Health Technology Assessment 2004; Vol. 8: No. 33

Psychosocial aspects of genetic screening of pregnant women and newborns: a systematic review

JM Green, J Hewison, HL Bekker,
LD Bryant and HS Cuckle

August 2004

Health Technology Assessment
NHS R&D HTA Programme

How to obtain copies of this and other HTA Programme reports.
An electronic version of this publication, in Adobe Acrobat format, is available for downloading free of charge for personal use from the HTA website (http://www.hta.ac.uk). A fully searchable CD-ROM is also available (see below).

Printed copies of HTA monographs cost £20 each (post and packing free in the UK) to both public **and** private sector purchasers from our Despatch Agents.

Non-UK purchasers will have to pay a small fee for post and packing. For European countries the cost is £2 per monograph and for the rest of the world £3 per monograph.

You can order HTA monographs from our Despatch Agents:

– fax (with **credit card** or **official purchase order**)
– post (with **credit card** or **official purchase order** or **cheque**)
– phone during office hours (**credit card** only).

Additionally the HTA website allows you **either** to pay securely by credit card **or** to print out your order and then post or fax it.

Contact details are as follows:

HTA Despatch
c/o Direct Mail Works Ltd
4 Oakwood Business Centre
Downley, HAVANT PO9 2NP, UK

Email: orders@hta.ac.uk
Tel: 02392 492 000
Fax: 02392 478 555
Fax from outside the UK: +44 2392 478 555

NHS libraries can subscribe free of charge. Public libraries can subscribe at a very reduced cost of £100 for each volume (normally comprising 30–40 titles). The commercial subscription rate is £300 per volume. Please see our website for details. Subscriptions can only be purchased for the current or forthcoming volume.

Payment methods

Paying by cheque
If you pay by cheque, the cheque must be in **pounds sterling**, made payable to *Direct Mail Works Ltd* and drawn on a bank with a UK address.

Paying by credit card
The following cards are accepted by phone, fax, post or via the website ordering pages: Delta, Eurocard, Mastercard, Solo, Switch and Visa. We advise against sending credit card details in a plain email.

Paying by official purchase order
You can post or fax these, but they must be from public bodies (i.e. NHS or universities) within the UK. We cannot at present accept purchase orders from commercial companies or from outside the UK.

How do I get a copy of *HTA on CD*?

Please use the form on the HTA website (www.hta.ac.uk/htacd.htm). Or contact Direct Mail Works (see contact details above) by email, post, fax or phone. *HTA on CD* is currently free of charge worldwide.

The website also provides information about the HTA Programme and lists the membership of the various committees.

Psychosocial aspects of genetic screening of pregnant women and newborns: a systematic review

JM Green,[1*] J Hewison,[2] HL Bekker,[2] LD Bryant[2] and HS Cuckle[3]

[1] Mother and Infant Research Unit, University of Leeds, UK
[2] Academic Unit of Psychiatry and Behavioural Sciences, University of Leeds, UK
[3] Leeds Screening Centre, University of Leeds, UK

* Corresponding author

Declared competing interests of authors: none

Published August 2004

This report should be referenced as follows:

Green JM, Hewison J, Bekker HL, Bryant LD, Cuckle HS. Psychosocial aspects of genetic screening of pregnant women and newborns: a systematic review. *Health Technol Assess* 2004;**8**(33).

Health Technology Assessment is indexed in *Index Medicus*/MEDLINE and *Excerpta Medica*/EMBASE.

NHS R&D HTA Programme

The research findings from the NHS R&D Health Technology Assessment (HTA) Programme directly influence key decision-making bodies such as the National Institute for Clinical Excellence (NICE) and the National Screening Committee (NSC) who rely on HTA outputs to help raise standards of care. HTA findings also help to improve the quality of the service in the NHS indirectly in that they form a key component of the 'National Knowledge Service' that is being developed to improve the evidence of clinical practice throughout the NHS.

The HTA Programme was set up in 1993. Its role is to ensure that high-quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined to include all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care, rather than settings of care.

The HTA programme commissions research only on topics where it has identified key gaps in the evidence needed by the NHS. Suggestions for topics are actively sought from people working in the NHS, the public, consumer groups and professional bodies such as Royal Colleges and NHS Trusts.

Research suggestions are carefully considered by panels of independent experts (including consumers) whose advice results in a ranked list of recommended research priorities. The HTA Programme then commissions the research team best suited to undertake the work, in the manner most appropriate to find the relevant answers. Some projects may take only months, others need several years to answer the research questions adequately. They may involve synthesising existing evidence or designing a trial to produce new evidence where none currently exists.

Additionally, through its Technology Assessment Report (TAR) call-off contract, the HTA Programme is able to commission bespoke reports, principally for NICE, but also for other policy customers, such as a National Clinical Director. TARs bring together evidence on key aspects of the use of specific technologies and usually have to be completed within a limited time period.

Criteria for inclusion in the HTA monograph series
Reports are published in the HTA monograph series if (1) they have resulted from work commissioned for the HTA Programme, and (2) they are of a sufficiently high scientific quality as assessed by the referees and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

The research reported in this monograph was commissioned by the HTA Programme as project number 93/56/99. As funder, by devising a commissioning brief, the HTA Programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

The views expressed in this publication are those of the authors and not necessarily those of the HTA Programme or the Department of Health.

ISSN 1366-5278

Published by Gray Publishing, Tunbridge Wells, Kent, on behalf of NCCHTA.
Printed on acid-free paper in the UK by St Edmundsbury Press Ltd, Bury St Edmunds, Suffolk.

Abstract

Psychosocial aspects of genetic screening of pregnant women and newborns: a systematic review

JM Green,[1*] J Hewison,[2] HL Bekker,[2] LD Bryant[2] and HS Cuckle[3]

[1] Mother and Infant Research Unit, University of Leeds, UK

[2] Academic Unit of Psychiatry and Behavioural Sciences, University of Leeds, UK

[3] Leeds Screening Centre, University of Leeds, UK

* Corresponding author

Objectives: To address five broad questions concerned with knowledge, anxiety, factors associated with participation/non-participation in screening programmes and the long-term sequelae of false-positive, true-positive in newborns and true-negative results.

Data sources: Five electronic databases, two journals and attempts were made to locate unpublished work.

Review methods: This review started from a substantial literature base that provided the basis for (a) scoping the literature, (b) informing search strategy terms and (c) identifying preliminary article inclusion and exclusion criteria. The main eligibility criteria were: any screening programme aimed at pregnant women or newborn babies that included a 'genetic' target condition, this included chromosomal anomalies; any study that reported psychosocial data collected directly from parents. The data extraction form developed for this study elicited data from the selected studies. The data were entered into a database, which provided a summary of the included papers.

Results: A total of 288 candidate publications were identified, 106 of which were eligible: 78 were concerned with antenatal screening and 28 with newborn screening. It was found that levels of knowledge adequate for decision-making were not being achieved despite information leaflets and videos having some effect. Studies that have succeeded in increasing knowledge have not observed a corresponding increase in anxiety, although some anxiety might be an appropriate response and may aid coping and decision-making. Anxiety is clearly raised in women receiving positive screening results, especially young women. However, evidence is lacking of a beneficial (i.e. reassuring) effect of receiving a screen-negative result. Anxiety in screen-positive women falls on receipt of subsequent reassuring results, but some residual anxiety may remain. A minority (perhaps up to 30%) of women receiving a screen-positive result in pregnancy expressed regret about their screening decision. Uptake of neonatal screening has been treated as a 'given' and not as a research topic.

Conclusions: The results of this review have many implications for the work of the National Screening Committee. The most pressing of these, in order of priority, relate to: the inadequacy of current procedures for achieving informed consent; the cost of providing a satisfactory service; the unmet needs of 'false-positives', and the unmet needs of women's partners, particularly in carrier screening. It is suggested that research is conducted on the above four topics in order to fill gaps in the evidence base that relate to screening technologies which have been available for many years. In addition, future screening programmes will create a new list of research questions, based on the same main agenda but applied to new areas, for example, new conditions such as haemoglobinopathies and fragile X syndrome; new client groups such as young women and minority ethnic groups; and new testing modalities such as ultrasound.

Contents

List of abbreviations

AFP	α-fetoprotein
ATD	α_1 antitrypsin deficiency
CF	cystic fibrosis
CVS	chorionic villus sampling
DMD	Duchenne muscular dystrophy
GHQ	General Health Questionnaire
HCG	human chorionic gonadotrophin
IRT	immunoreactive trypsinogen
MDCS	multi-dimensional classificatory system
MSAFP	maternal serum α-fetoprotein
NSC	National Screening Committee
NTD	neural tube defect
PKU	phenylketonuria
RCT	randomised controlled trial
STAI	State-Trait Anxiety Inventory

All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices in which case the abbreviation is defined in the figure legend or at the end of the table.

Executive summary

Background

More genetic screening takes place during pregnancy and the newborn period than at any other time. These are key points in the life course where people are accessible to the health services. However, these are also periods when parents are at their most vulnerable. With developments in technology, such tests are multiplying. It is therefore considered important to understand the psychosocial aspects of screening in order that screening programmes can be designed in ways which minimise harm. Our plan of investigation had two guiding principles:

- Screening programmes need to be considered according to how they are likely to be experienced by the recipients, rather than from the perspective of the service provider.
- The ultimate aim of the review is to learn lessons from psychosocial aspects of past screening programmes which can be used to inform genetic screening in the future. This does not preclude learning from the examples of non-genetic screening programmes, particularly where the evidence suggests that the genetic/non-genetic distinction is not highly salient from the recipients' point of view.

Objectives

The review aimed to address five broad questions concerned with knowledge, anxiety, other emotional aspects of screening, factors associated with participation/non-participation in screening programmes and the long-term sequelae of false-positive, false-negative, true-positive and true-negative results.

Three revisions were made. The literature on other emotional aspects of screening and on false-negatives was too fragmented for useful conclusions to be drawn, and discussion of true-positives is confined to newborn screening, for the same reason.

Methods

This review started from a substantial literature base that provided the basis for (a) scoping the literature, (b) informing search strategy terms and (c) identifying preliminary article inclusion and exclusion criteria. The main eligibility criteria were:

- Any screening programme aimed at pregnant women or newborn babies that included a 'genetic' target condition. 'Genetic' includes chromosomal anomalies.
- Any study that reported psychosocial data collected directly from parents.

There were no geographical or methodological limits except that studies asking only hypothetical questions and case reviews/single experiences were excluded.

Five electronic databases were searched, two journals were hand-searched and attempts were made to locate unpublished work. The data elicited from articles using the data extraction form developed for this study were entered into an SPSS database (version 10.1).

Results

A total of 288 candidate publications were identified, 106 of which were eligible: 78 concerned with antenatal screening and 28 with newborn screening. The main findings were as follows.

Knowledge

- Levels of knowledge adequate for decision-making are not being achieved.
- Information leaflets and videos have some effect but large gaps in knowledge usually remain.
- Procedural aspects of testing are better understood than material related to the meaning of risk calculations.
- Substantial social and cultural inequalities exist in knowledge about testing.
- The above findings almost certainly underestimate the extent of the problem, because only limited aspects of knowledge have been studied to date.

In addition
- Knowledge is not the same as understanding.
- Public understanding of the basic concepts associated with screening is poor.
- Knowledge that is only superficially acquired may not be retained.
- Informed consent for neonatal screening has been little studied.

Anxiety
- Studies that have succeeded in increasing knowledge have not observed a corresponding increase in anxiety.
- Anxiety is clearly raised in women receiving positive screening results but evidence is lacking of a beneficial (i.e. reassuring) effect of receiving a screen-negative result.
- Anxiety in screen-positive women falls on receipt of subsequent reassuring results but some residual anxiety may remain.
- The way in which carrier screening is offered may affect anxiety in screen-negative women.

In addition
- Knowledge that improves decision-making may not be the same as that which reduces anxiety.
- Some anxiety might be an appropriate response and might aid coping and decision-making.
- Young women may be more vulnerable to anxiety arising from positive screening test results.
- Knowledge and anxiety in men whose partners are undergoing screening have been little studied.

Attitudes and test uptake
- Most women hold positive attitudes towards prenatal screening.
- Women having screening tend to hold more negative attitudes to abnormality, to perceive their likelihood of having an affected child (or themselves being a carrier) as greater, to perceive the risks of subsequent procedures as lower, to perceive others as thinking they should have the test and are more likely to intend to have a termination if an abnormality is detected.
- Women who were more satisfied with their choices were also more falsely reassured, and made their choices less systematically, than women with lower satisfaction scores.
- A minority (perhaps up to 30%) of women receiving a screen-positive result in pregnancy expressed regret about their screening decision.
- Uptake of neonatal screening has been treated as a 'given' and not a research topic.

Policy implications and recommendations for future research

The results of the review have many implications for the work of the National Screening Committee. The most pressing of these, in order of priority, relate to:

- the inadequacy of current procedures for achieving informed consent
- the cost of providing a satisfactory service
- the unmet needs of 'false-positives'
- the unmet needs of women's partners, particularly in carrier screening.

We suggest that research is conducted on the above four topics in order to fill gaps in the evidence base that relate to screening technologies which have been available for many years. In addition, future screening programmes will create a new list of research questions, based on the same main agenda but applied to new areas, for example, to

- new conditions such as haemoglobinopathies and fragile X syndrome
- new client groups such as young women and minority ethnic groups
- new testing modalities such as ultrasound.

Research is needed which incorporates these topics into the mainstream of work, including that on informed consent, on the resource requirements of providing a satisfactory service, on people with false-positive results and on partners.

Chapter 1
Background

Definition of terms

Genetic

Discussions about genetic screening are confounded by ambiguous terminology. Both 'genetic' and 'screening' are words that can be used in somewhat different ways. In this report we take a **genetic disorder** to mean one that is attributable to a single-gene defect or a chromosomal anomaly. We will consider any screening test that is directed at such disorders (including heterozygote detection), whether or not the test itself is based on direct examination of genetic material.

Screening

Screening is a systematic attempt to identify, from apparently healthy individuals, those at high enough risk of a specific disease to warrant further action. Those in the high-risk group are offered interventions which are either too expensive or hazardous to be provided without such prior selection. A small number of screening tests are, in effect, diagnostic, but in most cases the screening test is only a marker for the disorder, that is, something frequently associated with it but which is not in itself a sign that anything is wrong. This means that, unlike diagnostic tests, most screening tests generate large numbers of false-positive results, that is, people are selected as high risk but do not have the disorder. There are also likely to be false-negatives, that is, people who have the disorder who have not been selected by the screen. Cut-offs are usually chosen to try and minimise the number of false-negatives. This has the effect of increasing the number of false-positives.

An essential characteristic of screening is that it is applied to a group of people who are not known to be more likely than anyone else to have the disorder being screened for. Genetic testing of individuals with a known family history of a particular disorder does not meet that definition of screening and is therefore not within the scope of this review.

Psychosocial aspects

The title of the commissioning brief referred to the 'psychosocial **impact** of screening'. However, we considered that this precluded consideration of antecedents such as people's reasons for accepting or declining screening. We have therefore chosen the word 'aspects' as being the most inclusive in order to provide the fullest possible picture of the psychosocial context of screening during pregnancy and the newborn period.

Antenatal screening

Maternal serum α-fetoprotein (MSAFP) screening for neural tube defects (NTDs) has been in common use in the UK since the late 1970s. The test is carried out at about 16 weeks. A woman with a high-risk result will be referred for diagnostic testing. This generally involves an invasive diagnostic procedure such as amniocentesis or chorionic villus sampling, which has a fetal loss rate of about 1%. If an abnormality is diagnosed, termination of pregnancy will be offered.

NTDs are not generally genetic in origin and therefore studies associated with these early programmes are not included. They have been reviewed elsewhere.[1–3] In the late 1980s and early 1990s, the same test started to be used to screen for chromosomal disorders, of which the most common is Down's syndrome. Since then it has been refined in various ways to improve its efficacy as a screen for Down's syndrome (e.g. the 'triple' test). We have included studies from the earlier period if the paper mentions that the test can be used to screen for Down's syndrome and also for neural tube defects. Before this, the only way to identify a woman with an above-average risk of having a baby with Down's syndrome was on the basis of her age, since risk increases with maternal age. Although, therefore, asking a woman her age is arguably a screening test, we have not considered it as such for the purposes of this review. An earlier Health Technology Assessment (HTA) report[4] covered technical aspects of antenatal screening for Down's syndrome, and also included a chapter on psychosocial aspects.

Ultrasound anomaly screening at 18–20 weeks is also now commonplace, but is focused on structural, rather than genetic, anomalies and was not considered to be within the remit of this review. The relevant literature has recently been reported in another HTA report.[5] Early ultrasound measurement of nuchal translucency[6] is used specifically to screen for chromosomal disorders, and was considered to be within the remit of this review.

Serious disorders caused by genetic mutations are much rarer than those with a chromosomal aetiology. Cystic fibrosis (CF) is the most common single gene disorder in Caucasian populations, with a prevalence in the UK of 0.4 per 1000 births. CF is inherited as a simple Mendelian autosomal recessive condition with a carrier frequency of 1 in 24. Thus one in 600 couples are both carriers and have a one in four chance of CF in every pregnancy. There are other common recessive conditions which in the UK occur primarily in ethnic minority populations (e.g. haemoglobinopathies and Tay–Sachs disease). Carrier testing for these recessively inherited conditions is within the scope of this review if carried out during pregnancy.

Newborn screening

Phenylketonuria (PKU) is a recessive genetic condition and one of the most common inherited metabolic disorders, with a birth prevalence of 1 in 15,000. Without treatment, PKU leads to permanent and severe learning difficulties. Clinical diagnosis can only be made after irreparable brain damage has occurred. Dietary restriction and supplementation are highly successful in preventing neurological disease, provided that treatment is started within the first weeks of life. Since there are no clinical diagnostic features in early infancy, this can only be achieved by newborn screening. The arguments in favour of a screening programme are therefore very strong.

The process of heelprick bloodspot testing of neonates for PKU was initiated in the mid-1960s by an American paediatrician Robert Guthrie. 'Guthrie testing' quickly became routine in developed countries. Nowadays the same blood sample (several drops of dried blood on a card) is often used to test for other disorders, most commonly congenital hypothyroidism, which has been routine in the UK since the late 1970s. Newborn screening programmes for a number of other conditions, including CF, have also been initiated in a number of countries (see Chapter 9). Any study concerned with Guthrie testing was considered to be within the remit of this review, whatever the disease focus (see below).

Why this review?

More genetic screening takes place during pregnancy and the newborn period than at any other time. These are key points in the life course where people are accessible to the health services, and this makes them attractive to public health planners because coverage will be high. In addition, most prenatal testing is directed either at assessing the health of the fetus or of the mother as a carrier of the fetus and therefore has by definition to take place during pregnancy. However, these are also periods when mothers are at their most vulnerable. Although compliance is likely to be high, because women want to do their best for their babies,[7] the emotions raised, especially by abnormal test results, have potentially far-reaching consequences. With developments in technology, such tests are multiplying. It is therefore considered important to understand the psychosocial aspects of screening in order that screening programmes can be designed in ways which minimise harm.

Earlier reviews

Psychosocial aspects of prenatal testing

The literature on psychosocial aspects of prenatal testing in general (i.e. not restricted to genetic screening) has been reviewed on a number of occasions.[1–3] These were not systematic reviews. Most of the studies covered, particularly in the earlier reviews, were concerned with women's experiences of α-fetoprotein (AFP) screening for neural tube defects, which do not meet the definition of 'genetic'. These reviews indicated that the major hazard of screening tests is the high level of anxiety associated with false-positive results. This was first reported by Farrant[8] and Fearn and co-workers[9] and has been confirmed in most subsequent studies.[10–12] Fearn and co-workers[9] found that the anxiety persisted even when women were told that there was not a problem after all. The most severe levels of anxiety were found in women who, having gone on to have amniocentesis, were not told the results. They were just told to assume that all was well if they did not hear to the contrary. A survey of 357 consultant obstetricians in England and Wales in 1993[13] showed that only 2% of obstetricians still followed such a policy.

There has been less research looking at the effect of screening on women whose result is normal. Early large-scale studies comparing anxiety in screened and unscreened women in Sweden[14,15] and the USA[16] concluded that any differences between screened and unscreened women were minor, favoured the screened women and did not suggest long-term harm resulting from participation in the screening programme. Two large British studies[17,18] also concluded that serum screening for neural tube defects was not causing

higher anxiety, but was being accepted by those who were more anxious initially.

Anxiety has been the main focus of earlier reviews, but there are many other psychosocial aspects of screening that have had a less high profile, such as the characteristics of those accepting and declining testing, longer term effects and other cognitions.

As far as we are aware, psychosocial aspects of newborn testing have not previously been the focus of a systematic review.

Related HTA reports

A report on antenatal ultrasound has recently been published[5] which includes a comprehensive section on psychosocial aspects. Other reports with points of overlap cover screening for fragile X syndrome,[19] newborn screening for inborn errors of metabolism,[20,21] antenatal screening for Down's syndrome,[4] informed decision-making,[22] screening for CF,[23] haemoglobinopathy screening[24,25] and false-negative results in screening programmes.[26]

Philosophy of this review

We believe that a review concerned with psychosocial aspects needs to work from the perspective of the test recipient, and that such a perspective is more concerned with the testing context than with the disease being sought. We know, for example, that pregnant women frequently do not know which tests they have had, or what disorders they may or may not detect.[27] Furthermore, in a number of situations a test may be capable of detecting more than one disorder: a pregnant woman may have a test to detect Down's syndrome and instead be told that her child has an extra Y chromosome. We therefore did not consider it appropriate that the boundaries of the review should be disease-based. Recipients are more likely to identify 'the test' as the procedure, such as 'the heelprick (Guthrie) test'. We therefore chose to include all studies that looked at participants in general screening programmes such as 'Guthrie testing' even when the study focused on a non-genetic disorder such as congenital hypothyroidism.

Chapter 2

Research questions and methods

Overview

Our plan of investigation had two guiding principles:

- Screening programmes need to be considered according to how they are likely to be experienced by the recipients, rather than from the perspective of the service provider.
- The ultimate aim of the review is to learn lessons from psychosocial aspects of past screening programmes which can be used to inform genetic screening in the future. This does not preclude learning from the examples of non-genetic screening programmes, particularly where the evidence suggests that the genetic/non-genetic distinction is not highly salient from the recipients' point of view.

One of the implications of these principles is that the range of literature to be covered may sometimes go beyond the boundaries of 'genetic'. For example, the blood sample obtained from the Guthrie ('heelprick') test that is carried out on all newborns in the UK is used to test for a variety of disorders, both genetic (PKU) and non-genetic (hypothyroidism). Few mothers know which disorders are tested for.[28] Hence our review needed to consider mothers' experience of this screening as an entity – it is not always possible to separate out aspects that are related only to the genetic part of the test.

Scoping the literature

This review was fortunate to start from a substantial literature base. One author (JMG) had carried out earlier reviews in the field[1–3] and JMG and JH had supervised four recent PhDs[29–32] whose bibliographies were available to us. Furthermore, three of us (HLB, HSC, JH) had co-authored earlier HTA reports on related topics.[19,22,23] These resources, plus the reference lists of three additional key review articles,[5,33,34] provided the basis for (a) scoping the literature, (b) informing search strategy terms and (c) identifying preliminary article inclusion and exclusion criteria.

Research questions

From the scoping exercise, it was clear that no single primary outcome was appropriate to focus the review area. Knowledge and anxiety were known to have been two major focuses but we wished to be open to other psychosocial aspects which may have been assessed such as understanding, decision-making, attachment, attitudes and beliefs. In consequence, the following questions were used to guide the focus of the review and the subsequent development of the data extraction form:

1. How well informed are screening programme participants and what factors are associated with different levels of knowledge/understanding?
2. What are the aspects of screening programmes that are associated with high/low levels of anxiety?
3. What do we know about other emotional aspects of screening, such as fetal attachment?
4. What factors are associated with participation/non-participation in screening programmes?
5. What do we know about the long-term sequelae of false-positive results, false-negative results, true-positive results and true-negative results?

Inclusion/exclusion principles

In order to address these questions, it was clear that the search strategy needed to be very broad in some respects, but with clear criteria to reduce the initial list to manageable numbers in order to carry out the detailed analysis that was going to be required. Accordingly, we adopted the following criteria to inform the search terms.

Methodologies

Studies in this area have used a range of methods. We knew that much of the literature of relevance to this review would be descriptive, both quantitative and qualitative. Restriction of the review to randomised controlled trials (RCTs), or even to quantitative outcomes, would be unrealistic and probably uninformative. Increasingly, reviews are moving away from their focus on RCTs to encompass a wider range of

evidence. The standard Centre for Reviews and Dissemination (CRD) guidelines are not always applicable under these circumstances. The recent HTA report on reviewing qualitative studies[35] was of benefit to us here.

Types of screening programme

Any genetic screening programme aimed at pregnant women or newborn babies. This included programmes based on the Guthrie test, even though these encompass both non-genetic and genetic disorders. In pregnancy, it included heterozygote testing for CF and haemoglobinopathies, and also both serum screening and ultrasound as part of a screening programme for Down's syndrome and other chromosomal abnormalities. It excluded generalised anomaly scanning and other screening programmes for non-genetic disorders such as NTDs. However, such screening programmes were included if they also referred to screening for chromosomal disorders (see Chapter 1).

Types of participant

Pregnant women and their partners or parents of newborn babies who are candidates for the screening programmes defined, including non-participants where data were available. Where a study included a comparison group of women to whom screening was not available, these were also included in the review.

Types of study

Any study which reported data collected directly from parents on the specified psychosocial aspects of genetic screening and which met other inclusion criteria. This included both comparative and descriptive studies.

Geographical limits

No geographical limits were set on the review since it was felt that information from screening programmes in a wide range of settings was desirable. For example, screening for thalassaemia in Cyprus, where carrier frequency is 1 in 10 and the care of affected children had become a major strain on the country's health budget, provides a very different scenario from that of most other countries. Far from making this irrelevant to UK practice, it provides the opportunity to look at the wider context through which we hoped to avoid the trap of generalising from the parochial. The majority of the literature of relevance to this review has, in fact, been published in English, or at least with English language abstracts which allowed initial screening.

Search methods

Electronic search strategy

A search strategy was devised by an experienced systematic reviewer (JM) who had been the first author of two previous HTA reports,[19,23] with additional input from information management experts at the University of Leeds. From the *a priori* reference lists, the following search terms were used (see Appendix 1 for search strategy applied to MEDLINE): tests used during pregnancy and the newborn period; measures of psychosocial variables such as knowledge, uptake, anxiety, beliefs and adjustment; specific disease or illnesses such as Down's syndrome, sickle-cell, cystic fibrosis, thalassaemia. The search strategy was applied first to the medically based electronic databases MEDLINE and CINAHL. When applied to the years 1966–2000, the total number of hits was 1005 and 57, respectively (see Appendix 1). The search strategy was then applied to the electronic databases PsycLIT, PUBMED and BIDS(UK).

The search terms were designed to be equally applicable to qualitative and quantitative studies. However, because qualitative research is often poorly indexed, there is a greater risk that a qualitative study could have been missed.

Grey literature

The pre-existing resources contained some unpublished work. Authors were contacted to obtain up-to-date references. Overseas researchers in the field were also contacted with requests for any unpublished work. We attended the 2000 EMPAG conference (European Meeting on Psychosocial Aspects of Genetics) and made a brief oral presentation about the review, specifically asking for unpublished information. Every delegate was given a flyer repeating this information and containing our contact details. No unpublished work was brought to our attention through either of these routes.

Handsearching

Two journals were handsearched from 1985 to 2000: *Prenatal Diagnosis* and *Journal of Reproductive and Infant Psychology*. *Prenatal Diagnosis* was chosen because of its centrality to the subject area. *Journal of Reproductive and Infant Psychology* was chosen because it was a likely source of papers with a psychosocial slant which was known not be listed on MEDLINE. Neither search revealed any additional papers. Given this, and pressures of time, we limited handsearching to these two journals only.

Exclusions

Publications that met any of the following criteria were excluded from the review:

- Studies concerned with only prenatal **diagnostic** testing and not screening.
- Review articles and other papers presenting only secondary data.
- Studies concerned only with health professionals rather than parents.
- Studies not assessing psychosocial aspects of screening.
- Studies not collecting data directly from parents, such as audits of medical records.
- Studies asking only hypothetical questions.
- Articles describing a case review and/or single experience.

Procedures

The electronic search was run in June 2000 and repeated in August 2001. Potential papers identified from the *a priori* resources and the searches were entered into a PROCITE database (version 5). Inclusion/exclusion criteria were applied to the abstracts of all these articles and subsequent exclusion/inclusion decisions were recorded on the PROCITE database. Full articles of all abstracts that met the inclusion criteria were retrieved; the articles of abstracts in which the information was vague and/or incomplete were also retrieved. All decisions to exclude articles were made by AW and checked with either CB, JMG, JH or HLB. Any disagreements in decisions made on the basis of the abstract information resulted in the full article being retrieved. The retrieved articles were divided between reviewers (CB, JMG, JH, HLB, LDB) and a data extraction form (see below) applied to each. The form was completed in full for all articles that met the inclusion criteria. Data were entered by AW, who also checked the decisions made by reviewers.

Materials: data extraction form

The data extraction form was developed over a 5-month period. The pilot form was informed by the review's research questions and the structure of extraction forms developed for similar types of HTA reports.[5,22,23,26,34] The form was piloted using a range of articles selected to cover the full and diverse range of research methodologies used in studies in this area, identified in the scoping exercise. The final form (Appendix 2) extracted the following information:

- Article details: review identification number; authors; journal specifics; authors with a psychosocial background; study location and year.
- Screening test characteristics: condition screened for; type of test; ante-/neonatal; participants; test outcome.
- Methods: theoretical framework; design; method of data collection; sample selection; sample size; eligibility criteria; variables measured; description of intervention, if any.
- Measures: any assessment of psychosocial factors such as knowledge, reasons, attitudes, beliefs, adjustment and anxiety.
- Results: description of findings for each outcome; description of theme generated if appropriate; statistic quoted if appropriate; effect (or not) noted.
- Quality I: description of reviewers' concern about methods; description of concern about analyses and results.
- Quality II: a score based on judgements of study quality in terms of validity, confounds, consistency of results with aims and interpretation and, for studies with quantitative data, sample size, selection and representation. This quality score was developed and piloted in the context of breast cancer follow-up treatment research.[36]

Data management and analysis

The data elicited from articles using the data extraction form were entered into an SPSS database (version 10.1). This allowed for basic descriptive analyses, frequencies and cross-tabulations, to provide summary data of the papers included in the review. Use of SPSS also kept open the option of meta-analysis if articles with sufficient homogeneity in the type and timing of measures were identified. The expectation was that data would be too heterogeneous and that integration of data would therefore be verbal rather than statistical and structured around the review research questions. This was in fact the case.

Chapter 3

Results of the search

Ineligible studies

A total of 288 candidate publications were identified and entered on to the PROCITE database. Of these 55 were clearly not eligible and a further 35 were excluded on the basis of the abstract alone. Hard copies of the remaining 192 were obtained. A further 86 were then excluded (in three cases because they were duplicates, therefore 83 ineligible), leaving 106 publications for inclusion. This process is shown in *Figure 1* and the reasons for exclusion are given in *Table 1*. Some studies were ineligible for more than one reason; the table shows only the first reason.

TABLE 1 *Reasons for exclusion*

Only concerned with screening for NTDs	29
No relevant psychosocial data from parents	20
No primary data	14
Only concerned with diagnostic tests	13
Data re health professionals only	11
Not pregnant women or parents of neonates	8
Policy/discussion paper or review	7
Only concerned with routine ultrasound	5
Hypothetical scenarios	4
High-risk group, not general population	3
No data re screening	3
Only concerned with other non-genetic condition	1
Duplicates	*3*
Total	121

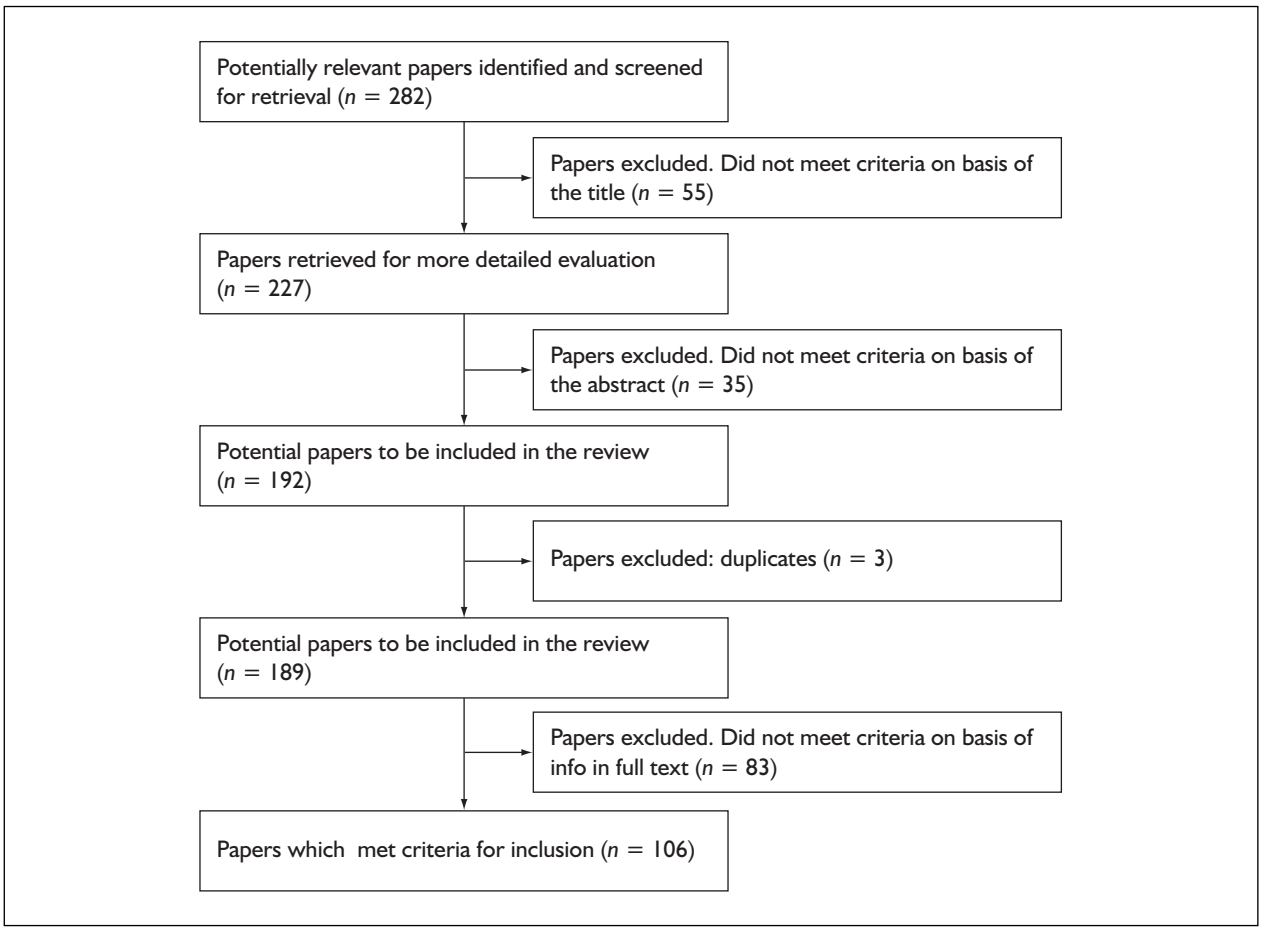

FIGURE 1 *Exclusion of papers identified by the search*

TABLE 2 *Condition that is the focus of the study*

	Antenatal studies	Neonatal studies	All
Chromosomal disorders			
Neural tube defects + Down's syndrome	27		27
Down's syndrome	27		27
Recessively inherited single gene defects			
Cystic fibrosis	19	8	27
Haemoglobinopathies	4	2	6
Tay–Sachs	1		1
Other			
Hypothyroidism		5	5
α_1 antitrypsin deficiency		4	4
phenylketonuria (and others)		3	3
Duchenne muscular dystrophy		3	3
Familial hypercholesterolaemia		1	1
Type 1 diabetes		1	1
Multiple rare genetic disorders		1	1
Total	78	28	106

TABLE 3 *Country of study*

	Antenatal studies	Neonatal studies	All
UK	34	5	39
USA	23	11	34
Sweden	0	8	8
Finland	6	0	6
Denmark	4	0	4
Canada	3	1	4
The Netherlands	3	1	4
Australia	1	2	3
Italy	1	0	1
Germany	1	0	1
France	1	0	1
Taiwan	1	0	1
Total	78	28	106

Characteristics of eligible studies

The 106 eligible publications are listed in Appendix 3. Seventy-eight concerned antenatal screening and 28 the screening of newborns (neonatal). There were no papers which covered both. Although 106 eligible publications were identified, some are multiple papers from a single study. The 28 neonatal papers represent approximately 22 separate studies; authors do not always make it clear when there is an overlap of samples with previously published results (see Appendix 4).

