomes were not reported in any of the included studies.

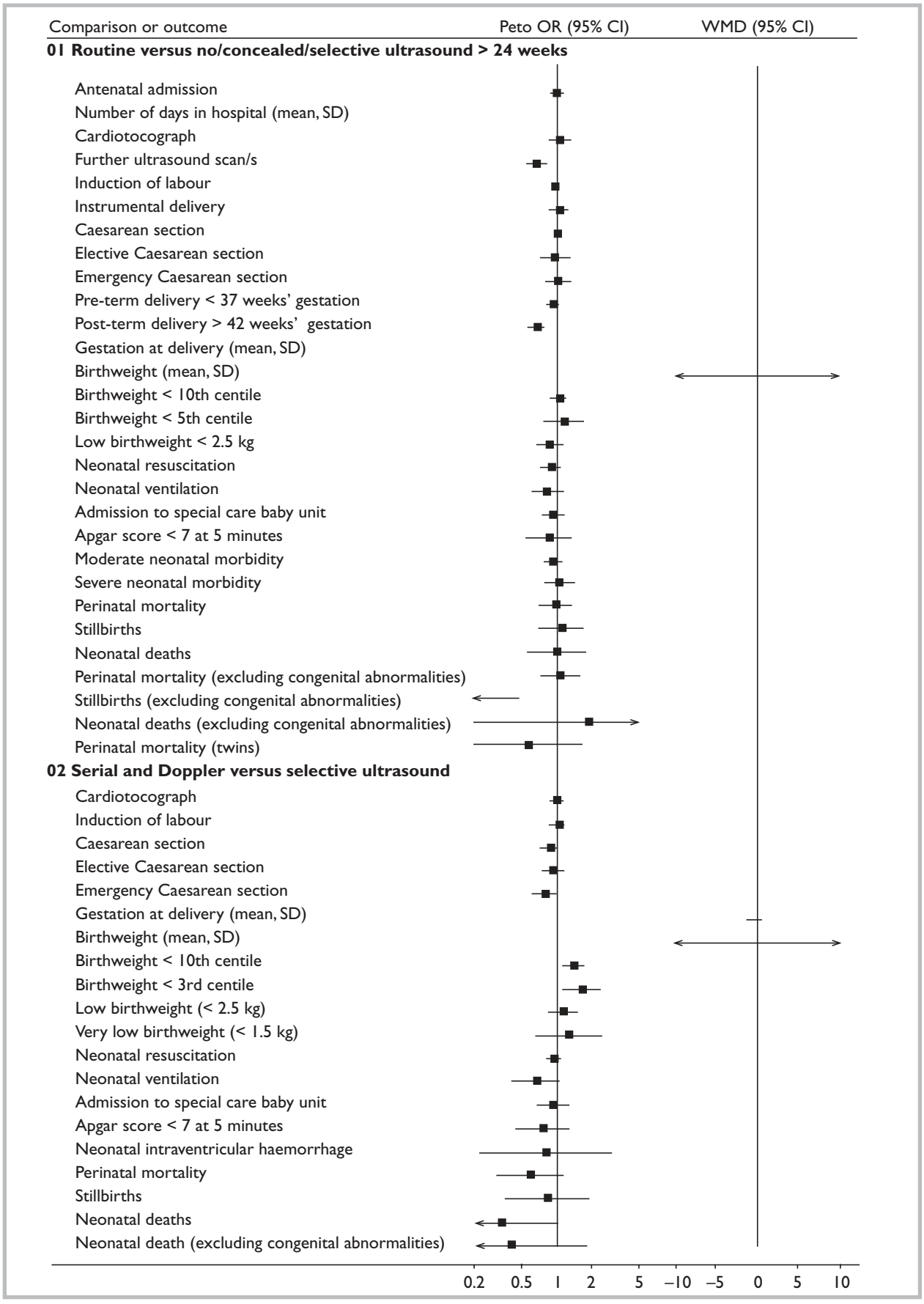
Serial ultrasound and Doppler ultrasound versus selective ultrasound

This comparison includes published and unpublished data from the Perth (Australia) 1996 trial. The results showed no significant differences between the two groups in antenatal admissions or other tests of fetal well-being; nor was there a significant difference in obstetric interventions, such as induction of labour, instrumental deliveries

TABLE 45 *Meta-analysis: routine ultrasound in late pregnancy (> 24 weeks gestation)*

Outcome	Number of studies	Number of participants	Statistical method	Effect size	Significant effect (see *Figure 5*)
Comparison 1: routine versus no/concealed/selective ultrasound at > 24 weeks					
Antenatal admission	4	5396	Peto OR (95% CI)	1.03 (0.90 to 1.17)	
Number of days in hospital (mean, SD)	2	2877	WMD (fixed) (95% CI)	0.17 (0.16 to 0.18)	
Cardiotocograph	1	2000	Peto OR (95% CI)	1.09 (0.87 to 1.36)	
Further ultrasound scan/s	2	2536	Peto OR (95% CI)	**1.70 (0.57 to 0.85)**	✓
Induction of labour	5	20,665	Peto OR (95% CI)	0.98 (0.92 to 1.05)	
Instrumental delivery	3	3886	Peto OR (95% CI)	1.06 (0.89 to 1.28)	
Caesarean section	4	19,037	Peto OR (95% CI)	1.05 (0.97 to 1.14)	
Elective Caesarean section	3	3886	Peto OR (95% CI)	0.99 (0.73 to 1.34)	
Emergency Caesarean section	3	3886	Peto OR (95% CI)	1.06 (0.82 to 1.36)	
Pre-term delivery < 37 weeks' gestation	2	17,151	Peto OR (95% CI)	0.95 (0.84 to 1.08)	
Post-term delivery > 42 weeks' gestation	2	17,151	Peto OR (95% CI)	**0.68 (0.58 to 0.81)**	✓
Gestation at delivery (mean, SD)	2	2877	WMD (fixed) (95% CI)	–0.13 (–0.13 to –0.12)	
Birthweight (mean, SD)	4	19,710	WMD (fixed) (95% CI)	–0.47 (–15.49 to 14.54)	
Birthweight < 10th centile	3	18,295	Peto OR (95% CI)	1.07 (0.91 to 1.26)	
Birthweight < 5th centile	2	2404	Peto OR (95% CI)	1.19 (0.80 to 1.78)	
Low birth weight < 2.5 kg	3	4510	Peto OR (95% CI)	0.91 (0.70 to 1.19)	
Neonatal resuscitation	3	4541	Peto OR (95% CI)	0.92 (0.75 to 1.13)	
Neonatal ventilation	2	3004	Peto OR (95% CI)	0.86 (0.63 to 1.16)	
Admission to special care baby unit	3	4541	Peto OR (95% CI)	0.97 (0.78 to 1.21)	
Apgar score < 7 at 5 minutes	3	3891	Peto OR (95% CI)	0.89 (0.56 to 1.42)	
Moderate neonatal morbidity	1	15,281	Peto OR (95% CI)	0.97 (0.80 to 1.16)	
Severe neonatal morbidity	1	15,281	Peto OR (95% CI)	1.03 (0.78 to 1.37)	
Perinatal mortality	6	22,278	Peto OR (95% CI)	1.03 (0.75 to 1.41)	
Stillbirths	4	19,710	Peto OR (95% CI)	1.15 (0.74 to 1.79)	
Neonatal deaths	4	19,710	Peto OR (95% CI)	1.04 (0.58 to 1.86)	
Perinatal mortality (excluding congenital abnormalities)	4	19,736	Peto OR (95% CI)	1.12 (0.74 to 1.68)	
Stillbirths (excluding congenital abnormalities)	2	2902	Peto OR (95% CI)	**0.13 (0.04 to 0.49)**	✓
Neonatal deaths (excluding congenital abnormalities)	2	2902	Peto OR (95% CI)	1.94 (0.20 to 18.7)	
Perinatal mortality (twins)	3	314	Peto OR (95% CI)	0.60 (0.20 to 1.76)	
Comparison 2: Serial and Doppler ultrasound versus selective ultrasound					
Cardiotocograph	1	2834	Peto OR (95% CI)	1.01 (0.87 to 1.17)	
Induction of labour	1	2834	Peto OR (95% CI)	1.03 (0.88 to 1.21)	
Caesarean section	1	2834	Peto OR (95% CI)	0.86 (0.72 to 1.04)	
Elective Caesarean section	1	2834	Peto OR (95% CI)	0.94 (0.74 to 1.19)	
Emergency Caesarean section	1	2834	Peto OR (95% CI)	0.80 (0.61 to 1.05)	
Gestation at delivery (mean, SD)	1	2834	WMD (fixed) (95% CI)	–0.1 (–1.20 to 1.00)	
Birthweight (mean, SD)	1	2834	WMD (fixed) (95% CI)	–25 (–67.53 to 17.53)	
Birthweight < 10th centile	1	2834	Peto OR (95% CI)	**1.41 (1.11 to 1.78)**	✓
Birthweight < 3rd centile	1	2834	Peto OR (95% CI)	**1.67 (1.11 to 2.53)**	✓
Low birthweight < 2.5 kg	1	2834	Peto OR (95% CI)	1.15 (0.84 to 1.56)	
Very low birthweight < 1.5 kg	1	2834	Peto OR (95% CI)	1.27 (0.65 to 2.50)	
Neonatal resuscitation	1	2834	Peto OR (95% CI)	0.96 (0.83 to 1.11)	
Neonatal ventilation	1	2834	Peto OR (95% CI)	0.67 (1.41 to 1.09)	
Admission to special care baby unit	1	2834	Peto OR (95% CI)	0.94 (0.67 to 1.33)	
Apgar score < 7 at 5 minutes	1	2834	Peto OR (95% CI)	0.76 (0.46 to 1.27)	
Neonatal intraventricular haemorrhage	1	2834	Peto OR (95% CI)	0.80 (0.22 to 2.97)	
Perinatal mortality	1	2834	Peto OR (95% CI)	0.59 (0.30 to 1.16)	
Stillbirths	1	2834	Peto OR (95% CI)	0.83 (0.36 to 1.93)	
Neonatal deaths	1	2834	Peto OR (95% CI)	0.34 (0.11 to 1.01)	
Neonatal deaths (excluding congenital abnormalities)	1	2834	Peto OR (95% CI)	0.42 (0.10 to 1.87)	

FIGURE 5 *Metaview: routine ultrasound in late pregnancy (> 24 weeks)*
(See Table 45 for statistical values, Peto ORs or WMDs and 95% CIs)



and Caesarean section. More babies in the screened group had a birthweight < 10th centile, (Peto OR, 1.41; 95% CI, 1.11 to 1.78) and < 3rd centile (Peto OR, 1.67; 95% CI, 1.11 to 2.53). There were no differences in other indices of perinatal or neonatal outcome.

Discussion

The ultrasound scan protocols in each trial varied. It is difficult to assess the effect of scans before 24 weeks' gestation on the outcome measures. For example, the finding of a reduction in post-term delivery in the screened group of the RADIUS 1993 study is probably due to better gestational age assessment at the 18–20 week scan. Furthermore, the reason for routine ultrasound scan after 24 weeks' gestation differed between trials. Ideally, subgroup analyses according to reason for the scan would resolve the possible difference in outcomes according to diagnostic approach but there are not enough studies to perform meaningful subgroup analyses. The results of the meta-analysis should be viewed in this light.

While the most accurate approach to assessment of the effect of routine late pregnancy ultrasound would be trials in which the intervention is late pregnancy ultrasound alone, no such trials exist. The fact that assessment of most parameters at late pregnancy ultrasound are based on gestational reference data, which, in turn, rely on accurate gestational dating in early pregnancy, further compounds this issue. It is neither realistic, therefore, nor pragmatic to consider routine late pregnancy ultrasound in isolation, and the included studies probably reflect existing practice.

Meta-analysis of the data shows no difference between groups in antenatal, obstetric and neonatal interventions. Overall perinatal mortality was no different for all fetuses/neonates and twin pregnancies. Although there was nonsignificant heterogeneity in perinatal mortality overall (chi-squared 10.73, $p > 0.05$), there was significant heterogeneity in perinatal mortality corrected for abnormality (chi-squared 8.31, $p < 0.025$). This was due to the data from the Peterborough 1987 trial that suggested a significant reduction in the number of congenitally normal stillbirths. This trial is unique in that it is an evaluation of placental grading as an adjunct to routine late pregnancy ultrasound. The authors state that this observation was not a formal prior hypothesis and may be an overestimate of the true effect of the test. In view of the nature of the trial, that is, single centre and limited power to assess perinatal outcome (2000 participants), and that it was performed over a decade ago (1987), this finding needs to be revisited in future research.

In the Perth (Australia) 1996 trial, there was an unexpected finding of significantly higher intrauterine growth restriction in the serial ultrasound and Doppler examination group (i.e. the intensive group). The authors state that while this may have been a chance finding, it is possible that frequent exposure to ultrasound may have influenced fetal growth. This finding was not associated with increased perinatal morbidity and mortality, and follow-up of these children at 1 year of age found that the difference was no longer discernible (Newnham, *et al.*, 1996). The authors stress the need for further investigation of the effects of frequent ultrasound exposure on fetal growth. Furthermore, if this were a true effect, the modality responsible (Doppler ultrasound versus real-time ultrasound) would need to be elucidated.

The only study that addressed detection of fetal anomalies in the third trimester was the 1993 RADIUS trial. The overall fetal anomaly detection rate in this trial was poor, at 35%. After 24 weeks' gestation, 34/156 (22%) anomalous fetuses were detected in the screened group and 10/155 (6.5%) anomalies were detected in the control group. However, the better detection rate in the screened group did not translate into an improvement in infant survival (relative survival rate 1.4, 95% CI, 0.9 to 2.3).

None of the trials addressed long-term neurodevelopmental outcome or maternal psychological outcome, and it is arguable that these are the most important outcomes. Exposure of the expectant mother to uncertainty and possible anxiety about the health of her baby has implications of which may be far reaching. In addition, perinatal survival does not automatically translate into long-term success, as little is known about the long-term prognosis of the *in-utero* compromised fetus.

Reviewer's conclusions

Implications for practice

There is no evidence that routine ultrasound in late pregnancy improves perinatal outcome. However, its use does not appear to increase the rate of interventions, and hence the risk of iatrogenic morbidity. As a result of this review, it is not clear what aspects of late pregnancy ultra-

sound may be valuable in centres where it is undertaken. However, placental grading appears to be useful and, perhaps, should be considered in late pregnancy ultrasound, whether routine or selective.

Implications for research

There are few data on the potential psychological effects of routine ultrasound in late pregnancy, and the effects on both short and long-term neonatal and childhood outcome. Future studies should address these issues.

Based on the available data about the value of placental grading, future research into late pregnancy ultrasound should include assessment of placental texture.

Characteristics of included studies

See *Table 46* for details of all included studies.

Characteristics of excluded studies

See *Table 47* for details of excluded studies.

References to studies

Included studies

Alesund 1999 (unpublished data only)
Eik-Nes SH, Okland O, Aure JC, Ulstein M. Ultrasound screening in pregnancy: a randomised controlled trial [letter]. *Lancet* 1984;**i**:1347.

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Glasgow 1984 (published data only)
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TABLE 46 *Characteristics of included studies*

Study	Method	Participants	Interventions	Outcomes	Notes
Alesund 1999	Randomisation by sealed envelopes	Nearly all women in that geographical area, including those with 'high-risk' pregnancies. Recruitment 1979–81, 1628 women.	Routine ultrasound examination at 18 weeks (biparietal diameter measured) and 32 weeks (biparietal diameter and mean abdominal diameter), with additional examination at 36 weeks' gestation if fetus small for gestational age and/or presenting by breech, versus selective examination for clinical indications only.	Obstetric interventions (antepartum and intrapartum) for singleton pregnancies only. Perinatal outcome indices for all pregnancies (including multiple pregnancies).	Trial reported in letter form only in 1984. Subsequently it became clear that there were inconsistencies in results and data has now been reanalysed. Data entered in this review are derived from most recent report (with authors approval), as yet unpublished but in press.
Glasgow 1984	Pseudo-randomisation according to last digit in hospital number	887 women attending hospital antenatal clinic between 34 and 36.5 weeks' gestation with uncomplicated singleton pregnancies, i.e. low risk pregnancies.	All women had ultrasound examination < 24 weeks' gestation for gestational dating. All had further ultrasound scan at 34–36.5 weeks' gestation to measure crown rump length and trunk area but, in study group, the two measurements were multiplied and results plotted and reported in case notes (i.e. revealed). Further management was responsibility of clinical staff. No requests for control group measurements to be revealed occurred but this option was available to clinicians.	Obstetric interventions (antepartum and intrapartum) and perinatal outcome indices.	Study addressed ultrasound screening for small for dates.
New Zealand 1993	Randomised by women selecting one of a number of envelopes (< 6) containing computer-generated random 1 or 2 and study number	All pregnant women who attended antenatal clinic < 24 weeks' gestation, i.e. unselected population. Multiple pregnancies excluded once diagnosed (and study numbers reused); 1527 women.	All women had dating scan at 16–24 weeks' gestation. Study group had further scan at 32–36 weeks' gestation (ideally, at 34 weeks) which aimed to detect small-for-gestational-age fetuses and, if estimated fetal weight fell below the 20th centile for gestation, this reported and additional scans recommended but not arranged. Clinicians were able to order further scans for control group if clinically indicated.	Mainly perinatal outcome indices. Number of further ultrasound scans.	Scan to detect small-for-gestational-age fetuses.

continued

TABLE 46 contd *Characteristics of included studies*

Study	Method	Participants	Interventions	Outcomes	Notes
Perth, Australia 1993	Sealed envelopes	2834 singleton pregnancies. Criteria for recruitment: gestational age 16–20 weeks, sufficient proficiency in English, expected to deliver at hospital, intention to remain in Western Australia so that childhood follow-up feasible.	'Regular' group had ultrasound examination at 18 weeks for fetal biometry, subjective amniotic fluid assessment and placental morphology and location; any further scans in pregnancy conducted at clinicians' request. 'Intensive group' had ultrasound examination, plus amniotic fluid index and continuous wave Doppler ultrasound of umbilical artery and arcuate artery within placental vascular bed at 18, 24, 28, 34 and 38 weeks' gestation. Doppler ultrasound parameter reported was systolic/diastolic ratio. Results of examinations recorded in hospital chart but no clinical management guidance given.	Obstetric interventions (antepartum and intrapartum) and perinatal outcome indices.	Published study reports results overall but few data are available for extraction. Authors were contacted and provided unpublished data.
Peterborough 1987	Randomisation by opaque sealed envelopes	2000 pregnant women attending ultrasound department for routine third trimester scans, including multiple pregnancies.	All women offered routine early pregnancy ultrasound and two routine scans in third trimester. Placental grading performed at routine third trimester scan. Results of placental grading in study group revealed and in control group concealed. Clinical management in both groups left entirely to clinician responsible for care.	Obstetric interventions (antepartum and intrapartum) and perinatal indices.	Study addresses value of placental grading at routine third trimester ultrasound.
RADIUS 1993	Randomisation by microcomputer after stratification by practice site: intention-to-treat	15,151 pregnant women who did not have 'an indication for ultrasonography' based on uncertain gestational age, previous or index pregnancy complication, medical disorder. Thus those eligible at low risk of adverse pregnancy outcome and comprised 40% of total population.	Ultrasound screen at 18–20 weeks' and 31–33 weeks' gestation, versus selective ultrasonography.	Perinatal outcome indices. Primary outcomes: perinatal mortality and moderate/severe neonatal morbidity.	
Trondheim 1984	Randomised by sealed-envelope method	1009 pregnant women in Trondheim attending for antenatal care between 1979 and 1980.	Study group offered ultrasound examinations at 19 and 32 weeks' gestation.	Obstetric interventions (antepartum and intrapartum) and perinatal outcome indices.	Some data only presented for singletons (mean birthweight, birthweight < 10th centile, low birth weight, neonatal resuscitation, admission to special care, Apgar scores).

TABLE 47 *Characteristics of excluded studies*

Study	Reasons for exclusion
Secher 1986	Methodology unclear as all suspected light-for-gestational age fetuses to be referred to obstetrician for further evaluation. However, 26 suspected light-for-gestational-age fetuses included in final analysis not reported to clinicians, primarily because they were part of another randomised study. The other randomised trial (Secher 1987) also not included (see below).
Secher 1987	In this study, third trimester ultrasound used to identify group of uncomplicated pregnancies when there was ultrasound suspicion but no clinical suspicion of poor intrauterine growth. Only these pregnancies randomised. Revealed group underwent serial tests of fetal well-being (non-stress cardiotocograph and serum oestriol and placental lactogen) and fetal growth and management planned depending on results of tests. Thus, study assesses value of various tests of fetal well-being if fetal growth retardation is suspected rather than the value of routine third trimester ultrasound alone.
Wladimiroff 1980	Primary aim of study was to assess ability of third trimester ultrasound in detecting small- and large-for-dates infants, and no clinical outcomes were evaluated.

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Grannum PA, Berkowitz RL, Hobbins JC. The ultrasonic changes in the maturing placenta and their relation to fetal pulmonary maturity. *Am J Obstet Gynecol* 1979;**133**:915–22.

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Appendix 3

Routine Doppler ultrasound in pregnancy: Cochrane review

This review has undergone the Cochrane Collaboration peer review process.

Cover sheet

Title: Routine Doppler ultrasound in pregnancy
Reviewer(s): Bricker L, Neilson JP
Date edited: 12/03/00
Date of last substantive update: 14/01/00
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Review first published: Issue 2, 2000
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Extramural sources of support None.