Conditions screened for

As *Table 2* shows, 54 antenatal publications were concerned with screening for Down's syndrome and other chromosomal abnormalities; half of these were in the context of AFP screening programmes targeted at NTDs. Twenty-four antenatal and 10 neonatal studies were concerned with recessively inherited single gene defects, principally CF. The remaining 18 neonatal studies covered a range of disorders which are described in Chapter 9.

Geographical location

As *Table 3* shows, the majority of studies identified were carried out in the UK and the USA, and nearly all others in Northern Europe. All were published in English. The search strategy did locate some non-English papers but they were either ineligible or repeated data already identified in an English language publication by the same authors.

TABLE 4 *Study design in 106 eligible studies*

	Antenatal studies	Neonatal studies	All
RCT	10 (12.8%)	4 (14.3%)	14 (13.2%)
Comparative (cohort, case–control)	16 (20.5%)	10 (35.7%)	26 (24.5%)
Survey (descriptive)	48 (61.5%)	14 (50.0%)	62 (58.5%)
Before and after	4 (5.1%)	0	4 (3.8%)
Total	78	28	106

TABLE 5 *Type of data collected in 106 eligible studies*

	Antenatal studies	Neonatal studies	All
Quantitative	45 (57.7%)	11 (39.3%)	56 (52.8%)
Qualitative	15 (19.2%)	4 (14.3%)	19 (17.9%)
Both	18 (23.1%)	13 (46.4%)	31 (29.2%)
Total	78	28	106

TABLE 6 *Method of data collection in 106 eligible studies*

	Antenatal studies	Neonatal studies	All
Questionnaire	42 (53.8%)	8 (28.6%)	50 (47.2%)
Interview	12 (15.4%)	13 (46.4%)	25 (23.6%)
Questionnaire and records	9 (11.5%)	0	9 (8.5%)
Questionnaire and interview	11 (14.1%)	3 (10.7%)	14 (13.2%)
Interview and records	3 (3.8%)	3 (10.7%)	6 (5.7%)
Questionnaire, interview and records	1 (1.3%)	1 (3.6%)	2 (1.9%)
Total	78	28	106

Design

As *Table 4* shows, less than half of the eligible studies were comparative in design. Only 14 studies (13.2%) were RCTs.

Type and method of data collection

Over half of the studies collected only quantitative data, 17.9% collected only qualitative data and 29.2% collected both quantitative and qualitative. Collecting both types of data was more common among the neonatal studies (*Table 5*). Most studies used questionnaires to collect data, either alone or supplemented by other methods (*Table 6*). Nearly one-quarter of the studies used interviews only, and this was also more common among the neonatal studies.

Timing of data collection

In order to answer the questions to be addressed by this review, data need to have been collected from participants at different stages of the process: before testing; after testing decision but before test result; and after test results are known. *Table 7* shows the timing of data collection in the eligible studies. Nearly all the neonatal studies are focused on the postresults phase. The antenatal studies are more varied, although the majority are also postresults. However, nearly one-quarter of the antenatal studies (20/78) collected data at more than one time point, five within the framework of an RCT.

Status of participants

Given the questions to be addressed by this review, eligible studies could involve both tested and untested individuals. Some questions can only be addressed when both are included. *Table 8* shows that the majority of studies (83.0%) involved only people who were tested. Only 17 studies (16.0%) included both people who were tested and those who were not. Only one of these studies concerned neonatal testing.

A number of studies were focused on people with a particular test result, most commonly, as *Table 9* shows, true-positives and false-positives. The focus on true positives was particularly strong in the neonatal studies. The table omits the 24 antenatal carrier screening studies, because of the ambiguities of this nomenclature in that context.

TABLE 7 *Timing[a] of data collection in 106 eligible studies*

	Antenatal studies	Neonatal studies	All
Before testing	15 (19.2%)	2 (7.1%)	17 (16.0%)
AT	3 (3.8%)	0	3 (2.8%)
After test results	40 (51.3%)	23 (82.1%)	63 (59.4%)
BT + AT + ATR	3 (3.8%)	0	3 (2.8%)
BT + AT	1 (1.3%)	0	1 (0.9%)
BT + ATR	13 (16.7%)	0	13 (12.3%)
AT + ATR	3 (3.8%)	3 (10.7%)	6 (5.7%)
Total	78	28	106

AT, after testing decision but before test result; ATR, after test result; BT, before testing.
[a] 'Timing' refers to the number of data collection points, but not all variables were necessarily measured on each occasion.

TABLE 8 *Inclusion of untested individuals in 106 eligible studies*

	Antenatal studies	Neonatal studies	All
Tested[a]	61 (78.2%)	27 (96.4%)	88 (83.0%)
Not tested	1 (1.3%)	0	1 (0.9%)
Both	16 (20.5%)	1 (3.6%)	17 (16.0%)
Total	78	28	106

[a] Includes the 17 studies that collected data only before testing.

TABLE 9 *Test results defining groups of interest in 82[a] eligible studies*

	Antenatal studies	Neonatal studies	All
NA[b]	29 (53.7%)	3 (10.7%)	32 (39.0%)
False-positives	11 (20.4%)	7 (25.0%)	18 (22.0%)
False-negatives	1 (1.9%)	0	1 (1.2%)
True-positives	0	13 (46.4%)	13 (15.9%)
True-negatives	2 (3.7%)	0	2 (2.4%)
False-positives and true-negatives	4 (7.4%)	0	4 (4.9%)
False-positives and true-positives	4 (7.4%)	1 (3.6%)	5 (6.1%)
True-positives and true-negatives	0	3 (10.7%)	3 (3.7%)
True-negatives, false-positives and true-positives	1 (1.9%)	1 (3.6%)	2 (2.4%)
False-positives, false-negatives and true-negatives	2 (3.7%)		2 (2.4%)
Total	54	28	82

[a] The 24 antenatal carrier screening studies have been omitted from this table. See text for explanation.
[b] NA = studies that did not define participants on the basis of test results, including those that only collected data before testing.

For example, 'true-positive' could mean a woman identified as a carrier, a carrier couple or an affected baby. Nine of these 24 studies did define groups of interest on the basis of test results and all nine included women who had been identified as carriers. Six included comparison with women who had tested negative.

Size of study

The size of the studies identified varied considerably (range 10–6442 participants for antenatal studies and 9–1387 for neonatal studies). In keeping with the differences already identified in the methodology and focus of studies, antenatal studies tended to be larger (mean 888 participants) than neonatal studies (mean 196 participants). A total of 26% of antenatal studies had less than 100 participants as opposed to 61% of neonatal studies. Only two neonatal studies (7%) had more than 1000 participants compared with 16 (19%) antenatal studies.

TABLE 10 *What was assessed in 106 eligible studies*

	Antenatal studies	Neonatal studies	All
Knowledge	51 (64.6%)	13 (46.4%)	64 (59.8%)
Anxiety	37 (46.8%)	12 (42.9%)	49 (45.8%)
Attitudes/beliefs	36 (46.2%)	12 (42.9%)	48 (45.3%)
Risk perception	17 (21.5%)	2 (7.1%)	19 (17.8%)
Other choices[a]	13 (16.5%)	3 (10.7%)	16 (15.0%)
Other cognitions	3 (3.8%)	2 (7.1%)	5 (4.7%)
Other affect[b]	8 (10.1%)	11 (39.3%)	19 (17.8%)
Uptake[b]	40 (51.3%)	1 (3.6%)	41 (38.7%)
Total	78	28	106

[a] E.g. choices about subsequent diagnostic tests or termination of pregnancy.
[b] Difference between antenatal and neonatal significant ($p < 0.001$).

Appendix 3 give details of study participants/comparison groups and sample sizes in each of the 78 antenatal and 28 newborn screening studies that were included in the review.

What was assessed

Table 10 shows the outcomes that were assessed in the eligible studies. As expected, a large percentage of studies assessed knowledge and anxiety, but many also assessed attitudes and beliefs. Test uptake was also an outcome measure in 38.7% of studies, all but one of them antenatal.

Study aims

The aims of the different studies were, of course, very varied. Appendix 3 lists details of each included publication including its aims.

Psychosocial and theoretical context

Since the review focuses on psychosocial aspects, we coded each study according to whether there was any apparent input from a psychologist or other social scientist. Overall, less than half of the studies had such input: 34 antenatal (43.6%) and 14 neonatal (50%). Very few studies had any theoretical framework: 13 antenatal (16.7%) and one neonatal (3.6%).

Quality of studies

A quality score was calculated as described in the previous chapter.[36] Some 31% of studies scored over 75%; one-quarter scored 25% or less. In fact, the dimensions assessed by this measure were not found to be useful, as will be described in subsequent chapters.

Structure of this report

Since antenatal and newborn screening are covered by non-overlapping literature, we chose to present them as separate sections of this report. Chapters 4–8 therefore deal with antenatal screening and Chapter 9 with newborn screening. Chapter 10 presents a final discussion of the findings from all scenarios.

The antenatal data are subdivided into studies concerned with screening for chromosomal anomalies and studies concerned with the detection of carriers of recessively inherited disorders. Within each chapter, findings are presented in terms of the extent to which they provide answers to important general questions. These questions will be seen to relate to those listed in the section 'Research questions' in the previous chapter (p. 5). They are not, however, identical because, at the time of formulating those questions, we did not know what the literature search would yield. Thus, for example, we were unable to pursue question 3, "What do we know about other emotional aspects of screening, e.g. fetal attachment?" since, as *Table 10* shows, there are insufficient studies assessing such outcomes. Similarly, the literature on false-negatives (question 5) was too sparse for useful conclusions to be drawn. Discussion of true-positives (question 5) is largely confined to newborn screening, since the information yielded by the antenatal studies was marginal and fragmented. Conversely, given the number of relevant studies, we have expanded issues around participation/non-participation (question 4) to present an entire chapter on decision-making (Chapter 8).

Chapter 4

Knowledge and understanding of prenatal screening for Down's syndrome

A number of general points need to be made about Down's syndrome screening and about how women's knowledge might be measured before the detailed results of the review are presented.

Serum screening for Down's syndrome grew out of the earlier programme of screening for neural tube defects. The new knowledge about the relationship between AFP levels and the probability of Down's syndrome meant that there was more to explain if women were to understand what the tests could do and what the implications of test results might be. Clinicians began to be concerned that giving women all the relevant information would make them anxious, and might put them off being screened. As a result, the focus of clinicians' concerns was originally anxiety, not knowledge: first, was anxiety raised by different aspects of the screening process, and second, did the provision of extra information make people less, or more, anxious? Transitory anxiety was of less concern than enduring anxiety, so there was interest in measuring anxiety weeks or months after screening and even postpartum.

One of the properties of screening programmes is that they generate additional categories of people, namely the false-positives, who may learn they are false-positives after subsequent tests or after the baby is born, and also the false-negatives, who usually only learn that after the baby is born. It was recognised early that false-negatives might be very distressed, but their numbers were likely to be small. False-positives, however, were being created in large numbers and their psychological wellbeing was another early concern. In all of these situations, anxiety was sometimes seen as an important topic in its own right, but also because anxiety might alter the woman's ability to remember and respond to the advice of healthcare professionals, and might even have physiological effects on the pregnancy and development of the baby.

It will be noted that what is missing from this agenda is the current emphasis on informed consent. The first papers on psychosocial aspects of Down's syndrome screening started appearing in the late 1980s and early 1990s. The change in priorities between then and now needs to be appreciated to understand why researchers asked the questions they did, why they collected certain kinds of information, when in pregnancy (and in relation to the chronology of prenatal testing) those data were collected and on which subgroups of women.

If informed consent is a priority, it follows that information on what women know and understand needs to be collected after efforts have been made to inform them, but before any decision has been enacted. If information on knowledge is collected before that, it may provide insight into levels of lay understanding, but that is a separate question, as what matters is the woman's understanding at the time the decision was made. If information on knowledge is collected later, after tests have been taken by some women, then knowledge about procedural aspects of testing is likely to have increased in the group as a whole because of direct experience and possibly because of further information imparted at the time of testing by the professional performing the procedure. Knowledge measures taken after testing cannot be interpreted as evidence of women's knowledge at the time they made the uptake decision. This limits considerably the conclusions that can be drawn from the existing literature.

A second limitation arises from the number of different measures of knowledge represented in the literature, which is only slightly less than the number of studies. Some teams have constructed a measure, then used it in several studies and occasionally, one team will adopt or modify a measure used by another, but in general, workers in this area have preferred to devise a knowledge measure specific to their interests at the time. As was indicated above, the interests of researchers reporting in the 1980s and early 1990s tended to be in knowledge as an influence on anxiety rather than knowledge in the context of informed consent. There was also a tendency for clinical researchers to judge what knowledge was essential, and hence should be measured – from the

maternity services perspective rather than from that of the pregnant woman. This led to an emphasis on procedural aspects of testing rather than, for example, on what it might be like to bring up a child with Down's syndrome. Obstetricians and fetal medicine specialists may in fact know relatively little about the latter, but specialist paediatricians seem to have had minimal input to projects in this area.

A third problem in reviewing research on knowledge about Down's syndrome screening is that self-assessment scales have often been used, that is, women have been asked if they have been given enough information and if they understood the information they were given. This approach is reasonable if the main interest is in anxiety, since feeling that one knows too little – or indeed too much – may well be a more important determinant of anxiety than the actual level of knowledge a woman possesses. However, self-assessment is much less useful if the interest is in informed consent, since a woman may be satisfied with very little information, and she may think she understands something fully, when in fact she has incomplete or indeed even incorrect understanding. Some studies have reported both factual and self-assessment knowledge data and have shown the extent to which the two may be discrepant. Details are given in the appropriate entry below.

Finally, if understanding of factual information is to be examined, the question arises as to how understanding is to be assessed. One or two studies have used open-ended questions with subsequent postcoding of free text, but most have used a multiple-choice questionnaire format. Results are then presented in terms of the separate items, for example the percentage of women who gave the correct answer (ticked the correct box on the multiple choice questionnaire), or totalled to produce a summary score (sometimes with points being deducted for 'obviously erroneous' answers), or subjected to data reduction techniques such as factor analysis and then presented as factor scores. Because no accepted yardstick of knowledge is available, scores on derived measures, or even simple total scores, cannot be interpreted without reference to the original questionnaire, and even then, total scores do not reveal which items people found difficult and which they found easy. Knowledge questionnaires which contain a lot of simple procedural questions, such as the fact that Down's syndrome screening uses a blood sample, are likely to generate much higher scores than those including a lot of questions about risk or other numerical material. Further, some material is easier to turn into multiple-choice questionnaire format than others, so that material is more likely to be included in knowledge questionnaires, whether or not it would be given a high priority on more conceptual criteria.

In this area, because of the absence of widely agreed measures, descriptive studies presenting only total or derived scores cannot be interpreted outside the context of the study. Knowing that 15% of a study sample got scores of 0–3 on a ten-item scale is not in itself informative, and using this information as an operational definition of, for example, 'poor' knowledge only disguises the problem. The problem is less severe in comparative studies, because the control or comparator group provides an anchor point and because interest often lies in whether one group was statistically different from another, rather than in the descriptive figures themselves.

There are many instances in which comparative information is required and in these cases it may be that the statistical advantages of using total or derived scores outweigh the interpretative problems they create. However, unusually in the health technology assessment field, basic descriptive information on levels of knowledge can also be very valuable. "How many people know that amniocentesis increases the risk of miscarriage?" is an important question in and of itself and illustrates the general point that studies presenting 'percentage correct' data for individual items have the advantage of being interpretable outside the context of the study.

Thirty studies reported findings pertaining to an aspect of women's knowledge of prenatal screening for Down's syndrome: seven employed pretest measures only;[17,37–42] six employed both before- and after-test measures;[43–48] 17 employed after-test measures only.[49–65] The main research question of these studies varied, with few aiming to ascertain whether or not participants had received sufficient information prior to the offer of testing (Appendix 3 describes the research aims of included studies).

Although there is currently no 'gold standard' knowledge questionnaire, professional guidelines (RCOG, 1993)[66] outline eight areas of which participants should be aware when making prenatal screening choices: the condition being screened for; the likelihood of detection; the testing method; the meaning of a positive result;

the meaning of a negative result; the options following a 'screen-positive' result; the options following a positive diagnosis; how further information can be obtained. However, there is little consensus and/or evidence to indicate what aspects of information within these eight areas should be assessed to illustrate sufficient knowledge and/or informed choice about prenatal screening.

Owing to the disparate research aims of studies, the poorly operationalised measures and the variation in timing of assessments, it is difficult to draw broad conclusions about women's knowledge and awareness. However, as no study included within this review systematically assessed issues relating to each of the eight information areas outlined above (RCOG, 1993),[66] it is unlikely that knowledge has been assessed adequately. A further validity issue of knowledge measures concerns the relationship between recalling facts and understanding of the information provided. There is some evidence from studies in this review that accurately recalling information provided by screening services is not the same as patients' understanding of the implications of testing. Despite the limitations of current knowledge measures, it is evident from these data that women's knowledge of prenatal screening is not comprehensive before testing and is prone to deterioration after receipt of results. Further in-depth integration of these knowledge data is carried out below.

Do women have enough knowledge about the purpose and properties of prenatal screening for Down's syndrome at the time they decide whether or not to have it?

The evidence suggests that there are some extremely low levels of understanding about basic aspects of testing. Many women could not name or had poor understanding of the condition being tested for, and many believed that screening tests provided definitive answers for having a child with Down's syndrome.

This section begins with the six observational studies that assessed knowledge before screening was offered and aimed to address the above research question.[37–39,41,42,46] Three were conducted in the UK,[37,39,41] one in Australia,[42] one in the USA,[38] and one in Canada.[46] The data collection methods are described and their findings critiqued.

Smith and colleagues, 1994.[37] A total of 353 women attending five UK hospitals completed a nine-item multiple-choice questionnaire about serum screening for Down's syndrome. No further details are given about the timing of data collection or the response rate achieved. Major shortcomings in understanding were identified (*Table 11*).

Grewal and colleagues, 1997.[39] Some 72% (572/800) of women attending antenatal booking clinics in Glasgow filled out a knowledge questionnaire about serum screening. Although unclear, the measure appeared to be in a multiple-choice format devised by the authors to assess knowledge of the test and implications of results.

In brief, 70% of the sample reported that they had received written information about the test and that, for most women, this information was provided at the same clinic as the questionnaires were completed. It is likely that women referred to this information to help them complete the questionnaire, which might result in an overestimation of the amount of knowledge women had available to them if they had made their choices on other occasions. More detailed results from this study are included in *Table 11*.

The authors concluded that leaflets should be provided prior to booking because "women in receipt of written information had better factual knowledge of the uses of the test and the sample used, and were two and a half times more likely to have already decided to undergo screening" (p. 112). However, it is possible that women who wanted screening were more likely than women who did not want screening to have noticed, sought out, read and remembered information provided about having the test.

Chilaka and colleagues, 2001.[41] About 82% (245/300) of women attending antenatal booking in Leicester filled out a questionnaire that assessed demographic details and knowledge about serum screening before counselling from staff and perceptions about the quality of information after the counselling session. Questionnaires were translated into several languages for this multi-ethnic sample; link workers were available for women who could not read. The results of this study are certainly informative but the absence of any knowledge assessment after hospital staff input is an important omission.

The authors defined preconsultation knowledge as good if Down's syndrome was "known to be a chromosomal abnormality associated with significant mental disability and structural abnormalities" (p. 160). Only 33% of the sample had good knowledge with substantial between group differences: 51% of Caucasians, 31% of UK-born Asians and 8% of non-UK-born Asians had 'good' knowledge. The factors related to Down's syndrome knowledge were quality of spoken English, knowing an affected child, parity and religion. Women whose sole source of information was the hospital had poorer knowledge scores than women whose source was their GP. The authors report that, "Despite counselling, only 48% of women knew they had a blood test for Down's syndrome during pregnancy" (p. 162). This figure differed by ethnic group: 66% in Caucasians, 38% in UK-born Asians and 28% in non-UK-born Asians.

The authors sought to relate knowledge to test uptake but their account is hard to follow. It appears as though women were asked prospectively, probably at the end of the booking visit, if they accepted the test, and this intention measure is referred to as 'uptake'. Knowledge scores elicited at the beginning of the booking visit were then related to this self-report of intention. The findings suggest that women with a good knowledge of Down's syndrome were more likely to accept the test than those with poor knowledge (53 versus 23%). Details of the inter-relationship between ethnicity, knowledge and uptake are not provided but the authors report that amongst those with poor knowledge – "complete ignorance" and/or "erroneous answers" – "race had no influence on the uptake of the test".

The authors comment in their discussion that "One surprising result of the present study was that a large number of women were ignorant of having been offered a Down's syndrome blood test and in addition could not admit to being screened, yet had consented to the tests" (p. 163). It is unclear when in relation to counselling and to giving a blood sample these data were collected and, therefore, how these data contributed to the conclusion.

Mulvey and Wallace, 2000.[42] One hundred women in Australia with "an interest in having prenatal screening for Down's syndrome" were interviewed at their first hospital antenatal visit; 63% were described as white Australian and 17% as white European. All women were sent written information before their visit as routine. Few details of the study are given, but the basic descriptive data suggest that little of this preconsultation information had been recalled: although 90% had heard of Down's syndrome, only 44% of the sample knew that Down's syndrome was associated with intellectual handicap.

Freda and colleagues, 1998.[38] All 53 women attending for routine prenatal care in an inner city New York health centre over a 6-month period agreed to take part in the study; 58% were Hispanic, 39% African-American and 3% Caucasian. After women had received a brief explanation about MSAFP testing from a staff member and watched a commercially produced 10-minute video, an interviewer asked them 12 open-ended questions about the video's content and vocabulary. Replies were tape recorded and analysed for correctness. Key findings are included in *Table 11*.

The authors summary of the findings were that "Many misconceptions were apparent, and for some knowledge items, as many as 80% of the women answered incorrectly." These results were based on very broad definitions of a correct response. For example, the answer "Down's baby" was scored as correct when the question asked "What does a positive low MSAFP test mean?" even though MSAFP is a screening test only and does not mean a baby with Down's syndrome. On noting that 80% of their sample planned to have the MSAFP test and signed a consent form, the authors commented that, "The question of how much comprehension is required to consider patients informed has not been answered."

Goel and colleagues, 1996.[46] Some 87% (1084/1241) of women attending routine second trimester care clinics in Canada filled in a 14-item scale designed to measure mothers' knowledge of serum screening. Women's views were elicited after a clinic visit that included a counselling session with a nurse. The authors planned their questionnaire content "to adhere closely to consumer maternal serum screening information pamphlets distributed to healthcare providers in Ontario" (p. 426). The measure went beyond the usual limited focus on assessing knowledge about testing, emphasising awareness of "target conditions and their perceived risks and test characteristics" (p. 426). Each questionnaire item was scored on a five-point Likert scale from –2 to +2, then domain scores (i.e. covering a particular topic area) were calculated by averaging across the relevant items. The mean score for the 'test

characteristics' domain was 0.81, for 'indications and timing' it was 0.63, for 'ancillary tests' 0.53 and for 'target conditions' 0.48.

The authors noted that the majority of patients having serum screening would have the test immediately after this counselling session visit. They concluded that their measure had shown "information gaps overall and in all domains, particularly for target conditions and indications and timing" (p. 428). Further, as their sample was both well educated and receiving a well-established care programme, the position elsewhere regarding informed consent about screening could be even worse.

Have attempts made to improve pretest knowledge about prenatal screening been successful?

This question needs to be addressed by employing a comparative study design, ideally an RCT design. The eight studies that evaluated an intervention or included a comparison group are discussed in more detail below in terms of the question they sought to address and the design issues that may limit the interpretation of their findings. Because of the direct relevance of these studies to policy making, their research design and methods are described in some detail. Knowledge was only assessed pretesting in one study,[40] four studies[43,44,47,48] assessed knowledge before and after the testing period and three studies[49,54,63] assessed knowledge after the testing period only.

Marteau and colleagues, 1993.[43] This study is the earliest in this section and reflects the focus of the time, namely increasing knowledge as a possible means of alleviating anxiety. Two interventions were evaluated: (a) a booklet plus the opportunity for a 5-minute discussion with a midwife and (b) the offer of anxiety management training in a group setting. These interventions were evaluated in a two-by-two design, with an additional comparison group intended to control for the effect of multiple questionnaire administration. Baseline (T1) knowledge was assessed using a multiple-choice questionnaire and anxiety by administering the Spielberger State-Trait Anxiety Inventory (STAI).[67] Measures were completed at the first antenatal visit, after which a follow-up appointment was made. At the follow-up clinic participants were randomly allocated to one of the five trial arms. The timing of subsequent events is unclear. The authors state that, "Interventions took place after the completion of the first questionnaire, and before the second questionnaire was distributed," but whether this meant at the end of the booking visit, the beginning of the clinic at which T2 data were collected, a visit in between or different timings for different women is not clear. They also say that data collection was designed as far as possible to fit in with clinic visits, and that a blood sample for serum screening was taken from those women choosing testing at 16–18 weeks. Women who did not attend the clinics at which data were collected and/or interventions offered were sent, as appropriate, the information leaflet, a leaflet about anxiety management and data collection questionnaires through the post. T2 in the results table is labelled as 'Post-test and intervention', so it seems that T2 data were obtained 'post-test' at the same visit as testing took place. These data cannot therefore be used to examine information prior to consent, as this would require data collected after the intervention but before testing. It seems rather that they were collected at a time chosen to test hypotheses about knowledge tempering anxiety in the period when women are waiting for test results, a question which is discussed later in this section. There were two further rounds of data collection in this study: T3 data were collected after the issuing of test results, 1–2 weeks after testing, and T4 after any subsequent tests and results.

The main problem with interpreting the results of this study arises from the selective nature of the data reported. Specifically, data at a particular time point are only reported for people who filled in questionnaires at all four time points. This reduced the sample from an initial 896 to only 469. No data are presented on people lost from the sample, although this would have been possible using T1 data, since coverage at this time point is likely to have been high. Other studies by the same team[48] (see below) have revealed the extent of the bias which can be introduced by omitting everyone with any missing data, and this study is likely to have been particularly prone to bias because clinic attenders are more likely to have filled in and returned questionnaires than people who were sent them by post.

As the focus of this study was whether knowledge might alleviate anxiety in people waiting for test results, it follows that people who were not tested, whether by choice or for any other reason, were not central to the argument. It is not clear whether these untested women were included in

these results and, if so, in what numbers and what their response rates were compared with tested participants.

Women allocated to receive the booklet were reported to be more knowledgeable about AFP testing at T2. These results are based on a complex analysis of factor scores derived from the questionnaire; no descriptive statistics are provided to aid this interpretation. Satisfaction with information stated as "at the time of testing", so presumably T2, was higher in women who had received a booklet, and also at T3 3 weeks later.

Michie and colleagues, 1997.[48] The same research group in 1997 used a similar methodology to investigate whether or not different information aids impacted on women's prenatal screening choices. Knowledge and anxiety were two measures used to evaluate the impact of the interventions. Knowledge was assessed using an 11-item multiple-choice questionnaire (not provided but probably based on an earlier nine-item version[37]) and anxiety using the short-form STAI.[68] The four trial arms were: receipt of a simple leaflet only; simple leaflet plus accompanying video; expanded leaflet only; expanded leaflet plus accompanying video. Women recruited at their booking appointment completed the baseline (T1) questionnaire and were then individually randomised by a researcher (if booking took place in the hospital clinic) or midwife (if booking took place in a community clinic). Follow-up data (T2) were collected at 16 weeks, "when the screening test was, or would have been, performed". Some 84% (1332/1580) of eligible women were recruited; data were reported for those women who completed all the questionnaires, 21% (324/1580). The mean knowledge scores at T2 were high across all four groups, with no mean group differences. The authors concluded that "a simple information leaflet alone is an effective means of informing women about serum screening for Down Syndrome".

One of the main concerns about this study is that women who did complete all questionnaires differed significantly from those who did not: uptake of testing (81% of completers versus 37% of non-completers); white ethnic origin (71% versus 53%); educated to GCSE or above (92% versus 86%). It is unclear, then, how representative these knowledge scores are and what impact the intervention had on the total population. In addition, without further details about the knowledge questionnaire, it cannot be concluded that knowledge levels were 'high'. The nine-item questionnaire previously used by this research group concentrated on assessing the practicalities of screening and the interpretation of risk results rather than other areas of importance as defined by the RCOG list. Finally, there is an ambiguity about the timing of the second knowledge assessment. This appears to have taken place after the consultation at which the test was performed. If so, women will have had additional contact with the health professional offering the test and, therefore, changes in knowledge cannot be attributed to the leaflet/video interventions alone.

Ormond and colleagues, 1996.[47] To assess changes in knowledge, 25 women were "divided randomly" into three groups: seven were given a 10-minute session with a genetic counsellor, seven had 10 minutes to read a leaflet and 11 received only 'usual physician care'. Knowledge was assessed by a 16-item multiple-choice questionnaire on 'multiple marker screening'; no instrument was published. All women had serum screening, but it was unclear if screening was an eligibility criterion for the study. 'Before' knowledge scores were collected at the booking appointment (T1) and 'after' knowledge scores at the end of a visit about 4 weeks later during which the interventions, or just usual care, had taken place (T2). It was unclear if testing took place before or after women completed the T2 questionnaires. As 90% of the sample were college educated, generalisability is likely to be limited. Mean knowledge scores are reported but no statistics were used. It is likely that some of the interpretations placed on the data by the authors would not have been supported by statistical analysis.

'Before' knowledge scores (T1) were very low. There was a large increase in knowledge between T1 and T2 for all three groups. This is probably a robust finding. Knowledge scores at T2 were slightly higher in the genetic counselling (13.36) and pamphlet (12.86) groups than in the usual care group (10.36), although it is unlikely that this difference would have reached statistical significance if adjustment had been made for differences at T1.

Glazier and colleagues, 1997.[40] In their well-designed intervention study in 1997, this Canadian group used their previously devised[46] 14-item knowledge measure to evaluate a revised patient information leaflet. About 94% (198/209) of pregnant women were randomised individually to receive either the revised pamphlet on triple

marker screening, or a pamphlet on daily activity during pregnancy. Immediately after the pamphlet had been read, women completed the knowledge questionnaire, referring to the pamphlet if they wished.

Using the –2 to +2 scoring system described in the previous section, the overall knowledge score was 0.52 in the daily living pamphlet group and 0.89 in the screening pamphlet group, a highly significant difference ($p < 0.001$). Nonetheless, scores of <0.5, which the authors describe as indicating a low level of knowledge, were still obtained by women in the screening pamphlet group for questions on the nature of amniocentesis, the possible outcomes when amniocentesis is positive for Down's syndrome and the relationship between neural tube defects and age. These items had also been the three lowest scoring items in the previous study.[46] *Table 11* provides more detailed information on these and other items.

Graham and colleagues, 2000.[44] A more recent intervention study compared the effects on knowledge of adding access to a touch-screen information system to the provision of a new information leaflet. Women were sent study information and baseline knowledge questionnaires through the post (T1), and were then recruited at booking clinics, where some additional T1 questionnaires were completed, and women were individually randomised. Recruitment (1050/1330) and questionnaire completion (875/1050) rates were high at this time, but the latter subsequently fell substantially, probably in part because later questionnaires were sent by post. It is unclear when the actual interventions took place, but it was probably at the recruitment clinic. T2 knowledge data were collected at 16 weeks, after testing had (or had not) taken place. A further (T3) follow-up took place at 20 weeks, after any anomaly scan had been conducted. The knowledge measure used a multiple-choice questionnaire format, but a copy is not provided.

There were several problems with this paper. Without further information on item content of the questionnaire, it is unclear what high knowledge scores mean. We know that assessed knowledge was intentionally limited to understanding the purpose of tests, which means that it cannot be used to address the wider issues of informed decision-making and consent. No data are reported from a time point which is postintervention but pretest. The results table refers to 'before' (T1) and 'after' (which might be T2 or T3 – text and table are contradictory here), but T2 was at 16 weeks, by which time the majority of participants had had the test and presumably been given additional information as part of that process. By 20 weeks (T3), test results are likely to have been given and discussed, so this time point is 'after' many more inputs than just the interventions being evaluated. Given this choice of time points, it seems likely that the authors' interest was still about information provision and its influence on anxiety rather than facilitating knowledge or understanding. Data are only reported for the 374 intervention group and 361 control group participants who completed T1 and T2 and/or maybe T3 questionnaires. Further, as 47% of the study sample had received higher education, the issue of generalisability of findings is raised.

Appropriate statistics (logistic regressions) were used to compare the trial arms and no differential improvement in knowledge was found in the touch-screen group. However, the descriptive statistics (means and p values) reported in the tables do not refer to this controlled comparison but to uncontrolled before-and-after (T1 versus T2 or T3) comparisons conducted within the two groups. These show large improvements in knowledge in both trial arms, but have the interpretation problems explained above. The most revealing finding of this study is the gaps in knowledge that still existed after the interventions at 16–20 weeks: nearly a quarter of participants still gave incorrect answers to an important question about the role of blood tests for example, and the majority were still unclear as to the purpose of chorionic villus sampling (CVS).

Thornton and colleagues, 1995.[49] The authors compared the effects of providing information via individual counselling or at antenatal classes on post-test anxiety at four time points: 16–18, 20, 30 and 46 weeks. Three groups were compared; a control group who received only basic information about testing ($N = 567$), an intervention group receiving the basic information plus an extra individual counselling session ($N = 561$) and an intervention group receiving the basic information plus an extra information session similar in format to an antenatal class ($N = 563$). Knowledge was assessed using a self-report measure and anxiety was measured using STAI[67] and the Hospital Anxiety and Depression Scale.[69] Women in both intervention groups reported greater understanding and satisfaction with information than controls, but no differences in terms of satisfaction with screening decision were seen. The

TABLE 11 *Knowledge about Down's syndrome screening at or before the time testing was offered (all data in %)*

	Smith et *al*., 1994[37] UK *N* = 353	Grewal et *al*., 1997[39] UK *N* = 572	Glazier et *al*., 1997[40] USA		Freda et *al*., 1998[38] USA *N* = 53
			Intervention *N* = 133	Controls *N* = 64	
Knew that serum screening can detect an increased risk of Down's syndrome	38	69			
Knew that test requires a maternal blood sample	72	82			84
Thought that test requires a sample of amniotic fluid		21			
Thought that test requires a sample of maternal urine		6			
Thought that test requires a fetal blood sample		2			
Knew that test offered to all women	74	85	74	69	
Knew that test undertaken between 16 and 18 weeks[a]	89	96			
Knew that about 1 in 20 results[b] suggest an increased risk of fetal abnormality	13	21			
Thought that up to 1 in 2 results were positive		4			
Thought only 1 in 100 results were positive		22			
Thought only 1 in 1000 results were positive		11			
Knew that positive results can occur in the absence of fetal abnormalities	32	57	78	54	
Knew that a negative result did not guarantee the absence of a fetal abnormality	36	55	83	63	28
Would expect a positive result to be followed up with further tests	67	69	87	75	62
Would expect immediate treatment or termination of pregnancy		10			
Knew amniocentesis associated with ~1% risk of miscarriage		47	83	44	
Thought that amniocentesis carried no risk at all		3			
Knew that the chance of having a baby with Down's syndrome is higher the older the mother			84	79	
Knew that if amniocentesis shows Down's syndrome, the only options are to have a baby with Down's syndrome or to terminate the pregnancy			49	52	

[a] 15–21 weeks for Grewal *et al*., 1997.[39]
[b] 1 in 10 for Grewal *et al*., 1997.[39]

antenatal classes were not well attended, and the authors suggested that they might not be an effective means of passing on information about prenatal testing. Since the focus of the research was on anxiety, knowledge scores and differential effects on improving knowledge were not reported. The participants were not differentiated into screen-positive and -negative groups, so it is not known whether an effect by screen result status existed.

Browner and colleagues, 1996.[54] The authors investigated the effects of a video intervention on knowledge, test uptake and anxiety. Two groups of screen-negative women were compared: those receiving the standard booklet issued by their care-giver ($N = 66$) and those receiving the booklet and a video designed for the study ($N = 64$). Knowledge was measured as part of an interview using a questionnaire based on items in the information booklet. The interviews took place within 3 months of the women being offered the screening test. The authors reported a significantly improved knowledge score in the video intervention group ($p < 0.001$) with no impact on anxiety or test uptake. However, they noted that in general knowledge levels were low and that procedural knowledge was generally higher than knowledge relating to the test purpose. Similar findings in relation to a low level of knowledge in the post-test period were reported in another paper by the same group.[50] Unfortunately, the retrospective measure used does not tell us the level of knowledge that the women had at the time they made their screening choice. In addition, as the study was conducted with screen-negative women, the interview measure of anxiety was unlikely to be sensitive enough to show effects of an information intervention 3 months previously.