Contribution of reviewers Both reviewers assessed studies and extracted data. Agreement about study inclusion and exclusion was reached and data extraction cross-checked. L Bricker entered data and wrote the review under the supervision of JP Neilson.

Acknowledgements Professor AM Weindling (Professor of Perinatal Medicine, University of Liverpool): for advice on neonatal outcomes. Dr JA Davies: for further data from the London trial. Professor J Newnham and Dr Sharon Evans: for unpublished results from the Perth trial.

Potential conflict of interest JP Neilson was a co-investigator in the Glasgow trial that was included in the review.

Synopsis

Routine Doppler ultrasound in pregnancy does not have health benefits for women or babies and may do some harm.

Doppler ultrasound uses sound waves to detect the movement of blood. It is used in pregnancy to study blood circulation in the baby, uterus and placenta. Using it in high-risk pregnancies, in which there is concern about baby's condition, reduces the risk of the baby dying and the need for interventions around birth, such as Caesarean section. However, its value as a screening tool in all pregnancies is limited by complications being rare, and the greater possibility of unnecessary intervention and adverse effects. The review of trials of routine Doppler ultrasound in pregnancy found that it does not improve the health of either the woman or baby, and it may do some harm.

Abstract

Background Doppler ultrasound study of umbilical artery waveforms helps identify the compromised fetus in 'high-risk' pregnancies and therefore deserves assessment as a screening test in 'low-risk' pregnancies.

One of the main aims of routine antenatal care is to identify the 'at-risk' fetus in order to apply clinical interventions that could result in reduced perinatal morbidity and mortality.

Objectives To assess the effects on obstetric practice and pregnancy outcome of routine Doppler ultrasound in unselected and low-risk pregnancies.

***S*earch strategy** The Cochrane Pregnancy and Childbirth Group Specialised Register of Controlled Trials and the Cochrane Controlled Trials Register were searched. Date of last search: September 1999.

Selection criteria Acceptably controlled trials of routine Doppler ultrasound (umbilical circulation

and/or uterine circulation) in unselected or low-risk pregnancies.

Data collection and analysis Both reviewers assessed trial quality and extracted data. Authors of two trials were contacted for additional information.

Main results Five trials were included which recruited 14,338 women. The methodological quality of the trials was generally good. Based on existing evidence, routine Doppler ultrasound examination in low-risk or unselected populations did not result in increased antenatal, obstetric and neonatal interventions, and no overall differences were detected for substantive short-term clinical outcomes, such as perinatal mortality. There is no available evidence to assess the effect on substantive long-term outcomes, such as childhood neurodevelopment. There is no available evidence to assess maternal outcomes, particularly psychological effects. In two studies there were unexpected findings suggesting possible harmful effects but the explanation for this is not clear, and further evaluation regarding the safety of Doppler ultrasound is required.

Reviewers' conclusions Based on existing evidence, routine Doppler ultrasound in low-risk or unselected populations does not confer benefit on mother or baby. Future research should be powerful enough to address small changes in perinatal outcome, and should include evaluation of maternal psychological effects, long-term outcomes such as neurodevelopment, and issues of safety.

Background

One of the main aims of routine antenatal care is to identify the 'at-risk' fetus in order to apply clinical interventions that could result in reduced perinatal morbidity and mortality. The routine use of a screening test should be based on proven clinical effectiveness, without subjecting a large group of normal women to anxiety and inappropriate intervention, and to subsequent risk of iatrogenic morbidity and mortality.

Doppler ultrasound is a non-invasive technique whereby the movement of blood (usually in a vessel) is studied by detecting the change in frequency of reflected sound. Doppler ultrasound has been used in obstetrics since 1977 to study the feto-placental (umbilical) circulation (Fitzgerald & Drumm, 1977) and, since the 1980s, to study the utero-placental (uterine) circulation (Campbell, *et al.,* 1983) and fetal circulation (Eik-Nes, *et al.,* 1980).

Doppler ultrasound of the umbilical and/or the uterine circulation has been the subject of more randomised trials than any other test of fetal well-being, despite its relatively recent introduction to obstetrics. The use of Doppler ultrasound of the umbilical artery in high-risk pregnancies (particularly in association with intra-uterine growth retardation and hypertensive disorders of pregnancy) is associated with a reduction in perinatal mortality and obstetric interventions, including antenatal admission, elective delivery and induction of labour (Neilson & Alfirevic, 1999). Furthermore, it has been shown in a longitudinal, observational study that Doppler ultrasound of the umbilical artery is more helpful than other tests of fetal well-being (namely, heart rate variability and biophysical profile score) in distinguishing between the normal small fetus and the 'sick' small fetus (Soothill, *et al.,* 1993). However, its exact role in optimising management, particularly timing of delivery, remains unclear and is currently being investigated in a multicentre trial (Growth Restriction Intervention Trial (GRIT); coordinator, Dr Jim Thornton, University of Leeds, UK).

The relationship between abnormal uterine artery Doppler velocimetry and pre-eclampsia, intrauterine growth retardation and adverse pregnancy outcome is well established. However, whether its use as a routine screening test ultimately results in a decrease in maternal and perinatal morbidity and mortality remains questionable. This is due to a number of factors, including the low positive predictive value of the test, the lack of an accepted standardised analysis of the uterine artery waveform, and the dependence on operator skill (Aquilina & Harrington, 1996). Furthermore, screening is only worthwhile if an effective preventive treatment is available. The debate about the benefit of prophylactic treatment with low-dose aspirin may not be completely resolved but the results of the two largest multicentre randomised trials (CLASP, 1994; ECPPA, 1996) were not encouraging.

Theoretically, the use of routine Doppler ultrasound in unselected or low-risk pregnancies would be to detect those pregnancies in which there has been failure to establish or maintain the normal low-resistance umbilical and uterine circulations (a pathological process leading to placental dysfunction and associated with intrauterine growth retardation and pre-eclampsia) before there is clinical evidence of fetal compromise. In practice, observational and longitudinal studies of Doppler ultrasound in unselected or low-risk pregnancies have raised

doubts about its application as a routine screening test and some authors have cautioned against its introduction into obstetric practice without supportive evidence from randomised trials (Sijoms, *et al.,* 1989; Beattie & Dornan, 1989; Goffinet, *et al.,* 1997). The relatively low incidence of significant, poor perinatal outcomes in low-risk and unselected populations presents a challenge in evaluating the clinical effectiveness of routine Doppler ultrasound, as large numbers are required to test the hypothesis.

The safety of Doppler ultrasound remains of concern. In particular, the use of pulsed Doppler (RCOG, 1997) involves the use of higher intensities compared with diagnostic ultrasound and, hence, may cause significant tissue heating and thermal effects. However, these thermal effects depend on the presence of a tissue/air interface and may not, therefore, be clinically significant in obstetric ultrasound examinations (Barnett, 1995). Clearly, while there is continuing concern regarding the safety of Doppler ultrasound, it should only be used if of proven value.

Objectives

To assess the effects on obstetric practice and pregnancy outcome of routine Doppler ultrasound in unselected and low-risk pregnancies.

A low-risk population is defined as a population in which those considered at risk have been excluded. Criteria of 'at risk' are variously defined and this is taken into consideration when the features of included studies are described.

Criteria for considering studies for this review

Types of studies

All acceptably controlled trials of routine Doppler ultrasound (umbilical circulation and/or uterine circulation) in unselected or low-risk pregnancies. Because of an anticipated paucity of RCTs, quasi-randomised trials were considered for inclusion.

Types of participants

Pregnant women in both unselected and low-risk populations.

Types of interventions

Routine Doppler ultrasound of the umbilical artery and/or uterine circulation in pregnancy in unselected or low-risk populations.

Types of outcome measures

All outcome measures

Perinatal outcome

– gestational age at birth
– birth-weight
– birth-weight < 10th percentile
– birth-weight < 3rd percentile
– preterm delivery < 28 weeks
– preterm delivery < 34 weeks
– preterm delivery < 37 weeks
– low birth-weight (< 2.5 kg)
– very low birth-weight (< 1.5 kg)
– need for resuscitation
– use of ventilation
– admission to a special care baby unit and length of stay
– low Apgar score (< 7 at 5 minutes)
– perinatal death

Detection of

– pre-eclampsia
– intrauterine growth retardation

Obstetric interventions

– antenatal admission
– antenatal fetal monitoring
  - Kick Count Chart
  - cardiotocography
  - biophysical profile
  - further Doppler
  - further ultrasound
– intention to deliver
– induction of labour
– operative delivery
  - elective Caesarean section
  - emergency Caesarean section
  - Caesarean section for distress
  - Caesarean section for distress antepartum
  - Caesarean section for distress intrapartum
  - instrumental vaginal delivery

Neonatal outcome

– acute neonatal problems
  - hypoxic ischaemic encephalopathy
  - necrotising enterocolitis
  - intraventricular haemorrhage
  - intraventricular haemorrhage with cystic periventricular leukomalacia
  - pulmonary haemorrhage
– neonatal death
– early neonatal death (first week of life)
– late neonatal death (1–4 weeks)
– infant death (1 month–1 year)
– neurodevelopment at age 2 years

Maternal outcome

– psychological effects (including stress, anxiety, depression, quality of life, reassurance)

Primary outcome measures
Only seven of the above outcome measures will be used for subgroup analyses as follows:

– induction of labour
– Caesarean section
– preterm delivery < 28 weeks
– preterm delivery < 34 weeks
– all deaths (perinatal, neonatal, and infant)
– neurodevelopment at 2 years of age
– maternal psychological effects.

Search strategy for identification of studies

This review drew on the search strategy developed for the Pregnancy and Childbirth Group as a whole.

Relevant trials were identified in the group's Specialised Register of Controlled Trials. See Review Group's details for more information.

In addition, the Cochrane Controlled Trials Register was searched. Date of last search: Issue 3, September 1999.

Methods of the review

All potential studies to be considered were identified as outlined in the search strategy. The two reviewers independently assessed the trials for methodological quality and appropriateness for inclusion. The reason for exclusion of any trial was clearly stated. The trials were not assessed blinded and the reviewers knew the author's name, institution, source of the publication and results when applying inclusion criteria. There were no disagreements but, if there had been, they would have been resolved by discussion until consensus was reached. Additional information was sought from the authors of two trials by personal communication.

Data extraction was performed by two reviewers and double-checked for discrepancies. Statistical analysis was performed using RevMan software.

If appropriate, stratified analyses of all outcome measures were performed in the following categories:

(i) all routine Doppler versus no Doppler/concealed Doppler examinations (i.e. caregivers not aware of results)
(ii) single Doppler versus no Doppler/concealed Doppler examinations
(iii) multiple Doppler versus no Doppler/concealed Doppler examinations.

If appropriate, subgroup analyses of the primary outcomes were only performed for the following categories:

(i) umbilical artery Doppler versus no Doppler/concealed Doppler examinations
(ii) uterine artery Doppler versus no Doppler/concealed Doppler examinations
(iii) umbilical and uterine artery Doppler versus no Doppler/concealed Doppler examinations.

Sensitivity analyses were performed if sufficient trials existed to make these appropriate, focusing on methodological quality, especially on allocation concealment.

Description of studies

See 'Characteristics of included studies' below.

Five trials comprising 14,338 women were included: France 1997; Glasgow 1994; Leeds 1993; London 1992; Perth (Australia) 1993.

Two trials (London 1992; Glasgow 1994) studied unselected populations, and three (Leeds 1993; France 1997; Perth (Australia) 1993 studied low-risk populations.

Only two trials evaluated both uterine and umbilical artery waveforms by Doppler ultrasound (London 1992; Perth (Australia) 1993) and both were different in design compared with the other three included trials, which evaluated umbilical artery Doppler ultrasound alone. The Perth (Australia) 1993 trial was unusual in that it combined intensive repeated ultrasound assessment of the fetus plus Doppler study of the umbilical and uterine arteries versus selective ultrasound. The data from this trial were therefore analysed in a separate comparison (serial ultrasound and Doppler ultrasound versus selective ultrasound), and have been included in another Cochrane review (Bricker & Neilson, 2000). The London 1992 trial was also unusual in that two different protocols were used for high- and low-risk populations, with the high-risk group (15% of the population) having serial Doppler examinations and the low-risk group having Doppler examinations on two occasions (19–22 weeks and 32 weeks). The data for each population were

not reported separately and, hence, could not be analysed separately. The Glasgow 1994 trial offered Doppler ultrasound of the umbilical artery to all participants but revealed results for the study group only. The intention of the London trial was for no Doppler ultrasound to be performed in the control group at any time during pregnancy. Doppler ultrasound was allowed, if clinically indicated, for the control group in the other trials (France 1997; Leeds 1993; Perth (Australia) 1993).

The trials studied, and therefore reported, different parameters of Doppler ultrasound. Three trials only studied umbilical artery Doppler (France 1997; Glasgow 1994; Leeds 1993), and reported parameters were resistance index, maximum A:B ratio and A:B ratio, respectively. The two trials which studied both umbilical artery and uterine artery Doppler (London 1992; Perth (Australia) 1993) reported pulsatility index and A:B ratio for the umbilical artery, respectively, and lowest resistance index and A:B ratio of an arcuate artery within the placental vascular bed, respectively. Furthermore, reference ranges used to determine whether normal or abnormal were different. For more details see 'Characteristics of included studies' below.

The results of the review should be considered in the light of these different factors, as the specific nature of the Doppler techniques and interpretation of reported parameters may have had some effect on the outcome measures.

No trials included a standardised management protocol for abnormal Doppler results.

Methodological quality of included studies

The methodological quality of all included studies was good in terms of allocation concealment. The Glasgow study (1994) included, for various logistic reasons (one operator who was, at times, not available; women who declined to participate; non-attendance at hospital-based antenatal clinics), only 40% of potential participants. However, the authors state that they believe this was representative of the total population, and compared the availability (revealed group) versus unavailability (concealed group) of Doppler ultrasonography. Furthermore, the characteristics of the two study groups were similar. Although the randomisation procedure in the Glasgow study (1994) was acceptable (sealed opaque envelopes containing groups generated by random-number tables), clerical error in preparation produced unbalanced numbers in the two groups. For details about losses to follow-up, see 'Characteristics of included studies' below.

Results

See meta-analysis table (*Table 48*) and metaview (*Figure 6*).

Few or no data were available for some of the prespecified outcome measures, particularly acute neonatal problems, long-term neurodevelopment and maternal psychological effects. There were no trials in which the use of routine mid-pregnancy uterine Doppler ultrasound to predict pre-eclampsia, intrauterine growth restriction or adverse pregnancy outcome was evauluated.

Due to the small number of included studies, no stratified or subgroup analyses were performed.

Routine Doppler ultrasound versus no/concealed/selective Doppler ultrasound

The results of meta-analysis of four trials (France 1997; Glasgow 1994; Leeds 1993; London 1992) showed no differences between groups in antenatal admissions, obstetric interventions, neonatal interventions and overall perinatal mortality. In the French trial (France 1997), the screened group were more likely to have further Doppler ultrasound examinations (Peto OR, 1.57; 95% CI, 1.30 to 1.90). Among the three trials (France 1997; Glasgow 1994; London 1992) that reported perinatal mortality for fetuses/neonates without congenital abnormalities separately, there is heterogeneity of the results (chi-squared 10.44, $p < 0.025$). This is because the data from the London trial (1992) found increased perinatal mortality in the screened group (Peto OR, 3.31; 95% CI, 1.37 to 7.97).

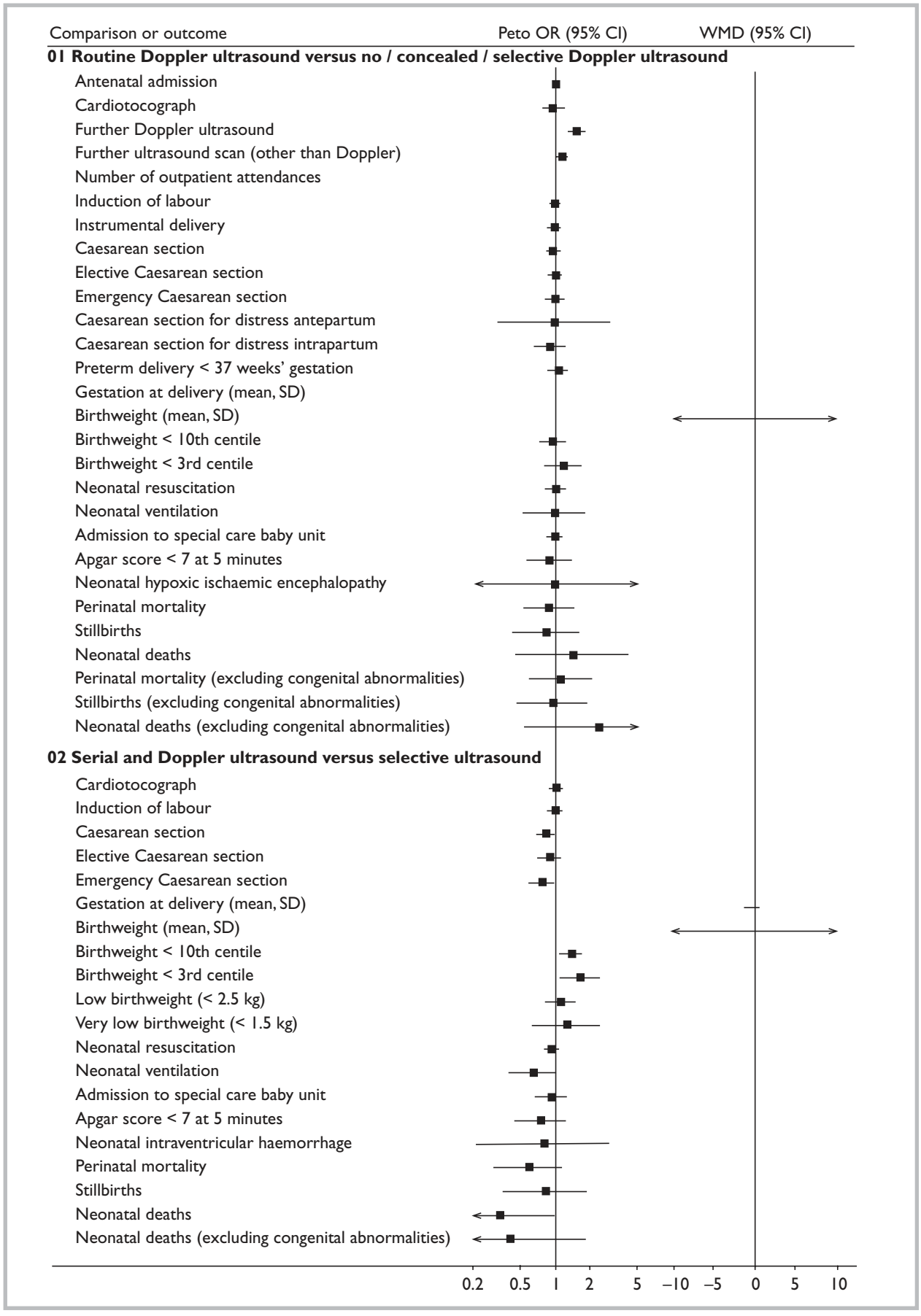
Serial ultrasound and Doppler ultrasound versus selective ultrasound

This comparison includes published and unpublished data from Perth (Australia) 1993. The results of this trial showed no differences between the two groups in antenatal admissions or other tests of fetal well-being, use of obstetric interventions (such as induction of labour, instrumental deliveries and Caesarean section) or perinatal and neonatal outcome. More babies in the screened group were of birthweight < 10th centile (Peto OR, 1.41; 95% CI, 1.11 to 1.78) and < 3rd centile (Peto OR, 1.67; 95% CI, 1.11 to 2.53).