Hewison and colleagues, 2001.[63] The authors compared the effects of providing information in the form of booklets or videos on knowledge, test uptake and anxiety using an RCT design. At the time they received their booking appointment date, 2000 women were randomly allocated to two information conditions: booklet only, or booklet and video. Data were collected after the test results were known to those who had had screening (17–19 weeks). Knowledge of Down's syndrome and understanding of risk were measured using a questionnaire; the Hospital Anxiety and Depression Scale[69] was used to measure anxiety (see also Chapter 5). A total of 359/449 of the video group and 420/552 in the control group returned the questionnaires. Knowledge scores were reportedly higher in the video group (7.3 versus 6.7, $p < 0.005$) with no impact on anxiety or test uptake; however, the questionnaire items were not reported, so it is not known if individual items of information were retained well or poorly. The authors concluded that a video can **in principle** increase knowledge without affecting test uptake or anxiety.

What do we know about knowledge in the period when women are waiting for test results?

Most studies collecting knowledge data in this period have done so in the context of trying to explain or reduce anxiety.[43–45,47,48] These studies are considered in Chapter 5. One further study[46] collected knowledge data in the period just after in addition to just before testing. As part of a test–retest reliability pilot, 72 women who had completed the measure at their initial hospital visit (following which screening had taken place if the woman chose to have it) completed the measure again 1–2 weeks later. Both screened and unscreened women were included in the main study that followed, but these details are not provided for the pilot. The correlation between enrolment and retest scores in the pilot was a very satisfactory 0.76, but mean knowledge scores rose from 0.62 to 0.76 over that period. Further, scores at enrolment were lower for non-respondents (mean 0.49) than respondents (0.66) to the retest. This magnitude of difference was similar to that seen between high school (0.40), college (0.57) and university (0.74) graduates in the main study, indicating that loss to follow-up can have an important effect on results in longitudinal studies of knowledge about prenatal testing.

Is there any evidence of inequalities in knowledge about prenatal testing?

Consistent differences in knowledge scores are observed by level of education, socio-economic status and ethnicity.[38–41,46,51,54,58,62,63] In addition, women who have had previous pregnancies or are older have higher knowledge scores.[51,58,63] There has been little systematic exploration of why these differences in knowledge scores occur or the extent to which they are – or can be – modified by input from health services.

Summary and conclusions

General patterns of findings that have emerged from the data are as follows: women seem to value personally delivered information rather than group-based;[49] prescreening information can increase knowledge scores;[40,43,47,49,54,63] videos but not computer-based media may be slightly more effective in communicating some types of information than leaflet-based interventions.[44,54,63] It is possible that a video is more likely to be watched than a leaflet read, especially in groups that cannot read and/or want to discuss testing with significant others outside a clinic.[54] Broadly, the most robust, if not the most useful, conclusions are that:

- Compared with the RCOG list, only limited aspects of knowledge have been the subject of intervention studies.
- Women's initial knowledge of the procedural and statistical aspects of prenatal screening is, perhaps not surprisingly, poor.
- Leaflets giving information about these aspects of testing improve knowledge, but substantial gaps in understanding of the material covered still remain.

Studies of knowledge that were designed with a focus on alleviating anxiety in people undergoing testing cannot necessarily be used as a source of evidence about how to help people make an informed choice as to whether to have a test or not. *Table 11* draws together knowledge data from several studies which collected comparable information.

Chapter 5

Prenatal screening for Down's syndrome – influences on anxiety

Over the last 20 years, research into the impact of receiving treatment for physical illness suggests that many procedures are stressful to patients, which impairs patient recovery and adherence to treatment regimens.[70,71] Anxiety has been measured to assess the presence of these iatrogenic consequences and the effectiveness of interventions designed to ameliorate these effects.[72] Anxiety is defined as an unpleasant emotional state "characterised by subjective feelings of tension, apprehension, nervousness and worry, and by activation or arousal of the autonomic nervous system".[73] The two most commonly used validated measures of anxiety in applied health settings are the Hospital Anxiety and Depression Scale (HADS)[69] and the State-Trait Anxiety Inventory (STAI).[67,74]

Twenty-four studies within the review measured anxiety, 12 employed the STAI,[12,17,43–45,47,48,75–79] one the STAI and HADS,[49] three used an unvalidated questionnaire measure[60,64,65] and ten ascertained anxiety levels by interview.[55,59,80–85] Of these studies, nine assessed anxiety before women were tested[12,17,43–45,47,48,76,77] and the rest after testing and/or after test results. Most studies were carried out in the UK,[12,17,43–45,48,59,65,83,84] five in North America,[47,74,78,79,85] three in Finland,[55,80,82] two in The Netherlands[60,64] and one each in Denmark[81] and Italy.[77]

As all studies in this chapter employing a validated measure of anxiety used the STAI, the STAI is discussed in more detail. The STAI measures both state and trait anxiety; state assesses an individual's response to a situation, trait an individual's predisposition to being anxious. The purpose of these studies was to ascertain the former, so only state anxiety is referred to further in this review. The full-form state measure includes 20 items, each rated on a four-point scale;[67] the short-form includes only six of these items, but the total is then pro-rated for comparability to the 20-item measure.[68] The range of scores for the STAI is 20–80 with a score of about 34 being rated as 'normal' and 48 'an acute anxiety response' to a stressful situation.

There are a number of methodological barriers to statistical integration of data across the studies in this review: only half the studies employed a validated measure; the aims of studies within the review were seldom in accord with those of the review and, therefore, the designs employed were not appropriate to elicit data to address the review's research questions; the data published were seldom those elicited from all participants but only those who completed all questionnaires at multiple time points. These issues are discussed in more detail when addressing the research questions used to integrate the results below. However, we tentatively suggest that (a) anxiety before having a screening test is slightly elevated compared with STAI norms and with anxiety levels in women after diagnostic test results and postpartum (STAI scores of about 38–39), (b) women receiving a screen-positive result have an acute anxiety response (STAI scores of 49–57), (c) there is insufficient evidence to indicate whether or not this acute response is appropriately dissipated and (d) there is little evidence to suggest knowledge is associated with reduced anxiety in the prenatal screening context.

What do we know about anxiety in the period before testing?

Of the nine studies which assessed anxiety before testing, only two[47,77] report anxiety scores for all study participants; the remainder present only data from those participants who completed anxiety measures at multiple time points, that is, subsamples of those recruited. Research reviewed earlier has demonstrated that participants lost to follow-up may differ systematically from those retained in terms of baseline scores as well as demographic characteristics; so the 'before' anxiety scores reported in these studies cannot be used as a guide to pretest anxiety levels in the group as a whole.

A further concern is whether an increase from pretest anxiety levels should necessarily be interpreted as evidence of harm. In most of these

studies, women attending the clinics are making a choice between testing and not testing. Decision-making theory suggests that increased arousal is a necessary component for individuals to be actively engaged in making a choice between options with serious consequences; this is a reflection of the inverted U-shaped relationship between arousal and information processing where low and very high arousal are associated with poor processing and slightly elevated arousal with effective processing.[74] Hence moderately increased anxiety scores may simply reflect increased arousal and be evidence of more effective decision-making. Few, if any, of the studies in this review acknowledge this dual interpretation of raised anxiety scores prior to choices about screening. The studies assessing anxiety before testing are critiqued in more detail below.

There are some methodological concerns with the two studies reporting complete data sets that suggest that the findings should be interpreted with caution. First, the sample sizes were small, $n = 46$[77] and 25.[47] Second, they assessed anxiety for women who had chosen to have screening after their booking appointment and dating scan at 11–13 weeks gestation. Assessing anxiety for those who had chosen screening leaves open the possibility that those declining testing might be more or less anxious. The mean anxiety scores for these studies were 33–36[47] and 38.[77] Although the authors[77] report that those choosing to have a test had similar anxiety scores to the normative scores of 816 non-pregnant women, a mean of 38 is slightly higher than STAI norm scores of 34.[77]

Of those studies that present the data from a subsample of original participants, six studies originated from the same research team in the UK,[12,17,43,45,48,76] and the other study from North America.[44] In general, these studies assessed anxiety at about 10–12 weeks gestation (booking appointment) and at about 16 weeks gestation [after (non-) screening and result].[44,48] Some have further assessments of anxiety at about 20 weeks gestation [after (non-) diagnostic testing result and 19-week scan], during the third trimester and postpartum.[12] The percentage attrition rate for these studies was at best 47%[48] and at worst 78%.[12] Before-testing anxiety scores for all participants in these studies have not been reported.

A further bias in anxiety scores for those participants included in these subsample studies concerns the under-representation of those choosing not to have a screening test.[12,45,48] Participants are more likely to complete a questionnaire when attending the hospital than when sent a questionnaire by post. Those having screening tests will attend the hospital more often than those declining testing.[12,45,48] In consequence, there is a greater attrition rate in those declining testing. There is one comparison between anxiety scores in those who did and did not have screening.[45] The authors report there were no differences in anxiety between those who did and did not have screening. However, this comparison uses baseline anxiety scores for the subset of those completing the measure at multiple time points, namely the subset that under-represented those declining screening. It remains an empirical question whether or not anxiety differs between those who chose not to have or have screening.

Is anxiety increased in people waiting for screening results?

Perhaps surprisingly, this question is virtually impossible to answer. The difficulty lies in identifying an appropriate comparison group, in other words, 'increased' compared with what? We can, in principle, compare people with themselves pretesting using a longitudinal design, but none of the longitudinal studies in this review measured anxiety while screening results were awaited. Even then, one would really want comparison data from a group who were not waiting for screening test results, to rule out other explanations for changes over time. Since we know from other sources[1] that people who accept testing tend to be more anxious than those who decline, women who had chosen not be tested would not be an appropriate comparison group for this purpose. The option of comparing with women in different geographical locations where screening is not available also has difficulties, since there are likely to be other differences between the groups.[15]

Does improving knowledge alleviate anxiety while waiting for test results?

This is a more answerable question, because the allocation of women to groups for comparison is at least potentially under researchers' control. Most interventions aimed at increasing women's knowledge tend to focus on improving the understanding of risk and the meaning of a positive and negative result. However, it remains an empirical question as to what information is helpful to women when (a) making a choice about

screening and/or (b) preparing them for the receipt of a positive or negative result.

Four studies describe findings that could address the question regarding knowledge and its role in alleviating anxiety while waiting for the test results;[43,44,47,48] one does not report the data relating to this waiting period directly.[44] The usefulness of these studies to address the above research question is considered below. In general, the main methodological concerns with these studies have been described before and are (a) the final data included in these analyses come from highly selected samples, (b) the changes over time cannot necessarily be attributed to the described intervention as many other events and/or contacts with health professionals occurred in the interim and (c) measures of knowledge are not uniform across studies and it is not yet clear what aspects of knowledge are pertinent to assessing testing impact.

As mentioned in the section 'What do we know about anxiety in the period before testing' (p. 25), two of these studies originate from the same research team, one in the early and one in the late 1990s.[43,48] The former[43] collected knowledge and anxiety data at four different time points, including a point at or soon after testing. The anxiety scores from 9% (84/896) of women who subsequently received a screen-positive result and completed all four questionnaires were reported. The authors do not comment on these preresults scores but mention that the knowledge and anxiety scores were unrelated; no further details are given. The latter[48] evaluated the effects of a simple leaflet, an expanded leaflet and/or a video on both anxiety and knowledge. The study reported no knowledge or anxiety differences between trial arms at 16 weeks, "when the screening test was or would have been performed". Four-fifths of study participants had undergone the screening test, and there were no differences in that proportion across study arms. However, amongst women excluded from the analysis because of questionnaire non-completion, only 37% were screened, suggesting a major selection effect of those included in the final analyses.

The final study in this section[47] collected anxiety and knowledge data 4 weeks after booking. The authors noted that anxiety had fallen in their leaflet and counselling groups but risen in the usual care group over time. However, these findings need to be interpreted with caution in part because of the small sample size (n = 25) but also because the anxiety scores of the three intervention groups were not equivalent at booking. It is unclear whether or not group differences would have been statistically significant if appropriate analyses had been performed. These authors also reported that there was no correlation between their knowledge and anxiety scores at baseline or subsequently.

In summary, this section reviewed the data from studies that were most likely to ascertain whether or not knowledge has a moderating or mediating role on anxiety in the period after screening but before the receipt of test results. However, the data from these studies are not convincing in establishing the knowledge–anxiety relationship, as the samples were small and/or unrepresentative.

Does anxiety increase on receipt of an abnormal screening test result?

Fifteen studies using both qualitative and quantitative methods have data indicating that women do experience an acute response to receiving a screen-positive result.[12,43,44,45,47,60,65,75,76,78–82,85] Those studies that employed the STAI reported scores rising to about 55 on receipt of a screen-positive result.[12,75,76,78,79] Others consistently reported women felt shock, panic, distress and worry upon receipt of a screen-positive test result.[12,60,65,80–82,85] This anxiety appeared to affect a number of factors, including changes to women's sleep patterns, appetite and feelings and attitudes about the pregnancy. A further pattern that appears in the literature is that 'older women' (35 years and over) appear to have significantly lower anxiety ratings than younger women upon receipt of a screen-positive result.[65,75,76,78] One explanation for this response difference may be that older women expect to be in a 'high-risk' group, whereas younger women expect to be at 'low risk'.[76,78] Again there are a number of methodological issues that limit the usefulness of these findings in addressing the above research question. These are discussed in more detail below.

The ambitious design of one previously described study[12] evaluated the psychological impact of abnormal MSAFP results – low or high – by employing seven separate data collection time-points: at 12 weeks (to provide baseline scores), 17 weeks (straight after test results known), 19 weeks (when results of further tests known), 28 and

36 weeks, then 2 days and 6 weeks postpartum. Only 372/1371 eligible women completed all seven questionnaires, of which ten had high (increased risk of spina bifida) and 16 had low levels (increased risk of Down's syndrome) of AFP. Women completing all questionnaires were older ($p < 0.01$), more likely to be born in the UK ($p < 0.001$), of higher social class ($p < 0.05$) and had lower levels of trait anxiety ($p < 0.01$) than those completing only some of the questionnaires. Women receiving screen-positive results were found to have higher anxiety scores than those receiving screen-negative results, but as the sample was small in size and unrepresentative of those eligible for inclusion in the study, further conclusions cannot be drawn.

A second study from the same group[43] reported the impact of receiving a screen-positive result for women receiving information about screening in different ways designed to alleviate anxiety: routine care; a leaflet; a class; and leaflet plus class. About 69% (469/736) of the sample completed all four questionnaires. Eighty-five women received a screen-positive result, 43 of them after their AFP test had been repeated owing to inaccuracies in gestation date estimates. The authors concluded that women "did not show any rise in anxiety either at the time of receiving their results or later" (p. 192) (i.e. after 28–36 weeks gestation, after a normal diagnostic test result). However, 15 of these women had no pretest data, so only 69 could be used to examine any rise in anxiety from baseline. Further, only 10 women in this sample did not receive an anxiety alleviating intervention. The findings that there were no differences in anxiety scores from baseline to receipt of a screen-positive result and between intervention groups should be interpreted with caution. As mentioned in previous sections, it is likely that women who do or do not complete four rounds of questionnaires differ in a number of important characteristics. The authors state that there were no differences in anxiety between women who did and did not complete all questionnaires, but the details of this comparison were not given. Further, these analyses were likely to be underpowered because of the small sample sizes. Certainly, as the mean anxiety scores for receipt of a screen-positive result in this study was around 40 and yet the same research group identified 55 as a response to the same result, it seems reasonable to suggest that women who completed all four questionnaires had lower anxiety reactions than those who did not take part in the study and, possibly, those who did not complete all four questionnaires.

Some authors[80] suggest that there are three distinct phases for raised anxiety in response to a positive result: upon receipt of the result; immediately following the decision to (not) have a diagnostic test; waiting for a diagnostic test result. However, there is little evidence to support these three stages. Indeed, little attention has been paid to indicate what a 'normal' reaction to a screen-positive result may be or how long this reaction should last. It is therefore difficult to identify when women are experiencing 'excessive' or 'unusual' anxiety to this stressful situation. Further, most of these studies do not report the anxiety levels of those who declined screening and/or were not offered screening. Taken into account with former statements regarding the anxiety levels of those who decline to take part in research, it is likely that women with higher anxiety scores were under-represented in these studies. These data, then, are limited in their usefulness when generating definitive statements about the impact of screening tests on women's anxiety. However, it seems likely that screen-positive results elicit an acute anxiety response in women and that some types of women (for example, younger) may be more vulnerable than others to this adverse response. More robust methods should be used to establish these potentially differential increases in anxiety and identify the factors causing and ameliorating their manifestation.

Does anxiety decrease if no abnormality is detected upon diagnostic testing?

In general, the findings from this review's studies suggest that anxiety scores return to normal levels upon receipt of a negative diagnostic test result and/or negative repeat MSAFP test.[78,81] However, a number of studies report some women experiencing a residual anxiety throughout the pregnancy and postpartum that impacts adversely on their experiences.[55,59,64,65,80,81] Some authors have suggested that this residual anxiety might be a result of the conflicting messages generated by health professionals offering reassurance that there is 'probably nothing to worry about' in conjunction with the offer of further testing suggesting just the opposite.[59,60] Further, like the differential anxiety responses identified in the previous section, this residual anxiety appears to be more of a concern in younger women.[76,86] However, it is unclear how many women experience this residual anxiety and whether these anxiety scores reflect response to screening or reactions to changes in the pregnancy. Certainly the degree to which residual anxiety

following a false-positive result is significantly greater than anxiety about fetal abnormality in the pregnant population generally has not been addressed. Some studies have suggested that a long-term consequence of this residual anxiety is that women receiving (false) positive results are less likely to have screening in subsequent pregnancies[55,81,87,85] and may experience changes to the mother-infant relationship.[65,80] These associations have yet to be established.

Some studies did describe whether or not women declining further diagnostic testing experienced this residual anxiety. One study reported a woman anticipating the birth "with fearful thoughts and only as an event to let her finally know whether or not her child would be disabled"[80] (p. 106). Another reported findings that after delivery the eight women who chose not to have a diagnostic test had higher anxiety ratings than those 18 who chose diagnostic testing.[12] However, further investigation of this study's results indicates that women in the diagnostic testing group had lower anxiety scores before screening than those declining diagnostic testing. It is likely that some pre-existing characteristic such as age was predictive of women's choice (not) to have a diagnostic test, but this was not accounted for in the analysis. Certainly findings described in this review suggest that adjusting for age is important in any analysis seeking to compare anxiety, at baseline or subsequently, in screened and unscreened women over the results period. This potential confound and the small sample size suggest that few robust conclusions can be drawn from this study regarding residual anxiety in those declining diagnostic testing upon receipt of a screen-positive screening result.

From the studies reviewed in this section, it is unclear whether anxiety is reduced in all women accepting or declining diagnostic tests upon receipt of a screen-positive screening result and why some women may experience residual anxiety whereas others do not. Further, if the results from a diagnostic test are not sufficient to alleviate anxiety, profound questions are raised about women's trust and understanding of the whole prenatal testing process. Studies employing more robust research designs are needed to address these questions.

Does improving knowledge alleviate anxiety after a screen positive test result?

Fifteen studies explored the role of knowledge in alleviating anxiety after a screen-positive test result.[43,44,49,55,59,63–65,78–80,81–84] Some studies evaluated the provision of information before screening,[43,44,49,63,82] a few the provision of information after receipt of a screen-positive result[78–80] and some aimed to described what type of information women found useful.[55,59,64,65,80–84]

It is evident from these studies that increasing women's knowledge by providing more information prior to testing does not **raise** post-test anxiety;[43,44,49,63] the role of pretest information in **alleviating** post-test anxiety is less clear. One intervention providing routine information plus additional one-to-one counselling reported some overall benefits in anxiety but the authors did not differentiate between women receiving a screen-positive or -negative result.[49] An intervention described in more detail in the section 'Does anxiety increase on receipt of an abnormal screening test result?' (p. 27) found no difference in anxiety levels in those screen positives who had received either detailed written information, anxiety management, both or neither.[43] The methodological concerns with this paper have been described before (section 'Does anxiety increase on receipt of an abnormal screening test result?' (p. 27)). Suffice to say their findings should be interpreted with caution. A more recent study published in 2000 compared the provision of information using a computer-based touch-screen or leaflet medium.[44] Anxiety and knowledge were assessed at booking (T1), at 16 weeks (T2) and at 20 weeks (T3). Overall, there were no differential changes in anxiety and knowledge to support the hypothesis of a relationship between the two and direct knowledge–anxiety correlations were not reported. Although one subgroup, nulliparous women on the touch-screen intervention, did demonstrate a decrease in anxiety between T1 and T3, there were other differences between the trial arms that suggest that the fall in anxiety may not have been attributable to the information intervention alone. Those in the touch-screen intervention were also noted to have had significantly more anomaly scans than the controls. Although this could be a chance finding, it is also plausible that the intervention had led them to seek extra scans and that for nulliparous women in particular the extra scans were reassuring.

Those studies that reported the provision of information and/or counselling following receipt of a positive test result did report small decreases in anxiety.[78–80] In addition, studies report that women value prompt and accessible information, especially if delivered verbally.[55,59,81–84] Lack of

professional support or insensitive handling of test results – such as leaving the test result on an answer-machine – tends to compound anxiety and make coping more difficult.[55,59,65]

There has been little research that systematically assesses what type of information is useful to women in this postresult situation, how this information differs from other stages in the screening process, whether different information is required to dispel residual anxiety and how needs may differ depending on women's choices and their consequences. Most of the information interventions within this review focus on improving understanding of risk and the meaning of a positive and negative result.[44,49,78,79] These aspects of knowledge are regarded as necessary to enable women to make informed choices about screening and/or diagnosis. The effectiveness of these interventions in facilitating choice is discussed in Chapter 6. The information required to facilitate decision-making is not necessarily the same as the information that might prepare women for their results postchoice, as demonstrated by the quote from one of the studies assessing women's reactions to a screen positive result:[80]

> "Although because of her education she knew that few positive results indicated real abnormality, her first thought on learning of her positive result was 'disaster'. That evening she was unable to sleep and felt like crying desperately. The next day she described herself as being 'out of control'. Simply having technical knowledge did not prevent a negative emotional reaction" (p. 104).

One study evaluated an anxiety management intervention delivered before receipt of the test result,[43] and focusing on general pregnancy worries, in an attempt to allay postresult anxieties. Anxiety management techniques are useful when individuals have excessive anxiety responses to situations. Although it is possible that some women are experiencing an abnormal anxiety response to receipt of a screen-positive result, it is likely that most women are responding appropriately to the result.[64,80] That is to say, an intervention managing an abnormal anxiety response has little impact on reducing anxiety in this context because anxiety is a normal response to a stressful situation. There is some evidence to indicate that anxiety responses do differ amongst study samples when analysed by characteristics such as age, prenatal testing experience and level of education.[80,81] These findings indicate that some women are experiencing greater distress than others. However, few studies have attempted to explain what aspects of women's knowledge and experience about testing and pregnancy are associated with reductions in anxiety. It is possible that evidence-based information about how others react, feel or cope with the receipt of a screen-positive test result increases women's preparation for an adverse test result and is a more effective strategy in reducing test-specific anxiety.

Summary

Most of the research in this area was informed by at least one of the following concerns of health professionals that (a) the screening process was resulting in iatrogenic consequences such as raised anxiety, (b) screening services could be improved by reducing women's anxiety responses and (c) increasing knowledge about prenatal screening and diagnosis might help reduce inappropriate anxiety responses. Concerns lingered, however, that the increased knowledge would make matters worse, so findings that knowledge could be increased without increasing anxiety were also of value. There are a number of methodological concerns described in the previous section that limit the extraction of robust conclusions. However, the findings of studies in this review suggest that (a) knowledge does not increase women's anxiety about testing and (b) receipt of a screen-positive result raises women's anxiety. The application of inappropriate theoretical frameworks has resulted in two basic misconceptions about knowledge and anxiety, which has informed the measures, interventions and study designs of prenatal screening research in the last decade. In consequence, insufficient and/or incomplete data from the studies have been elicited to draw any further conclusions. These misconceptions are summarised below.

Misconception 1: information that increases knowledge is the same as that which reduces anxiety

The information interventions in this review have been informed by two literatures:

- The first literature draws upon research carried out over the last 20 years that demonstrates preparing individuals for medical interventions is associated with reduced distress.[71] The type of information that is useful in this context is: instruction regarding relaxation techniques; specific information about the procedures; descriptions of how they may feel and/or sensations they will experience; techniques to help cope with the 'health threats'.

- The second literature concerns the information to which women should have access in order to enable them to make informed choices about prenatal testing (see Chapter 4). Guidelines (RCOG, 1993)[66] identified the type of information with which women should be familiar before and during decision-making, including information about risks and benefits of the options and consequences and meanings of test results (see Chapter 4).

Within this review, numerous information aids have been developed to facilitate knowledge about testing but little research has focused on information that enhances preparation for receipt of a screen-positive result. In addition, most study designs have considered it appropriate to provide just one type of information intervention at one point in the screening process, usually when women are choosing whether or not to have screening. With hindsight, it is clear that information needed to facilitate decision-making is qualitatively different from that needed to reduce distress and aid coping. It also seems likely that the provision of information about coping with a test result should occur after the testing choice has been made, perhaps after having the test or upon receipt of the result. Future research is required to identify what information is most effective in reducing anxiety and when in the screening process it is most appropriate to deliver this intervention.

Misconception 2: increased anxiety is inappropriate, abnormal and undesirable

As we have already discussed, anxiety is an unpleasant emotional state experienced by the individual when the autonomic nervous system is activated. It is not unknown for treatment regimens for physical health problems to make people anxious and minimising such iatrogenic consequences is desirable not least because reduced distress is associated with increased patient adherence and recovery. However, the anxiety associated with screening tests is not always inappropriate, abnormal or undesirable.

- First, increased anxiety may indicate that individuals are employing more effective information processing strategies during decision-making. Increased arousal is necessary to enable individuals to attend to decision-relevant information when making choices about treatment, although too high a level of anxiety will impair effective decision-making.[74]
- Second, the expression of anxiety may be of benefit to long-term coping. There is some evidence to indicate that the expression of affect during decision-making about treatment options is associated with reduced long-term distress.[72]
- Third, an acute response to a stressful situation is a normal reaction; anxiety is an appropriate response on receiving a screen-positive result.

Most studies in this review have assumed increased anxiety to be an abnormal response and/or an iatrogenic consequence of prenatal testing. Certainly the only intervention designed specifically to alleviate anxiety was informed by a technique to manage anxiety-related problems. It is likely that some women did experience an abnormal response to aspects of the screening process. In other words, some women's anxiety levels were abnormally high. However, what is unclear from the plethora of anxiety scores in this area is what constitutes a level that is associated with an abnormal response to a stressful situation or evidence of effective information processing. Further research is required to identify these levels of optimum and/or normal anxiety responses in order for interventions to be evaluated on their effectiveness to reduce the iatrogenic consequences of undergoing prenatal testing.

Chapter 6

Knowledge about prenatal carrier screening for cystic fibrosis and other genetic disorders

Part one: cystic fibrosis

CF is a recessively inherited disorder with an estimated carrier prevalence in the UK of approximately 1 in 24. To date over 800 mutations in the CFTR gene have been identified, although not all have been found to be disease causing. The most common UK mutation is the three base pair deletion, ΔF508, which accounts for 75% of carriers. Because it is not practical to test for every possible mutation, the tests detect only around 80–85% of carriers, depending on the distribution of mutations in the population being tested. Thus, a positive test result tells someone that they definitely are a carrier, and a negative result tells them that they do not carry the most common mutations, but still leaves a residual probability that they may carry a rarer mutation. Carrier testing can, in principle, take place at any stage in the life cycle. In practice, testing in pregnancy has been seen as an attractive pragmatic option. For further information about carrier screening for CF, see the earlier HTA report by Murray and colleagues.[23]

A number of general points need to be made about prenatal testing for CF carrier status before a more detailed review is embarked upon.

Because prenatal CF testing is a relatively new technology, it is in practice likely to be an add-on to an existing testing programme, that is, one that already offers testing for Down's syndrome. This is likely to be true both in research projects and in clinical practice, although the details may vary with the age of the woman and local policy regarding age thresholds for offering Down's syndrome testing. In women who are offered both Down's syndrome and CF testing, if a woman is to make an informed choice about CF testing it will not be enough to establish basic knowledge about test properties (blood? saliva? when offered?); it will also be necessary to ensure that the woman understands the very different kinds of logic behind the two tests, for example, regarding future pregnancies and the role of her partner. Women who are not offered Down's syndrome testing are likely to be younger and may not have previously considered that their baby was at risk of having any kind of abnormality, so the increased vulnerability already observed in younger women found to be screen positive for Down's syndrome may also arise in CF testing.

The meaning of the word 'screening' and the relationship between screening and diagnostic testing are different in Down's syndrome and CF programmes. In Down's syndrome programmes, the screening stage has the same function of risk revision in people who turn out to be screen positive and people who turn out to be screen negative, that is, both sets of people receive only probabilistic information, and both may proceed to diagnostic testing if they wish. In CF programmes, women who are screen negative receive the probabilistic information that they are at low risk of being a CF carrier; the risk is not zero, because not all mutations are tested for, so 'false-negatives' exist. Screen-positive women in CF programmes do not receive probabilistic information: they learn that they are carrying a CF gene. For them, the screening test has in effect 'diagnosed' carrier status, and the probabilistic element has moved on to questions about their partner and, eventually, after the same process has been repeated, perhaps then to questions about the baby.

A further complication arises because of the distinction between stepwise and couple screening programmes. In stepwise programmes, if a woman is found to be a carrier, an offer of testing is made to her partner. In couple screening, both partners submit a sample, but initially only the woman's is tested. If she is a carrier, the partner's sample is tested. If either parent tests negative, a screen-negative result is issued to the couple. This approach was advocated[88] to avoid the distress and subsequent counselling demands associated with women learning they were carriers in the stepwise programmes, only to learn later that their partner was not a carrier.

Screening programmes for Down's syndrome have to be conducted in pregnancy, because their purpose is to learn something about the baby.

Screening programmes for CF carrier status can be (and are) conducted outside of pregnancy, because their purpose is initially to collect information about adults who are, or might become, parents; only later in prenatal programmes, and only if both parents are found to be carriers, is information sought about the baby.

The above information is complex. Not all of it needs to be understood by a pregnant woman offered prenatal CF carrier testing, but most of it does, in addition to the material not rehearsed here about genes and chromosomes, the meaning of risk figures, what CF is like and what it might be like to bring up a child with CF, treatments for CF and what they might achieve and of course, procedural aspects of testing. Studies in the literature have been much less ambitious in their knowledge assessments, and have many of the same preoccupations with the mechanisms of inheritance and with risk figures seen in the Down's syndrome literature reviewed earlier.

Do women have enough knowledge about the purpose and properties of prenatal screening for cystic fibrosis at the time they decide whether or not to have it? And have attempts made to improve pretest knowledge been successful?

In the Down's syndrome review, the above two questions were examined separately. Interestingly, and perhaps because CF carrier testing is a newer technology, practitioners and researchers seem to have assumed that women need to be given information about it. All of the studies reviewed used some sort of information leaflet and, in most cases, that is all that they did use. Hardly any data are available on different methods of improving pretest knowledge, and in most cases only simple descriptive information of the 'per cent correct' variety is reported.

Ten papers[89–98] refer to knowledge before or around the time of testing.

Mennie and colleagues, 1992,[89] Livingstone and colleagues, 1993[90] and Mennie and colleagues, 1993.[91] A Scottish group published early work in the field. These are important papers because they asked questions that had not been asked before. They do, however, share some of the problems identified in the Down's syndrome literature, one of these being the timing of knowledge assessments in relation to uptake and hence to informed consent, and the other being a narrow definition of the kind of knowledge that needs to be assessed.

The authors of the papers use the word 'trial' to refer to a package of activities comprising the offer of CF carrier testing and accompanying evaluation activities, that is, questionnaire completion. There is no comparative element to the studies, and most of the data are only presented for trial entrants, that is, people who had the test and filled in questionnaires. In the 1992 study,[89] women were sent a leaflet about the trial with their booking appointment. At the booking clinic, a midwife ensured that women were "fully aware of the consequences of CF carrier screening" (p. 310), in a session which used visual aids and included one-to-one counselling. If women chose to have the test, it was conducted at the booking clinic, and self-completion questionnaires were given out for filling in at home. Over the period of the study, 161 women agreed to be tested and 19 declined, and there was an 81% response rate (135/161 accepters and 10/19 decliners). There are two main problems in interpreting the results of this study. First, knowledge data were collected by self-assessment and so may not be a valid measure of what women actually knew and understood. Second, it is unclear what knowledge women had at the time when they decided to take the test – additional information was presumably gathered by tested women during the process of being tested. As in the case of many of the Down's syndrome screening studies, assessing informed consent was not the authors' priority; they were interested in the relationship between knowledge and anxiety in people being tested, so assessments after testing were adequate to their purpose.

A paper the following year (1993) by the same group[90] reported early data from using the information leaflet within the Edinburgh couple screening programme. In this study, knowledge questionnaires were posted out with the booking appointment, the information leaflet about the CF carrier screening programme and tubes for saliva sample collection from both parents. Details are not given, but it seems likely that the completed questionnaire was returned at the clinic and that samples for those wanting testing were handed in at the same time. The response rate to the questionnaires was 80% (out of 312 parents), and 65% opted to have the test. Knowledge data are reported for the combined sample of those tested and those declining.

Most of the knowledge data were collected by self-assessment, as in the authors' earlier study,[89]

except for one question which asked "What do you think is your risk of both carrying a CF gene?" More than one-third of respondents answered this factual question incorrectly, which throws doubt on the otherwise satisfactory self-assessments, and inevitably leads one to ask: what else did they not understand?

In the Edinburgh work,[89,90] the explicit purpose of sending an information leaflet in the post prior to the booking visit was to avoid the need for a longer booking appointment. It therefore seems unlikely that opportunities were routinely provided during the visit to check and perhaps improve understanding, and if necessary to review the uptake decision. Women and their partners choosing testing had already provided mouthwash samples by this stage, on the basis of the posted information leaflet. Subsequent analysis of the questionnaires shows that in at least one-third of cases, the decision to provide or not provide samples was not an informed one, and shows also that 42% of respondents wanted more information.

In the third Edinburgh paper,[91] also published in 1993, the emphasis was on psychological wellbeing rather than knowledge, but questions on perceived carrier risk (in multiple choice questionnaire format) were included in the 'prescreening questionnaire', which was sent with an information leaflet and the booking appointment. However, data are only presented on those women who went on to accept CF carrier testing. Despite having the leaflet to refer to, only 59% of women (1055/1798) perceived their carrier risk correctly. A large number (378, 21%) had no perception of their risk, a minority (36, 2%) thought their risk was much lower than the 1 in 25 stated in the leaflet and 329 (18%) thought their risk was 1 in 4. It is possible that from the respondents' point of view, this information was not assimilated because factors other than carrier risk were more relevant to their decision about having the test, but the results do also raise questions about people's ability to understand numerical information, particularly if it is presented in printed form.

Cuckle and colleagues, 1996.[96] An English study used the approach of sending out information leaflets with hospital booking appointments and supplemented this with distribution via GPs. Extra copies were also made available in clinics. Knowledge questionnaires were given out at the beginning of hospital clinics and returned at the end. Information given in the leaflet was reinforced by a face-to-face explanation from a doctor or midwife, lengthening the visit by 10 minutes. The CF carrier test was offered (and if wanted, undertaken) on the same occasion.

The questionnaire response rate was 59%. Of respondents, 91% said they had understood the leaflet and 94% said they had understood the face-to-face explanation. However, 25% answered an important question on the risk of being a CF carrier incorrectly. The response rate and knowledge data are not presented in relation to uptake, so there may be other issues relating to informed consent which were not examined.

Leonard and colleagues, 1995.[97] This study compared knowledge in two groups of women (total $N = 409$) receiving either a traditional information brochure or an expanded one including a story. The women were attending a prenatal genetics centre, usually because they were ≥33 years old. The different brochures were handed out on alternate weeks and questionnaires were filled in towards the end of the same clinic visit. The questionnaires included variables derived from the Health Belief Model in addition to knowledge items. All the latter were about risk.

No relationship was found between brochure type and either knowledge about risk or the uptake of the screening test. Prior knowledge was unrelated to any other variable, but the brochures increased the woman's perception of her own risk of having a child with CF (measured on a 1–5 Likert scale) and increased also her perception of the severity of the condition. The average score achieved, on the aspects of knowledge assessed, was 65%, and increase in score was found to make a modest contribution (12% of variance explained) to predicting test uptake.

There have also been five papers arising from longitudinal studies which included some reference to knowledge early in a screening programme. One from Edinburgh[98] mentions but does not report pretest knowledge assessments; one from Germany[93] mentions, but does not measure, "beliefs" as an influence on anxiety. The other three papers[92,94,95] report complex and large-scale studies, designed to answer policy questions about how CF carrier screening might be offered in pregnancy.

Miedzybrodzka and colleagues, 1995.[94] The earliest of the three, published in 1995, reports a randomised comparison of stepwise and couple screening, conducted in Aberdeen. Randomisation

was not at the individual level, but rather was performed on a weekly basis, and it is unclear what participants knew of the arrangement. Recruitment took place at antenatal clinics, where parents were given an information leaflet and counselling by a midwife. Knowledge data were collected on the same occasion and mouthwash sample(s) were provided by those accepting the test. Response rates to the questionnaire were 92% in women and 71% in men, probably reflecting who attended clinic and who was asked to complete questionnaires later. Knowledge was assessed using multiple-choice questionnaire format or Likert scales, and a good range of items was included. *Table 12* gives some multiple-choice questionnaire results, which show first that a substantial minority of people did not understand important facts and second that the position was considerably worse for men. The authors state that only about 50% of partners were in attendance, so it seems likely that many male respondents got all their information from their partner and the leaflet. It is not apparent that male partners had forewarning that tests requiring their informed consent would be offered at the clinic, but if they were not present, their consent could only be sought on a 'second-hand' basis. Risk estimate data from the Likert scales are also presented, but are harder to interpret, so emphasis is placed on the comparison of trial arms. No differences at baseline were found between trial arms or between women and their partners, but the measure was not designed to be sensitive to differences likely at baseline, and differential response rates between men and women may also have influenced the results.

Uptake of the test by women was reported as 91% for stepwise and 89% for couple screening, and these were said to be very similar to local Down's syndrome screening uptake rates. Uptake was not found to be related to questionnaire response rates or to knowledge in those responding. It does seem likely, however, that many people, especially men, are having tests the purpose of which they do not understand, and probably others not having tests for the same reason. Misunderstandings about CF screening in particular or 'genetic tests' in general are likely to be increased in people who get their information second hand. The possibility of reviewing decisions at a later date also seems limited, and this may have been especially true in a study in which randomisation was according to weeks, not families. Women attending without their partners may have accepted testing to keep their options open in these circumstances.

Witt and colleagues, 1996.[92] A 1996 American study reports a study of stepwise screening in which women read a brochure and watched a video in a group setting, then filled in questionnaires and responded to the offer of screening, all on the same occasion. A non-randomised comparison group only received the brochure. Few details are given, but women who saw the video obtained knowledge scores averaging 7/10, compared with the brochure-only group who got 4/10. People who accepted testing only scored half a point higher than those declining, and adjusting for demographic differences did not alter this finding.

Grody and colleagues, 1997.[95] In another American study, women attending antenatal clinics were invited to consent to a 'protocol' consisting of educational information, questionnaires and the offer of the carrier screening test. Knowledge of the clinical and genetic aspects of CF was assessed using a multiple-choice questionnaire before and after the instructional session, which consisted of an 8-minute video in English or Spanish and the opportunity to ask questions.

Data from these knowledge assessments are only presented for the minority who filled in a total of three questionnaires, including a third administered at a later stage in the screening process. Numbers are unclear but this seems to have been between 1200 and 1500 out of a sample of 3700. At the time of consenting to testing, 11/17 items exceeded 80% of people answering them correctly, but for the two lowest scoring items the figure was only 45–55%. Large increases of between 30 and 100% were reported for pre- to postinstruction. In a non-randomised comparison of brochure with and without the video, the mean postinstruction knowledge score out of 17 was about 9 in the full protocol and about 7 in the streamlined protocol. Some 38% of those declining to take part in the protocol said that this was because they did not want to fill in questionnaires, rather than because they did not want testing. Amongst participants, test uptake was about 98%.

What do we know about knowledge in the period when women are waiting for test results?

Unlike in the Down's syndrome screening literature, this has not been seen as a distinct question in the CF work. Some of the studies reviewed above collected their knowledge data at the time of testing and this therefore provides a reasonable guide to what people knew while waiting for their results. Information on the meaning of test results

TABLE 12 *Knowledge about CF and carrier status at the time of testing: % correct*

	Miedzybrodzka *et al.*, 1995[94] UK		Livingstone *et al.*, 1993[90] UK		Mennie *et al.*, 1993[91] UK	Cuckle *et al.*, 1996[96] UK	Grody *et al.*, 1997[95] USA
	Women *N* = 1841	Partners *N* = 1427	Women *N* = 288	Partners *N* = 278	Women *N* = 1798	Women *N* = 275	Women *N* = 3543
What proportion of British[a] people are carriers? (1/25)[b]	89	80			59	75	~90
Which sex is more likely to be carriers? (Equally likely)[b]	85	66					
Are all carriers related to someone with cystic fibrosis? (No)[b]	77	63					
If both parents are cystic fibrosis carriers, can they have a normal baby? (Yes)[b]	84	79					
What is the risk of both parents carrying a CF gene? (1/600)[b]			59	58			

[a] 'Americans of N. European descent' for Grody *et al.* (1997).[95]
[b] Correct answers in parentheses.

is presumably particularly valuable at this time, so it is of concern that questions about risk were not well answered in the studies reviewed earlier.

Is there any evidence of inequalities in knowledge about prenatal testing?

Some of the studies reviewed[92,98] mentioned socio-demographic data, but only in the context of checking the comparability of other kinds of groups, such as screen positives and matched controls[98] or consenters and decliners of testing.[92] It seems likely, however, that inequalities seen in the Down's syndrome context are also seen in CF screening, and the gaps may if anything be wider because of the reliance on written forms of information giving.

Do people remember enough information about their CF carrier status to help them make reproductive choices in the future?

Eight studies reported data which can be used to address this question.[92,94,95,98–102]

Witt and colleagues, 1996.[92] In an American study which sought to evaluate video as a means of pretest education about (stepwise) screening, knowledge at the time of testing was assessed with a multiple-choice questionnaire and shown to be improved in the video group. Carriers (n = 76) and a subsample of screen negative controls (n = 192) were followed up after they had had their babies, but unfortunately the knowledge questionnaire was not repeated. Women instead took part in an interview, on the basis of which 97% of carriers and 83% of controls were judged to have excellent or good comprehension of their screening results. About 17% carriers had "some low residual concern that their baby could have CF, but none had serious concerns" (p. 828).

Grody and colleagues, 1997.[95] In another American study, 40% of screen-positive women believed that there was no risk of CF after their partner tested negative. This belief was held by only 7% of women who themselves tested negative. The authors considered that the higher figure in the screen positives was evidence of false reassurance, possibly arising from relief experienced when partners tested negative.

Harris and colleagues, 1996[102] and Hartley and colleagues, 1997.[101] The pilot study of general practice-based screening[102] included a 1-year follow up in which 69% (44/64) of the original questionnaire sample took part. The authors noted that "factual recall was good, and 35/44 (80%) of patients had retained information about cystic fibrosis and were able correctly to answer three out of five questions relating to literature given at the beginning of pregnancy" (p. 226). Further details of recalled and non-recalled items are not given. The main study which followed[101] did not assess recall, but did ask screen-negative women questions about risk perception, 2 weeks after they had received their results. Overall, 29% (82/278) of non-carriers believed that their baby was now at no risk of CF and the level of false reassurance was similar in both stepwise (28%,37/134) and couple screened groups (31%, 45/144). The 12 women who were carriers all correctly recalled their carrier status.

Clausen and colleagues, 1996.[100] A Danish study with a mixed sample of routine and CVS patients asked women some questions to test their understanding soon after they had received their test results. There were 123 women with a positive result and 142 with a negative result in the sample. It is not clear exactly how the question was asked, but "Significantly more women with a positive than a negative test result could remember the pretest information that 'everyone is a carrier for some genetic disorders' ($p < 0.00001$)" (p. 202). Some 84% (103/123) of carriers remembered soon after the results that their risk of having a child was reduced but not zero if their partner's test was negative, but over 1 year later this figure had fallen to only 61% (75/122). Amongst screen-negative women, 94% (131/140) believed at follow-up that they were not carriers and only 4% endorsed the response option, "It is highly unlikely that I am a carrier", which the authors had chosen as the correct answer.

It is likely that terminology was causing extra problems here. Staff tell a screen-positive woman that she is a carrier – the term is widely used. They do not tell a screen-negative woman that she is not a carrier. It is but a short step for the latter to conclude that she is not a carrier – she is after all not being treated as a carrier.

The picture was a little better when a more straightforward question was asked: 39% (54/140) of screen negatives could remember after more than 1 year that their risk of having a CF child was reduced but not zero. Less satisfactorily, 46% (64/140) believed they could not have a CF child and a further 15% (21/140) said they could not remember.

Miedzybrodzka and colleagues, 1995.[94] In the Aberdeen study of stepwise and couple screening

(the latter involving non-disclosure), women's knowledge was assessed shortly after they had had their baby (*Table 13*). About 21% of screen-negative women from the stepwise group and 13% from the couple group perceived incorrectly that they had no risk of being a carrier; 19% of the stepwise group and 17% of the couple group perceived incorrectly that they had no risk of having a baby with CF. Partners had a significantly greater perception of their own carrier risk than did women ($p < 0.01$), which was incorrect in the couple arm of the study. Some 21% (53/253) of women with negative couple results were unaware that repeat testing would be required with a new partner. The authors draw attention to these points. In addition, it is notable that overall, 22% of female participants (323/1470) did not know that if both parents are CF carriers they can have a normal baby; the corresponding figure for men was 26% (379/1457). Further, 47% of women (691/1470) and 57% of men (830/1457) did not know that males and females are equally likely to be CF carriers.

Mennie and colleagues, 1993[98] and 1997.[99]
Two papers by the Edinburgh group include information on recalled knowledge. In the 1993 paper,[98] 64 women carriers identified through stepwise screening completed a knowledge multiple-choice questionnaire, derived from the prescreening information leaflet, 6 weeks after their test results. A total of 63 screen-negative partners, 101 female controls (from the same booking clinic, of the same parity but with a negative test result) and 100 of their partners also completed questionnaires. Particularly poor levels of understanding were shown by male controls, that is, the partners of women found to be screen negative. In a stepwise programme, these men would not themselves have been tested, so may have had only limited and indirect information to draw upon (*Table 13*).

The 1997 Edinburgh paper[99] reports a long-term follow-up to the studies of stepwise[91] and couple[90] screening reviewed earlier. A total of 171 carriers from the stepwise programme who had screen-negative partners were sent a questionnaire 3–4 years after screening. For each carrier, two controls matched for age and social class were selected from women who had received screen-negative results in the stepwise programme, plus another matched control from screen negatives in the couple screening programme. For the latter group, the questionnaires arrived about 2 years after screening.

Some 64% of carriers (109/171) replied, as did 52% of stepwise controls (179/342) and 66% of controls from the couple programme (113/171). Over 97% of participants correctly recalled their carrier status, although a small number of women thought they had been screened in their GP surgery, suggesting the possibility of some confusion with Down's syndrome screening.

In interpreting the results from this study, it is important to remember that non-disclosure of individual results was practised in couple screening, that is, only couples in which both partners were carriers learned their individual carrier status. Couples were 'not encouraged' to ask for individual results, but 1.5% of screen-negative couples sought and were given them.

Screen-negative women tested by the stepwise method were more likely than their couple screened counterparts to understand that a CF carrier is healthy and will not develop the disease, and also to understand that a baby can only develop CF if both parents pass on their CF gene. Carriers were more likely than either screen-negative group to know that parents who were both carriers could have a baby without the disease, and to know that a screen-positive result meant that someone definitely was a CF carrier, whereas a screen-negative result did not mean someone definitely was not a CF carrier (*Table 13*).

The authors concluded that screen-negative women in (non-disclosure) couple programmes were significantly less knowledgeable about the genetics of CF than their counterparts in stepwise programmes. The authors note that one of the attractions of couple screening is that it is less time consuming, so better able to be accommodated in busy antenatal clinics, but they go on to comment, "It would be a pity if in the interests of efficiency, the fundamentally important information and counselling component of the screening process was lost" (p. 859). They voice the further concern that information leaflets may become substitutes rather than supplements to orally presented information and counselling, and draw the conclusion that better written information is therefore essential.

Few would dispute the need for high-quality written information, but the assumption that the need for 'efficiency' will necessarily rule out the possibility of adequate staff input should not go unchallenged. Even leaving aside moral considerations, providers of screening services may be open to legal challenge if their procedures are

TABLE 13 *Recalled knowledge about CF and carrier status: % correct*

	Hartley et *al.*, 1997[101] UK (after test results)		Grody et *al.*, 1997[95] US (stepwise) (after test results)		Mennie et *al.*, 1993[98] UK (stepwise) (6 weeks after test results)				Miedzybrodzka et *al.*, 1995[94] UK (after birth of baby)					Clausen et *al.*, 1996[100] Denmark (1 year after testing)		Mennie et *al.*, 1997[99] UK (2–4 years after testing)		
	Screen-negative women		Screen-negative women	Screen-positive women	Screen-positive women	Screen-negative women	Partners of screen positives	Partners of screen negatives	Screen-negative women		Screen-negative partners	All women	All partners	Screen-positive women	Screen-negative women	Screen-positive women	Screen-negative women	
	Stepwise (*N* = 134)	Couple[a] (*N* = 144)	(*N* ≈ 1200)	(*N* = 30)	(*N* = 64)	(*N* = 101)	(*N* = 63)	(*N* = 100)	Stepwise (*N* = 1092)	Couple (*N* = 253)	Couple (*N* = 248)	(*N* = 1470)	(*N* = 1457)	(*N* = 123)	(*N* = 140)	(*N* = 108)	Stepwise (*N* = 179)	Couple (*N* = 113)
If one partner tests negative, is there still a risk of having a child with CF?[b] (Yes)[c]	72	69	93	60	89	90	87	82	81	83				61	39	56	36	37
If you had a pregnancy in future with a different partner, would you need to have another carrier test? (No for stepwise, Yes for couple screening)[c]									67	79	72							
If both partners are CF carriers, can they have a normal baby? (Yes)[c]												78	74			95	72	59
Which sex is more likely to be carriers? (Equally likely)[c]												53	43					

[a] With disclosure.
[b] In Mennie *et al.* (1997),[99] question related to residual carrier risk only.
[c] Correct answers in parentheses.

demonstrably inadequate; and protecting against that by providing further counselling (and possibly re-screening) in subsequent pregnancies is likely to erode the efficiency benefits achieved the first time round.

Overall, serious shortcomings are apparent in what people remember about CF carrier screening. As in Down's syndrome screening, self-reported understanding and ratings of the adequacy of information materials are both likely to create a misleading impression that satisfactory levels of understanding are reached and maintained. None of the studies reviewed which used objective assessments of women's knowledge and understanding have shown satisfactory levels of information retained, and some areas of real concern have been identified. The position of men is likely to be even less satisfactory.

Prenatal CF carrier screening: summary and conclusions

Reaching the end of the work on knowledge about CF carrier screening, a number of similarities to the Down's syndrome literature can be identified:

- Knowledge is improved by giving people information in the form of a leaflet, but significant gaps remain.
- Narrow definitions of knowledge are commonly used.
- Self-assessment overestimates knowledge.
- Evidence is limited on the effects of supplementary methods such as videos.
- It is likely that fairly large numbers of people are having tests the purpose of which they do not understand.

Some further points arise in connection with antenatal CF carrier screening:

- Men's need for information is even less well served than is the case for women.
- Some service providers have agreed to offer CF carrier screening without agreeing to provide extra time in antenatal clinics to obtain informed consent.
- Leaflets have been seen as a substitute for discussion with a professional, but sometimes they have not even been sent out in advance of the consultation at which the test offer was made.
- The time frame in which people are expected to absorb information and make a decision about having a test has been artificially constrained in order to fit in with the ongoing routines of antenatal clinics. Research ethics committees nowadays expect potential participants to have 24 hours to decide whether they wish to fill in research questionnaires; by contrast, parents in some of the studies reported above seem only to have had minutes to decide whether or not they, and possibly their partner, would be tested for CF carrier status.
- Retention of information relevant to future reproductive choices is inadequate.

Part two: prenatal carrier screening for other genetic disorders

In addition to the studies of CF carrier screening, a further five studies related to prenatal screening programmes for other recessively inherited disorders.[103–107] All were for conditions that are prevalent in specific minority ethnic groups.

Wallerstein and colleagues, 1994.[104] One paper is about screening for Tay-Sachs disease. Set in America, it is concerned with Ashkenazi Jewish women's reasons for declining screening.

Rowley and colleagues, 1988,[103] Loader and colleagues, 1991[105] and Rowley and colleagues, 1991.[107] Three of the papers were based on the Rochester Prenatal Haemoglobin Screening Project in the USA. The programme is described in detail in another paper,[108] and is also discussed in Chapter 7. One paper[107] presents findings on predictors of screening intentions and another[103] presents interim findings on factors associated with postscreening behaviours. Only the paper from the Rochester Project that contains information on knowledge[105] is considered in this section.

The Rochester Prenatal Haemoglobin Screening Project, which ran in the mid–late 1980s, asked the question "Should haemoglobinopathy carrier screening be part of routine prenatal care?" Nineteen local providers of prenatal care undertook to supply the project with blood taken at the first antenatal visit for other purposes. This and all subsequent testing and counselling were at no cost to either the parents or the providers.

> "The provider had the option of asking the patient for consent to be screened. However, only one of the 19 centres chose to do this and then only for the first several years; the other providers felt that they had their patients' implicit consent for relevant diagnostic blood tests"[108] (p. 440).

A blood test taken as part of a screening programme can only be regarded as a diagnostic test in a very specific sense (the 'diagnosis' of carrier status), so the assumption of implicit consent was probably convenient rather than evidence based.

Women who screened positive were contacted by the project and invited to attend for genetic counselling to discuss the result. Whether or not women responded to this invitation was taken as a measure of their interest, as was whether those counselled then got their partners to be tested, which was the main message of the counselling. Women completed questionnaires immediately before and after counselling to assess their knowledge of the manifestations of haemoglobinopathy and of prenatal diagnosis. Higher levels of postcounselling knowledge were shown by women who were younger, had more education and who had known about trait previously.

Green and France-Dawson, 1997.[106] The last paper to be considered in this section is also concerned with sickle cell screening, specifically with the experiences of women of African descent living in the West Midlands in the UK.

This study makes an interesting contrast to the Rochester study, taking the women rather than the screening programme as its starting point. The study was an extension to the Cambridge Prenatal Screening Study,[18,28,109] which was a prospective longitudinal study of women's experiences of routine screening for fetal abnormalities in the early 1990s. The main study only covered MSAFP screening for neural tube defects and therefore is not eligible for this review. The study reviewed here was an extension of the project into an area of the UK with a high proportion of people of African origin, specifically in order to investigate experiences of screening for sickle cell disorders in pregnancy. A total of 159 women of African descent completed an additional questionnaire in the second trimester specifically about sickle-cell testing. About 52% of these (N = 83) said that they had been tested for sickle at some time in their lives, 37% (N = 58) said that they had never been tested and 11% (N = 18) were not sure; 41% of the last two groups wanted to be tested, but 46% were not sure because they did not know what it would entail.

Of the 83 who said that they had been tested, only 36% (N = 30) felt that they had had a clear explanation of the test; 4% said that they had only realised they had been tested when results came in the post and another three women (4%) said that they had been given no information at all. Two-thirds of those tested were given a result (N = 55); 38% of these believed 'trace of sickle-cell' meant they had a serious illness. 15% believed the term 'carrier' meant one was at risk of illness (and one example is given of a carrier who worried about dying from sickle-cell disease). Women were less likely to understand the implications for transmitting the gene if the term used was 'trait' or 'trace of sickle-cell' compared with use of the word 'carrier'. There was also very poor knowledge of what it meant to 'have sickle-cell'.

The authors concluded that women had received very little information about either the carrier test or the condition during their pregnancies. The terminology used was a major source of confusion. Even those women who knew they had been tested and knew their results did not necessarily know what the results meant.

In summary, very little is known about psychosocial aspects of prenatal carrier testing for disorders other than CF. The limited evidence available suggests that women do not understand the tests or their purpose. If language difficulties compound the problem – as they do in the UK thalassaemia testing programme, for example – it is unlikely that informed consent is routinely achieved.

Chapter 7

Prenatal carrier testing for cystic fibrosis and other genetic disorders – influences on anxiety

The previous chapter showed that women's knowledge about prenatal carrier testing has only really been studied in the case of CF. Part one of this chapter examines anxiety in the context of prenatal CF carrier screening. Part two provides a brief postscript about anxiety in the context of screening for other genetic disorders.

Part one: cystic fibrosis

What do we know about anxiety in the period before carrier testing?

Six papers[89–91,94,95,110] made reference to anxiety in the period before or around the time of testing. Four of these[89–91,110] are papers from the Edinburgh group (see Chapter 6), but one[89] only provides self-reported anxiety information, and only for people who had been tested (see below). Another[90] gives self-reported data from a study of couple screening: 13% of women and 10% of men reported that the thought of taking the CF carrier test 'made them anxious'. It is not very clear what aspects of testing respondents had in mind here, since the actual samples were collected using a mouthwash procedure.

Mennie and colleagues, 1993.[91] The third of the Edinburgh papers presents data from women accepting testing in a stepwise programme (uptake rate not given here), using standardised measures: the 12-item version of the General Health Questionnaire (GHQ) and the Symptom Rating Test. These were contained in a 'prescreening questionnaire', sent with the antenatal booking appointment and an information leaflet. Joining the 'trial' entailed having the screening test and completing questionnaires. Women who had not completed questionnaires at home did so at the clinic. GHQ data were used to identify 'women suffering from a psychological disturbance before receiving a positive CF test result' (p. 544). Those people scoring above the 3/4 cut-off point were asked at the clinic to fill in the Symptom Rating Test, which produced separate scores for anxiety, depression, inadequacy and somatic symptoms, and they were interviewed by a genetic nurse to identify the 'likely source of their disturbance'. Of the 1798 participants, 32% were found to be above the GHQ cut-off, although only 2/576 attributed their disturbance to worry about the CF test. Self-reported anxiety was felt by 23%, but no relationship was found with perceived carrier risk, even though the latter showed considerable variation.

In discussing their results, the authors comment on levels of concurrent distress seen in women entering a screening programme, and comment too on the 'multiple provoking agents' which may be encountered in pregnancy, such as receiving a high AFP result and having an amniocentesis after learning one was a carrier for CF.

Livingstone and colleagues, 1994.[110] The fourth Edinburgh paper reported GHQ data in the context of couple screening. The first of four GHQ assessments was completed before testing, although it is unclear whether questionnaires were sent in the post at the same time as the information leaflet, sample containers and booking appointment, or whether they were filled in at the clinic. Most appointments were for about 3 weeks after the letter arrived, so couples had time to deliberate. GHQ data are presented only for the 'first 300 couples who completed the GHQ at all four time points' (pretesting, 10 days after testing, 6 weeks after testing and 6 weeks postpartum), and who had been tested. Altogether, 5922 couples were screened out of 7822 who were eligible, but the numbers failing to complete all four GHQ rounds in the time needed to recruit 300 couples are not given. Over 30% of female and over 10% of male GHQ respondents had scores of ≥3 at recruitment, that is, they had fairly high levels of distress at the point of embarking on the screening programme, although the prospect of screening might of course have contributed to this. The authors did not comment on this last possibility, pointing out only that no procedures had at this stage been carried out. They also commented that the figures were very similar to those seen in their stepwise programme.[91]

Grody and colleagues, 1997.[95] In the 1997 American study, anxiety data were collected (using

TABLE 14 *Mean STAI anxiety scores of women during CF carrier screening programmes*

	At recruitment	After test result	After all results	After birth of baby
Miedzybrodzka *et al.*, 1995,[94] UK				
Allocated to stepwise ($N \approx 1106$)	32.7			
Allocated to couple ($N \approx 250$)	34.2			
Screen positives ($N = 34$)		52.3	36.1	32.3
Screen negatives (stepwise) ($N = 1072$)			32.1	31.2
Screen negatives (couple, no disclosure) ($N = 250$)			35.4	32.0
Hartley *et al.*, 1997,[101] UK				
Stepwise ($N = 134$)			36.9	
Couple (with disclosure) ($N = 144$)			33.3	

an 'adapted' STAI) before and after an instructional session consisting of an 8-minute video and the opportunity to ask questions. Only participants who filled in another STAI, after test results, are included in the figures for the two earlier time points. Scores were reported to fall over the instructional period, from 2.07 to 1.86, but these adapted figures are not easy to interpret.

Miedzybrodzka and colleagues, 1995.[94] Lastly in this section, the Aberdeen study noted that women offered couple screening were more anxious at recruitment than those offered stepwise screening ($p = 0.02$). This comparison used the short-form STAI (*Table 14*).

Is anxiety increased in people waiting for carrier screening results?

The studies which throw the most light on anxiety at the beginning of a screening programme have been reviewed above. There is, however, no corpus of work in CF looking specifically at anxiety while waiting for antenatal carrier screening results, unlike in the Down's syndrome literature. In a number of the studies reviewed above, anxiety data were collected on the same occasion as testing was conducted. Researchers have not made fine distinctions between anxiety measured before giving a mouthwash sample and anxiety measured afterwards, and this is probably reasonable in the circumstances.

Mennie and colleagues, 1992.[89] One of the Scottish studies provides a guide to anxiety at this time. In the 1992 paper, anxiety data were collected by self-report and only presented for people who had had testing (because only they were regarded as having joined 'the trial': 161/180 had testing and 135/161 returned questionnaires). Only 3% of respondents reported themselves as 'anxious', 38% were 'slightly apprehensive' and 59% were 'reassured'. The authors reported no correlation between anxiety and women's reports of having difficulty understanding the leaflet or the purpose of screening.

Does anxiety go up on receipt of an abnormal screening test result? Does it go down on receiving a screen negative result?

The distinction between stepwise and couple screening programmes needs to be repeated here. In stepwise programmes, if a woman is found to be a carrier, an offer of testing is made to her partner. In couple screening, both partners submit a sample, but initially only the woman's is tested. If she is a carrier, the partner's sample is tested. If either parent tests negative, a screen-negative result is issued to the couple. Couple screening was proposed when many screen-positive women identified by stepwise programmes were found to be very anxious, and in need of counselling, which had resource implications.

Eight studies need to be discussed under this heading. Four of these[91,94,95,110] are longitudinal studies encountered earlier and the other four[93,101,102,111] all began their data collection after the receipt of screening test results.

Grody and colleagues, 1997.[95] In the American study which used a brochure and a video as instructional materials, mean scores on an adapted STAI were 1.86 at the time of testing (down from 2.07 at recruitment, before the educational intervention). Anxiety in women receiving screen-positive results was not reported (although they were said to show concern while awaiting their partner's result), but it was observed to fall to 1.40 in those receiving screen-negative results. Adapted STAI scores are not easy to interpret, but in this large study (minimum $N = 1224$), the difference between the three time points was reported to be 'significant to $p < 0.001$'.

Mennie and colleagues, 1993.[91] The earlier of the two studies from the Edinburgh group examined the psychological effects of stepwise screening on carriers and their partners. Out of 1798 women screened, 69 were found to be CF carriers, and in all cases the male partner was tested. For each carrier, two controls were chosen. These were women of the same parity (and with a partner also willing to complete questionnaires), but who had received negative test results. Carriers, partners and controls were assessed on four occasions using the GHQ and Symptom Rating Test: on receiving the carrier's positive test result, on receiving the partner's negative test result, 6 weeks later and 6 weeks after the birth. Of those continuing to be eligible on clinical grounds, 64/65 carrier women completed all questionnaire rounds, as did 62/65 of their partners. A total of 116 female and 115 male controls agreed to take part and, of these, 101 women and 100 men completed the study to stage 3.

On receiving positive screening test results, the proportion of carriers with a GHQ score above threshold was 53%, compared with 27% of controls ($p < 0.001$). These groups had been very similar at baseline (22 and 25%, respectively). On the Symptom Rating test, there was a significant difference between carriers and controls in the total score for generalised psychological disturbance ($p < 0.005$) and specifically in the subscores for anxiety and depression ($p < 0.001$). There were no differences between partners and their controls on the GHQ or total symptom rating test score but anxiety and inadequacy subscores were significantly higher in partners than controls ($p < 0.05$ and $p < 0.02$, respectively) at this time.

Livingstone and colleagues, 1994.[110] In the other longitudinal study from the Edinburgh group, men and women who had taken part in couple screening were told (in the information leaflet) that if they had heard nothing from the programme coordinator 10 days after giving samples, they were not a high-risk couple. Four couples out of 5922 were screen positive. The screen negatives filled in 12-item GHQs 10 days after being tested. The proportion of respondents with above-threshold (≥3) GHQ scores was observed to fall from about 33% at baseline to about 18% after results in women and from about 12% to about 4% in men (figures estimated from graph). When data were collected again 6 weeks after testing, there had been hardly any change in women, but a rise of 4–5 percentage points in men. Six weeks after the baby was born, the percentage of people with above threshold scores was nearly back to baseline levels in women and exceeded it in men. All of these figures are based on the first 300 couples to complete the GHQ at all four time points. Potential drawbacks to this approach were discussed above.

On the basis of these data, the authors concluded that couple screening appeared to cause little anxiety in participants. However, it is unclear how typical were the 300 couples who contributed full GHQ data, and figures are only given for people who had the screening test. Further, the score at baseline could have been elevated by the prospect of testing, providing scope for a fall when (screen-negative) results were received. Without comparison data at baseline from people not offered screening, it is possible that anxiety was elevated at an early stage in the screening programme, and since measurements were not taken at day 9, when results were due, it is unknown whether anxiety was raised at that time also.

In their discussion, the authors compared the anxiety profile seen in the couple screening study[110] with that seen in the stepwise study,[91] and noted that the pattern seen in couple screening was very similar to the pattern seen in non-carriers and male controls in stepwise screening. They went on, "However, the sharp peak in anxiety affecting over half of the carrier women awaiting their partner's results in two step screening was conspicuously absent in this trial." (p. 1461).

Miedzybrodzka and colleagues, 1995.[94] The Aberdeen study was a comparison of stepwise versus couple screening. Randomisation was employed, but on a weekly not an individual basis. Anxiety was measured using the short form of the STAI, and anxiety data were collected from women at baseline, after test results and after delivery. An additional questionnaire was sent to carriers in the stepwise arm after their partners' results were known. The study did not assess anxiety in partners.

Screening uptake was very similar in the two arms (stepwise 1487/1641, 91%; couple 321/361, 89%). Response rates to questionnaires fell from 92% at recruitment to 82% with the test result and 77% after delivery. The response rate amongst carriers after learning their partners' results was 88% (42/48).

Women who received negative results in the couple screening arm were significantly more

anxious (STAI mean 35.1) than women receiving negative results in the stepwise arm (STAI mean 32.8) ($p < 0.001$), and this difference remained when adjustment was made for the former's slightly (but significantly) higher scores at recruitment (STAI means 34.2 and 32.7, respectively). Women who learned they were carriers in the stepwise arm had very high levels of anxiety (STAI mean 52.3) (*Table 14*).

Returning to the title of this section, it is clear from both the Edinburgh and Aberdeen studies that in stepwise screening, anxiety rises on receipt of a positive screening result. However, the question is harder to answer for people receiving negative results, as the appropriate yardstick is less clear. In the Aberdeen study, people in both arms receiving negative results had very similar scores to those recorded in their arm at baseline, but there is no information on how anxious people were before testing was proposed, and no information either on whether anxiety went up in anticipation of receiving results. The Edinburgh data leave the same questions unanswered. Anxiety might have gone down on receipt of a negative result, but that cannot be decided on the basis of the data collection schedules that these studies have employed.

Jung and colleagues, 1994.[93] Moving on to the papers which only report anxiety postresults, the German study offered stepwise screening to a mixed sample of attenders at antenatal and genetics clinics. Women were given an information letter about CF and carrier screening, together with the offer of an immediate personal consultation if they had any queries. Nobody took up this offer, and only one person out of 638 declined carrier screening. Twenty women who were screen positive attended an individual 1–2-hour counselling session, and the 18 true positives (there were two laboratory errors) all went on to have partner tests. The 20 couples "showed a high degree of anxiety", which was attributed by the authors largely to "misunderstanding of heterozygosity as an indication of fetal disease" (p. 21). Anxiety was observed to be relieved by the explanation provided in the counselling session, but "strong fears" were noted in nine cases.

Clausen and colleagues, 1996.[100] In this Danish study, two groups of women were offered antenatal CF carrier screening: those referred for CVS (usually because of maternal age) and those receiving routine antenatal care, 7400 women in all. Women were sent an information leaflet before their clinic appointment and questions were answered by the clinic nurse or midwife. A total of 6599 women accepted testing: 98% of the first group ($N = 3545$) and 80% of the second ($N = 3054$). Screen-negative women were sent a letter explaining that the most common CF mutation had not been detected, but that this did not completely rule out the risk of having a child with CF. The 172 women found to be screen positive were informed by letter and telephone call and further information and counselling were provided on that occasion. The partners of all but 10 women agreed to be tested. To assess the impact of test results, 160 carrier women and 200 randomly chosen screen-negative controls were sent questionnaires to complete on two occasions: soon after the result (although precisely when in relation to partner testing is unclear) and 14–30 months later. The response rate for the first questionnaire was 77% for the carrier group and 71% for the controls; for the second questionnaire, the figures were 76 and 70%, respectively, although the questionnaires were anonymous, so it was not possible to link the replies on the two occasions.

Women's recollections of anxiety in response to test results was assessed in the second questionnaire (i.e. a fairly long time afterwards), using a five-point rating scale, and a very large difference was found between the groups. Screen positives were more likely than controls to rate themselves as having had some (31 versus 6%) or a little (50 versus 21%) anxiety, and less likely to report having had no anxiety (11 versus 68%). The proportions of people who had been 'very' anxious were similar in both groups (7 versus 4%).

Hartley and colleagues, 1997[101] and Harris and colleagues, 1996.[102] Two other studies, one a pilot for the other, have examined anxiety in the context of offering prenatal CF screening in primary care. Women booking antenatal care were allocated alternately to stepwise or couple screening (it is unclear whether the women were aware of this). After counselling by their GP, they were given an information leaflet. If they accepted testing, they provided a mouthwash sample. Women accepting couple screening also took home a leaflet and mouthwash container for their partner; 75/76 eligible women accepted testing. The authors reported that integrating carrier testing into routine antenatal care added about 10 minutes to the consultation. All participants were given their individual result, by their GP within 5 days if screen positive, by post after 2 weeks if screen negative. Two weeks after the test

result, a questionnaire including the STAI was posted, followed by a semi-structured interview 1 month later and another 1 year later. STAI data are not reported for the pilot study,[101] and although it is noted that overall 30% of women reported at the 1-month interview having felt "a little more worried" while waiting for the test result, the implications are unclear as 42 women had undergone stepwise and 34 couple screening.

The main study[101] protocol differed from that of the pilot only by including a second leaflet specific to either stepwise or couple screening, by sending all results by post and by omitting the 1-year follow-up interview. As a result of concerns about the limited time available to obtain informed consent, the main study also included a variant in which women took home the leaflet and mouthwash tubes and returned them to the practice if they wanted the tests. Other study practices later modified their own procedures in response to the same concerns.

Overall, test uptake was 85% (529/623). Forty-two women declined the test and another 52 took information and equipment home but did not return samples. Of the 262 women allocated to couple screening, the partner's sample was not returned in 26 cases. A total of 382 questionnaires were returned, with response rates (allowing for changing eligibility) of 79 and 85% in the stepwise and couple groups, respectively.

Women's recollection of their anxiety while waiting for the test result was compared, as in the pilot, using a rating scale, but this time excluding the 10 women found to be screen positive in the stepwise group, as it was unclear which time period they were recalling. No difference in recalled anxiety was observed between non-carriers in the stepwise group and in the couple screening group, with 63 and 61%, respectively, reporting that they had been no more worried than usual.

It can be seen that the last four studies reviewed in this section do not change the conclusions drawn earlier. The German[93] and Danish[100] studies both noted high levels of anxiety in women receiving screen-positive results in stepwise programmes. The English study[101,102] does not contribute data to answering the question, however, for two reasons: STAI data were collected after all screening results had been received, not just the mother's, and the questions about recalled anxiety were about waiting for results, not reactions to results.

Does anxiety go down if further tests show the fetus is not at increased risk?

The main group of interest here are people in stepwise programmes in which the woman has been found to be screen positive, that is, to be a CF carrier. If partner results are negative, the fetus is not at increased risk, so a reduction in anxiety might be expected. If partner results are positive, the fetus is at 1 in 4 risk, and a diagnostic test would be offered. Couple screening programmes identify couples only at the stage where the baby is at 1 in 4 risk. In both types of CF carrier screening, only very small numbers of couples fall into this category, so assessments of anxiety while people are waiting for, and/or following, diagnostic test results are not included in evaluations of screening programmes. It should be noted that this is different from Down's syndrome screening, in which large numbers of women receive screen-positive results and go on to diagnostic testing, so assessments of their psychological well-being form an important part of programme evaluation.

Mennie and colleagues, 1993.[91] There were 64 carriers followed up in the Edinburgh stepwise study. They had been much more anxious than controls on learning their own carrier status. However, when they were measured after learning their partners' negative test result (the study excluded three couples in which the partner also tested positive), the carrier group did not have a higher proportion of GHQ scores above threshold than did the controls (26 and 20%, respectively, estimated from graph, down from 53 and 27% just after receiving their own screening results.) The picture was unchanged 6 weeks after the test and 6 weeks after the birth. Partners and their controls did not differ on the GHQ at any of the time points assessed. A similar pattern was seen on the Symptom Rating Test. On receiving partners' negative results, carriers' scores – which had been elevated – returned to control levels and remained there at both follow-up periods.