TABLE 48 *Meta-analysis: routine Doppler ultrasound*

Outcome	Number of studies	Number of participants	Statistical method	Effect size	Significant effect (see *Figure 7*)
Comparison 1: routine Doppler versus no/concealed/selective Doppler ultrasound					
Antenatal admission	3	9359	Peto OR (95% CI)	1.05 (0.95 to 1.15)	
Cardiotocograph	1	3898	Peto OR (95% CI)	0.98 (0.80 to 1.97)	
Further Doppler ultrasound	1	3898	Peto OR (95% CI)	**1.57 (1.30 to 1.90)**	✓
Further ultrasound scan (other than Doppler)	2	6373	Peto OR (95% CI)	1.16 (1.02 to 1.32)	
Number of outpatient attendances	1	2475	WMD (fixed) (95% CI)	0.1 (–0.11 to 0.31)	
Induction of labour	4	11,375	Peto OR (95% CI)	1.03 (0.93 to 1.13)	
Instrumental delivery	2	6373	Peto OR (95% CI)	1.01 (0.89 to 1.15)	
Caesarean section	2	6373	Peto OR (95% CI)	1.00 (0.86 to 1.15)	
Elective Caesarean section	4	11,375	Peto OR (95% CI)	1.02 (0.87 to 1.19)	
Emergency Caesarean section	2	5461	Peto OR (95% CI)	1.01 (0.84 to 1.23)	
Caesarean section for distress antepartum	1	3898	Peto OR (95% CI)	1.00 (0.32 to 3.10)	
Caesarean section for distress intrapartum	2	6884	Peto OR (95% CI)	0.91 (0.67 to 1.24)	
Pre-term delivery < 37 weeks' gestation	3	9359	Peto OR (95% CI)	1.09 (0.89 to 1.33)	
Gestation at delivery (mean, SD)	1	2016	WMD (fixed) (95% CI)	–0.02 (–0.19 to 0.15)	
Birthweight (mean, SD)	1	2016	WMD (fixed) (95% CI)	–27 (–74.23 to 20.23)	
Birthweight < 10th centile	1	2475	Peto OR (95% CI)	0.97 (0.74 to 1.25)	
Birthweight < 3rd centile	1	3898	Peto OR (95% CI)	1.17 (0.79 to 1.73)	
Neonatal resuscitation	2	6373	Peto OR (95% CI)	1.02 (0.83 to 1.26)	
Neonatal ventilation	1	2986	Peto OR (95% CI)	0.99 (0.54 to 1.83)	
Admission to special care baby unit	3	7477	Peto OR (95% CI)	0.99 (0.82 to 1.19)	
Apgar score < 7 at 5 minutes	4	11,375	Peto OR (95% CI)	0.88 (0.56 to 1.40)	
Neonatal hypoxic ischaemic encephalopathy	1	2016	Peto OR (95% CI)	0.99 (0.06 to 15.78)	
Perinatal mortality	4	11,375	Peto OR (95% CI)	0.89 (1.52 to 1.50)	
Stillbirths	3	9359	Peto OR (95% CI)	0.83 (0.42 to 1.63)	
Neonatal deaths	3	9359	Peto OR (95% CI)	1.38 (0.45 to 4.30)	
Perinatal mortality (excluding congenital abnormalities)	3	9359	Peto OR (95% CI)	1.10 (0.59 to 2.07)	
Stillbirths (excluding congenital abnormalities)	3	9359	Peto OR (95% CI)	0.93 (0.46 to 1.87)	
Neonatal deaths (excluding congenital abnormalities)	3	9359	Peto OR (95% CI)	2.33 (0.53 to 10.28)	
Comparison 2: serial ultrasound and Doppler ultrasound versus selective ultrasound					
Cardiotocograph	1	2834	Peto OR (95% CI)	1.01 (0.87 to 1.17)	
Induction of labour	1	2834	Peto OR (95% CI)	1.03 (0.88 to 1.21)	
Caesarean section	1	2834	Peto OR (95% CI)	0.86 (0.72 to 1.04)	
Elective Caesarean section	1	2834	Peto OR (95% CI)	0.94 (0.74 to 1.19)	
Emergency Caesarean section	1	2834	Peto OR (95% CI)	0.80 (0.61 to 1.05)	
Gestation at delivery (mean, SD)	1	2834	WMD (fixed) (95% CI)	–0.1 (–1.20 to 1.00)	
Birthweight (mean, SD)	1	2834	WMD (fixed) (95% CI)	–25 (–67.53 to 17.53)	
Birthweight < 10th centile	1	2834	Peto OR (95% CI)	**1.41 (1.11 to 1.78)**	✓
Birthweight < 3rd centile	1	2834	Peto OR (95% CI)	**1.67 (1.11 to 2.53)**	✓
Low birth weight < 2.5 kg	1	2834	Peto OR (95% CI)	1.15 (0.84 to 1.56)	
Very low birth weight < 1.5 kg	1	2834	Peto OR (95% CI)	1.27 (0.65 to 2.50)	
Neonatal resuscitation	1	2834	Peto OR (95% CI)	0.96 (0.83 to 1.11)	
Neonatal ventilation	1	2834	Peto OR (95% CI)	0.67 (1.41 to 1.09)	
Admission to special care baby unit	1	2834	Peto OR (95% CI)	0.94 (0.67 to 1.33)	
Apgar score < 7 at 5 minutes	1	2834	Peto OR (95% CI)	0.76 (0.46 to 1.27)	
Neonatal intraventricular haemorrhage	1	2834	Peto OR (95% CI)	0.80 (0.22 to 2.97)	
Perinatal mortality	1	2834	Peto OR (95% CI)	0.59 (0.30 to 1.16)	
Stillbirths	1	2834	Peto OR (95% CI)	0.83 (0.36 to 1.93)	
Neonatal deaths	1	2834	Peto OR (95% CI)	0.34 (0.11 to 1.01)	
Neonatal deaths (excluding congenital abnormalities)	1	2834	Peto OR (95% CI)	0.42 (0.10 to 1.87)	

FIGURE 6 *Metaview: routine Doppler ultrasound in pregnancy (See Table 45 for statistical values, Peto ORs or WMDs and 95% CIs)*



There was no difference in other indices of perinatal or neonatal outcome.

Discussion

The higher perinatal mortality of normal fetuses/neonates in the screened group of the London trial (1992) suggests that routine Doppler ultrasound in unselected pregnancies may do more harm than good. However, the authors acknowledge that this was an unexpected finding which may have occurred by chance. Furthermore, they state that the study was not designed to test the ability of routine Doppler ultrasound examinations to reduce perinatal mortality, as a much larger number of women would need to be included in such a trial to test this hypothesis. In this review, meta-analysis of perinatal outcome in normal fetuses includes data from 9359 pregnancies from three trials (France 1997; Glasgow 1994; London 1992). No differences in perinatal mortality are demonstrated but this number of participants remains too small to detect small but significant changes in perinatal outcome.

In the London trial (1992), there was only one single case of absent umbilical artery end-diastolic flow, a worrying feature, but this was associated with pregnancy-induced hypertension, resulting in intra-uterine death of a fetus with birthweight < 10th centile.

In the Perth study (Australia 1993), there was an unexpected finding of a greater risk of intrauterine growth restriction in the serial ultrasound and Doppler examination group (i.e. the intensive group). The authors state that while this may have been a chance finding, it is possible that frequent exposure to ultrasound may have influenced fetal growth. This finding was not associated with increased perinatal morbidity and mortality, and follow-up of these children at 1 year of age found that the difference in growth was no longer discernible (Newnham, *et al.,* 1996). This is, however, a further finding that suggests more harm than good, and the authors stress the need for further investigation of the effects of frequent ultrasound exposure on fetal growth.

No trial addressed long-term neurodevelopmental outcome or maternal psychological outcome and it is arguable that these are the important outcomes. The finding of increased further Doppler examinations in the screened group of the French study (France 1997), implies exposure of the expectant mother to uncertainty and possible anxiety about the health of her baby, the implications of which may be far-reaching. In addition, perinatal survival does not automatically translate into long-term success, as little is known about the long-term prognosis of the compromised fetus *in utero.*

Reviewers' conclusions

Implications for practice

Existing evidence suggests that the use of routine Doppler ultrasound in low-risk or unselected populations does not benefit either mother or baby, and may be harmful. At present, Doppler ultrasound examination should be reserved for use in high-risk pregnancies (see Cochrane review: Neilson & Alfirevic, Cochrane Library, Issue 3, 2000).

Implications for research

If there is to be future research into Doppler ultrasound examination in low-risk or unselected populations, a large trial with adequate power to test hypotheses related to perinatal outcome is required. Trials should include assessment of maternal outcomes, particularly psychological effects, neonatal morbidity, long-term neurodevelopment and safety. The value of routine mid-pregnancy uterine Doppler ultrasound to predict pre-eclampsia, intrauterine growth restriction and other adverse outcomes should be assessed in randomised trials.

Characteristics of included studies

See *Table 49* for characteristics of included studies.

Characteristics of excluded studies

See *Table 50* for characteristics of excluded studies.

References to studies

Included studies

France 1997 (published data only)
Doppler French Study Group. A randomised controlled trial of Doppler ultrasound velocimetry of the umbilical artery in low risk pregnancies. *Br J Obstet Gynaecol* 1991;**14**:419–22.

Glasgow (UK) 1994 (published data only)
Whittle MJ, Hanretty KP, Primrose MH, Neilson JP. Screening for the compromised fetus: a randomised trial of umbilical artery velocimetry in unselected pregnancies. *Am J Obstet Gynaecol* 1994;**170**:555–9.

Leeds (UK) 1993 (published data only)
Mason GC, Lilford RJ, Porter J, Nelson E, Tyrell S. Randomised comparison of routine versus highly selective use of Doppler ultrasound in low risk pregnancies. *Br J Obstet Gynaecol* 1993;***100***:130–3.

London (UK) 1992 (published and unpublished data)
Davies J, Spencer J, Gallivan S. Randomised trial of Doppler screening in a general obstetric population [abstract]. British Congress 1992.

Davies JA, Gallivan S, Spencer JAD. Randomised controlled trial of Doppler ultrasound screening of placental perfusion during pregnancy. *Lancet* 1992;**340**:1299–1303.

Spencer JAD, Davies JA, Gallivan S. Randomised trial of routine Doppler screening during pregnancy [conference abstract]. *J Matern Fetal Invest* 1992;**1**:126.

Perth (Australia) 1993 (published and unpublished data)
Newnham JP, Evans SF, Michael CA, Stanley FJ, Landau LI. Effects of frequent ultrasound during pregnancy: a randomised controlled trial. *Lancet* 1993;**342**:887–91.

Newnham J, MacDonald W, Gurrin L, Evans S, Landau L, Stanley F. The effect of frequent prenatal ultrasound on birthweight: follow up at one year of age [conference abstract]. In: Proceedings of Australian Perinatal Society, in conjunction with the New Zealand Perinatal Society; March 1996.

Excluded studies (Published data only)

Gonsoulin. Umbilical artery Doppler waveform analysis: a randomised study on effect on outcome [abstract]. *Am J Obstet Gynaecol* 1991;**164**:370.

Schneider KTM, Amberg-Wendland D, Renz S, Furstenau U. Prospective randomised study of the clinical value of Doppler sonography as a screening procedure [translation]. *Gynakol Rundsch* 1991;**31**:139–40.

Schneider KTM, Renz S, Furstenau U, Amberg-Wendland D, Prochaska D, Graeff H. Doppler flow measurements as a screening method during pregnancy: is it worth the effort [conference abstract]? *J Matern Fetal Invest* 1992;**1**:125.

Studies awaiting assessment

Ellwood D, Peek M, Curren J. Predicting adverse pregnancy outcomes with ultrasound [unpublished data]. A randomised controlled trial. Personal communication, 1997.

Scholler J, Putz M, Sainz HG, Altrichter R, Philipp K. Value of Doppler sonography in management of non-risk pregnancies at term [translation]. *Gynakol Rundsch* 1993;**33** (1 suppl):118–19.

Other references

Additional references

Aquilina J, Harrington K. Pregnancy hypertension and uterine artery Doppler ultrasound. *Curr Opin Obstet Gynecol* 1996;**8**:435–40.

Barnett SB. Ultrasound safety in obstetrics: what are the concerns? *Ultrasound Q* 1995;**13**:228–39.

Beattie RB, Dornan JC. Antenatal screening for intrauterine growth retardation with umbilical artery Doppler ultrasonography. *BMJ* 1989;**298**:631–5.

Bricker L, Neilson JP. Routine ultrasound in late pregnancy (after 24 weeks gestation) (Cochrane review). In: Cochrane library, Issue 1, 2000. Oxford: Update Software; 2000.

Campbell S, Diaz-Recasens J, Griffin DR, Cohen-Overbeek TE, Pearce JM, Wilson K, *et al.* New Doppler technique for assessing utero–placental blood flow. *Lancet* 1983;**i**:675–7.