Livingstone and colleagues, 1994.[110] The Edinburgh study of couple screening cannot contribute data to this section, because couple screening has no phase in which a screen-positive woman has to wait for her partner's screening results. As for diagnostic tests, four screen-positive couples were found in this study and two were found to be carrying affected fetuses. The numbers are clearly too small and the circumstances too particular for conclusions about psychological state to be drawn.

Miedzybrodzka and colleagues, 1995.[94] In the Aberdeen study, women identified as carriers in the stepwise arm had had very high levels of anxiety, but this dissipated after receiving a negative result for their partners, and the new level was similar to that of women with a negative couple result (carriers' STAI mean down from 52.3 to 36.1, women with negative couple result, 35.4). There was no difference in anxiety between groups after delivery (*Table 14*).

Jung and colleagues, 1994.[93] In the German study which assessed anxiety by observation, the partners of all 18 screen-positive women were tested. Couples were given their results in a second counselling session and in 17 cases learned that the male partner had screened negative. "Considerable relief" was observed. (One couple learned that the fetus was at 1 in 4 risk. CVS at 13 weeks revealed that the fetus was homozygous for a mutant CF gene and the woman had an abortion.) The authors commented that all of the screen positives (including the couple at 1 in 4 risk) agreed that "screening was psychologically acceptable and that a positive result could be handled if adequate counselling was given to explain the disease" (p. 21). Interestingly, however, the authors also noted that offers of postnatal CF testing made to screen-positive women during pregnancy were accepted at the time but then not taken up. When they actively invited two women to a counselling session, "we had the impression that we had caused new anxiety, which then had to be addressed and dispelled, and therefore we refrained from further active approaches." (p. 22).

Grody and colleagues, 1997.[95] Thirty carriers were followed up in the study in Los Angeles after their partners' negative test results had become available. Some 70% recalled that they had been worried while waiting for their partner's result and 45% recalled that their partner had been worried during that period. However 97% said they were reassured by their partner's negative outcome and 71% said they were no longer worried about their baby's CF risk.

Clausen and colleagues, 1996[100] **and Hartley and colleagues, 1997.**[101] The Danish study[100] did not collect any information on anxiety relating to the period after partners had received their results and the English study of antenatal screening in general practice[101] used different measures of anxiety (ratings and STAI scores) at different stages in the project, so changes over time could not easily be assessed.

What methods have been tried of reducing anxiety while waiting for, or after receiving, test results?

It was stated above that most investigations of antenatal CF carrier screening have taken it as a given that women would have little prior knowledge of CF screening and that information would need to be provided. Unlike the position in Down's syndrome screening, the effects of knowledge on anxiety have not therefore been a preoccupation of researchers in the field and knowledge interventions have been evaluated in their own terms rather than as a means to an end.

However, the issue of stepwise versus couple screening must be revisited here, as the latter was proposed explicitly as a means of reducing the anxiety and attendant counselling demands, seen in the early days of stepwise screening.

Livingstone and colleagues, 1994.[110] As the Edinburgh group noted in 1994, couple screening did not produce the anxiety peak observed in screen-positive women in their earlier stepwise screening project.[91]

Miedzybrodzka and colleagues, 1995.[94] The Aberdeen study, which compared the two methods within the same project, confirmed the existence of the peak in screen-positive women, but also drew attention to anxiety levels in women who had just received screen-negative results: these were slightly but significantly higher in the couple screening arm than in the stepwise arm (STAI means 35.4 versus 32.1, $p < 0.001$).

Hartley and colleagues, 1997.[101] The English general practice-based study used a quasi-random design to compare the two types of screening and collected STAI data 2 weeks after final results had been received. These figures revealed lower anxiety in the couple group – which in this study included disclosure of individual results – than in the stepwise group (means 33.3 and 36.9, respectively, $p = 0.002$). However, it is stated in the discussion that anxiety scores were only available for 312 women, that is, that the reported means reflected 73% of women in the couple group compared with only 60% of the stepwise group, so several interpretations of the group difference are possible (*Table 14*).

The results are not as contradictory as they appear, however, for two reasons. The stepwise group in the Aberdeen comparison is made up simply of screen negatives, whereas in the English comparison the stepwise group contains, in

addition to the screen negatives, screen positives whose partners subsequently tested negative. Further, screen-negative couples in the Aberdeen programme were not given individual results, whereas in the English study there was full disclosure of the individual results of both parents.

It follows that most of the couple-screened women in the English study would have known that neither parent was a CF carrier, whereas their stepwise-screened comparators would at best have known that the woman was screen negative (but with no information about her partner), and at worst have known that she herself was screen positive (though her partner was not). In these circumstances, it is not surprising that couple-screened women were **less** anxious. In the Aberdeen study, by contrast, there was more uncertainty in women screened negative in the couple arm (either or neither parent might be a carrier) than in the stepwise arm (only their partner might be a carrier). In these circumstances, it is not surprising that couple screened women were **more** anxious.

This review has highlighted that the stepwise versus couple screening question is both difficult to research and unlikely to have one simple answer. It is not clear that participants in any of the studies knew that two sorts of programme existed and understood the differences between them. On a policy level, it could be that couple screening with full disclosure would bring the best of both worlds from the perspective of parental anxiety. Individual carrier parents would have extra information needs, but at the same time as learning they were carriers they would also learn the baby was not at increased risk, so the heightened anxiety seen in carriers in stepwise programmes would be much less likely to arise. The resource implications might be very much less in these circumstances.

Antenatal CF carrier screening and anxiety: summary and conclusions

Before summarising the effects of prenatal CF carrier screening on anxiety, three general points need to be made:

- As in many of the Down's syndrome studies, researchers into CF carrier screening have often limited the generalisability of their findings by reporting anxiety data only from people who decided to be tested.
- In assessing the effects of offering CF carrier screening, other influences on anxiety in pregnancy need to be considered.
- The way in which screening is offered (stepwise versus couple) may influence anxiety before any procedure has taken place.

The findings can be summarised as follows:

- Anxiety is clearly raised in women receiving positive screening test results compared with those receiving negative results, but evidence of an actual beneficial effect on anxiety of receiving a low-risk result is not available.
- Anxiety in women undergoing stepwise screening does fall on learning their partners' negative results. Anxiety in the longer term, and in men, has been less well studied.
- In screen-negative women, couple screening without disclosure leads to somewhat higher anxiety than stepwise screening.
- Couple screening with disclosure may lead to lower anxiety than stepwise screening, but a full evaluation has not been conducted.

Part two: other antenatal genetic screening programmes

Five papers were identified at the end of Chapter 6 which had examined knowledge in women undergoing carrier screening in pregnancy for conditions other than CF.[103–107] None of these yield substantive information about anxiety. The UK study of sickle-cell screening offered to women of African descent in the West Midlands[106] reports only that 54% (of 83 participants) had been worried to some degree about having the test.

Interestingly, anxiety was not examined in any of the papers about the Rochester Prenatal Haemoglobin Screening Project.[103,105,107,108] The authors note,[103] however, that one of the arguments against screening in pregnancy is that it is "too anxiety producing to be efficacious" (p. 450). They then conclude that one of the benefits of their programme is the "opportunity for parental reassurance in the case of fetuses found healthy" (p. 452), but do not consider the possibility that reassurance would not have been needed if there had been no screening programme. Women's receptivity in coming for counselling, and getting their partner tested, is taken as indicating that there was no need to be worried that screening in pregnancy is "too anxiety producing to be efficacious". Rather,[108] "These results indicate that, despite pregnancy, patients are highly receptive to genetic information. This is especially remarkable since the decision as to whether to ask patients for

consent to be carrier tested was in the hands of the prenatal care providers and many providers did not ask patients for consent. Thus our data is of special interest because it describes significant receptivity to genetic screening in an essentially unselected population." (p. 446). It is unclear the extent to which receptivity would have been maintained if informed consent, as it is understood today, had been sought.

Chapter 8

Understanding decision-making about prenatal genetic screening

All 52 studies included in this section referred to a measure that aimed to understand women's prenatal testing choices; 34 were concerned with Down's syndrome screening,[17,45,48,51–55,57–65,75,81–84,86,112–122] and 18 with prenatal carrier testing.[89,90,92,94,96–104,107,123–126] Seven studies employed an RCT design; five evaluated interventions offering screening information in two or more ways[48,62,63,97,124] and two that provided screening in different ways (couple versus stepwise carrier screening).[94,101]

Nine studies referred to the psychological literature when developing a measure or coding frame to assess women's decision-making strategies. Of these, five were based on expectancy-value models adapted for understanding health behaviours,[17,97,103,107,124] three on information processing theory[45,48,62] and one on feminist psychological theory.[117] As there is little similarity in the measures employed across studies, statistical integration of findings is not possible. However, the elicited decision-making cognitions were classified broadly into those assessing attitudes, perceptions of risk, perceptions of the social norm, preferences for service delivery, reasons for choices and other decision-related outcomes (*Table 15*).

About one-third of the Down's syndrome screening (11/34) and half of the prenatal carrier testing studies (8/18) compared differences in those screened with those not screened. Fifteen papers assessed cognitions associated with just one of the possible screening options, such as those that accepted screening only or only those that decided to have a diagnostic test. Most studies employed questionnaire or interview survey methods to explore women's choices, seven administered before the testing decision was made,[89,94,96,97,123,124,126] nine after testing but before receipt of results[17,45,48,90,92,107,113,115,125] and the rest after receipt of results. These variations in research design mean it is likely that many findings about cognitions during decision making were prone to some bias, either representing the cognitions associated with just one aspect of the screening process or reporting cognitions that are in some way 'readjusted' postdecision-making.

In consequence, the main methodological concerns of these studies in terms of understanding participant's decision-making are (a) few studies referred to a theory to inform the selection of measures and/or the analysis and interpretation of data, (b) a significant number of studies included only those cognitions associated with one of the consequences of being offered testing, such as those who had had testing and screened positive or those that declined testing, and (c) no studies employed information tracing techniques to assess cognitions concurrently with decision-making, most elicited cognitions retrospectively or prospectively. Despite these varied research designs, disparate measures and possible bias in reported findings, some general patterns concerning women's decision-making about prenatal testing can be discerned. Note that because of the heterogeneity of methods employed, these findings are stronger in some studies than others. These broad patterns of findings are integrated below.

Do women want prenatal testing?

Twenty-one studies elicited women's views on the value of prenatal screening, 12 for chromosomal disorders[52,53,55,57,59,60,64,113,114,117,119,121] and nine for carrier testing.[80,90,92,94,96,98,102,124,125] About 80% of women preferred to have the screening option to just the diagnostic test alternative[64,119] and would consider paying for these services.[55,104,119] Further, about 60–75% of women stated they valued prenatal testing,[52,53,59,89,92,94,96,98,113,114,117,121,124] felt it empowered and enabled women to make informed choices[57,114] and perceived it as a maternal responsibility to ensure the health of the baby.[57,114] A smaller percentage of women (about 10%) stated that prenatal testing medicalises pregnancy,[53] generates worry,[53,90,122,125] creates a false sense of control[53] and may lead to increased

stigmatising of disability in society.[53] These findings suggest that most women evaluate positively prenatal testing programmes but some have concerns of their usefulness and impact on the pregnancy experience and society.

Do we know why women choose to have or not have testing?

Evidence from two types of findings can be used to understand why women do or do not have testing: studies that ask women to generate reasons for their testing choices ('reason studies') and those that elicit women's attitudes and risk perceptions and used them to predict testing behaviour ('predictor studies') (*Table 15*). As mentioned, most studies (76%) elicited women's views after the decision had been made, using questionnaires or interviews. It is likely that these cognitions reflect women's postchoice justifications rather than those strategies employed by women when reaching their decisions. Further, the range of measures employed, samples assessed and timing of data collection have generated a wealth of evidence that varies in reliability and validity. However, some findings are consistently generated that illustrate that women hold a variety of cognitions about (not) testing. The 'reason studies' (n = 21) suggest that women have clear and different reasons for choosing to have or not have testing. The 'predictor studies' (n = 36) suggest most women evaluate the same type of decision information but the cognitions vary in strength between those who do and do not have testing. These differences in findings are summarised below.

The following reasons were generated as to why women had their tests. The large variation in the percentage of women responding across studies reflects the methodological inconsistencies between studies mentioned earlier. For example, not all women were prompted to address this issue directly within quantitative studies and, for open-ended items within quantitative surveys, not all women identified the following as a reason for having or not having a test. In consequence, the following summaries highlight issues that are a factor in women's decision-making but are unable to provide a 'weight' or an indication of degree of importance. Between 11 and 82% of women stated that testing provides information to help avoid 'nasty surprises' and inform later decisions about abortion of, or preparation for, a child with an abnormality.[51,53,57,64,82,89,90,92,96,102,113,114,122,123,125] Between 8 and 73% of women stated they needed to know for certain whether or not the child had an abnormality[51,86,92, 96,97,101] or they carried a disease gene.[89,102,125] Between 17 and 88% of women had a test for reassurance that everything was OK.[51,53,57,60,65,92,102,114,123] A small proportion (16–26%) could think of no reason not to have these prenatal or genetic tests.[51,60, 90,92,114] A small proportion (6–24%) said they were following the recommendation of a health professional or spouse.[86,89,123]

The following reasons were generated as to why women chose not to have a test. Between 17 and 71% said they would not act on[92,113,115,117] or did not want to worry about the screening result information;[92,117,123] one study reported that 3% of women just "did not want to know".[126] Between 32 and 100% of those having no test stated that they would not have an abortion.[51,89,90,96,115,117,118,123] A significant number (10–55%) stated the screening test result did not provide a definite answer and was unreliable.[51,86,113,115,117,118,123,126] Between 21 and 64% perceived their pregnancies to be at low risk of abnormality[104,115,123] and/or the abnormality not to be serious.[96,123] A smaller proportion (1–32%) referred to their own or others' poor screening experiences.[51,89,115,117] A minority (8%) referred to a lack of resources, such as child care and time, as reasons for not having testing.[104,117]

The 'predictor studies' assessed the following cognitions of women choosing to have or not have testing: attitudes towards the abnormality;[17,53,57,61,80,94,96,97,103,107,112,123] perceptions of risk of having a healthy baby or baby with an abnormality;[17,51,57,60–62,65,74,80,86,89,92, 94,96,97,103,107,123,124] perceived risks of subsequent interventions;[60,103,107,117,118] perceptions of social norms, that is, what health professionals and/or friends and family think the woman should do;[17,53,57,61,82,89,90,104,116] perceived benefits and barriers to testing;[124] attitudes or intentions to terminate;[52,58,61,65,80,92,94,100,115–117,123,126] and in the case of carrier testing, the intention to refer partner for testing.[83,103,107] In general, those having the test differed from those not having the test by holding more negative attitudes towards an abnormality, perceiving their likelihood of being a carrier/having an affected child as greater, perceiving the risks of subsequent interventions as lower, more likely to perceive others as thinking they should have the test and were more likely to intend to have an abortion.

These findings illustrate that although the reasons generated between those having and not having a

TABLE 15 *Studies assessing factors that may explain prenatal genetic testing choices and behaviours*

Attitudes: to screening programmes, termination, to abnormality, perceived seriousness	**Risk perception: of susceptibility to abnormality, miscarriage, healthy baby**	**Social norms: includes assessments of those others that may have been important in decision-maker's choice**	**Preferences for service delivery: such as how results are presented and need for more information**	**Decision-making processes: includes reasons for and against choice, deliberation and effectiveness of decision**	**Decision-making outcomes: measures such as satisfaction or regret with the choice**
Marteau *et al.*, 1992[17]	Marteau *et al.*, 1992[17]	Marteau *et al.*, 1992[17]	Carroll *et al.*, 2000[57]	Marteau *et al.*, 1992[17]	Michie *et al.*, 1997[48]
Press and Browner, 1998[50]	Santalahti *et al.*, 1998[51]	Santalahti *et al.*, 1998[51]	Statham and Green, 1993[59]	Michie *et al.*, 1999[45]	Browner *et al.*, 1996[54]
Heikkila *et al.*, 1997[52]	Carroll *et al.*, 2000[57]	Moyer *et al.*, 1999[53]	Marteau *et al.*, 2000[62]	Michie *et al.*, 1997[48]	Salonen *et al.*, 1996[55]
Moyer *et al.*, 1999[53]	Statham and Green, 1993[59]	Carroll *et al.*, 2000[57]	Hewison *et al.*, 2001[63]	Santalahti *et al.*, 1998[51]	Statham and Green, 1993[59]
Salonen *et al.*, 1996[55]	Roelofsen *et al.*, 1993[60]	Priest *et al.*, 1998[61]	Burn *et al.*, 1996[83]	Moyer *et al.*, 1999[53]	Marteau *et al.*, 2000[62]
Carroll *et al.*, 2000[57]	Priest *et al.*, 1998[61]	Santalahti *et al.*, 1998[82]	Dodds and Newburn, 1997[84]	Browner *et al.*, 1996[54]	Burn *et al.*, 1996[83]
Al-Jader *et al.*, 2000[58]	Marteau *et al.*, 2000[62]	Dodds and Newburn, 1997[84]	Leonard *et al.*, 1995[97]	Salonen *et al.*, 1996[55]	Witt *et al.*, 1996[92]
Priest *et al.*, 1998[61]	Evans *et al.*, 1988[75]	Jan *et al.*, 1996[86]	Harris *et al.*, 1996[102]	Carroll *et al.*, 2000[57]	Mennie *et al.*, 1993[98]
Santalahti *et al.*, 1996[80]	Santalahti *et al.*, 1996[80]	Mennie *et al.*, 1992[89]	Rowley *et al.*, 1988[103]	Al-Jader *et al.*, 2000[58]	Clausen *et al.*, 1996[100]
Santalahti *et al.*, 1998[82]	Mennie *et al.*, 1992[89]	Livingstone *et al.*, 1993[90]	Press and Browner, 1997[114]	Statham and Green, 1993[59]	Hartley *et al.*, 1997[101]
Mennie *et al.*, 1992[89]	Witt *et al.*, 1996[92]	Clausen *et al.*, 1996[100]	Phillips *et al.*, 1998[119]	Roelofsen *et al.*, 1993[60]	Harris *et al.*, 1996[102]
Livingstone *et al.*, 1993[90]	Miedzybrodzka *et al.*, 1995[94]	Wallerstein *et al.*, 1994[104]	Fairgrieve, 1997[120]	Priest *et al.*, 1998[61]	Santalahti *et al.*, 1999[116]
Witt *et al.*, 1996[92]	Cuckle *et al.*, 1996[96]	Press and Browner, 1997[114]	Jorgensen, 1995[121]	Santalahti *et al.*, 1998[82]	Mennie *et al.*, 1994[125]
Miedzybrodzka *et al.*, 1995[94]	Leonard *et al.*, 1995[97]	Jorgensen, 1995[115]	Browner and Press, 1995[122]	Jan *et al.*, 1996[86]	
Cuckle *et al.*, 1996[96]	Rowley *et al.*, 1988[103]	Santalahti *et al.*, 1999[116]		Mennie *et al.*, 1992[89]	
Leonard *et al.*, 1995[97]	Rowley *et al.*, 1991[107]	Markens *et al.*, 1999[117]		Livingstone *et al.*, 1993[90]	
Clausen *et al.*, 1996[100]	Markens *et al.*, 1999[117]	Loader *et al.*, 1996[123]		Witt *et al.*, 1996[92]	
Harris *et al.*, 1996[102]	Esen and Olajide, 1997[118]			Cuckle *et al.*, 1996[96]	
Rowley *et al.*, 1988[103]	Loader *et al.*, 1996[123]			Leonard *et al.*, 1995[97]	
Rowley *et al.*, 1991[107]	Fang *et al.*, 1997[124]			Hartley *et al.*, 1997[101]	
Hall *et al.*, 2000[112]				Harris *et al.*, 1996[102]	
Jorgensen, 1995[115]				Wallerstein *et al.*, 1994[104]	
Santalahti *et al.*, 1999[116]				Kornman *et al.*, 1997[113]	
Markens *et al.*, 1999[117]				Press and Browner, 1997[114]	
Phillips *et al.*, 1998[119]				Jorgensen, 1995[115]	
Loader *et al.*, 1996[123]				Esen and Olajide, 1997[118]	
Fang *et al.*, 1997[124]				Phillips *et al.*, 1998[119]	
Mennie *et al.*, 1994[125]				Browner and Press, 1995[122]	
Mennie *et al.*, 1993[126]				Loader *et al.*, 1996[123]	
				Mennie *et al.*, 1994[125]	
				Mennie *et al.*, 1993[126]	

test differ and appear distinct, those choosing to have or not have a test evaluate the same decision attributes. It is likely that the verbal justifications or reasons for a choice do not access or represent the cognitions that underpin the testing behaviour. It is important to note that although there are similar patterns of findings to those in research about the prenatal diagnosis decision, screening decisions are not predictive of diagnostic testing and/or termination choices.[114] It is likely that similar decision attributes are evaluated for each of these prenatal choices, such as attitudes and risk perceptions towards abnormality, but aspects of the different decisions will vary and/or change over time. For example, screening tests are non-invasive so few studies in this review evaluated women's views towards procedure-related miscarriage; attitudes and risk perceptions towards abnormality may change upon receipt of a screen-positive result.

Are women making informed decisions?

A decision is said to be informed when the relevant information about the advantages and disadvantages of all the possible courses of action is evaluated in accord with the decision-maker's beliefs, in order to reach a decision and take steps to make a choice.[22,72,127,128] This definition is based on a model of effective decision-making that judges decision quality on the way in which a decision is made and not on attributes of the final choice. Currently there is no published questionnaire-based measure that assesses the quality of the decision process, that is, informed decision-making. However, some cognitions are associated with the employment of a more thoughtful and/or effective decision-making process: awareness of decision-relevant information; accuracy in individual's risk perceptions; degree of systematic processing; stability in individual's values over time; satisfaction with the decision; and perceived decisional conflict.[48,74,127,129,130,131,132] Although no studies within the review explicitly measured informed decision-making, there is evidence from these types of cognitions to assess the degree to which women were making informed choices about prenatal testing.

As summarised in previous chapters, it is clear that women value the opportunity to make informed testing choices and, when asked directly, most women (65–93%) state that their choices were informed.[59,64,98,102] However, it is evident that women's understanding of screening is poor and not based on an accurate evaluation of the decision-relevant information (see Chapters 4 and 6). Further, few women (6–15%) deliberated about the testing information before making their choice[45,48,54,55,60,86,114] and women varied in the degree to which they made up their own minds about testing (between 21 and 86%).[82,84,86,115] Some studies documented that health professionals explicitly stated that testing was the woman's choice and voluntary,[65,82] whereas others found evidence of some women (3–17%) being persuaded by staff and significant others about their choice.[84,100,115] A number of studies[58,60,82,90,100–102,114–116] also reported that between 2 and 28% of women found it difficult to decline these screening tests when offered by health professionals. Finally, between 10 and 42% of women found making these choices difficult and requested more support and/or time when making these testing choices.[57–59,82,102,114,116]

These results and those integrated in previous chapters indicate that most women are not evaluating complete decision-relevant information in accord with their beliefs before making their screening choices, that is, most are not making informed choices about screening. Further, although women want to make informed choices and, when questioned directly, state that their choices were informed, there is evidence that women do not have the necessary understanding about prenatal tests to have made an informed choice. In addition, many women reported that they did not deliberate about the decision and some actually requested help with making a choice. These findings suggest there to be a gap between women's desire to make informed choices with their awareness of what constitutes an informed decision and the skills with which to achieve it. Although studies have assessed interventions aimed at improving the quality of information women receive about testing,[48,62,63,97,124] few, if any, have evaluated interventions aimed at aiding women's decision-making about prenatal screening.

Are informed decisions good for decision-makers?

There is a paucity of evidence within the medical decision-making literature that has assessed both informed decision-making and outcome measures.[72] What evidence there is from associated literature suggests it is likely that more informed decisions result in better postdecision

outcomes.[72,133] As mentioned, the studies in this review did not assess informed decision-making but some evaluated aspects of decision effectiveness. These findings are discussed below.

When asked, most women (over 92%) stated they had made the right choice and were satisfied with their choice,[48,54,92,101] but between 3 and 30% of those screening positive expressed regret about their screening decision.[55,83,98,100,102] In addition, those women who were more satisfied with their choices were also more falsely reassured and made their choices less systematically – as measured by a three-item questionnaire – than women with slightly lower satisfaction scores.[48,54,134] However, those making decisions more systematically and reporting greater knowledge rated higher on worry scales.[48,63] These results suggest that making more informed decisions may be associated with increased anxiety. This finding is consistent with the decision-making literature that states that more effective decision-making strategies require individuals to be more alert and, therefore, to have raised anxiety during decision-making.[74] One hypothesis that would fit these data is that focusing on the cognitions and emotions during decision-making is experienced as more demanding or less satisfying than using a simpler cognitive strategy (heuristic).[74] However, this more systematic evaluation of decision information is necessary to make informed decisions and is associated with reductions in false reassurance and increases in decisional satisfaction.[74]

Summary

Of the 52 studies assessing aspects of participants' decision-making about prenatal genetic screening, only eight (17%) were informed by a decision-making theory, 18 (35%) assessed both the choice to have or not have a test and six (11%) assessed prechoice cognitions. There was little consistency in measures employed across studies. Further, it is likely that some of the elicited cognitions were not appropriately represented within these data and others were subject to 'cognitive readjustments' or postchoice bias. However, it is evident that general patterns of findings were observed. First, the factors predicting, and reasons generated for, (not) having a test were similar for both Down's syndrome and carrier screening. Second, overall participants have favourable attitudes towards screening but report ambiguous or conflicting evaluations of the role of screening and the information it provides to the individual and society. Third, a significant proportion of women are not making fully informed decisions about screening and/or prenatal carrier testing but are relying on simpler heuristics to make the choice such as reassurance and/or recommendations from health professionals.

It is worth reiterating that the original research questions of the studies included in this chapter were not necessarily concerned with assessing and/or facilitating informed choice. It is fair to say that early studies were concerned with (a) ascertaining the acceptability of prenatal screening to the general population, (b) identifying the predictors that explained why women did (not) have testing and (c) monitoring the iatrogenic consequences of being offered and/or undergoing testing. Definitions of informed, and measures of effective, decision-making have only been available since the mid to late 1990s.[22,130,131,135] Today, researchers and service developers are explicitly concerned with identifying measurable aspects of understanding and/or informed decision-making in order to design and evaluate appropriate interventions.[34,35,72,135] One future direction is to establish the relationship between increased understanding and informed choice with individuals' satisfaction with screening and screening decisions. In addition, there needs to be a more thorough investigation of the changes required to enable professionals and patients to adopt the informed model of patient–professional interaction.[128] What evidence there is within this chapter suggests women are not fully aware of the 'active participant' role they are required to adopt,[128,135] and evidence from other sources suggests that professionals are not sufficiently trained to enable this role.[72]

Chapter 9
Newborn screening

As we saw in Chapter 3, the focus of nearly all the investigations of newborn screening has been the effects of true-positive or false-positive results. In contrast to the situation with prenatal screening, there is very little available information about pretesting and process issues, although a number of studies do draw attention to process with regard to the giving of results. Similarly, decision-making and uptake tend not to be variables of interest because these are taken as givens. Hence, 'informed consent', which has become such an important issue in other arenas, especially with regard to genetic testing, has received very little study in the context of newborn screening. In a number of cases, notably in the USA, participation in the programme was mandatory. Elsewhere, mandatory testing has been resisted. In a recent case in Ireland where a couple refused PKU testing for their infant, their right to refuse was upheld by the Irish Supreme Court,[136] even though the judges considered their decision to be "manifestly unwise and disturbing" (p. 1149).

As described in Chapter 3, the most commonly measured variables have been knowledge, anxiety, other affects and attitudes. Virtually all studies have focused on one specific disorder, such as CF or hypothyroidism (see *Table 2*). This is despite the fact that the sample on which the result will have been based will also have been used for testing for other disorders such as PKU (see below).

The emphasis of different studies has been different for different disorders, partly as a result of different false-positive rates. Where false-positive rates are high, as in the early days of hypothyroidism and CF screening, studies have focused on false-positives, but otherwise the main focus of attention has been on true-positives. Within this subgroup, four of the studies concerned specifically with CF[111,137–139] have made comparisons between those detected by newborn screening and those detected symptomatically at a later stage.

A number of studies have followed up parents over a period of time – often a number of years – after the receipt of test results. *Table 16* shows the timing of data collection from parents in 28 newborn screening studies.

The disorders and screening scenarios

The papers reviewed cover screening programmes for a wide range of disorders. This section will describe the salient features of the disorders and the screening scenarios.

Phenylketonuria

Newborn screening for PKU is the most widely used genetic screening test in the world. It is therefore notable that we found no studies which looked at parents' responses to the process or results of PKU screening and only a very small number looking at knowledge and attitudes to Guthrie testing in general.[28,140,141] One reason for this may be that the test is unusual in having virtually no false-positives or false-negatives (but see below). This is because the test is a direct test for phenylalanine, rather than using a marker as many screening tests do. Therefore, it is effectively diagnostic. Although PKU is a genetic (single gene) disorder, it does not lend itself to DNA analysis because there are over 700 probable disease-related mutations. Nowadays phenylalanine is tested by tandem mass spectrometry and many other disorders can, in principle, be detected at the same time.

In the UK and most of Europe, blood for the Guthrie test is taken when the baby is about 5 days old. Earlier than this could cause false-negative results because blood phenylalanine concentrations of PKU children are not elevated at birth owing to equilibration with maternal blood *in utero*. This has apparently caused occasional problems in the USA where screening is typically carried out before the baby leaves hospital, often within the first 24 hours. The same blood spot (or a second sample taken at the same time) is often used to test for other disorders, most commonly congenital hypothyroidism (see below), which has been routine in the UK since the late 1970s.

Cystic fibrosis

Newborn screening programmes for CF have been ongoing from the early 1980s and eight papers have reported on psychosocial aspects: two from Australia, one from the UK and five from the USA. Four of the American papers[137,142–144] arise

TABLE 16 *Timing of data collection from parents in 28 neonatal screening studies*

Authors, year	Condition	Sample size	Timing of data collection	Age of child at any subsequent follow up
Statham *et al.*, 1993[28]	PKU (Guthrie)	1387	Children aged ~6 weeks	
Al-Jader *et al.*, 1990[111]	CF	58	1–4 years after diagnosis	
Baroni *et al.*, 1997[137]	CF	98	children <10 years old (different for different groups)	
Boland and Thompson, 1990[138]	CF	58	~2–2.5 years after screening/diagnosis (unscreened comparison group mean age >8 years)	
Helton *et al.*, 1991[139]	CF	92	Range: 4 days–5 years after diagnosis for neonatal screened group, 3 days–10 years postdiagnosis for unscreened group	
Holtzman *et al.*, 1983[140]	PKU (Guthrie)	628	Either preconsent procedure for screening or postconsent	
Faden *et al.*, 1982[141]	PKU (Guthrie)	628	Either preconsent procedure for screening or postconsent	
Mischler *et al.*, 1998[142]	CF	415	After sweat test result (~3 months)	1 year and at end of study (children aged <1–9 years)
Tluczek *et al.*, 1992[143]	CF	104	After positive result of IRT and before results of sweat test	1 year
Tluczek *et al.*, 1991[144]	CF	115	Either at 6 weeks or 4 years old	
Bodegard *et al.*, 1983[145]	Hypothyroidism	102	Children aged 6–12 months	6–12 months
Fyro and Bodegard, 1988[146]	Hypothyroidism	11	1–4 years after screening	
Fyro and Bodegard, 1987[147]	Hypothyroidism	16	At the time of retesting (children aged 23–30 days)	6–12 months, 4–5 years
Fyro, 1988[148]	Hypothyroidism	102	At the time of retesting (23–30 days after birth) (results then given by telephone 7 days later)	6–12 months after birth. Information also collected from a variety of official records up to age 5 re health, parents' marital status, etc.
Tymstra, 1986[149]	Hypothyroidism	31	4–12 months after screening	
Hildes *et al.*, 1993[151]	DMD	11	3–6 years after diagnosis	
Parsons *et al.*, 1996[152]	DMD	41	~6 months postscreening	
Bradley *et al.*, 1993[153]	DMD	9	~6 months postscreening	
Grossman *et al.*, 1985[154]	Sickle-cell disease	91	Soon after neonatal diagnosis, both before and after counselling	4–8 months
Warren *et al.*, 1982[155]	Sickle-cell disease	18	Children aged ~2 years	
Yu *et al.*, 1999[156]	Type 1 diabetes	88	Children aged 5–7 weeks (baseline)	4–5 months after results
Senior *et al.*, 1999[157]	Hypercholesterolaemia	24	1–10 days after children identified as high risk	
Thelin *et al.*, 1985[158]	ATD	107	5–7 years after test result	
Sveger and Thelin, 1981[159]	ATD	40	4 years after diagnosis	
Sorenson *et al.*, 1984[160]	Multiple rare disorders	60	After specimen for repeat test collected	After test results for repeat specimen given (within 14 days)
Thelin *et al.*, 1985[162]	ATD	214	5–7 years after test result	
Thelin *et al.*, 1985[163]	ATD	214	5–7 years after test result	
Dudding *et al.*, 2000[164]	CF	87	Information not given but presume 1–16 years postdiagnosis	

from the Wisconsin study, which was carried out in the context of an established newborn screening programme testing for PKU, galactosaemia, maple syrup urine disease and hypothyroidism. State law required that all neonates be tested, refusal being allowed only on religious grounds. Immunoreactive trypsinogen (IRT) was added, experimentally, as a free-of-charge optional extra in 1985 to screen for CF. Infants with a screen-positive IRT result were then called for a sweat test. Some 13% of these (46/369) were positive, that is, for the remaining 87% the result was a false-positive. IRT is a non-genetic marker for a genetic condition, but following the identification of ΔF508 in 1989, it became possible to couple the IRT assay with DNA analysis, which improved the sensitivity and increased the positive predictive value to 16% (21/132). This procedure has the side-effect of also identifying heterozygotes, that is, children who are not themselves affected but who are CF carriers.

The Wisconsin study aimed to assess the benefits and risks of newborn screening and to determine if early diagnosis would improve the prognosis of children with CF. To this end, all children were screened (unless their parents objected on religious grounds), but half were randomised to a delayed disclosure arm, that is, the CF screening result was not disclosed until the child was 4 years old or became symptomatic, whichever occurred first.

Congenital hypothyroidism

Congenital hypothyroidism is not generally considered to be a 'genetic' condition. However, we have included it in the section on newborn screening for the reasons described in Chapter 1. Five papers describe sequelae of screening programmes for congenital hypothyroidism. All are concerned only with parents who had false-positive results. Four papers are from the same group of Swedish authors[145–148] and the fifth is Dutch.[149] Three of the Swedish papers[145,147,148] report on the same group of parents. These were part of an integrated pilot newborn screening programme for congenital hypothyroidism carried out in the mid–late 1970s. At this time the positive predictive value of the initial screen was only 5%, that is, 95% of screen positives were actually false-positives. This is also the rate cited for the Dutch programme. By the time of the second Swedish study[146] (1979–81), technical refinements had raised the positive predictive value to 50%.

α_1 Antitrypsin deficiency (ATD)

α_1 Antitrypsin is a blood protein, and a deficiency carries a high risk for chronic obstructive lung disease in adulthood. The risk can be diminished considerably through avoidance of concentrated air pollutants, especially cigarette smoke. Nation-wide newborn screening for ATD was conducted in Sweden from 1972 to 1974, but discontinued thereafter owing to paediatricians' observations that the early identifications of ATD appeared in some cases to have notably negative psychological effects on the parents and the parent–child relationship. The important characteristic to note is that ATD carries a risk for adult ill health, but those affected are not necessarily ill as children (although a small number have liver problems). Furthermore, the action to be taken in the event of a positive screen is primarily a modification of parental health behaviour (not smoking) rather than anything with which the child needed to comply such as a reduced diet (PKU) or taking tablets (hypothyroidism).

Duchenne muscular dystrophy (DMD)

DMD is an X-linked recessive genetic disorder which has an incidence of <1 in 4000 of live-born males. Wasting and muscle weakness are progressive so that the majority of boys are in wheelchairs by the age of 10 and very few survive beyond their late teens. There is no treatment that can materially alter the course of the disorder. The rationale for newborn screening is not therefore primarily to benefit the child but to benefit the family in that earlier diagnosis of affected boys leads to greater opportunities for reproductive choice, including earlier identification of carrier female relatives. It also spares parents the distress of the diagnostic delays that are typical.[150] About one-third of cases are the result of a new mutation in the affected boy and in another one-third the mother carries a new mutation. In the remaining one-third of cases the mother will have inherited the gene from her own mother, in which case other female relatives may also be carriers.

Newborn screening has been possible since 1975, but has not been widespread because of doubts about its benefits, given the untreatable nature of the disorder. Two newborn screening programmes have reported psychosocial findings, one in Manitoba in Canada (1986–89)[151] and the other in South Wales (1990–92).[152,153]

Haemoglobinopathies

Newborn haemoglobinopathy screening is limited to sickle-cell disorders. There is very little information available about parents' experiences of newborn screening for sickle-cell disorders, which is a particularly notable omission since such screening programmes are widespread for people

of Afro-Caribbean origin. Two eligible studies were identified,[154,155] one in New York State in 1975–77 and the other in Baltimore in 1980–81. Like CF, sickle-cell disorders are recessively inherited. Thus a child can only be affected if both parents are carriers. As with the later CF programmes, DNA analysis means that the 'false-positives' identified by the screening process are heterozygotes (carriers). These infants are in a different situation to the 'false-positives' for, say, congenital hypothyroidism, because their genetic status does have possible reproductive implications both for the child and for the parents, even though the child is not ill. At the time of these studies, not all newborn screening programmes were informing parents of carrier 'trait' results.

Other disorders

Just two studies have reported on the effects of a genetic screening test for **susceptibility** to a disease: type 1 diabetes[156] and cardiovascular disease[157] [although it could be argued that ATD (see above) falls into this category]. Unlike the other screening programmes described, the purpose of these two programmes was primarily to identify a cohort of high-risk newborns for scientific study rather than to benefit directly either the children or the families.

What do parents know before testing?

Only one study has collected data from parents before testing.[140,141] This was an investigation which took place in the USA, in 1978, when the State of Maryland introduced mandatory informed consent for newborn screening (PKU, hypothyroidism, branched-chain ketoaciduria and homocystinuria). Women were randomised to be interviewed either before or after having been through the consent procedure. There were no significant differences between groups in their attitudes as to the necessity for consent to be given: 80% felt that consent was not necessary although most still wanted to be informed that the test was being carried out. There was strong evidence that women had gained a substantial amount of information from the consent form. Women with higher knowledge scores were more likely to think that testing should be mandatory, that is, that consent should not be sought. There were significant differences in the knowledge scores of women at different hospitals, which the authors ascribe to differences in the timing of seeking consent.[140] Only 0.05% of mothers refused screening (27 out of 50,000). Interviews were sought with these women, although most could not be located or declined to be interviewed. Among the seven who were interviewed, reasons for declining testing generally showed misunderstandings, for example, that there was no need for the test because the child was healthy.[141] The authors argue[140] that **informing** and **consent** should be distinguished and that only the former is appropriate in this context.

What do parents know after testing?

A British study[28] collected data from mothers when their babies were 6 weeks old, but was also primarily concerned with informed consent issues rather than effects of screening. Participants were 1387 mothers sampled from nine districts in south-east England in 1990 who were asked to indicate which of a number of conditions listed the test covered. Most women believed the test to have been fully explained. However, knowledge about which conditions were tested for was very poor, particularly among younger and less educated women. Multiparas were no better informed than primiparas. The majority of the sample failed to identify PKU, hypothyroidism and CF (which babies in six of the districts would have been screened for) but, conversely, many believed that the test detected more disorders than it could. The authors conclude that this clearly challenges any notion that women are giving informed consent for their babies to be tested.

An American study of 104 parents with false-positive CF results[143] had similar findings regarding parents' low levels of knowledge and also found better educated parents to be more knowledgeable.

Table 17 summarises the findings regarding knowledge and information from parents of children who were confirmed either as true-positives or false-positives in ten studies.

It is virtually impossible to sum up the data reported since the 'knowledge' being assessed is so variable and will have been asked in a variety of ways. In one study, for example,[157] 93% of respondents said that they wanted more information, suggesting either a very severe lack of information or a question phrasing that made it easier to say 'yes' than 'no' (or both). It is possible that a similar result could have been generated in other studies had the same question been asked. However, only three of the studies represented in the table have particularly highlighted poor levels

TABLE 17 *Summary of findings regarding knowledge and information from ten papers studying parents after neonatal screening results*

Authors, years	Condition and place of publication	Findings	Notes
Mischler *et al.*, 1998[142]	CF (Wisconsin)	In false-positive families, 95% understood at the time that their child definitely did not have CF, and 92% 1 year later. True positives: at 3 months 90% could correctly identify recurrence risk (97% at 1 year). Most, but not all, parents of carriers retained and understood this information	
Tluczek *et al.*, 1992[143]	CF (Wisconsin)	The majority of families (73%) knew of neonatal screening. Significant relationship between knowledge and level of education. Telephone communication leads to more misunderstanding than face-to-face communication	
Tluczek *et al.*, 1991[144]	CF (Wisconsin)	Parents of children in early disclosure group were much more knowledgeable than those told 4 years after test took place. Parents informed of negative sweat test result by telephone had significantly lower understanding than those informed face-to-face	
Tymstra, 1986[149]	Hypothyroidism (Netherlands)	Parents often did not understand the events surrounding the screening very well. Health professionals did not give sufficient information. Those who screened false-positive were dissatisfied with the service and were still bothered by questions and insecurities	
Hildes *et al.*, 1993[151]	DMD (Manitoba)	All 9 responders correctly knew the basic facts about DMD although only 7 out of 11 had correct recall of their own carrier status	
Grossman *et al.*, 1985[154]	Sickle-cell disease (Baltimore)	Knowledge levels increased after counselling but parents who chose not to be counselled were better informed at baseline than those who were counselled. Demographic variables were not predictive of postcounselling knowledge scores	
Warren *et al.*, 1982[155]	Sickle-cell disease (New York state)	Almost all parents knew the name of their child's condition, that painful crises could occur, that the child would be susceptible to infections and that they should telephone the physician when the child became ill. Two-thirds were able to state the recurrence risk but not all of those could explain what that meant	
Thelin *et al.*, 1985[158]	ATD (Sweden)	63% of mothers and 59% of fathers thought ADT posed an immediate and possibly serious threat in childhood. Half of parents had negative views about how they were informed of diagnosis. Over two-thirds had negative attitudes towards the amount of information provided. Lack of information was reported to contribute towards negative affect in 25% of parents	Follow-up data collected when children aged 5–7 years
Sveger and Thelin, 1981[159]	ATD (Sweden)	44% still lacked understanding of the condition. Half knew further children had 25% risk of having ADT. 20% knew child also had PKU testing. 93% requested that more information about the condition be given	Parents of 4-year-olds detected via neonatal screening
Sorenson *et al.*, 1984[160]	Multiple genetic disorders (Boston)	45% knew initial test was abnormal. 55% had not been told the reason for the repeat test. 36% of parents expressed concern about the child's health, around half of these expressing great concern. This was not related to parents' knowing the reason for the repeat test but was related to perceived lack of information	Parents of children with false-positive results

of knowledge: the Dutch hypothyroidism study,[149] the ATD study[158,159] and Sorenson and colleagues' study, which covered a range of rare genetic disorders.[160] The Swedish hypothyroidism studies do not appear in the table because they did not assess knowledge, but the later one[146] did report that the majority of parents felt that they had received no information and were unprepared for the test results. Sorenson and colleagues' study[160] similarly highlights lack of information as parents' main complaint about the screening process.

The Baltimore sickle study[154] was investigating the feasibility of informing and counselling the parents of all children found to be heterozygotes. Only 32/91 were in fact counselled. Pre- and post-tests demonstrated an increase in knowledge as a result of counselling. Interviews at 4–8 months showed that counselled parents had retained their knowledge. The scores of uncounselled trait parents were higher than the precounselling scores of the counselled parents but there were no differences at follow-up. Hence those who do not attend for counselling may in these circumstances be those least in need because they have other sources of information.

One CF study[143] highlights the effect of the method of conveying diagnostic results following a (false) positive screen. There were two participating centres. At Centre A, parents waited at the clinic for the sweat test result, which they were then given face-to-face. At Centre B, parents were telephoned at home later with the result. Whereas all parents from Centre A correctly reported that the sweat test result was normal and that this meant that their child did not have CF, six parents from Centre B had not understood that their child did not have CF.

Anxiety and other emotional responses

It is generally assumed both that the receipt of positive newborn screening results engenders anxiety and that good practice can reduce this. In this section we will examine the research evidence relating to these assumptions.

In contrast to the prenatal screening literature, where the use of the Spielberger State Trait Anxiety Inventory is widespread, this scale was used by only one of the neonatal studies.[138] Two studies[137,156] used the Parenting Stress Index. It is not clear how appropriate this may have been in the study where the children were only a few months old.[156] The fact that 25/88 respondents omitted at least one item may be suggestive. In all other cases where anxiety or other affective outcomes were reported this was on the basis of parents' self-report, usually retrospective, either in a questionnaire or interview, and cannot be compared across studies.

Table 18 summarises the findings of those papers which reported on anxiety or other emotional responses.

Most studies on the effects of newborn testing cite an early paper by Rothenberg and Sills[161] on 'Iatrogenesis: the PKU anxiety syndrome'. This was published in 1968 and is not a research study but reported on the authors' clinical experience in New York City with parents who had had continuing anxiety following an initial false-positive result. These doctors reported that they were dealing with this first by warning parents at the time of testing that results could be false-positives and second by:

> "an intensive follow-up programme … in which paediatricians with psychiatric consultation provide ongoing opportunities for the parents … to ventilate their feelings and receive support and reassurance until their anxiety has been properly controlled. (The mothers, for example, are able to observe, with the paediatrician, the landmarks of their babies' normal growth and development and see the evidence that retardation is not present)" (p. 692).

What they describe, therefore, is a support programme with major resource implications since approximately 90% of initial positive results in that programme were false-positives. Unfortunately, these authors do not seem to have published any evaluation of their support regime or otherwise reported on its efficacy.

The earliest American study[160] looking at parental anxiety was in the context of the Massachusetts Newborn Screening programme. Sixty parents of infants recalled for retesting after an equivocal newborn screening result were interviewed twice: once after retesting and again after the retest result was given. (Those with an abnormal retest result were excluded from the study.) About 45% of the parents understood that the retest was necessary because the first result was abnormal. The remainder believed retesting to be routine or the result of an error or were told nothing specific. There were no differences between these groups in terms of anxiety or depression (assessed by the Multiple Affect Adjective Checklist) or belief that there might be something wrong. Similarly,

TABLE 18 *Summary of findings related to anxiety and other affective outcomes from 15 papers studying parents after neonatal screening results*

Study	Location	Findings	Notes
False positives: Hypothyroidism			
Tymstra, 1986[149]	Netherlands	The suspicion of thyroid deficiency was a great strain on parents; this adversely affected the parent/child relationship. Those who screened false positive were dissatisfied with the service and were still bothered by questions and insecurities.	4–12 months after screening
Bodegard *et al*., 1983[145]	Stockholm	Strength of emotional reaction negatively related to coping ability.	4 years after screening. Same parents as Fyro and Bodegard, 1987[147]
Fyro and Bodegard, 1987[147]	Stockholm	'Integration' shown in most families. Nine out of 12 children who showed no distress had integrated parents: while eight out of 12 parents of disturbed children had unsatisfactory integration.	4 years after screening. Same parents as Bodegard and colleagues, 1983[145]
Fyro and Bodegard, 1988[146]	Stockholm	Ten out of 11 families reacted strongly – felt they had received no information and were unprepared for the test results. Six out of 11 had increased concern for the infant while awaiting results of follow up.	1–4 years after screening. Later study by same authors as Bodegard *et al.*, 1983[145] and Fyro and Bodegard, 1987[147] different parents, different screening protocol
False positives: cystic fibrosis			
Baroni *et al*., 1997[137]	Wisconsin	Parents of false +ve children generally had *lower* scores than other groups (i.e. better emotional well-being).	Comparison of screened and conventionally diagnosed children and false positives and healthy controls for each of these groups. Up to age 10.
Tluczek *et al*., 1991[144]	Wisconsin	Children whose parents were still anxious following a negative sweat test were more likely to have had a low Apgar score at birth. Delayed disclosure group just as likely to express anger as anxiety when given result. Parents in both groups reported negative emotional response to +ve result. Response to delayed disclosure: anger at being misled, fear that child affected, anxiety and grief, although some reassured because child was asymptomatic.	Trial in which disclosure of positive test result delayed for half the parents until child symptomatic or age 4
Tluczek *et al*., 1992[143]	Wisconsin	Most parents reported strong emotional responses to the initial IRT result. Increased anxiety about seeing the baby in the 3 days awaiting sweat test results; emotional responses of shock and depression. Those with lingering concerns about CF after sweat test had lower Apgar scores.	False positives

continued

TABLE 18 *Summary of findings related to anxiety and other affective outcomes from 15 papers studying parents after neonatal screening results (cont'd)*

Study	Location	Findings	Notes
False positive: multiple genetic disorders			
Sorenson *et al*., 1984[160]	Boston	Both anxiety and depression scores significantly less after retesting for both groups. No significant difference between those who understood reason for repeat test and those that didn't at either first or second interview. 36% of parents expressed concern about the child's health, around half of these expressing great concern. This was not related to general anxiety/depression.	False positives. Two groups: those who understood reason for retesting and those who did not.
True positives: inherited α_1 antitrypsin deficiency			
Sveger and Thelin, 1981[159]	Malmo	20% reported shock or depression on first being told. At 4 years 12% felt depressed, 6% felt guilty. 26% indifferent, 12% relieved. 50% viewed early diagnosis positively, 5% viewed it negatively, remainder ambivalent. Between 32% and 49% of parents still smoked despite risk to child.	4 years after testing. Same parents included in the sample for Thelin and colleagues, 1985.[158]
Thelin *et al*., 1985[158]	Malmo	78% of mothers and 58% of fathers had an immediate negative emotional reaction to the diagnosis. 86% of mothers, 43% father reported very strong negative emotions. 30% of mothers and 44% of fathers reported the reactions lasted for more than a year. The emotional reactions of parents who were aware that their child had some condition at the first contact and those that didn't were comparable. Lack of information was reported to contribute towards negative affect in 25% of parents.	5–7 years after testing. Includes some of the same parents as Sveger and Thelin, 1981[159]

continued

TABLE 18 *Summary of findings related to anxiety and other affective outcomes from 15 papers studying parents after neonatal screening results (cont'd)*

Study	Location	Findings	Notes
True positives: CF comparison between neonatal and traditional symptomatic diagnosis			
Baroni *et al*., 1997[137]	Wisconsin	Parents of children diagnosed through screening were more likely to have 'at risk' scores.	Comparison of screened and conventionally diagnosed children and false positives and healthy controls for each of these groups.
Boland and Thompson 1990[138]	New South Wales	Mothers in screened symptomatic group scored significantly lower on 'fostering dependency' scale. Mothers in screened asymptomatic group scored significantly higher on intrusiveness scale. In unscreened infants, mothers desire to foster dependency decreased with length of delay in diagnosis. Absence of observable symptoms at diagnosis did not appear to increase mothers' protectiveness as indicated by anxiety scale.	Three groups of children with CF: those screened as newborns subdivided into those now symptomatic and those not, plus unscreened symptomatic.
Al-Jader *et al*., 1990[111]	Wales	A total of 11 out of 29 parents experienced diagnostic delays resulting in 'extreme anxiety' – nine were in the screened group.	Sample included both screened and conventionally diagnosed children.
Helton *et al*., 1991[139]	Colorado	No significant differences between groups on their report of depression and anxiety at the time of diagnosis, most rated it a time of high anxiety whenever it occurred.	Comparison of screened and conventionally diagnosed children.
True positives: diabetes type 1 predisposition			
Yu *et al*., 1999[156]	Colorado	Median change in parenting stress score was not significantly associated with any of the independent variables measured in the study including risk status.	'Parenting stress' measured at 4–5 weeks (before test results known) and 4–5 months after results. Groups were high ($N = 3$) or moderate ($N = 20$) risk vs low risk ($N = 65$).

whether the parents had been contacted specifically about the need for retesting or had been informed at a routine visit made no difference.

The authors interpret this as evidence that telling parents the reason for retesting does no psychological harm. Indeed, lack of information was parents' main complaint about the process and this was associated with concern about the child's health after retesting, even if there had not been concern at the first interview. The authors make the point that some parents will need to be told more than just the results of the test; they also need contextual information about the screening process in order to make sense of that. This is an important point. As we have seen with studies of antenatal screening, there is considerable variation between studies in what knowledge is assessed and therefore, one presumes, in the items of information that it is considered desirable for parents to have.

The other early report on anxieties engendered by newborn screening comes from the Swedish newborn ATD screening programme. It was only after the programme had been discontinued (on the grounds of the anxiety that it was causing to parents) that psychological follow-up of the parents was undertaken,[158,159,162,163] and parents accounts of the screening process are therefore necessarily retrospective. Data have been reported, by the same group of authors, on two groups of parents of children diagnosed with ATD through the newborn screening programme. Three papers[158,162,163] all report on the same group of parents of 61 children 5–7 years after testing. An earlier paper[159] reports on the parents of 26 children 4 years after testing. It is not made explicit to what extent the samples overlap, but it seems inevitable that they do given limited numbers of the target families. However, the findings are oddly disparate in places. For example, one (later) paper[158] says that 78% of mothers and 58% of fathers had an immediate negative emotional reaction to the diagnosis. The early paper,[159] however, says that "On receiving the first information regarding ATD, 80% reacted with indifference or had not altogether understood the consequences of the disorder" (p. 174) and that just 20% reported shock or depression on first being told. It is not possible to deduce the reason for this mismatch. It is also reported[163] that at 5–7 years mothers, but not fathers, scored worse than controls on three out of eight physical and mental health measures.

In the Wisconsin CF Neonatal Screening Project,[143,144] anxiety amongst parents of children with false-positive results was associated with lower Apgar scores, suggesting that parents who may already have some grounds for concerns about their baby's health may be more vulnerable to this additional uncertainty. One study[137] reported that parents of children with false-positive results generally had better emotional well-being scores than other groups (true-positives, healthy controls and conventionally diagnosed children with CF). However, group sizes were small and there were demographic differences between healthy controls and the other groups, so this finding may not be reliable.

Those CF studies that have been able to compare parents of children diagnosed through screening and those diagnosed symptomatically[111,137–139] have not found major differences. However, we should note that 14/18 parents of false-positives in the Wisconsin trial who were randomised to the 'delayed disclosure' group reacted very negatively to the discovery that potentially important information about their child's health had been withheld from them for 4 years.[144] All were false-positives. Responses to delayed disclosure included anger at being misled, fear that the child was affected, anxiety and grief.

Reproductive decision-making

One of the distinguishing characteristics of single gene disorders is that there are potentially implications for future pregnancies and for other family members. One of the arguments put forward for screening for such conditions where there is not a clear benefit to the child is that it provides parents with the option of avoiding future affected pregnancies. Within the studies meeting the criteria for this review, just six of the neonatal studies considered issues to do with subsequent reproductive decision-making.[111,139,142,143,151,164] Five were concerned with CF and one[151] with DMD. Four report data on reproductive behaviour,[139,142,151,164] the remainder only on attitudes. It is difficult to generalise from these studies because many of the samples are small and the populations vary.

Reproductive behaviour

The Wisconsin CF Neonatal Screening Project followed up the parents of true-positives on a number of subsequent occasions.[142] Final follow-up was when the trial ended in 1994, when the oldest children diagnosed through the programme would have been 9 years old and the youngest less than 1 year old. Of the 73 families contacted, 52% had

not conceived again since diagnosis, but 74% of these had had other children already. In families where the child with CF was the first born, 70% had further pregnancies (43 pregnancies in 31 families). Prenatal diagnosis was used by eight families (26%) for 21% of the pregnancies. The authors conclude that a neonatal diagnosis of CF had little effect on reproductive behaviour. In contrast, an Australian study[164] reported a stronger desire to avoid a further affected pregnancy: 53 out of 124 mothers had had a further pregnancy. Two-thirds had prenatal CF testing and 69% of these either decided to terminate or said that they would have terminated if the fetus had been affected. There were 12 affected pregnancies and 10 were terminated. There are a number of methodological differences between this study and that from Wisconsin, which may account for some differences, but are in fact as likely to bias the findings in the other direction. It is likely that differences in attitude to termination of pregnancy account for some of the difference in the findings of these two studies. In a study in Colorado,[139] 30% of 55 families had had further pregnancies, two had prenatal testing and three terminated, two of those without testing. The final study to look at reproductive behaviour was the Manitoba DMD study.[151] There were seven subsequent pregnancies in women identified and counselled as being high-risk carriers subsequent to newborn screening. Prenatal diagnosis was performed in only two of these seven pregnancies, and two further affected boys were born. Although this is only a small sample from which to generalise, it does suggest that discovering carrier status before the index child is symptomatic does not have the impact on reproductive behaviour that later diagnosis has. It may be that people need lived experience of the disorder, not just the intellectual knowledge that comes from being related to a presymptomatic child, before they are likely to act on the information given. A similar effect might account for some of the variation between the CF studies, all of which included some fairly young children.

Reproductive attitudes

The Wisconsin CF study[142,143] also looked at 'false-positives', both those who had been tested only with IRT, and who were therefore genuine false-positives, and those who had been tested using IRT followed by DNA analysis, who were therefore CF carriers. All were asked 1 year later whether their experience had changed their feelings about having more children. About 4% (reported as 8% of 104 in Tluczek and colleagues' study[143]) of 106 IRT families and 17% of 58 IRT/DNA families said yes. Two additional studies asked parents of children with CF, some of whom were detected through newborn screening, about their attitudes to terminating a further CF pregnancy. In a study in Wales,[111] 11/18 parents said that they would terminate. In Colorado,[139] 61% of the newborn screened group who were interviewed (N = 40) said that they would not terminate for CF and 22% were unsure. Only 6% spontaneously mentioned family planning as a benefit of newborn screening.

The effects of service delivery and organisation on anxiety

The issues might be thought to be different for parents of children who are 'true-positives' and those who are 'false-positives' insofar as the first group do have a health problem which may be a legitimate source of anxiety and the second group do not. However, consideration of the published studies shows that the situations are not as different as might be expected. First, the conditions in question represent a continuum of health problems or health threats rather than a simple dichotomy. At one extreme are serious and untreatable conditions such as DMD where parental anxiety might be considered inevitable and the key question is whether there is a net benefit to parents of affected boys in knowing presymptomatically. However, most of the conditions considered do not fall into this category, rather they are conditions where some form of treatment will be available and, in many cases, (e.g. hypothyroidism, PKU), the child can expect to lead a fairly normal life. There is even an area of overlap for 'true' and 'false' positives in that for some conditions (e.g. ATD, familial hypercholesterolaemia) a 'true-positive' child is unlikely to have imminent health problems, although a vulnerability exists, and the same is true for 'false-positives' for sickle conditions. However, in all cases, whether 'true' or 'false' positive, anxiety appears to be linked to a lack of understanding about the child's true health status – whatever that may be. This can almost be taken as a given. What is less clear is the best course of action for averting misunderstanding.

We have seen that in two cases[158,161–163] the early drivers of subsequent screening (or non-screening) have been clinicians' anecdotal observations rather than research studies. This is not to say that the clinicians' observations are incorrect, only that the specific causes of distress and the assumptions about how best to proceed thereafter are untested. This was clearly recognised in Sweden when a

screening programme for congenital hypothyroidism was to be introduced in the mid-1970s.[145,147,148] With the ATD screening experience still very recent, the psychological aspects of the hypothyroidism pilot programme seem to have been given considerable forethought. The likelihood of distress being caused by false-positive results was anticipated and a protocol was in place for following up parents. All the false-positive families were telephoned by the same well-informed member of the clinic team (a social worker with psychotherapeutic training) with a set form of words, who then visited them at home and conducted follow-up interviews at 6–12 months. Nevertheless, the authors concluded that:

- False alarms cause pronounced acute strain in the majority: 20% of families showed distress 6–12 months later and related this to the result. Initial assessment of amount of worry and coping methods predicted risk of lasting distress.[145]
- Follow-up after 4 years showed that long-lasting distress in families, in some cases affecting the children also, may originate in the psychological reactions to the false-positive result.[147]
- Comparison of families with high and low distress scores showed no large differences in terms of life stress scores.[148]

In 1979, the new congenital hypothyroidism programme was introduced into routine practice. The main difference between the two screening scenarios was that the giving of results was not governed by the protocol that had applied in the pilot study. The fourth Swedish paper[146] was a follow-up of a further 11 families who had had a false-positive result in the period 1979–81. Most of these parents described their experiences as dramatic and chaotic. Communication with health professionals was clearly poor, reminiscent of the retrospective ATD study findings. However, unfortunately, the way in which results were communicated was not the only difference between the two screening scenarios, so comparison of findings is difficult, despite the involvement of the same principal author. The nature of the author's involvement with the parents was different and technical refinements to the test meant that the positive predictive value of the initial screen had risen from 5% to 50%. Hence there were considerably fewer false-positives and receipt of an initial positive result was much more likely to indicate a true problem.

Poor and chaotic communication with health professionals was also characteristic of the Dutch hypothyroidism study,[149] where parents of 31 children who had had a false-positive result were interviewed 4–12 months after the event. A number of examples of prevarication and misinformation from primary healthcare professionals were reported. In a follow-up study of parents with a sickle-cell condition detected through newborn screening,[155] there were also examples (4/15) of parents who had previously been told (erroneously, evidently) that they were not themselves carriers and therefore not at risk. In this study, two-thirds of parents said that they felt isolated and unprepared to deal with their child's health problems.

One of the arguments for newborn screening for CF and for DMD is that parents can be spared the protracted process of diagnosis that is otherwise the norm. It is therefore sobering to see that in one CF study in Wales,[111] which confirmed that diagnostic delays resulted in 'extreme anxiety', 11/29 parents experienced such delays and that nine of these 11 had been diagnosed through screening. The negative effects of such delays evidently still apply even if the child is presymptomatic. Two mothers were very negative about screening as a result and felt that the process had interfered with their relationship with their baby. Clearly, we cannot be complacent in assuming that the existence of a screening programme automatically removes diagnostic delays. It is also worrying that such a result comes to light as a by-product of a study on the attitudes of parents of CF children, rather than as part of a screening programme evaluation. This may imply that the standards achieved by normal service delivery fall short of those reported in evaluation studies.

The reports from the South Wales screening programme for DMD[152,153] focus on the experiences of the families with a true-positive result, but also give considerable information about the process of screening and the emphasis on minimising parental distress. This – and the facilitation of informed parental choice – has been the guiding principle of the protocol that was developed for the programme. This has apparently been successful at least in terms of parental satisfaction.[152]

Chapter 10

Authors' synthesis and comments on the review

Introduction

This review has examined 106 publications concerned with psychosocial aspects of genetic screening in pregnancy and the newborn period. The definition of genetic screening is problematic, as we described in Chapter 1, because the same test may screen for a number of different disorders, some genetic and some not. As a result, we have, despite the title of the review, collected some information on experiences of screening for 'non-genetic' disorders, notably MSAFP screening for neural tube defects and 'Guthrie testing' for congenital hypothyroidism.

Although the review was circumscribed by the emphasis on 'genetic' disorders, it was as inclusive as possible in other regards. We attempted to include any paper that reported relevant psychosocial data collected directly from parents, even if the main thrust of the paper was not psychosocial. Our stipulation that the paper should include data collected directly from parents seemed necessary for a review focused on psychosocial aspects. However, this does mean that we excluded studies that **only** reported on parental behaviour such as uptake of subsequent tests or termination of pregnancy. Such studies would complement what we are able to say from the literature on parental reports about the psychosocial aspects of testing.

Overview of findings

Antenatal and newborn screening

Relatively few studies of newborn screening programmes were found: 28 versus 78 antenatal. This is of some interest when we consider that newborn genetic screening is universal in developed countries. The number of studies certainly is not a reflection of conditions being screened for. Why have psychosocial aspects of antenatal screening been seen as more worthy of research investigation than neonatal? We can only speculate, but there would seem to be a number of possible explanations. One is to do with historical context. Newborn screening for PKU started in the 1960s when people were not, on the whole, asking questions about people's responses to the decisions that doctors made on their behalf. Once a programme has been running for some years, the impetus to start asking research questions is not there unless there are demonstrable problems or good reasons to expect them. This is presumably the reason why we could not find a single study looking at parents' responses to screening for PKU, despite it being the most widely used genetic screening test in the world. It also explains why the newborn studies that we did find were mainly concerned with 'add-ons' to the basic Guthrie test, but not with PKU.

Psychosocial aspects assessed

Earlier reviews had led us to expect an emphasis on knowledge and anxiety as the principle psychosocial outcomes assessed. This emphasis was indeed replicated here, although a majority of publications also looked at attitudes and beliefs. In seeking to interpret all this information on knowledge and anxiety, we have found ourselves questioning some of the underlying assumptions associated with these two constructs, and this will be discussed in the following sections.

Knowledge

Chapters 4 and 6 showed that assessing knowledge is not a straightforward task, even in one context and with one set of study aims. Summing up the data reported on knowledge in different studies is even more problematic, since the 'knowledge' being assessed is so variable and has been measured in a variety of ways. This is true both for prenatal and newborn testing.

There are, however, a few robust findings:

- Levels of knowledge adequate for decision making are not being achieved.
- Efforts to improve knowledge using information leaflets are effective in the sense that people given a leaflet know more than people not given a leaflet, but ineffective in the sense that large gaps in knowledge usually remain.
- Providing supplementary material in a video seems to produce a small additional improvement, but does not begin to solve the problem.

- Procedural aspects of testing are better understood than material related to the meaning of risk calculations.
- Substantial social and cultural inequalities exist in knowledge about testing.
- The above findings almost certainly underestimate the extent of the problem, because only limited aspects of knowledge have been studied to date.

Before further evaluation studies are conducted, a clearer consensus is required about the knowledge that it is necessary and sufficient for women to have when they are making decisions about prenatal and newborn genetic testing. Put more bluntly, what it is that people **do** need to know and whose business it is to decide that. Professionals have been preoccupied with conveying certain kinds of information (e.g. procedural matters, risk estimates) but have virtually ignored others (e.g. what it might be like to bring up a child with the condition in question), and an approach based on parents' needs rather than staff needs is long overdue. The National Screening Committee (NSC) may be the forum in which this debate is conducted.

Other, more detailed, points arising from this review that might assist future deliberations are:

- Knowledge is not the same as understanding. Correct recitation of a risk figure does not necessarily mean that the concept of risk is understood.
- Public understanding of the basic concepts associated with screening is poor, so little can be assumed when explanations are given.
- Knowledge that is only superficially acquired may not be retained.
- Considerations of 'efficiency' that limit the time available to inform women may be misguided if achieved levels of understanding are inadequate, and may be a false economy if women's knowledge is so unreliable that no future decision can depend upon it.
- As different genetic tests are introduced, the cumulative knowledge demands become substantial, increasing the possibility of inadequate or incorrect understanding.
- More complicated testing scenarios may amplify inequalities in understanding, especially if time constraints mean that leaflets are used as substitutes for face-to-face explanations.
- Most male partners get their information about genetic testing second hand. Serious misunderstandings can occur, such as men thinking that future children are not at risk when they are, and vice versa.
- Informed consent for newborn screening has been little studied.

Before concluding this section on knowledge, attention needs to be drawn to the ambiguity of the word 'informed' and some of the implications of using it in different ways. It may be used as a verb, 'The midwife informed the woman', or as an adjective, 'She made an informed choice'. However, in the phrase, 'The woman was informed by the midwife' it is not clear whether the emphasis is on the activity performed by the health professional or on the resulting state of enlightenment experienced by the woman. This would not matter if the former necessarily led to the latter but, as shown above, there is plenty of evidence to suggest that it does not.

If it is not a valid assumption that information given equals information received, then a really crucial question follows: do we design services to ensure that everybody is given the same information, or do we seek to ensure that everybody achieves an agreed level of understanding? There is a related question: what are the 'givens'? Is it a 'given', for example, that the routine activities of antenatal clinics must have priority, so that informing all women about genetic testing must be fitted into the same prespecified, and necessarily very limited, period of time? If it is clear that informed consent cannot be achieved for many women in these circumstances, what are the service implications, and how are decisions then taken about priorities and about the resource consequences of meeting stated objectives?

Informed decision-making about prenatal testing has recently become a research topic in its own right. However, as the above discussion has indicated, there is at present no agreement even about what constitutes being 'informed'. Operationalising 'informed decision-making' presents researchers with major conceptual and methodological challenges that are only just beginning to be appreciated.

The sections below present material on anxiety and attitudes. Knowledge is likely to influence both, although not necessarily via simple pathways, and – as has been shown – knowledge levels are unsatisfactory. It follows that the information currently available on anxiety and attitudes represents the feelings and views of many people who are not in fact well informed about the topic under discussion. The feelings and views of people who were well informed cannot readily be

ascertained from the material reported below, and this must be borne in mind when considering the policy relevance of the results reported.

Anxiety

Researchers have had fewer problems measuring anxiety than measuring knowledge, because 'off the peg' self-completion measures of general anxiety, with good psychometric pedigrees, are available. There are, however, problems in interpreting the data obtained, particularly regarding the relationship between knowledge and anxiety. In the early days of screening, clinicians thought that too much knowledge would worry people and many were reluctant to give very much information for that reason (and because it might put people off being screened). However, since knowledge was demonstrably poor, it was also possible that too little information was causing anxiety. Studies were therefore conducted to see if increasing knowledge could reduce anxiety and other studies were conducted to see if knowledge could be increased without increasing anxiety.

The above is not as illogical as it sounds, because knowledge about different things might plausibly have different effects on anxiety. We have already argued that no proper debate has taken place regarding the knowledge that women need to make choices about testing. By extension, we can add that detailed aspects of the relationship between knowledge and anxiety have not been investigated and are not properly understood.

The most robust findings from the work on anxiety are:

- Studies that have succeeded in increasing knowledge have not observed a corresponding increase in anxiety.
- Anxiety is clearly raised in women receiving positive screening results but evidence is lacking of a beneficial (i.e. reassuring) effect of receiving a screen-negative result.
- Anxiety in screen-positive women undergoing stepwise carrier screening falls on learning their partners' negative result; in Down's syndrome screening, and in newborn screening, anxiety falls if no abnormality is detected on a diagnostic test.
- Anxiety in 'false' positives may, however, not return to normal levels; some residual anxiety may remain, possibly over extended periods of time.
- The way in which carrier screening is offered may affect anxiety in screen-negative women. Couple screening without disclosure leads to higher anxiety in screen-negative women than does stepwise screening. Couple screening with disclosure may lead to lower anxiety than stepwise screening, but a full evaluation has not been conducted.

In addition to the above findings, a number of general comments can be made arising from the literature on anxiety.

- Knowledge that improves decision-making may not be the same as that which reduces anxiety.

  Numerous information aids have been developed to facilitate knowledge about testing, but little research has focused on information that enhances preparation for receipt of a screen-positive result. Information interventions have been provided at just one point in the screening process, usually when women are choosing whether or not to have screening. It now seems likely that the information to facilitate choice is qualitatively different from that to reduce distress and aid coping. It also seems likely that the provision of information about coping with a test result should occur after the testing choice has been made, perhaps after having the test or upon receipt of the result. Future research is required to identify what information is most effective in reducing anxiety and when in the screening process it is most appropriate to deliver this intervention.

- Some anxiety might be an appropriate response and might aid coping and decision-making.

  Increased arousal is necessary to enable individuals to attend to decision-relevant information when making choices about treatment, so increased anxiety at that time may indicate individuals are employing more effective information strategies. Too high a level of anxiety will, however, impair effective decision-making. Unfortunately, it is unclear what constitutes a level of anxiety that is associated with effective information processing and what constitutes an abnormal response to a stressful situation.

  In an earlier HTA report on Antenatal screening for Down's syndrome,[4] the authors noted that:

  > "Anxiety was assessed in most of the studies but in many it was not acknowledged that anxiety is a necessary cost of realising that there is an increased risk of a serious disease or a fetal abnormality. Often the studies have simply confirmed that

> antenatal serum screening causes anxiety. Some authors have viewed this as an adverse finding. This is only the case if the anxiety is excessive and could have been appropriately avoided" (p. 85).

We agree, but anticipate that there will be difficulties in defining and agreeing what counts as 'excessive' anxiety and 'appropriate' avoidance. The phrase 'necessary cost', furthermore, implies a set of values that may not be shared by all participants in screening programmes, especially those who did not make an informed choice to take part. Further research is required to identify levels of optimum and/or normal anxiety responses, in order for interventions to be evaluated on their effectiveness to reduce the iatrogenic consequences of undergoing prenatal testing.

- Young women may be more vulnerable to anxiety arising from positive screening test results.

  Studies of Down's syndrome screening have found some evidence that young women may be especially vulnerable to psychological distress if screening test results are positive.[165] The reasons are not fully understood, but it may be that younger women do not think of themselves as being 'at risk' of having a baby with any kind of abnormality, so a positive screening result may challenge many assumptions they have made about the well-being of their baby. The finding of enhanced vulnerability is consistent with other literature on this age group, and has service implications because antenatal screening for Down's syndrome will soon be offered to large numbers of younger women following recommendations by the National Screening Committee.

- Knowledge and anxiety in men whose partners are undergoing screening have been little studied.

  Although a point can be made about the general lack of attention paid to men's views, the most obvious shortcoming relates to carrier screening. In the studies of prenatal carrier screening for CF, women who had themselves been given only very limited information were expected to obtain the informed consent of their partners to a genetic test which could have far-reaching consequences for both of them as individuals, the pregnancy, any existing children and any potential future children. Providing a mouthwash sample is not itself very threatening, so compliance with that procedure should not be taken as evidence of the men's informed consent. Anxiety data are difficult to interpret in these circumstances, for reasons mentioned above.