CLASP (Collaborative Low-Dose Aspirin Study in Pregnancy) Collaborative Group. CLASP: a randomised trial of low-dose aspirin for the prevention and treatment of pre-eclampsia among 9364 pregnant women. *Lancet* 1994;**343**:619–29.

ECPPA (Estudo Colaborativo para Provencao da Pre-eclampsia com Aspirina) Collaborative Group. ECPPA: randomised trial of low dose aspirin for the prevention of maternal and fetal complications in high-risk pregnant women. *Br J Obstet Gynaecol* 1996;**103**:39–47.

Eik-Nes SH, Brubaak AO, Ulstein MK. Measurement of human fetal blood flow. *BMJ* 1980;**280**:283–4.

Fitzgerald DE, Drumm JE. Non-invasive measurement of the human circulation using ultrasound: a new method. *BMJ* 1977;**2**:1450–1.

Goffinet F, Paris J, Heim N, Nisand I, Breart G. Predictive value of Doppler umbilical artery velocimetry in a low risk population with normal fetal biometry. A prospective study of 2016 women. *Eur J Obstet Gynecol Reprod Biol* 1997;**71**:11–19.

Neilson JP, Alfirevic Z. Doppler ultrasound in high risk pregnancies (Cochrane review). In: Cochrane library, Issue 3, 1998. Oxford: Update Software; 1998.

RCOG Working Party. Ultrasound screening for fetal abnormalities. London: RCOG; 1997.

Sijoms EA, Reuwer PJHM, Van Beek E, Bruinse HW. The validity of screening for small-for-gestational-age and low-weight-for-length infants by Doppler ultrasound. *Br J Obstet Gynaecol* 1989;**96**:557–61.

Soothill PW, Ajayi RA, Campbell S, Nicolaides KH. Prediction of morbidity in small and normally grown fetuses by fetal heart rate variability, biophysical profile score and umbilical artery Doppler studies. *Br J Obstet Gynaecol* 1993;**100**:742–5.

Zelen M. A new design for the randomised clinical trial. *N Engl J Med* 1979;**300**:1242–5.

TABLE 49 *Characteristics of included studies*

Study	Method	Participants	Interventions	Outcomes	Notes
France 1997	Centrally prepared, consecutively numbered, sealed envelopes. Protocol violation at 3 centres; hence 115 women excluded from analysis.	3898 pregnant women recruited, at 20 centres throughout France, with normal routine ultrasound at 28–34 weeks' gestation: fetal biometry > 10th percentile. Low-risk population, excluded women with clinical indication for Doppler ultrasound, listed as: medical history of hypertension or diabetes; obstetric history of fetal death, intrauterine growth retardation, or hypertensive disorders of pregnancy; hypertension or diabetes in index pregnancy; and those who had Doppler before 28 weeks' gestation for any reason. 174 women lost to follow-up (4.5%).	Single Doppler ultrasound examination at 28–34 weeks' gestation. Continuous wave or pulsed wave (according to centre) Doppler ultrasound of umbilical artery to calculate resistence index, derived from mean of six velocity waveforms, and fetal heart rate. No management protocol if abnormal results. Doppler allowed in control group if developed clinical indication.	Obstetric interventions (antenatal and intrapartum); occurrence of pregnancy complications/ disorders (hypertensive disorders, antepartum haemorrhage, fetal growth and amniotic fluid abnormalities); perinatal outcome.	
Glasgow (UK) 1994	Sealed opaque envelopes containing group generated by random-number tables (though clerical error in preparation produced unbalanced numbers in the two groups)	2986 singleton pregnancies less than 26 weeks' gestation at first antenatal visit. Only exclusion criterion was multiple pregnancy. No comment on losses to follow-up – assume none.	Umbilical artery Doppler ultrasound at 26–30 and 34–36 weeks' gestation in all women, who were randomised into revealed and concealed groups. No management protocol if abnormal result. No requests to reveal Doppler in concealed group. Parameter calculated was maximum A:B ratio of five analysed waveforms (positive result – A:B ratio > 95th centile for gestation). Absent end diastolic flow specified if present.	Obstetric interventions (antepartum, but mainly intrapartum) and perinatal outcome indices.	Weakness of study was that, for various logistic reasons (one operator was sometimes not available; women declined to participate; non-attendance at hospital-based antenatal clinics), only 40% of potential participants included. However, authors consider this was representative of total population, and trial compared availability (revealed group) versus unavailability (concealed group) of Doppler ultrasonography. Characteristics of study groups similar.

continued

TABLE 49 contd *Characteristics of included studies*

Study	Method	Participants	Interventions	Outcomes	Notes
Leeds (UK) 1993	Numbered opaque envelopes; randomised at booking as per method described by Zelen, 1979	2145 primigravid women with negative medical and gynaecological histories and physical examinations attending one centre for antenatal booking; 120 (5.6%) either miscarried or moved away (i.e. lost to follow-up), and nine twin pregnancies excluded from analysis.	Continuous wave umbilical artery Doppler ultrasound at 28 and 34 weeks' gestation. Calculated mean A:B ratio over 5 waveforms (positive result defined as mean A:B ratio > 4.5). Positive results further categorised according to severity, as reduced or no end diastolic flow. No management protocol if abnormal result, clinical team informed of positive results, and decided further management. Doppler ultrasound available for control population if clinically indicated, e.g. if developed intrauterine growth retardation and/or hypertensive disorders of pregnancy; 42 (3.9%) of control group underwent Doppler ultrasound for clinical indications.	A few perinatal outcome indices. Two obstetric interventions mentioned – induction of labour and elective Caesarean section.	Little usable outcome data compared with other included trials.
London (UK) 1992	Sealed opaque envelopes; randomisation in four blocks of 500 and three blocks of 200	2600 singleton pregnancies randomised at 19–22 week anomaly scan at single centre. Unselected population: 79% of eligible population recruited; 125 (4.8%) excluded from analysis (106 delivered elsewhere, eight miscarried, two multiple pregnancy erroneously randomised, nine incomplete data). Analysis undertaken on remaining 2145 women recruited.	Two protocols. High-risk protocol: monthly umbilical and uterine artery Doppler ultrasound. High-risk pregnancies identified by presence of one or more of the following factors: pre-existing medical condition (e.g. diabetes, hypertension), previous small-for-gestational-age live birth, previous stillbirth or neonatal death, hypertension in previous pregnancy or at booking, or smoking > 10 cigarettes per day. Low risk protocol: umbilical and uterine artery Doppler ultrasound at 19–22 and 32 weeks' gestation and, if result abnormal, managed according to high-risk protocol but transferred back to low-risk protocol if subsequent examination normal. Women in control group not intended to have Doppler ultrasound at any time during pregnancy but 15 (1.2%) did so (one in error, two at clinician's request and 12 as part of intensive investigation in fetal medicine department). Parameters used were lowest resistance index from uterine arteries, and pulsatility index from umbilical artery, reported as normal, raised (> 95th centile for gestation), or showing absent end diastolic flow. If initial uterine artery resistance index was abnormal, test repeated at 24 weeks before being deemed abnormal.	Obstetric interventions (antepartum and intrapartum) and perinatal outcome indices.	More detail on some data obtained by contacting first author. Of study population, 15% were 'high risk'. Data for high-risk population not available for separate analysis. Number of high-risk pregnancies similar in Doppler and control groups (192 vs. 189). Only one case of absent umbilical artery end-diastolic flow, associated with pregnancy-induced hypertension, resulting in intrauterine fetal death of a fetus with birth weight < 10th centile.
Perth (Australia) 1993	Sealed envelopes prepared in blocks of 20, with computer-generated random numbers	2834 singleton pregnancies. Criteria for recruitment: gestational age 16–20 weeks, sufficient proficiency in English, expected to deliver at hospital and intention to remain in Western Australia so that childhood follow-up would be feasible. Losses to follow-up: 33 (1.2%)	'Regular' group had ultrasound examination at 18 weeks for fetal biometry, subjective amniotic fluid assessment and placental morphology and location; any further scans in pregnancy conducted on clinician's request. 'Intensive group' had ultrasound examination, plus amniotic fluid index and continuous wave Doppler ultrasound of umbilical artery and arcuate artery within placental vascular bed, at 18, 24, 28, 34 and 38 weeks' gestation. Doppler ultrasound parameter reported was A:B ratio. Results recorded in hospital chart. No management protocol if results abnormal.	**Obstetric interventions (antepartum and intrapartum) and perinatal outcome indices.**	Published study reports results overall but few data available for extraction. Authors contacted and provided unpublished data.

TABLE 50 *Characteristics of excluded studies*

Study	Reasons for exclusion
Gonsoulin 1991	Conference abstract: not clear whether high-risk/low-risk/unselected pregnancies and no data suitable for inclusion. Number of women included in study was small (147) and would not affect meta-analysis. Further details sought from author, without success.
Schneider 1992	Conference abstract in English language identified: unexplained difference in numbers (250 vs. 329) in Doppler vs. control groups suggesting allocation bias. Definitive publication after translation from German did not explain this difference and failed to outline trial methodology.

Appendix 4

Search strategy for the review of the detection of fetal abnormalities by routine ultrasound

A literature search for primary studies published after 1995 assessing the detection of fetal anomalies by routine ultrasound was undertaken to update the review by Chitty.[9]

MEDLINE was searched from 1995 onward using the strategy shown in the box below (including truncation of terms where appropriate).

Science Citation Index (BIDS) was searched for papers that cited Chitty (1995):[9] nine papers were identified (two of which overlapped with the MEDLINE search above).

Four further studies were identified as possibly relevant – one which was published after the above search was performed, and three which were identified when the studies used to report detection rates for specific abnormalities in the RCOG Working Party document were cross-referenced with the results of the literature search.

All papers used for data extraction by Chitty (1995)[9] were retrieved and reviewed to assess whether they fulfilled our inclusion criteria, viz. Rosendahl and Kivenen (1989),[10] Saari-Kemppainen and colleagues (1990),[11] Chitty and colleagues (1991),[12] Levi and colleagues (1991),[13] Shirley and colleagues (1992),[14] Luck (1992),[15] Crane and colleagues (1994),[16] and Levi and colleagues (1995).[17]

The studies reviewed by the economists (see chapter 8) were checked to identify any further literature that could be included in the clinical review. No extra studies were identified here.

Date of last search: December 1998.