Attitudes and test uptake

The main findings from this part of the review are:

- The majority of women hold positive attitudes towards prenatal screening.
- Women having screening tend to hold more negative attitudes to abnormality, to perceive their likelihood of having an affected child (or themselves being a carrier) as greater, to perceive the risks of subsequent procedures as lower, to perceive others as thinking they should have the test and to intend to have a termination if an abnormality is detected.
- Women who were more satisfied with their choices were also more falsely reassured, and made their choices less systematically, than women with lower satisfaction scores.
- A minority of screen-positive women (ranging from 3 to 30% in different studies) expressed regret about their screening decision.
- Uptake of newborn screening has been treated as a 'given' and not a research topic.

The question about knowledge has already been raised. Many women do not have enough knowledge to make informed decisions about having screening, but because most will receive screen-negative results, their understanding is not put to the test. Rather, they receive reassuring results and become 'satisfied customers'. However, as Green and colleagues noted over a decade ago, "it is quite likely that women would find screening less reassuring if they understood its limitations."[166] It is not being argued here that fully informed women would not have positive attitudes to screening, only that their enthusiasm might be tempered by a more realistic appreciation of potential costs in addition to benefits.

Finding that screened and unscreened groups show some differences in attitudes is not the same as saying that attitudes are good predictors of behaviour at an individual level. The attitude–behaviour relationship has long preoccupied psychologists, but across many studies in many settings, only a small proportion of variation in behaviour can be explained by variation in attitudes.[167] Further, screening decisions are not necessarily predictive of other decisions about diagnostic tests or the termination

of pregnancy. Since lay knowledge is poor and improved by leaflets and also by contacts with health professionals, it may be that attitudes change over time. Measuring them at one stage in the process may therefore give an oversimplified picture of the attitude–behaviour relationship.

Clinical impressions confirm the attitude data in showing that most women want prenatal tests. They also want neonatal tests, and do not necessarily expect their consent to be sought for them. Inadequate understanding of screening is again an issue, however, which can escape attention because the very great majority of screen negatives will never have their sense of reassurance disturbed, and the parents of true positives feel that the best medical care is being provided for their baby.

These points have implications for the role of service users in planning and policy making. Attitudes to screening in women who have never been screened, or in women who have only received reassuring (or helpful) results, can only tell a part of the story. The views of women whose experience was less favourable must also be incorporated if a balanced picture is to be obtained.[85]

What difference does it make that the condition is 'genetic'?

This review is limited to screening for 'genetic' disorders, defined for these purposes as chromosomal or single gene disorders. We argued in Chapter 1 that tests needed to be categorised from the perspective of the recipient and the characteristics of the specific disorder being screened for may be irrelevant if parents do not have a full understanding of the testing process. For this reason, some data relating to testing for conditions which are not genetic have been included. This has proved valuable because it allows us to see that responses are fairly similar across a range of disorders.

To take one example, we might expect there to be a greater concern with subsequent pregnancies for genetic than for non-genetic disorders. This may well be the case, but we do not have the evidence to report on it here, first because this review has not covered non-genetic disorders in the same way and second because it is unlikely that the question will often have been asked of parents in these cases. However, we do have some information from the studies that we have covered, which reminds us that we need to focus on parents' interpretations of terms rather than those of professionals. The first example comes from one of our non-genetic examples: congenital hypothyroidism. A qualitative study[149] of parents with a false positive result showed that some of parents' residual concerns **did** focus on future pregnancies:

> "We're thinking about having another child but my husband says 'isn't it too much of a risk with that thyroid gland defect?'" "You sometimes hear that with heart defects the first child has a little bit, and the second a little bit more and with the third it's really serious" (p. 96).

Leaving aside the fact that the index child in these cases did not in fact have congenital hypothyroidism, it is obvious that the parents take it for granted that disorders run in families, whether or not there is any Mendelian basis for that belief. This is consistent with the wider literature both of people's attempts to make sense of illness and of lay understandings of genetics. So, although the distinction between genetic and non-genetic disorders may be important from the point of view of those providing tests, it may be less salient to recipients.

Another perspective on this comes from a second qualitative study, involving parents of 24 babies who had been identified as having familial hypercholesterolaemia,[157] an inherited predisposition to heart disease. The key finding to emerge from this study was that parents' response to the diagnosis depended on whether they focused on the fact that it was to do with cholesterol or that it was 'genetic'. Those focusing on cholesterol saw the disorder as relatively unthreatening and controllable. The word 'genetic', on the other hand, clearly conveyed messages of "some terrible condition rather than some dietary thing", something that was "a death sentence"; "there's nothing you can do about it" (p. 1859).

When we see comments of this sort, it becomes clearer how misunderstandings occur so easily. As another paper[144] referring to CF screening reported:

> "When parents were faced with ambiguous, incomplete or uncertain information, they filled their information gap in any way they could. Information seeking had the consequences of inaccurate sources and increased anxiety for parents" (p. 35).

Parents read so much into the words used and rarely have the opportunity for any follow-up

discussions with well-informed health professionals who can dispel misconceptions. Recommendations which have been made in other spheres for giving diagnoses have included giving parents a tape recording of the consultation and giving them a follow-up appointment to come back with questions that will have arisen in the meantime. Such measures may well prove valuable in the screening setting also. The evidence of this review suggests that this would be needed for parents of children with false-positive results in addition to true-positives.

Methodological characteristics and quality of studies reviewed

One of the clearest messages to arise from previous reviews[3] is the importance of historical context for understanding participants' responses to screening. We also knew from the outset of this review that different research questions are asked at different points in the history of any technology, and that this confounding means that some questions can never be properly answered. For example, tests which are at an early stage of their history may well only be offered within the context of a research study. Study participants are likely to be keener, better informed and better educated than the general population of people who might be offered the same test in later years when it has become routine, and staff characteristics may also differ.

There is also a tendency for different methodologies to be associated with different findings in this field.[1] For example, qualitative studies have generally reported more extreme anxiety responses than quantitative studies. Farrant,[8] in 1980, reported women smoking more, taking tranquillisers or drinking half a bottle of spirits in one day while waiting for amniocentesis results. Such extremes of anxiety are rarely reflected in quantitative studies. One straightforward explanation for this is that extreme responses are simply absorbed in quantitative studies, which report on groups rather than on individuals. An unexpected finding in the quantitative papers, however, was that many of the samples used were biased towards the experiences of highly cooperative research participants, so this may also have been a contributory factor.

We should be aware that as reviewers we only have the information available to us that authors have included in their papers. Most papers have an 'agenda', often to demonstrate the benefits or the disbenefits of a particular course of action. Inevitably the information presented (or indeed gathered) is selective. This is particularly true when we come to consider aspects of service delivery and organisation. Typically, detailed information about the protocol for informing and supporting parents is not given, although there are notable exceptions. Even when the protocol is given, however, we rarely have any audit of that protocol to know whether this is what really happened. In the authors' defence, it must be said that many problems arose because we wanted to use data for a purpose that differed from that of the original study. Our intention is certainly not to imply that investigators should have asked our questions rather than their own, but only to warn that there are pitfalls when data collected to answer one research question is drawn upon in an attempt to answer another.

Also unexpected was the limited usefulness to the review of traditional research quality ratings. Not only did an overall quality score miss the point that some features mattered more than others, many serious problems were not detected at all using these methods.

The publication policy of many academic journals also does not help here, as editors usually prefer concise papers to detailed ones. Crucial information on the implementation of an intervention, or the timing of data collection, may therefore be omitted in order to meet a word count designed for a different type of research altogether.

Putting the last few points together, the usefulness of published data in answering our questions could not be easily determined from traditional quality ratings. This mismatch has implications beyond the present review.

A further unexpected point – but one which probably could have been anticipated – is that prospective studies of prenatal screening do not usually generate enough true-positives and false-negatives for quantitative study. Studies of the latter usually have to draw their samples from a wider population than those investigated in screening studies, particularly the kind of screening studies included here, which collect psychological data (sometimes on several occasions) from participants. This review therefore adds less than we had originally expected to understanding the experiences of people with true-positive and false-negative results from prenatal screening. The position is different in

newborn screening, where 'before and after testing' studies were not attempted, and researchers concentrated on subgroups of people with particular kinds of test result.

Genetic screening and the role of psychology

We embarked on this review hoping to construct a multi-dimensional classificatory system (MDCS) which would allow us to go beyond a simple description of outcomes. Our aim was to construct a multi-dimensional framework on which all screening scenarios could be located. It was intended that this would provide us with a structured tool for making comparisons across studies and thus to draw conclusions about the relative importance of the various parameters.

We hoped that this would enable us to go beyond the traditional 'reactive' kind of psychology, which measures and describes the psychological effects of genetic screening, and in addition help to predict, explain and anticipate people's behaviour.[168]

The following variables were postulated for inclusion in the MDCS:

- timing of testing, including
  - when in pregnancy/neonatally
  - timing in relationship to other events, for example, when having other tests
  - when in the history of the test, that is, is the test new or well established?
- who offers the test and where
- how much information people have about the testing procedures
- how much information people have about the disorder
- attitudes to the disorder
- how results are given
- the certainty of the test results, both positive and negative predictive value
- the certainty of the prognosis (as opposed to the diagnosis)
- what can be done with the information
- the implications of the test result.

All are factors that could in principle vary between different screening programmes for the same disorder. Most were incorporated into our thinking and have been extensively discussed in the pages of this report. It proved premature, however, to draw up a classification table and use it to examine outcomes, because there was little variation on some of the dimensions, because there were insufficient data to examine the effect of one variable while holding the others constant, and because there was little evidence that women understood important implications of the distinctions being made. No attempt at meta analysis was made for the same reasons.

Service delivery and organisation

The factors that could be identified as important from the existing evidence base were primarily concerned with service delivery and organisation. We are referring here to the same aspects of care commented upon in an earlier HTA report on screening for Down's syndrome:[4]

> "Much that is often considered as the 'psychosocial' aspect of screening concerns the self-evident need to provide a well-informed compassionate service that respects the wishes of individuals. Nevertheless, it is often in this area that screening fails and causes 'casualties' that could, with appropriate care, be avoided" (p. 85).

Being 'self-evident' is clearly not sufficient to ensure that a need is met. The neonatal literature (Chapter 9) provides some particularly detailed descriptions of the problems that can arise,[111,138,146,155] but similar problems also occur in prenatal screening. Strongly negative psychological responses to the screening process were typically related to misunderstandings, which could frequently be traced back to unsatisfactory communication with health professionals. This could take the form of non-communication or delayed communication, but there were also examples where parents have been misinformed or underinformed.

One paper[149] was explicit about the dilemma for health professionals, who have to tread a fine line between treating the screening result as very important and scaring the parents ('it makes you think he's dying') and dismissing the result (and the parents' concerns) as trivial.

These authors' recommendations for good practice in giving results[149] deserve repeating here:

1. Good written information.
2. The period of uncertainty should be kept as short as possible.
3. A good 'rounding-off' interview between the parents and a well-informed health professional.

4. Better education of health professionals taking the initial samples and those who may have contact with parents thereafter.

As pointed out above, we should also recognise that anxiety is an appropriate response to any perceived threat to the baby's health and the goal of eradicating it is unrealistic. We should instead be aiming for appropriate anxiety, which, in the case of false-positive results, means that the anxiety should be resolved by the results of subsequent tests.

The above recommendations represent no more than a commonsense minimum standard. Importantly, the studies also indicate that resolution of anxiety is not always achieved even with a strong protocol in place. This suggests that improving the quality of existing patterns of care will reduce but not solve the problem. The fourth point above – better education of health professionals – may be key, and it is to be hoped that the planned work of the NSC in this area will be seen to have an impact. Similar conclusions can almost certainly be drawn about knowledge outcomes as well as anxiety, and about prenatal and newborn screening.

Policy implications and recommendations for future research

Although the research reviewed in this report was largely conducted before the establishment of the NSC, the results of the review have many implications for the committee's work. The NSC's Antenatal and Newborn Programme monitors the establishment and maintenance of services offering antenatal screening for Down's syndrome and the haemoglobinopathies, and newborn screening for sickle-cell, phenylketonuria and a number of other inborn errors of metabolism. From April 2004, all pregnant women in the UK, regardless of age, are to be offered Down's syndrome screening. Screening for haemoglobinopathies has begun with work on newborn screening for sickle-cell disease. Initially, specific programmes were developed by the NSC for specific conditions, but the aim of the Antenatal and Newborn Programme is to integrate the various screening programmes with each other, and with the overall pattern of antenatal and neonatal care.

Antenatal screening guidance from the NSC complements clinical guidelines on antenatal care recently published by the National Institute for Clinical Excellence.[169] The NHS Plan contains a commitment for effective and appropriate screening programmes for women and children by 2004.[170] The National Service Framework for Children, Young People and Maternity Services is due to be published in 2004, following an interim consultation document published in 2003.[171] All of these documents make frequent reference to information and choice for women. The results of this review have implications for both the implementation and monitoring of antenatal and newborn screening programmes, themselves provided in the context of national policies emphasising the importance of information and choice in the delivery of healthcare.

Large-scale staff training exercises are being implemented as part of the NSC's Down's syndrome and haemoglobinopathy screening programmes. It may be that the combination of better trained staff and new information materials developed to accompany the programmes will lead to significant improvements in women's level of understanding. Efforts will also be made in NSC programmes to improve public awareness of genetics. Comparative research will need to be sensitive to major changes of this kind in national screening policy and practice.

The most pressing implications of this review for the NSC Antenatal and Newborn Programme, in order of priority, relate to:

1. **The inadequacy of current procedures for achieving informed consent.**
   New approaches need to be developed and evaluated as a matter of urgency. Both development and evaluation need to be conceptually and methodologically more sophisticated, and more oriented towards service users' information needs – rather than professionals' concerns about avoiding anxiety – than has been the case in the past. Research is needed not only about the **content** of what potential test recipients want to know, and about its timing and format, but also about the value that different people place on being informed. There are certainly grounds for thinking that there are people who value 'being informed' as something separate from 'giving consent'.[31,140] Differences in the information and support needs of women at different stages in the screening pathway need to be examined, as does the impact of staff attitudes on the information giving process. Future research on this topic should also explicitly examine the ability of interventions to reduce inequalities in

understanding between social, educational and ethnic groups. Different approaches may be required to meet the needs of different demographic groups. User involvement and the reduction of health inequalities are two of the cornerstones of NSC policy, so there is an urgent need for research evidence to support programme development and management in these areas.

2. **The cost of providing a satisfactory service.** Research is required into the costs and effectiveness of different approaches to achieving informed consent and into the implications for service delivery and organisation of implementing effective services. Informational materials will need to be provided in a variety of languages and in audio in addition to written format, to meet the needs of people with limited literacy. The cost of achieving adequate levels of understanding may be different in different demographic groups.

3. **The unmet needs of "false positives" from screening programmes.** Psychological distress in 'false-positives' might be largely a product of inadequate understanding and might be reduced if more effective means of conveying information were available. In the meantime, the information and support needs of this group need to be better understood, and factors (individual and service related) predicting particular vulnerability to distress also need further investigation.

4. **The unmet needs of women's partners, particularly in carrier screening.** Data from men were collected only very occasionally in the studies reviewed for this report. When they were collected, for example in some of the work on carrier screening for CF, unsatisfactory levels of understanding were revealed. Since many of the men were reliant on their partners for information, and since the women themselves were often poorly informed, low levels of understanding in men were – with hindsight – only to be expected. Better methods of conveying information to women will probably reduce the problem in the future, but a direct approach to men is also likely to be required if important misunderstandings are to be minimised. Research on men is required in relation to both antenatal and newborn screening: men's information and support needs have to be better understood, and factors (individual and service related) predicting particular vulnerability to distress need further investigation.

We suggest that research is conducted on the above four topics in order to fill gaps in the evidence base that relate to screening technologies which have been available for many years. In addition, future screening programmes will create a new list of research questions, based on the same main agenda but applied to new areas, for example to:

- new conditions, such as haemoglobinopathies, fragile X syndrome
- new client groups, such as young women, minority ethnic groups
- new testing modalities, such as ultrasound.

Research has begun to appear on these topics, but too recently for inclusion in this review. Further research is needed, which – most importantly – does not treat these topics in isolation, but which incorporates them into the mainstream of work, including that on informed consent, on the resource requirements of providing a satisfactory service, on people with false-positive results and on partners.

Acknowledgements

We would like to express our thanks to the following people. Jenni Murray, Alison Winterburn and Carla Bratten all made very substantial contributions to the study: searching, reviewing abstracts, acquiring papers, extracting data and entering data on to the database. Additional readers were Vicky Ramwell and Shenaz Ahmed. The substantial secretarial work on the report was carried out with efficiency and good humour by Stephanie Bridgford, Rebecca Wilding and Emilie Cumming.

Contributions of authors

Josephine Green (Professor of Psychosocial Reproductive Health) had overall responsibility for direction and management, as well as writing and editing the report. Jenny Hewison (Professor of Psychology of Healthcare) carried out direction and management, as well as report writing. Hilary Bekker (Senior Lecturer in Behavioural Sciences) was involved in direction and management, setting up the database and overseeing data extraction. HB also contributed report writing. Louise Bryant (Research Fellow, Psychology) carried out literature trawling, data extraction and report writing. Howard Cuckle (Professor of Reproductive Epidemiology) carried out direction and management; as well as reading and commenting on the report.

References

1. Green JM. *Calming or harming? A critical review of psychological effects of fetal diagnosis on pregnant women*. London: Galton Institute, Occasional Papers, Second Series, No. 2; 1990.
2. Green JM. Women's experiences of prenatal screening and diagnosis In Abramsky L, Chapple J, editors. *Prenatal diagnosis: the human side*, 2nd ed. Cheltenham: Nelson Thornes. 2003. pp. 37–53.
3. Green JM, Statham H. Psychosocial aspects of prenatal screening and diagnosis. In Marteau TM, Richards MPM, editors. *The troubled helix: social and psychological implications of the new human genetics*. Cambridge: Cambridge University Press; 1996. pp. 140–63.
4. Wald NJ, Kennard A, Hackshaw A, McGuire A. Antenatal screening for Down's syndrome. *Health Technol Assess* 1998;**2**(1).
5 Bricker L, Garcia J, Henderson J, Mugford M, Neilson J, Roberts T, *et al*. Ultrasound screening in pregnancy: a systematic review of the clinical effectiveness, cost-effectiveness and women's views. *Health Technol Assess* 2000;**4**(16).
6. Nicolaides KH, Snijders RJM, Gosden CM, Berry C, Campbell S. Ultrasonographically detectable markers of fetal chromosomal abnormalities. *Lancet* 1992;**340**:704–7.
7. Richards MPM, Green JM. Attitudes toward prenatal screening for fetal abnormality and detection of carriers of genetic disease: a discussion paper. *J Reprod Infant Psychol* 1993; **11**:49–56.
8. Farrant W. Stress after amniocentesis for high serum alpha-feto-protein concentrations. *BMJ* 1980;**281**:452.
9. Fearn J, Hibbard BM, Laurence KM, Roberts A, Robinson JO. Screening for neural-tube defects and maternal anxiety. *Br J Obstet Gynaecol* 1982; **89**:218–21.
10. Berne-Fromell K, Uddenberg N, Kjessler B. Psychological reactions experienced by pregnant women with an elevated serum alpha-fetoprotein level. *J Psychosomatic Obstet Gynaecol* 1983;**2**:233–7.
11. Burton BK, Dillard RG, Clark EN. The psychological impact of false positive elevations of maternal serum alpha-fetoprotein. *Am J Obstet Gynaecol* 1985;**151**:77–82.
12. Marteau TM, Cook R, Kidd J, Michie S, Johnston M, Slack J, *et al*. The psychological effects of false positive results in prenatal screening for fetal abnormality: a prospective study. *Prenat Diagn* 1992;**12**:205–14.
13. Green JM. Serum screening for Down's syndrome: the experiences of obstetricians in England & Wales. *BMJ* 1994;**309**:769–72.
14. Berne-Frommel K, Kjessler B, Josefson G. Anxiety concerning fetal malformation in women who accept or refuse alpha-fetoprotein screening in pregnancy. *J Psychosom Obstet Gynaecol* 1983;**2**:94–7.
15. Berne-Frommel K, Kjessler B. Anxiety concerning fetal malformations in pregnant women exposed or not exposed to an antenatal serum alpha-fetoprotein screening program. *Gynaecol Obstet Invest* 1984;**17**:36–9.
16. Burton BK, Dillard RG, Clark EN. Maternal serum alpha-fetoprotein screening: the effect of participation on anxiety and attitude toward pregnancy in women with normal results. *Am J Obstet Gynecol* 1985;**152**:540–3.
17. Marteau TM, Johnston M, Kidd J, Michie S, Cook R, Slack J, *et al*. Psychological models in predicting uptake of prenatal screening. *Psychol Health* 1992;**6**:13–22.
18. Statham H, Green J, Snowdon C. Psychological and social aspects of screening for fetal abnormality during routine antenatal care. In Robinson S, Thomson A, Tickner V, editors. *Proceedings of the 1992 Research and the Midwife Conference*. Manchester: School of Nursing. University of Manchester; 1993. pp. 44–62.
19. Murray J, Cuckle H, Taylor G, Hewison J. Screening for fragile X syndrome. *Health Technol Assess* 1997;**1**(4).
20. Pollitt RJ, Green A, McCabe CJ, Booth A, Cooper NJ, Leonard JV, *et al*. Neonatal screening for inborn errors of metabolism: cost, yield and outcome. *Health Technol Assess* 1997;**1**(7).
21. Seymour CA, Thomason MJ, Chalmers RA, Addison GM, Bain MD, Cockburn F, *et al*. Newborn screening for inborn errors of metabolism: a systematic review. *Health Technol Assess* 1997;**1**(11).
22. Bekker H, Thornton JG, Airey CM, Connelly JB, Hewison J, Lilleyman J, *et al*. Informed decision making: an annotated bibliography and systematic review. *Health Technol Assess* 1999;**3**(1).

23. Murray J, Cuckle H, Taylor G, Littlewood J, Hewison J. Screening for cystic fibrosis. *Health Technol Assess* 1999;**3**(8).

24. Zeuner D, Ades AE, Karnon J, Brown J, Dezateaux C, Anionwu EN. Antenatal and neonatal haemoglobinopathy screening in the UK: review and economic analysis. *Health Technol Assess* 1999;**3**(11).

25. Davies SC, Cronin E, Gill M, Greengross P, Hickman M, Normand C. Screening for sickle cell disease and thalassaemia: a systematic review with supplementary research. *Health Technol Assess* 2000; **4**(3).

26. Petticrew MP, Snowden AJ, Lister-Sharp D, Wright K. False-negative results in screening programmes: systematic review of impact and implications. *Health Technol Assess* 2000;**4**(5).

27. Marteau TM, Johnston M, Plenicar M, Shaw RW, Slack J. Development of a self-administered questionnaire to measure women's knowledge of prenatal screening and diagnostic tests. *J Psychosom Res* 1988;**32**:403–8.

28. Statham H, Green J, Snowdon C. Mothers' consent to screening newborn babies for disease. *BMJ* 1993;**306**:858–9.

29. Bekker HL. Decision making and prenatal testing. PhD thesis, University of Leeds; 1999.

30. Middleton A. Attitudes of deaf and hearing individuals towards issues surrounding genetic testing for deafness. PhD thesis, University of Leeds; 1999.

31. Ahmed S. Thalassaemia carrier testing in pregnant Pakistani women: perceptions of 'information' and 'consent'. PhD thesis, University of Leeds; 2002.

32. Bryant LD. Understandings of Down's syndrome in the prenatal testing context. PhD thesis, University of Leeds; 2003.

33. Marteau TM. Towards informed decisions about prenatal testing: a review. *Prenat Diagn* 1995; **15**:1215–26.

34. Jepson R, Clegg A, Forbes C, Lewis R, Sowden A, Kleijnen J. The determinants of screening uptake and interventions for increasing uptake: a systematic review. *Health Technol Assess* 2000;**4**(14).

35. Murphy E, Dingwall R, Greatbach D, Parker S, Watson P. Qualitative research methods in health technology assessment: a review of the literature. *Health Technol Assess* 1998;**2**(16).

36. Collins RF, Bekker HL, Dodwell DJ. Follow-up care of patients treated for breast cancer: a structured review. *Cancer Treat Rev* 2004;**30**:19–35.

37. Smith DK, Shaw RW, Marteau TM. Informed consent to undergo serum screening for Down's syndrome: the gap between policy and practice. *BMJ* 1994;**309**:776.

38. Freda MC, DeVore N, Valentine-Adams N, Bombard A, Merkatz IR. Informed consent for maternal serum alpha-fetoprotein screening in an inner city population: how informed is it? *J Obst Gynecol Neonatal Nurs* 1998;**27**:99–106.

39. Grewal GK, Moss HJ, Aitken DA, Bjornsson S, Cameron AD, Pell JP. Factors affecting women's knowledge of antenatal serum screening. *Scot Med J* 1997;**42**:111–13.

40. Glazier R, Goel V, Holzapfel S, Summers A, Pugh P, Yeung M. Written patient information about triple marker screening: a randomised controlled trial. *Obstet Gynecol* 1997;**90**:769–74.

41. Chilaka VN, Konje JC, Stewart CR, Narayan H, Taylor DJ. Knowledge of Down syndrome in pregnant women from different ethnic groups. *Prenat Diagn* 2001;**21**:159–64.

42. Mulvey S, Wallace EM. Women's knowledge of and attitudes to first and second trimester screening for Down's syndrome. *Br J Obstet Gynaecol* 2000;**107**:1302–5.

43. Marteau TM, Kidd J, Michie S, Cook R, Johnston M, Shaw RW. Anxiety, knowledge and satisfaction in women receiving false positive results on routine prenatal screening – a randomized controlled trial. *J Psychosom Obst Gynaecol* 1993;**14**:185–96.

44. Graham W, Smith P, Kamal A, Fitzmaurice A, Smith N, Hamilton N. Randomised controlled trial comparing effectiveness of touch screen system with leaflet for providing women with information on prenatal tests. *BMJ* 2000; **320**:155–60.

45. Michie S, Smith D, Marteau TM. Prenatal tests: how are women deciding? *Prenat Diagn* 1999; **19**:743–8.

46. Goel V, Glazier R, Holzapfel S, Pugh P, Summers A. Evaluating patient's knowledge of maternal serum screening. *Prenat Diagn* 1996;**16**:425–30.

47. Ormond KE, Pergament E, Fine BA. Pre-screening education in multiple marker screening programs: the effect on patient anxiety and knowledge. *J Genet Couns* 1996;**5**:69–80.

48. Michie S, Smith D, McClennan A, Marteau TM. Patient decision making: an evaluation of two different methods of presenting information about a screening test. *Br J Health Psychol* 1997;**2**:317–26.

49. Thornton JG, Hewison J, Lilford RJ, Vail A. A randomised trial of three methods of giving information about prenatal testing. *BMJ* 1995; **311**:1127–30.

50. Press N, Browner CH. Characteristics of women who refuse an offer of prenatal diagnosis: data

from the California maternal serum alpha fetoprotein blood test experience. *Am J Med Genet* 1998;**78**:433–45.

51. Santalahti P, Aro AR, Hemminki E, Helenius H, Ryynanen M. On what grounds do women participate in prenatal screening? *Prenat Diagn* 1998;**18**:153–65.

52. Heikkila A, Ryynanen M, Kirkinen P, Saarikoski S. Results and views of women in population-wide pregnancy screening for trisomy 21 in east Finland. *Fetal Diagn Ther* 1997;**12**:93–6.

53. Moyer A, Brown B, Gates E, Daniels M, Brown HD, Kuppermann M. Decisions about prenatal testing for chromosomal disorders: perceptions of a diverse group of pregnant women. *J Womens Health Gender-Based Med* 1999;**8**:521–31.

54. Browner CH, Preloran M, Press NA. The effects of ethnicity, education and an informational video on pregnant women's knowledge and decisions about a prenatal diagnostic screening test. *Patient Educ Couns* 1996;**27**:135–46.

55. Salonen R, Kurki L, Lappalainen M. Experiences of mothers participating in maternal serum screening for Down's syndrome. *Eur J Hum Genet* 1996;**4**:113–19.

56. Gekas J, Gondry J, Mazur S, Cesbron P, Thepot F. Informed consent to serum screening for Down syndrome: are women given adequate information? *Prenat Diagn* 1999;**19**:1–7.

57. Carroll JC, Brown JB, Reid AJ, Pugh P. Women's experience of maternal serum screening. *Can Fam Physician* 2000;**46**:614–20.

58. Al-Jader LN, Parry-Langdon N, Smith RJ. Survey of attitudes of pregnant women towards Down syndrome screening. *Prenat Diagn* 2000;**20**:23–9.

59. Statham H, Green J. Serum screening for Down's syndrome: some women's experiences. *BMJ* 1993; **307**:174–6.

60. Roelofsen E-E, Kamerbeek L-I, Tymstra Tj. Chances and choices: psycho-social consequences of maternal serum screening: a report from The Netherlands. *J Reprod Infant Psychol* 1993;**11**:41–7.

61. Priest JH, Fitzgerald JM, Haag MM, Streets K, Vanisko M, Johnson JP. Acceptance of amniocentesis by women in the state of Montana (USA) who are screen positive for Down's syndrome. *J Med Screen* 1998;**5**:178–82.

62. Marteau TM, Saidi G, Goodburn S, Lawton J, Michie S, Bobrow M. Numbers or words? A randomized controlled trial of presenting screen negative results to pregnant women. *Prenat Diagn* 2000;**20**:714–18.

63. Hewison J, Cuckle H, Baillie C, Sehmi I, Lindow S, Jackson F, *et al*. Use of videotapes for viewing at home to inform choice in Down syndrome screening: a randomised controlled trial. *Prenat Diagn* 2001;**21**:146–9.

64. Weinans MJ, Huijssoon AM, Tymstra T, Gerrits MC, Beekhuis JR, Mantingh A. How women deal with the results of serum screening for Down syndrome in the second trimester of pregnancy. *Prenat Diagn* 2000;**20**:705–8.

65. Robinson J. Prenatal screening: a retrospective study. *Br J Midwifery* 2001;**9**:412–17.

66. Royal College of Obstetricians and Gynaecologists. *Report of the working party on biochemical markers and the detection of Down's syndrome*. London: RCOG Press; 1993.

67. Spielberger C, Gorsuch RL, Lushene R, Vagg PR, Jacobs GA. *State-trait anxiety inventory: STAI form Y*. Palo Alto, CA: Consulting Psychologists Press; 1970.

68. Marteau TM, Bekker H. The development of a six-item short-form of the state scale of the Spielberger state-trait anxiety inventory (STAI). *Br J Clin Psychol* 1992;**31**:301–6.

69. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983; **67**:361–70.

70. Ley P, Llewellyn S. Improving patients' understanding, recall, satisfaction and compliance. In Broome A, Llewellyn S, editors. *Health psychology: processes and applications*. 2nd ed. London: Chapman and Hall; 1995; Chapter 5.

71. Johnston M. Hospitalisation in adults. In Baum A, Newman S, Weinman J, West, R, McManus C, editors. *Cambridge handbook of psychology, health and medicine*. Cambridge: Cambridge University Press; 1997. pp. 121–3.

72. Bekker HL, Hewison J, Thornton JG. Understanding why decision aids work: linking process with outcome. *Patient Educ Couns* 2003; **50**:323–9.

73. Schwarzer R, Quast H-H, Jerusalem M. The impact of anxiety and self-consciousness on cognitive appraisals in the achievement process. In Schwarzer R, van der Ploeg HM, Spielberger CD, editors. *Advances in test anxiety research*, Vol. 5. Lisse: Swets & Zeitlinger; 1987. pp. 39–52.

74. Bekker HL, Legare F, Stacey D, O'Connor A, Lemyre L. Is anxiety a suitable measure of decision aid effectiveness: a systematic review? *Patient Educ Couns* 2003,**50**:255–62.

75. Evans MI, Bottoms SF, Carlucci T, Grant J, Belsky RL, Solyom AE, *et al*. Determinants of altered anxiety after abnormal maternal serum alpha-fetoprotein screening. *Am J Obstet Gynecol* 1988;**159**:1501–4.

76. Marteau TM, Kidd J, Cook R, Johnston M, Michie S, Shaw RW, *et al*. Screening for Down's syndrome. *BMJ* 1988;**297**:1469.

77. Quagliarini D, Betti S, Brambati B, Nicolini U. Coping with serum screening for Down syndrome when the results is given as a numeric value. *Prenat Diagn* 1998;**18**:816–21.

78. Abuelo DN, Hopmann MR, Barsel-Bowers G, Goldstein A. Anxiety in women with low maternal serum alpha-fetoprotein screening results. *Prenat Diagn* 1991;**11**:381–5.

79. Keenan KL, Basso D, Goldkrand J, Butler WJ. Low level of maternal serum alpha-fetoprotein: its associated anxiety and the effects of genetic counselling. *Am J Obstet Gynecol* 1991;**164**:54–6.

80. Santalahti P, Latikka AM, Ryynanen M, Hemminki E. Women's experiences of prenatal serum screening. *Birth* 1996;**23**:101–7.

81. Jorgensen FS. User acceptability of an alpha-fetoprotein screening programme. *Dan Med Bull* 1995;**42**:100–5.

82. Santalahti P, Hemminki E, Latikka AM, Ryynanen M. Women's decision-making in prenatal screening. *Soc Sci Med* 1998;**46**:1067–76.

83. Burn J, Fairgrieve S, Franks P, White I, Magnay D. Audit of maternal serum screening: strategies to augment counselling in response to women's views. *Eur J Hum Genet* 1996;**4**:108–12.

84. Dodds R, Newburn M. Support during screening – an NCT report. *Mod Midwife* 1997;**7**:23–6.

85. Alteneder RR, Kenner C, Greene D, Pohorecki S. The lived experience of women who undergo prenatal diagnostic testing due to elevated maternal serum alpha-fetoprotein screening. *Am J Maternal Child Nurs* 1998;**23**:180–6.

86. Jan S-W, Chen C-P, Huang L-H, Huang F-Y, Lan C-C. Attitudes toward maternal serum screening in Chinese women with positive results. *J Genet Couns* 1996;**5**:169–80.

87. Rausch ND, Lambert-Messerlain GM, Canick JA. Participation in maternal serum screening following screen positive results in previous pregnancy. *J Med Screen* 2000;**7**:4–6.

88. Wald NG. Couple screening for cystic fibrosis. *Lancet* 199I;**338**:1318–19.

89. Mennie ME, Liston WA, Brock DJH. Prenatal cystic fibrosis carrier testing: designing an information leaflet to meet the specific needs of the target population. *J Med Genet* 1992; **29**:308–12.

90. Livingstone J, Axton RA, Mennie M, Gilfillan A, Brock DJH. A preliminary trial of couple screening for cystic fibrosis: designing an appropriate information leaflet. *Clin Genet* 1993; **43**:57–62.

91. Mennie ME, Compton ME, Gilfillan A, Liston WA, Pullen I, Whyte DA, *et al*. Prenatal screening for cystic fibrosis: psychological effects on carriers and their partners. *J Med Genet* 1993;**30**:543–8.

92. Witt DR, Schaefer C, Hallam P, Wi S, Blumberg B, Fishbach A, *et al*. Cystic fibrosis heterozygote screening in 5,161 pregnant women. *Am J Hum Genet* 1996;**58**:823–35.

93. Jung U, Urner U, Grade K, Coutelle C. Acceptability of carrier screening for cystic fibrosis during pregnancy in a German population. *Hum Genet* 1994;**94**:19–24.

94. Miedzybrodzka ZH, Hall MH, Mollison J, Templeton A, Russell IT, Dean JC, *et al*. Antenatal screening for carriers of cystic fibrosis: randomised trial of stepwise v couple screening. *BMJ* 1995; **310**:353–7.

95. Grody WW, Dunkel-Schetter C, Tatsugawa ZH, Fox MA, Fang CY, Cantor RM, *et al*. PCR-based screening for cystic fibrosis carrier mutations in an ethnically diverse pregnant population. *Am J Hum Genet* 1997;**60**:935–47.

96. Cuckle H, Quirke P, Sehmi I, Lewis F, Murray J, Cross D, *et al*. Antenatal screening for cystic fibrosis. *Br J Obstet Gynaecol* 1996;**103**:795–9.

97. Leonard KP, Bartholomew LK, Swank PR, Parcel GS. A comparison of two approaches to education about carrier testing for cystic fibrosis. *J Genet Couns* 1995;**4**:97–113.

98. Mennie M, Compton M, Gilfillan A, Axton RA, Liston WA, Pullen I, *et al*. Prenatal screening for cystic fibrosis: attitudes and responses of participants. *Clin Genet* 1993;**44**:102–6.

99. Mennie ME, Axworthy D, Liston WA, Brock DJH. Prenatal screening for cystic fibrosis carriers: does the method of testing affect the longer-term understanding and reproductive behaviour of women? *Prenat Diagn* 1997;**17**:853–60.