Number	Records	Request
1	117	"ABNORMALITIES"/ultrasonography
2	39,302	PREGNAN*
3	102	PREGNAN*
4	39,302	#1 and PREGNAN*
5	8685	PRENATAL*
6	40,813	PREGNAN* or PRENATAL*
7	104	#1 and #6
8	319,362	ANIMAL in TG
*9	103	#7 not #8

Appendix 5

Data extraction sheet for the review of the detection of fetal anomalies by routine ultrasound

Author			Year		Country
Study type	RCT	Prospect	Retrospect	Mixed	Unclear
Study aim					
Population					
No. women			No. fetuses/neonates		
Intervention/screening test including gestation					
Ultrasound alone assessed					
Quality control					
Scan regime described					
Period					
Postnatal ascertainment					
Setting		Tertiary	Primary	Mixed	
Operator, including training and skills					
Equipment					
Definition of anomaly described	Only major	All	Only minor	Soft markers	
Mean no. scans per subject					
No. scans repeated for technical reasons					
No. scans repeated by more experienced observer					
No. anomalous fetuses	Major		Minor	Soft markers	
No. anomalies	Major		Minor	Soft markers	
Anomalies detected < 24 weeks:			Anomalous fetuses detected < 24 weeks:		
Sensitivity					
Specificity					
Positive predictive value					
Negative predictive value					
Anomalies detected > 24 weeks:			Anomalous fetuses detected > 24 weeks:		
Sensitivity					
Specificity					
Positive predictive value					
Negative predictive value					
No. terminations of pregnancy		Abnormal pregnancies	Normal pregnancies		
Perinatal outcome					
Description of false-positives					
Mention/report on soft markers/chromosomal markers					

System	Notes	Ultrasound detected			Prevalence	Detected, %
		< 24 weeks	> 24 weeks	Total		
CNS						
Anencephaly						
Spina bifida						
Encephalocele						
Hydrocephaly						
Holoprosencephaly						
Other						
Pulmonary						
Congenital diaphragmatic hernia						
Congenital adenomatous						
malformation of the lung						
Pleural effusion						
Other						
Cardiac						
Ventricular septal defect						
Atrial septal defect						
Atrioventricular septal defect						
Single ventricle						
Valve abnormalities						
Outflow tract abnormalities						
Other complex						
Other						
Gastrointestinal tract						
Tracheo-oesophageal fistula						
Exomphalos						
Gastroschisis						
Small bowel obstruction/atresia						
Other						
Urinary tract						
Obstructive uropathy						
Renal dysplasia						
(Unilateral)						
(Bilateral)						
Renal agenesis						
(Unilateral)						
(Bilateral)						
Prune belly						
Other						
Skeletal						
Limb reduction defect						
Talipes						
Spinal abnormality						
Dwarfism						
Other						
Other						
Cystic hygroma						
Facial cleft						
Hydrops						
Multiple abnormality/syndrome						
Chromosomal						
Trisomy 21						
Trisomy 18						
Trisomy 13						
Turners						
Other						
Soft markers		Number	True-positives	False-positives		
CPCs						
Renal pelviectatsis						
Echogenic bowel						
NT						
Golf balls						
Ventriculomegaly						
Short limbs						
Odd-shaped skull						
Other						
Other						
2 soft markers						
3 soft markers						
4 soft markers						
Total						

Appendix 6

Search strategy for the review of ultrasonic soft markers

MEDLINE was searched from 1990 onwards, using the strategy presented in the box below (including truncation of terms where appropriate).

Number	Records	Request
1	4826	Choroid
2	6996	Plexus
3	10,952	Cyst
4	29	Choroid plexus cyst
5	71,326	Ultraso*
6	10,953	Sonog*
7	23,664	Doppler*
8	27	#4 and (Ultraso* or Sonog* or Doppler*)
9	849	Echogenic
10	16,584	Bowel*
11	26	Echogenic bowel*
12	71,326	Ultraso*
13	10,953	Sonog*
14	23,664	Doppler*
15	26	#11 and (Ultraso* or Sonog* or Doppler*)
16	80,939	Renal
17	3	Pelviectasis
18	71,326	Ultraso*
19	10,953	Sonog*
20	23,664	Doppler*
21	2	Renal pelviectasis and (Ultraso* or Sonog* or Doppler*)
22	53	#8 or #15 or #21
23	22,650	Soft
24	93,804	Marker*
25	3	Soft marker*
26	56	#22 or #25
27	907,944	Animal in TG
28	56	#26 not (Animal in TG)

Appendix 7

Some terms for finding references on women's views of ultrasound

A. Person	B. Procedure	C. Feelings	D. Ultrasound	E. Prenatal
Woman/women	Scan(ning)/s	Experience/s	Ultrasound	Pregnant/cy
Mother/s	Screen(ing)/s	Expectations/s	Ultrasonography	Ante(-)natal
Maternal	Monitor(ing)	Satisfaction	Sonography	Pre(-)natal
Patient/s	Test(ing)/s	View(point)/s	Doppler	Obstetric
Consumer/s	Diagnosis/diagnostic	Acceptance/ability		Fetus/fetal
Fetus/fetal		Inform(ing/ation)		Maternal
		Belief/s		
		Attitude/s		
		Response/s		
		Preference/s		
		Emotion(al)/s		
		Feel(ing)/s		
		Anxiety/anxious		
		Stress(ful)		
		Behavio(u)r(al)/s		
		Mood/s		
		Well(-)being		
		Psychology/psychological		
		Psych(-)social		
		Social		
		Feedback		

Appendix 8

Search strategy for systematic review of cost and cost-effectiveness studies

The keyword searching was based on the following strategy (including truncation of terms where appropriate).

Ultrasound OR ultrasonography OR sonography OR Doppler
AND
pregnancy OR antenatal OR prenatal OR obstetric OR fetal OR maternal
AND
cost OR economic OR resource.

Electronic bibliographic databases searched included the following (specify 'anonymous').

- MEDLINE
- Cumulative Index of Nursing and Allied Health Literature (CINAHL)
- EMBASE
- EconLIT
- PsycLIT
- Science Citation Index (SCI)
- Social Science Citation Index (SSCI)
- British Library Inside Information (BLII)
- Cochrane Library
- Database of Abstracts of Reviews of Effectiveness (DARE)
- NHS Economic Evaluation Database
- ASSIA
- System for Information on Grey Literature in Europe (SIGLE)
- NUKOP/BOPCAS
- ASLIB Index to Theses
- Current Research in Britain (CRIB)
- COPAC
- ProCite databases held at the National Perinatal Epidemiology Unit (especially Econ2 – a unique collection of references on the costs/economics of antenatal, perinatal and neonatal care)

To ensure comprehensive coverage of relevant material, additional searches were undertaken, as follows:

- current journals for 1998 in perinatal care, health management and health economics
- hand-searching of books, pamphlets and other grey literature held in the library of the National Perinatal Epidemiology Unit
- manuscripts were identified by other means and through personal contacts with fellow health economics researchers.

Date of last search: December 1998.

Appendix 9

Example of data extraction sheets for systematic review of costs and cost-effectiveness studies

Study type, methods and key results

Study number	1	2	3	4	5
First author					
Year of publication					
Type of study					
Economic evaluation (cost-effectiveness/ cost–benefit/ cost–utility analysis					
Descriptive cost study					
Effectiveness study with some assessment of cost implications					
Other (specify)					
Quality: pass or ?					
Aim of study					
Routine ultrasound					
Non-routine ultrasound					
Other, e.g. serum (specify)					
Country					
Setting					
Number of sites for data collection					
Effects					
Costs					
Period of data collection					
Participants					
Forms of care					
Baseline					
Experimental					
Outcomes measured					
Cases detected					
Cases averted					
Incremental					
Average					
Other (specify)					
Methods for clinical effectiveness					
RCT					
Secondary effectiveness study					
Unspecified					

Cost assessment					
Viewpoint					
Model for costing					
Study design (primary or secondary costing or both)					
Data sources					
Number of observations					
Marginal costing					
Cost estimates					
Price year					
Currency					
Charges/market prices/other (e.g. opportunity cost)					
Incremental costs estimated?					
Period covered					
Discount rate					
Valuation of outcomes					
Utility/wtp/other					
Method of estimation					
Whose values?					
Assumptions recorded and tested (sensitivity? – specify)					
Economist as co-author?					
Funding sources					
Comments?					
Sector of economy					
Health care					
Hospital					
Other (specify)					
Community services					
General practice					
Household					
Patient (e.g. travelling cost)					
Family					
Other care providers					
Local authority					
Voluntary organisation (e.g. Life)					
Other (specify)					
Wider economy					
Loss/gain of working time to community (e.g. wage rate)					
Other (specify)					

Form for extraction of cost data from studies included in the systematic review of economic studies of ultrasound scanning

Study number								
Unit breakdown of costs								
			Name	**Price**	**Currency**	**Year**	**Discount rate**	**Conversion to £UK**
Item of machinery, e.g. Doppler								
Other equipment (specify)								
Consumables/ disposables								
Overheads								
Capital charges								
Other (specify: e.g. societal)								
Staff	**Type**	**Grade**	**Time spent**	**Wage rate/cost**				
Summary costs			**Name**	**Price**				
Cost of scan								
What does cost include? (specify)								
Cost of tests (e.g. serum) (specify)								
Average cost per case detected								
(Or other outcome: specify)								
Incremental cost per case detected								
(Or other outcome: specify)								

Appendix 10

Staff diary for time scanning

	Date							Session		a.m.		p.m.		
	Scan number		1	2	3	4	5	6	7	8	9	10	11	12
1	Scan type	Dating												
		Anomaly												
		repeat Dating												
		repeat Anomaly												
		Detail												
		Growth												
		Doppler												
		Biophysical profile												
		Amniotic fluid index												
		Estimated fetal weight												
		Placental												
		Presentation												
		Other (specify)												
		Twins												
		Triplets												
2	Indication for scan	Routine												
		Pregnancy induced hypertension												
		Antepartum haemorrhage												
		Suspected small for gestational age												
		Suspected large for gestational age												
		Suspected oligohydramnios												
		Suspected polyhydramnios												
		Pain												
		Diabetes												
		Premature rupture of membranes												
		History: intrauterine growth retard'n												
		Known anomaly												
		Viability												
		Rec misc												
		High alpha fetoprotein												
		Smoker												
		Reduced fetal movement												
		Other (specify)												
3	Prescan talk	< 5 minutes												
		5–10 minutes												
4	Scan	< 5 minutes												
		5–9 minutes												
		10–14 minutes												
		15–19 minutes												
		20–24 minutes												
		25–29 minutes												
		30–35 minutes												
5	Postscan talk	< 5 minutes												
		5–9 minutes												
		10–15 minutes												
6	Documentation	< 5 minutes												
		5–9 minutes												
		10–15 minutes												
7	Other arrangements	< 5 minutes												
		5–9 minutes												
		10–15 minutes												
	Specify													
8	Training	Yes/No												

Specify Part 1

Scan number	
1	
2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	

Specify Part 2

Scan number	
1	
2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	

Specify Part 3

Scan number	
1	
2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	

Appendix 11

Data sheet for scans/procedures performed at the Fetal Centre, Liverpool Women's Hospital

1 **Date**

2 **Patient details** Name ____ Number ____

Booked LWH ____ Tertiary referral ____

3 **Indication for consultation** ____

4 **Procedure** Scan ☐ Detailed ☐ Cardiac ☐ Growth ☐ Doppler ☐ BPP ☐ AFI ☐ LV (max pool) ☐

Other ☐ specify ____

Amnio ____ CVS ____ FBS ____

Other ☐ specify ____

5 **Time spent** (minutes)

		< 5	5	10	15	20	25	30	35	40	45	50	55	60	Other
Counselling visit	Y/N														
a Pre-counselling time															
b Documentation															
Procedure/scanning visit															
c Precounselling time															
d Procedure/scanning time															
Trainee	Y/N														
Supervisor															
e Post-counselling time															
f Database entry															
g Other arrangements															
(specify)															

6 **Others present**

Midwife	☐	All the time	☐
Doctor	☐	Part of time (indicate)	5a 5b 5c 5d 5e 5f 5g
Healthcare assistant	☐	Extra time (specify)	
Radiographer	☐		
Other	☐		

BPP, biophysical profile; AFI, amniotic fluid index; LV, liquor volume; FBS, fetal blood sampling

Appendix 12

Patient information and questionnaire for survey of women's costs of ultrasound scans

PATIENT INFORMATION LEAFLET

An evaluation of what it costs to attend for antenatal tests

Before you fill in the questionnaire it is important that you read this leaflet. It outlines why we are asking you (and many other women) to fill in the questionnaire. Please ask if you do not understand or would like more information. You do not have to agree to fill in the questionnaire and your care will not be affected in any way.

The aim of the questionnaire
Pregnant women are offered a number of tests, including ultrasound scan, blood tests, and so on. However, very little is known about the hidden costs of these tests to the health service, to women and to society at large. An evaluation of the costs would be incomplete if we did not consider the cost to the women when attending for a test. By doing this we can find out if the service we provide is valuable for each individual and society as a whole. The information we get from this questionnaire will be part of a larger study evaluating the cost-effectiveness of ultrasound scanning in pregnancy. This does not mean we will stop performing ultrasound scans in pregnancy but that we will have a better idea of how and when is the best time to do them.

What you need to do
We would appreciate it if you would take the time to fill in the questionnaire. It shouldn't take longer than 5–10 minutes. You do not have to put your name on the questionnaire and therefore the information you provide remains anonymous.

How this will benefit you
In the short term this will not benefit you as nothing will change in the way you are cared for during your pregnancy. However, it will help us plan and hopefully improve certain aspects of antenatal care in the future, which will ultimately benefit you and other pregnant women.

Contact person for the study

Leanne Bricker (Clinical Research Fellow)

Liverpool Women's Hospital
Extension 4149
or bleep via switchboard

Questionnaire for measuring women's costs of attending for antenatal tests

Thinking about your visit today

1. What would you have been doing today if you were not attending the clinic?
   - Paid employment ❑
   - Looking after children or relatives ❑
   - Studying at school/college ❑
   - Other *Please specify* _____

If you are in paid employment, please answer question 2, if not go to question 3.

2. What arrangements did you make to take time off work? (Please tick one box)
   - Paid absence from work ❑
   - Unpaid absence from work ❑
   - Will make the time up ❑
   - Came to clinic outside work time ❑
   - Took holiday ❑
   - Other arrangements *Please specify* _____

3 (a) Did you travel here today by:
   - Walking ❑
   - Bicycle ❑
   - Private car ❑
   - Public transport ❑
   - Other *Please specify* _____

(b) If you came by private car, were you given a lift by someone else?
Yes ❑ No ❑

(c) If you came by private car, how much was paid in car park fees? £_____ p_____

(d) If you came by public transport how much did it cost? £_____ p_____
(write down the single fare; if a return fare, halve it)

4. How long did the whole journey take? _____ minutes

5. Did anyone come with you to the hospital
and wait for you while you received your care? Yes ❑ No ❑

If yes, did they take time off work? Yes ❑ No ❑
If more than one person, please specify _____

6. How long did you spend at the hospital today from arrival to departure?
(don't count the time spent filling in this questionnaire) _____ minutes

Some women having more detailed tests may be advised to take time off work

7. Have you been advised to take time off work after today's visit? Yes ? No ?
If yes, how long? _____ minutes

8. What money income, if any, are you losing today by coming to hospital?
None ❑ £_____ p_____

9. If you have children or other dependants
   Have you paid someone to look after them? Yes ❑ No ❑ Not applicable ❑
   If yes, how much has it cost? £_____ p_____
   OR
   Has someone taken time off work to look after them? Yes ❑ No ❑

If you have any comments about your costs for attending the hospital or anything else about this study please write them below.

Thank you for your co-operation and help

To be filled in by staff member before giving out questionnaire

Date: _____

Attended:

Ultrasound Department ❑
Fetal Centre ❑
Obstetric Day Unit ❑
Other ***(please specify)*** _____

Procedure/s attended for: **(please tick)**

❑ **ultrasound scan:**	**dating**	❑	**anomaly**	❑
	repeat dating	❑	**repeat anomaly**	❑
	detailed	❑	**growth**	❑
	placental	❑	**Doppler**	❑
	BPP	❑		
	other	❑	**(please specify)** _____	

❑ **amniocentesis**
❑ **chorionic villus sampling**
❑ **cardiotocograph**
❑ **other** ***(please specify)*** _____

Appendix 13

Combining detection rates from scans done at different times

Detection rates from scans done at different times are combined because the scans are not independent of each other.

Suppose women are scanned in the first trimester; there is a 10% chance of a lethal anomaly being detected. That 10% of women would go on to have further tests. Only the 90% remaining would go on to have a routine anomaly scan with a 76% chance of detecting a lethal anomaly.

Thus, the combined detection rate for both these scans is:

$$0.1 + (0.9 \times 0.76) = 0.784$$

Appendix 14

National Screening Committee's criteria for appraising the viability, effectiveness and appropriateness of a screening programme: with comments in the light of this study

The criteria, which are set out below, are based on the classic criteria first promulgated in a WHO report in 1966 but take into account both the more rigorous standards of evidence required to improve effectiveness and the greater concern about the adverse effects of healthcare; regrettably some people who undergo screening will suffer adverse effects without receiving benefit from the programme.

These criteria have been prepared taking into account international work on the appraisal of screening programmes, particularly that in Canada and the USA. It is recognised that not all of the criteria and questions raised in the format will be applicable to every proposed programme, but the more that are answered will obviously assist the NSC to make better evidence-based decisions.

All of the following criteria should be met before screening for a condition is initiated.

The condition

1. The condition should be an important health problem.

Ultrasound screening during pregnancy does not aim to detect a single health problem. Rather it aims at establishing gestational age to assist subsequent clinical care (if complications occur), detect multiple pregnancies and fetuses with structural malformations. The incidence of one or more major anomalies at birth is about 2% and the responses below concentrate on this issue.

2. The epidemiology and natural history of the condition, including development from latent to declared disease, should be adequately understood and there should be a detectable risk factor, or disease marker and a latent period or early symptomatic stage.

The purpose of screening for fetal anomalies is primarily to allow the woman the option of termination of pregnancy. Occasionally, prenatal diagnosis allows intrauterine therapy or pre-planning of neonatal medical and surgical care.

3. All the cost-effective primary prevention interventions should have been implemented as far as practicable.

There are few proven measures that prevent fetal malformations (e.g. folic acid to prevent neural tube defects). Health promotion information about folic acid is routinely available.

The test

4. There should be a simple, safe, precise and validated screening test.

Ultrasound is an operator-dependent diagnostic technique and accurate detection of anomalies requires experience and expertise. As discussed in this report, studies of safety have been broadly reassuring, but little is known about the safety of newer technologies, for example, transvaginal ultrasound which uses higher frequencies and pulsed Doppler, and continued vigilance is advised. Furthermore, while some anomalies are detected with a high sensitivity (e.g. CNS abnormalities), others are frequently missed (e.g. cardiac and skeletal abnormalities).

5. The distribution of test values in the target population should be known and a suitable cut-off level defined and agreed.

Not applicable.

6. The test should be acceptable to the population.

As discussed in this report, ultrasound is popular with pregnant women – as long as the findings are reassuring.

7. There should be an agreed policy on the further diagnostic investigation of individuals with a positive test result and on the choices available to those individuals.

There is no single appropriate response to this multi-dimensional investigation.

The treatment

8. There should be an effective treatment or intervention for patients identified through early detection, with evidence of early treatment leading to better outcomes than late treatment.

See above.

9. There should be agreed evidence-based policies covering which individuals should be offered treat-ment and the appropriate treatment to be offered.

See above.

10. Clinical management of the condition and patient outcomes should be optimised by all healthcare providers prior to participation in a screening programme.

See above.

The screening programme

11. There must be evidence from high quality RCTs that the screening programme is effective in reducing mortality or morbidity.

Where screening is aimed solely at providing information to allow the person being screened to make an 'informed choice' (e.g. Down's syndrome, cystic fibrosis carrier screening), there must be evidence from high quality trials that the test accurately measures risk. The information that is provided about the test and its outcome must be of value and readily understood by the individual being screened.

Only one randomised trial has shown a reduction in perinatal mortality as a result of ultrasound screening. This Finnish study was the only trial to target detection of anomalies and detect anomalies effectively and take place in a community with high acceptance of termination of pregnancy.

12. There should be evidence that the complete screening programme (test, diagnostic procedures, treatment/ intervention) is clinically, socially and ethically acceptable to health professionals and the public.

See report. Appears acceptable.

13. The benefit from the screening programme should outweigh the physical and psychological harm (caused by the test, diagnostic procedures and treatment).

This is discussed at some length in the report.

14. The opportunity cost of the screening programme (including testing, diagnosis, treatment, administration, training and quality assurance) should be economically balanced in relation to expenditure on medical care as a whole (i.e. value for money).

We have not compared the costs of ultrasound screening and diagnostic sequelae and termination of pregnancy, with the costs of care of surviving children with anomalies, nor have we compared combinations of ultrasound screening with other screening options in antenatal care.

15. There must be a plan for managing and monitoring the screening programme and an agreed set of quality assurance standards.

In the UK, this is patchy to say the least. Where regional fetal abnormality registers exist (e.g. Northern Region, Mersey, West Midlands), there is potential for such monitoring.

16. Adequate staffing and facilities for testing, diagnosis, treatment and programme management should be made available prior to the commencement of the screening programme.

The adequacy of staff and facilities throughout the UK is unknown. This is, in part, the consequence of 'creeping' rather than strategic introduction.

17. All other options for managing the condition should have been considered (e.g. improving treatment, providing other services), to ensure that no more cost-effective intervention could be introduced or current interventions increased within the resources available.

Not applicable.

18. Evidence-based information, explaining the consequences of testing, investigation and treatment, should be made available to potential participants to assist them in making an informed choice.

While we are aware of individual hospitals that supply such material, we know of no way of assessing the national situation.

19. Public pressure for widening the eligibility criteria for reducing the screening interval, and for increasing the sensitivity of the testing process, should be expected. Decisions about these parameters should be scientifically justifiable to the public.

Not applicable.

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