100. Clausen H, Brandt NJ, Schwartz M, Skovby F. Psychological and social impact of carrier screening for cystic fibrosis among pregnant woman – a pilot study. *Clin Genet* 1996;**49**:200–5.

101. Hartley NE, Scotcher D, Harris H, Williamson P, Wallace A, Craufurd D, *et al*. The uptake and acceptability to patients of cystic fibrosis carrier testing offered in pregnancy by the GP. *J Med Genet* 1997;**34**:459–64.

102. Harris H, Scotcher D, Hartley N, Wallace A, Craufurd D, Harris R. Pilot study of the acceptability of cystic fibrosis carrier testing during routine antenatal consultations in general practice. *Br J Gen Pract* 1996;**46**:225–7.

103. Rowley PT, Loader S, Walden M. Pregnant women identified as hemoglobinopathy carriers by prenatal screening want genetic counselling and use information provided. *Birth Defects: Original Article Series* 1988;**23**:449–54.

104. Wallerstein R, Seshadri K, Brady-Yasbin S, Shih L. A retrospective survey of community based utilization of Tay Sachs screening in eight New Jersey counties. *J Genet Couns* 1994;**3**:125–31.

105. Loader S, Sutera CJ, Walden M, Kozyra A, Rowley PT. Prenatal screening for hemoglobinopathies II. Evaluation of counselling. *Am J Hum Genet* 1991;**48**:447–51.

106. Green J, France-Dawson M. Women's experiences of routine screening during pregnancy: the sickle cell study. Targeting health promotion: reaching those in the West Midlands. In Clarke A, Parsons E, editors. *Culture, kinship and genes: towards cross-cultural genetics*. New York: St. Martin's Press; 1997. pp. 120–32.

107. Rowley PT, Loader S, Sutera CJ, Walden M, Kozyra A. Prenatal screening for hemoglobinopathies III. Applicability of the health belief model. *Am J Hum Genet* 1991;**48**:452–9.

108. Rowley PT, Loader S, Sutera CJ, Walden M, Kozyra A. Prenatal screening for hemoglobinopathies I. A prospective regional trial. *Am J Hum Genet* 1991;**48**:439–46.

109. Green JM, Statham H, Snowdon C. Women's knowledge of prenatal screening tests. 1: Relationships with hospital screening policy and demographic factors. *J Reprod Infant Psychol* 1993;**11**:11–20.

110. Livingstone J, Axton RA, Gilfillan A, Mennie M, Compton M, Liston WA, *et al*. Antenatal screening for cystic fibrosis: a trial of the couple model. *BMJ* 1994;**308**:1459–62.

111. Al-Jader LN, Goodchild MC, Ryley HC, Harper PS. Attitudes of parents of cystic fibrosis children towards neonatal screening and antenatal diagnosis. *Clin Genet* 1990;**38**:460–5.

112. Hall S, Bobrow M, Marteau TM. Psychological consequences for parents of false negative results on prenatal screening for Down's syndrome: retrospective interview study. *BMJ* 2000; **320**:407–12.

113. Kornman LH, Wortelboer MJ, Beekhuis JR, Morssink LP, Mantingh A. Women's opinions and the implications of first- versus second-trimester screening for fetal Down's syndrome. *Prenat Diagn* 1997;**17**:1011–18.

114. Press N, Browner CH. Why women say yes to prenatal diagnosis. *Soc Sci Med* 1997;**45**:979–89.

115. Jorgensen FS. Declining an alpha-fetoprotein test in pregnancy, why and who? *Acta Obstet Gynecol Scand* 1995;**74**:3–11.

116. Santalahti P, Hemminki E, Aro AR, Helenius H, Ryynanen M. Participation in prenatal screening tests and intentions concerning selective termination in Finnish maternity care. *Fetal Diagn Ther* 1999;**14**:71–9.

117. Markens S, Browner CH, Press N. 'Because of the risks': how US pregnant women account for refusing prenatal screening. *Soc Sci Med* 1999; **49**:359–69.

118. Esen UI, Olajide F. Expectations and fears of women regarding two methods of prenatal screening. *Int J Gynaecol Obstet* 1997;**57**:193–4.

119. Phillips OP, Seely L, Wan JY, Wachtel SS, Shulman LP. A survey of attitudes about maternal serum screening for fetal chromosome abnormalities in women 35 years of age and older. *Fetal Diagn Ther* 1998;**13**:357–60.

120. Fairgrieve S. Screening in pregnancy. Screening for Down's syndrome: what the women think. *Br J Midwifery* 1997;**5**:148-51.

121. Jorgensen FS. Attitudes to prenatal screening, diagnosis and research among pregnant women who accept or decline an alpha-fetoprotein test. *Prenat Diagn* 1995;**15**:419–29.

122. Browner CH, Press NA. The normalization of prenatal diagnostic screening. In Ginsburg F, Rapp R, editors. *Conceiving the new world order: the global politics of reproduction*. Berkeley, CA: University of California Press; 1995. pp. 307–22.

123. Loader S, Caldwell P, Kozyra A, Levenkron JC, Boehm CD, Kazazian HH Jr, *et al*. Cystic fibrosis carrier population screening in the primary care setting. *Am J Hum Genet* 1996;**59**:234–47.

124. Fang CY, Dunkel-Schetter C, Tatsugawa ZH, Fox MA, Bass HN, Crandall BF, *et al*. Attitudes toward genetic carrier screening for cystic fibrosis among pregnant women: the role of health beliefs and avoidant coping style. *Womens Health* 1997; **3**:31–51.

125. Mennie ME, Compton ME, Liston WA, Brock DJH. Gene therapy for cystic fibrosis: will it affect the uptake of prenatal carrier screening. *Prenat Diagn* 1994;**14**:1158–62.

126. Mennie ME, Gilfillan A, Compton ME, Liston WA, Brock DJ. Prenatal cystic fibrosis carrier screening: factors in a woman's decision to decline testing. *Prenat Diagn* 1993;**13**:807–14.

127. O'Connor AM, O'Brien-Pallas LL. Decisional conflict. In McFarland GK, McFarlane EA, editors. *Nursing, diagnosis and intervention*. Toronto: Mosby; 1989. pp. 486–96.

128. Charles C, Whelan T, Gafni A. What do we mean by partnership in making decisions about treatment? *BMJ* 1999;**319**:780–2.

129. Marteau TM, Dormandy E, Michie S. A measure of informed choice. *Health Expect* 2001;**4**:99–108.

130. O'Connor AM. Validation of a decision conflict scale. *Med Decis Making* 1995;**15**:25–30.

131. Holmes-Rovner M, Krol J, Schmitt N, Rovner DR, Breer ML, Rothert ML, *et al*. Patient satisfaction

with health care decisions: the satisfaction with decision scale. *Med Decis Making* 1996;**16**:58–64.

132. Michie S, Dormandy E, Marteau TM. The multi-dimensional measure of informed choice: a validation study. *Patient Educ Couns* 2002;**48**:87–91.

133. Baron J. *Thinking and deciding*. 2nd ed. Cambridge: Cambridge University Press; 1994.

134. Doherty RA, Palomaki GE, Kloza EM, Erickson JL, Haddow JE. Couple-based prenatal screening for cystic fibrosis in primary care settings. *Prenat Diagn* 1996;**16**:397–404.

135. Bekker HL. Genetic testing: facilitating informed choices. In Cooper DN, Thomas N, editors. *Nature encyclopaedia of the human genome*. New York: Nature; 2003. pp. 926–30.

136. Payne D. Couple has the right to refuse test on newborn child. *BMJ* 2001;**323**:1149.

137. Baroni MA, Anderson YE, Mischler E. Cystic fibrosis newborn screening: impact of early screening results on parenting stress. *Pediatr Nurs* 1997;**23**:143–51.

138. Boland C, Thompson NL. Effects of newborn screening of cystic fibrosis on reported maternal behaviour. *Arch Dis Child* 1990;**65**:1240–4.

139. Helton J, Harmon RJ, Robinson N, Accurso FJ. Parental attitudes toward newborn screening for cystic fibrosis. *Pediatr Pulmon Suppl* 1991;**7**:23–8.

140. Holtzman NA, Faden R, Chwalow AJ, Horn SD. Effect of informed parental consent on mothers' knowledge of newborn screening. *Pediatrics* 1983; **72**:807–12.

141. Faden R, Chwalow AJ, Holtzman NA, Horn SD. A survey to evaluate parental consent as public policy for neonatal screening. *Am J Public Health* 1982;**72**:1347–52.

142. Mischler EH, Wilfond BS, Fost N, Laxova A, Reiser C, Sauer CM, *et al*. Cystic fibrosis newborn screening: impact on reproductive behavior and implications for genetic counseling. *Pediatrics* 1998;**102**:44–52.

143. Tluczek A, Mischler EH, Farrell PM, Fost N, Peterson NM, Carey P. Parents' knowledge of neonatal screening and response to false-positive cystic fibrosis testing. *Dev Behav Pediatr* 1992; **13**:181–6.

144. Tluczek A, Mischler EH, Bowers B, Peterson NM, Morris ME, Farrell PM, *et al*. Psychological impact of false-positive results when screening for cystic fibrosis. *Pediatr Pulmon Suppl* 1991;**7**:29–37.

145. Bodegard G, Fyro K, Larsson A. Psychological reactions in 102 families with a newborn who has a falsely positive screening test for congenital hypothyroidism. *Acta Paediatr Scand* 1983; **304**:1–21.

146. Fyro K, Bodegard G. Difficulties in psychological adjustment to a new neonatal screening programme. *Acta Paediatr Scand* 1988;**77**:226–31.

147. Fyro K, Bodegard, G. Four-year follow-up of psychological reactions to false positive screening tests for congenital hypothyroidism. *Acta Paediatr Scand* 1987;**76**:107–14.

148. Fyro K. Neonatal screening: life stress scores in families given a false positive result. *Acta Paediatr Scand* 1988;**77**:232–8.

149. Tymstra T. False positive results in screening tests: experiences of parents of children screened for congenital hypothyroidism. *Fam Pract* 1986;**3**:92–6.

150. Green JM, Murton FE. Diagnosis of Duchenne muscular dystrophy: parents' experiences and satisfaction. *Child Care Health Dev* 1996;**22**:113–28.

151. Hildes E, Jacobs HK, Cameron A, Seshia SS, Booth F, Evans JA. Impact of genetic counselling after neonatal screening for Duchenne muscular dystrophy. *Am J Med Genet* 1993;**30**:670–4.

152. Parsons E, Bradley D, Clarke A. Disclosure of Duchenne muscular dystrophy after newborn screening. *Arch Dis Child* 1996;**74**:550–3.

153. Bradley DM, Parsons EP, Clarke AJ. Experience with screening newborns for Duchenne muscular dystrophy in Wales. *BMJ* 1993;**306**:357–60.

154. Grossman LK, Holtzman NA, Charney E, Schwartz AD. Neonatal screening and genetic counselling for sickle cell trait. *Am J Dis Child* 1985;**139**:241–4.

155. Warren NS, Carter TP, Humbert JR, Rowley PT. Newborn screening for hemoglobinopathies in New York State: experience of physicians and parents of affected children. *J Pediatr* 1982; **100**:373–7.

156. Yu MS, Norris JM, Mitchell CM, Butler-Simon N, Groshek M, Follansbee D, *et al*. Impact on maternal parenting stress of receipt of genetic information regarding risk of diabetes in newborn infants. *Am J Med Genet* 1999;**86**:219–26.

157. Senior V, Marteau TM, Peters TJ. Will genetic testing for predisposition for disease result in fatalism? A qualitative study of parents' responses to neonatal screening for familial hypercholesterolaemia. *Soc Sci Med* 1999; **48**:1857–60.

158. Thelin T, McNeil TF, Aspegren-Jansson E, Sveger T. Psychological consequences of neonatal screening for α_1 antitrypsin deficiency. Parental reactions to the first news of their infants' deficiency. *Acta Paediatr Scand* 1985;**74**:787–93.

159. Sveger T, Thelin T. Four year old children with α_1 antitripsin deficiency. Clinical follow up and parental attitudes towards neonatal screening. *Acta Paediatr Scand* 1981;**70**:171–7.

160. Sorenson JR, Levy HL, Mangione TW, Sepe SJ. Parental response to repeat testing of infants with 'false-positive' results in a newborn screening program. *Pediatrics* 1984;**73**:183–7.

161. Rothenberg MB, Sills EM. Iatrogenesis: the PKU anxiety syndrome. *J Am Acad Child Psychol* 1968, **7**:689–92.

162. Thelin T, McNeil T-F, Aspegren-Jansson E, Sveger T. Identifying children at high somatic risk: possible long-term effects on the parents' attitudes toward themselves as parents and toward having more children. *Acta Psychiatr Scand* 1985;**72**:74–80.

163. Thelin T, McNeil TF, Aspegren-Jansson E, Sveger T. Identifying children at high somatic risk: possible long-term effects on the parents' views of their own health and current life situation. *Acta Paediatr Scand* 1985;**71**:644–53.

164. Dudding T, Wilcken B, Burgess B, Hambly J, Turner G. Reproductive decisions after neonatal screening identifies cystic fibrosis. *Arch Dis Child Fetal Neonatal Ed* 2000;**82**:124–7.

165. Bryant LD, Green JM, Hewison J. Prenatal screening for Down's syndrome: some psychosocial implications of a 'screening for all' policy. *Publ Health* 2001;**115**:356–8.

166. Green JM, Statham H, Snowdon C. Screening for fetal abnormalities: attitudes and experiences. In Chard T, Richards MPM, editors. *Obstetrics in the 1990's: current controversies*. London: McKeith Press; 1992. pp. 65–89.

167. Connor M, Norman P. *Predicting health behaviour*. Milton Keynes: Open University Press; 1996.

168. Green, JM. Genetic screening: something for everyone (including psychologists). Introductory paper given to a symposium on genetic screening at the Annual Conference of the British Psychological Society, University of Warwick, 1–4 April 1995. Summarised in *The Psychologist*, 1995;**8**:305–6.

169. National Institute for Clinical Excellence. *Antenatal care: routine care for the healthy pregnant woman. Clinical Guideline 6*. London: National Institute for Clinical Excellence; 2003.

170. Department of Health. *The NHS Plan: a plan for investment, a plan for reform*. London: Stationery Office; 2000.

171. Department of Health. *The national service framework for children, young people and maternity services – emerging findings*. London: Stationery Office; 2003.

Appendix 1

Medline Search Strategy run 2.6.00

1 (screen$ or test$ or diagnos$ or amniocentesis or ultrasound).ti,ab
2 (terminat$ adj1 pregnan$).mp. [mp=title, abstract, registry number word, mesh subject heading]
3 1 or 2
4 ((biochemical or serum) adj screen$).ti,ab.
5 4 or 3
6 (maternal or antenatal or pregnan$ or newborn$ or neonat$ or pernatal or fetal or foetal).ti,ab.
7 6 and 5
8 (maternal or antenatal or pregnan$ or newborn$ or neonat$ or pernatal or fetal or foetal).ti,ab. adj10 (((biochemical or serum) adj screen$).ti,ab. or ((screen$ or test$ or diagnos$ or amniocentesis or ultrasound).ti,ab. or (terminat$ adj1 pregnan$).mp.))
9 exp patient acceptance of health care/
10 exp behavior/
11 exp truth disclosure/
12 12 exp attitude to health/
13 exp patient participation/
14 exp knowledge/ or understanding.mp. or practice/ [mp=title,abstract, registry number word, mesh subject heading]
15 exp anxiety/
16 exp false negative reactions/
17 exp false positive reactions/
18 patient understanding/
19 Professional-patient relations/
20 informed consent.ti,ab.
21 informed decision making.ti,ab.
22 patient decision.ti,ab.
23 or/9-22
24 23 and 7
25 (aneuploid$ or genetic or chromosomal or congenital or trisomy or down's syndrome or down sydnrome or cystic fibrosis or CF or duchenne or AFP or neural tube defect$ or fetoprotein or NTD$ or edwards syndrome or klinefelter$ syndrome or turner$ syndrome or fragile X or tay sachs or haemoglobinopath$ or hemoglobinopath$ or alpha antitrypsin or sickle cell or thalass?emia or inborn errors or PKU or phenyketonuria or adrenal hypoplasia or hypothyroidism).ti,ab
26 25 and 24
27 27 exp neoplasms/
28 exp HIV/
29 exp heart/
30 exp sexually transmitted diseases/
31 exp cervix uteri/
32 exp huntington disease/
33 33 or/27-3234
34 26 not 33

Appendix 2

Data extraction form

Article details

Paper ID No:	
Authors	
Any authors with psychosocial background?	Yes / No (delete as appropriate)
Title	
Journal details (name.yr;:vol:pgs)	
Stated aims or study outline	
Database	Medline / PsycLIT / IDS / Hand / WOS
Reviewer date	Sent / Returned /
Reviewer	LB / SA / HB / AM / JG / JH / CH / AW / VR

Study characteristics

Study location	Country: City:
Year(s) of screening	
Screening test characteristics	a) Established / Experimental b) Widely available / Limited to study / Modified for study
Screening test uptake for clinic	Not Reported / n =
Conditions screened	DS / CF / Thal / Sickle / Tay–Sachs / Hypothyroidism / PKU / Haem(NS) / Genetic (NS)/ NTDs Other, specify
Test type	Blood / Urine / Ultrasonography / Sweat / Mouthwash Other, specify
Timing	Antenatal / Neonatal
Participants	Pregnant women / Male partners / GPs / Obstetricians / Parents (mother) / Parents (both) / Other, specify
Groups studied (note all those that apply)	Attenders / Non-attenders / Both (attenders and non-attenders) False +ves / False –ves / True +ves / True –ves

Methods

Theoretical framework	Yes / No, If yes specify
Design	RCT / prospective cohort / before and after / survey / Case–control / Other (specify)
Method of data collection	Questionnaire / Interview / Existing Records / Other If other specify
Sample selection	Total available population / Systematic sample / Volunteer (convenience) / Not adequately described
Sample size (regarding the study outcomes – not background clinic figures)	Total no. available – Total no. initially invited – No. initial respondents – No. excluded – Reason(s) for exclusion No. in final sample –
Any eligibility criteria	Yes / No (If yes specify)
Sample characteristics (any information regarding)	Yes / No (If yes specify)
Control characteristics (any information regarding)	Yes / No (If yes specify)
Any concerns regarding design and methods?	Yes / No (If yes specify)

Variables measured

VARIABLE	DATA SOURCE	MEASUREMENT TOOL	TIMING AND FREQUENCY OF MEASUREMENT
Test uptake			
Knowledge			
Anxiety			
Attitudes/beliefs			
Risk perception			
Other choices (e.g. termination)			
Other cognitions (e.g. social norm)			
Other affect (e.g. depression)			
Other service measure (e.g. satisfaction)			
Sociodemographic (state all)			

Description group and/or intervention groups

Group	Brief description	No. in group
Group 1		
Group 2		
Group 3		
Group 4		
Group 5		

Results of findings (outcomes relating to review objectives – questions to be addressed by the review)

Variable	Findings	Statistical comparisons	Effect yes/no

Results: authors' summary

Quality I: concerns about results, findings, interpretation

Analysis	
Confounds	
Interpretation	
Generalisability	

Quality of study

	YES	NO	Unclear	N/A
Sample				
Adequate sample size	☐	☐	☐	☐
Stratified/random sample	☐	☐	☐	☐
Representative of study population	☐	☐	☐	☐
Low attrition	☐	☐	☐	☐
Intervention studies only				
Clearly defined intervention (reduction of confounds)	☐	☐	☐	☐
Assessors blinded to treatment allocation	☐	☐	☐	☐
Randomisation low risk of bias (i.e. 3rd party)	☐	☐	☐	☐
Different groups similar at baseline	☐	☐	☐	☐
Analysis intention to treat	☐	☐	☐	☐
Interpreting results				
Mostly validated measures	☐	☐	☐	☐
Mostly appropriate timing of measures (length)	☐	☐	☐	☐
Measures consistent with aims	☐	☐	☐	☐
Conclusions consistent with results	☐	☐	☐	☐

Yes = 1
No = –1
Unclear = 0

Total quality score ☐/

Appendix 3

Details of papers included

Antenatal

Authors, year	City, country	Stated aim of article	Study group 1	*N*	Comparison group(s)	*N*
Serum screening for Down's syndrome (or Down's and NTDs)						
Marteau *et al.*, 1992[12]	London, UK	To describe the impact of false-positive results from initial MSAFP screening	Women who received normal MSAFP result	346	Women who received abnormal MSAFP result (none found to have abnormalities on further testing and none gave birth to children with Down's syndrome or spina bifida)	26
Marteau *et al.*, 1992[17]	London, UK	To determine which psychological models are most useful in predicting uptake of a prenatal screening test	Women who undertook screening	902	Women who declined screening (gave reasons) Women who declined testing (no reason given)	51 47
Smith *et al.*, 1994[37]	UK	To assess the link between knowledge and consent in women undergoing screening	Women attending one of 5 hospitals up to 18 weeks gestation	353		
Freda *et al.*, 1998[38]	Bronx, New York, USA	To determine whether women getting information and watching a videotape about MSAFP screening understood enough to give informed consent	Women attending antenatal class, candidates for test	53		
Grewal *et al.*, 1997[39]	Glasgow, UK	To assess pregnant women's knowledge of antenatal screening tests for fetal anomaly and implication of results	Women attending antenatal class, candidates for test	572		
Glazier *et al.*, 1997[40]	Ontario, Canada	To investigate how a new educational pamphlet affects knowledge and to identify subgroups of women who do not benefit	Women receiving leaflet on triple marker screening	133	Women receiving leaflet on daily activity during pregnancy	64
Chilaka *et al.*, 2001[41]	Leicester, UK	To assess level of awareness and understanding of Down's syndrome in cohort of women from different ethnic groups receiving hospital antenatal care	Caucasian women	117	Asian women born outside UK Asian women born in UK Others	86 32 10
Mulvey & Wallace, 2000[42]	Clayton, Australia	To explore women's preferences for first or second trimester screening	Women at first antenatal visit	100		
Marteau *et al.*, 1993[43]	London, UK	To test two hypotheses in a 2 × 2 design: 1. Detailed information about MSAFP will increase knowledge 2. Training in anxiety management techniques will reduce anxiety	Women received a booklet about MSAFP	22	Women received early antenatal class on anxiety management Women received both booklet and class Women did not receive either booklet or class	14 23 10

continued

Authors, year	City, country	Stated aim of article	Study group 1	*N*	Comparison group(s)	*N*
Graham *et al*., 2000[44]	Aberdeen, UK	To compare a touch screen system with leaflets for providing women with information on prenatal tests	Intervention group both leaflet and touch screen	524	Leaflet-only group	526
Michie *et al*., 1999[45]	London, UK	To describe the extent to which women offered prenatal screening for Down's syndrome were making decisions systematically	Women who had serum screening	261	Women who declined screening	63
Goel *et al*., 1996[46]	Toronto, Canada	To develop an instrument for assessing knowledge about MSS	Women registering for antenatal care	1084		63
Ormond *et al*., 1996[47]	Burlington, Vermont, USA	To determine, prospectively, differences in knowledge or anxiety between women who received additional pretest education re MSS in either written or verbal form, and those who received standard care	Women educated by genetic counsellor	7	Women who read a pamphlet Women who received standard care (educated by physician during consultation)	7 11
Michie *et al*., 1997[48]	London, UK	To investigate whether videos and leaflets with decision trees lead to more systematic decisions about testing and whether systematic decisions lead to better outcomes	Simple leaflet	88	Decision tree leaflet Simple leaflet and video Decision tree leaflet and video	93 76 67
Thornton *et al*., 1995[49]	Bradford and Leeds, UK	To test the effect of extra non-directive information about prenatal testing, given individually or in a class	Women given routine information	567	Women offered extra prenatal testing information individually Women offered extra information in a class	561 563
Press and Browner, 1998[50]	Southern California, USA	To describe which women are more likely to reject MSAFP screening; to understand the reasons for refusal and the meanings associated with it	Women who accepted MSAFP screening: Interviewed Medical charts	 127 452	Women who declined MSAFP screening: Interviewed Medical charts	 31 143
Santalahti *et al*., 1998[51]	Jyvaskyla, Kuopio,Turku, Finland	To examine women's knowledge and perceptions of, and reasons for participation in, prenatal screening	Serum screening	909	Ultrasound screening	424
Heikkila *et al*., 1997[52]	East Finland	To study the attitudes of women in population-wide pregnancy screening for Trisomy 21	Screen-negative women who had a healthy baby	100	Screen-positive women who had a healthy baby. Screen-positive women who had an affected baby	100 14

continued

Authors, year	City, country	Stated aim of article	Study group 1	*N*	Comparison group(s)	*N*
Moyer *et al*., 1999[53]	San Francisco, USA	To elucidate factors that influence women's decisions about genetic screening and testing and to learn about their experiences	Ethnically diverse pregnant women participating in focus groups	75		
Browner *et al*., 1996[54]	Southern California, USA	To examine the efficacy of different ways of presenting information about prenatal screening	Women who self-reported that they had seen the video	64	Women who stated they had not seen the video or didn't know	66
Salonen *et al*., 1996[55]	Helsinki, Finland	To investigate how best to inform mothers about Down's syndrome testing and the meaning of results and how to minimise anxiety caused by positive screening results	Screen positives	625	Screen negatives	240
Gekas *et al*., 1999[56]	Amiens, France	To evaluate MSS test uptake, satisfaction with testing and knowledge and implications of MSS	Women over 38 years with positive MSS result	200		
Carroll *et al*., 2000[57]	Ontario, Canada	To explore ideas, opinions, feelings, and experiences of women regarding prenatal genetic screening (MSS)	Women who had given birth since Jan 1994 and no affected babies, not currently pregnant	60		
Al-Jader *et al*., 2000[58]	Glamorgan, UK	To examine whether pregnant women made informed decisions based on an accurate understanding of the antenatal screening process and to explore their attitudes to screening and termination of a Down's syndrome fetus	Women offered screening and accepted	20	Women not offered screening and not screened Women offered screening and refused	9 5
Statham and Green, 1993[59]	UK	To describe the experiences of a small group of women who had positive results after serum screening for Down's syndrome	Positive screening result yet negative amniocentresis	8	Positive screening result, no amniocentesis Positive screening result, terminated following amniocentesis Positive screening result with unknown amniocentesis results	2 8 2
Roelofsen *et al*., 1993[60]	Groningen, The Netherlands	To describe how women experience MSAFP screening, how the screening affects them, how they interpret the results and what consequences they consider the results to have	Women whose MSAFP showed high risk and who had amniocentesis – all waiting for result at time of interview	20	Postnatal women below official age limit (36 years) for MSAFP (80% had MSAFP) Women over 36 years who had had CVS/amniocentesis in preceding 6 months	105 155

continued

Authors, year	City, country	Stated aim of article	Study group 1	*N*	Comparison group(s)	*N*
Priest *et al.*, 1998[61]	Helena, Montana, USA	To assess factors influencing uptake of amnio after positive screen and identify ways to increase uptake	Women who chose amniocentesis following screen positive	30	Women who chose not to have amniocentesis following screen positive	23
Marteau *et al.*, 2000[62]	London, UK	To assess women's understanding when presented with screen-negative results verbally or with figures	Women presented with risk verbal 'low risk'	112	Women presented with risk figures, e.g. '1 in 500'	97
Hewison *et al.*, 2001[63]	Hull, UK	To assess the effect of Down's syndrome screening video on test uptake, knowledge and psychological stress	Women receiving video and booklet	993	Women receiving booklet	1007
Weinans *et al.*, 2000[64]	Groningen, The Netherlands	To gain insight into users' opinions about maternal serum screening for Down's syndrome in The Netherlands	Pregnant women over 36 years who had not opted out of serum screening	81	Women under 36 years who opted in for serum screening and screened positive (all had amniocentesis and all tested negative)	63
Robinson, 2001[65]	London, UK	To explore the experiences of women who had given birth to a 'normal' baby after screening high risk for Down's syndrome in their quadruple test	Women who screened high risk for Down's syndrome. 6 had amniocentesis, 4 did not. All gave birth to babies unaffected by Down's syndrome	10		
Evans *et al.*, 1988[75]	Detroit, USA	To assess the psychological impact of receiving abnormal MSAFP results	Abnormal screening result	32	Advanced maternal age	37
Marteau *et al.*, 1988[76]	London, UK	To study the psychological impact of receiving false positive results	Women ≥ 38 years with false positive results	21	Women <38 years with false positive results	21
Quagliarini *et al.*, 1998[77]	Milan, Italy	To evaluate how the level of anxiety in women undergoing 2nd trimester serum screening varied when results were given a numeric value (not as positive or negative)	Women undergoing 2nd trimester serum screening	46	Non-pregnant women	816
Abuelo *et al.*, 1991[78]	Rhode Island, USA	To measure anxiety in pregnant women who had low MSAFP, received genetic counselling and chose to undergo amniocentesis for fetal chromosome analysis	Women <35 years with low MSAFP and having amniocentesis at 16–18 weeks	50	Women ≥ 35 years having amniocentesis due to maternal age at 13–14 weeks	50
Keenan *et al.*, 1991[79]	Albany, USA	To investigate anxiety in women <35 years with a low MSAFP result and show the effectiveness of genetic counselling on this anxiety	Women with low levels of MSAFP <35 years attending private practice and obtained counselling	52	Women with normal MSAFP <35 years attending same practice	25

continued

Authors, year	City, country	Stated aim of article	Study group 1	*N*	Comparison group(s)	*N*
Santalahti *et al*., 1996[80]	Jyvaskyla and Kuopio, Finland	To examine the impact of screening positive for Down's syndrome and NTD on women's experience of pregnancy	Had positive serum screen result	45	Matched control – tested negative	46
Jorgensen, 1995[81]	Hvidovre and Sonderjylland, Denmark	To understand the impact of false positive screening results on women	Women having false-positive screening results, then normal results after ultrasound	123	Women having false-positive screening results, then ultrasound and amniocentesis	96
Santalahti *et al*., 1998[82]	Kuopso and Iyraskyla, Finland	To examine how women describe their decision-making in the different phases of serum screening	Women who received positive screening results	45	Group individually matched who received negative screening results	46
Burn *et al*., 1996[83]	Northumberland, UK	To audit participants' views of Down's syndrome screening, including adverse psychological sequelae	Same study as Fairgrieve, 1997[120]			
Dodds & Newburn, 1997[84]	Nationwide, UK	To investigate women's experiences of antenatal screening with a focus on the information and support received	Women responding to NCT questionnaire	2722		
Alteneder *et al*., 1998[85]	Ohio, USA	To explore the experiences of women with elevated MSAFP who had diagnostic procedures to determine fetal status	Women who had amniocentesis	16		
Jan *et al*., 1996[86]	Taipei, Taiwan	To describe women's attitudes to MSFAP screening when they had a positive result	Women screening positive and referred for amniocentesis	214		
Hall *et al*., 2000[112]	UK	To determine psychological consequences for parents of children with Down's syndrome of having received a false-negative result on prenatal screening	Parents with affected child who had screened false-negative	141	Parents with affected child who had not been offered screening Parents with affected child who had declined screening	103 57
Kornman *et al*., 1997[113]	Groningen, The Netherlands	To investigate women's opinions of first vs second trimester screening for Down's syndrome	Women attending routine antenatal clinic at 15 weeks – after deciding on uptake of screening	158	Women attending antenatal diagnosis clinic entitled to CVS	96
Press and Browner 1997[114]	California, USA	To examine the routine application of prenatal screening tests and its implications	Women offered MSAFP screening aged 18–35 years	110		
Jorgensen, 1995[115]	Copenhagen, Sonderjylland, Denmark	To determine and explore reasons for non-uptake of MSAFP test	Women declining MSAFP test (questionnaire at 16 or 18 weeks)	336	Women accepting MSAFP testing (questionnaire at 30 weeks)	3331

continued

Authors, year	City, country	Stated aim of article	Study group 1	*N*	Comparison group(s)	*N*
Santalahti *et al*., 1999[116]	Jyvaskyla, Kuopio, Turku, Finland	To examine how prenatal screening tests are presented to women, factors associated with women's participation in screening, their experiences of decision-making and intention concerning pregnancy and termination	Women offered serum screening	909	Women offered ultrasound screening	424
Markens *et al*., 1999[117]	California, USA	To compare women's explanations for refusing MSAFP screening with other women's reasons for accepting it	Women who refused MSAFP	25	Women who had MSAFP	not stated
Esen and Olajide, 1997[118]	South Shields, UK	To evaluate women's perceptions and expectations re anomaly ultrasound and MSAFP/HCG testing methods of prenatal screening	Women who accepted MSAFP/HCG	456	Women who declined MSAFP/HCG accepted anomaly ultrasound	154
Phillips *et al*., 1998[119]	Tennessee, USA	To describe responses of recent mothers to the question: what test (MSS or prenatal diagnosis) she would choose for herself if she were of advanced maternal age and had the information sent with the questionnaire about chromosomal abnormalities and accuracy, risks and costs of MSS and prenatal diagnosis	Women who had undergone amniocentesis/CVS for advanced maternal age within last 2 years	92	Women aged 30–34 years who had undergone MSS within last 2 years	80
Fairgrieve, 1997[120]	East Northumberland, UK	To audit level of support for and consumer satisfaction with a Down's syndrome screening service (not a Down's syndrome diagnostic service)	Women who had been screened (both pregnant and delivered, screened low or high risk)	1774	Women (all of whom had delivered, screened low or high risk, Down's syndrome status of babies not stated), completed another version of the questionnaire	1676
Jorgensen, 1995[121]	Copenhagan and County of Sonderjylland, Denmark	To describe the opinion of pregnant women about MSAFP screening with view to determining whether every pregnant woman should be offered a diagnostic test and ultrasound scan	Women who had agreed to have the MSAFP test	3331	Women who declined the AFP test	336
Browner & Press, 1995[122]	Southern California, USA	To investigate pregnant women's feelings about prenatal testing (MSAFP), and the considerations they take account of when deciding whether to use it	Women who received a negative MSAFP result	30		
CF carrier screening						
Mennie *et al*., 1992[89]	Edinburgh, UK	To obtain the views of patients on an information leaflet inviting them to participate in a pilot trial of CF carrier testing	Women who accepted screening	135	Women who declined screening	10

continued

Authors, year	City, country	Stated aim of article	Study group 1	*N*	Comparison group(s)	*N*
Livingstone *et al.*, 1993[90]	Edinburgh, UK	To design an information leaflet which would permit the target population to make an informed decision about volunteering for couple screening for CF	Couples who decided to be screened	253	Couples who decided against screening	59
Mennie *et al.*, 1993[91]	Edinburgh, UK	To assess the psychological impact of screening for CF carrier status in a population of pregnant women	Carriers of CF whose partners were tested and found not to be carriers	62	Matched control couples where women screened negative for CF	101
Witt *et al.*, 1996[92]	Northern California, USA	To examine issues of the ability to counsel large numbers of patients for CF, the problems posed by inherent test insensitivity and the uncertainty of adverse psychological effects, particularly for couples in which only one partner is identified as a carrier	Couples, given information, offered CF screening (mouthwash), consented to screening	5161	Couples, given information, offered screening, declined screening Controls (from another hospital), not given information, not offered screening	947 334
Jung *et al.*, 1994[93]	Berlin, Germany	To investigate the acceptability of carrier screening for CF during pregnancy	Women offered screening	638		
Miedzybrodzka *et al.*, 1995[94]	Aberdeen, UK	To perform a rigorous comparative evaluation of stepwise and couple approaches to antenatal carrier screening	Stepwise screening (mother first)	1641	Couple screening (couples)	361
Grody *et al.*, 1997[95]	Los Angeles, USA	To determine the technical feasibility, patient acceptance and understanding and psychosocial impact of large-scale CF carrier screening	Women who participated in screening	3688		
Cuckle *et al.*, 1996[96]	Leeds and Hull, UK	To assess the practicality of implementing antenatal screening for CF in one area	Women who were offered screening	6071		
Leonard *et al.*, 1995[97]	Houston, Texas, USA	To test the efficacy of two types of educational materials for genetic counselling: a traditional information brochure and one adding a role model story re CF	Group given 'traditional information' brochure which included info on CF and risk of being a carrier; treatment; inheritance; availability and sensitivity of carrier screening for CF	330	Group given 'role model' brochure which included traditional info and a story, interspersed throughout, of a family whose second child was affected by CF	330
Mennie *et al.*, 1993[98]	Edinburgh, UK	To assess the attitudes, understanding and responses of carriers and their partners detected through CF carrier screening in pregnancy	Carriers, identified through screening	64	Carriers' partners – identified as non-carriers through screening Control mothers – identified as non-CF carriers through screening Partners of control mothers (not screened)	63 116 115

continued

Authors, year	City, country	Stated aim of article	Study group 1	*N*	Comparison group(s)	*N*
Mennie *et al.*, 1997[99]	Edinburgh, UK	To determine whether the method of prenatal CF carrier testing (couple vs two-step) influenced women's understanding of the implications of the test result or subsequent reproductive behaviour or intentions	Women screen positive identified using two-step method (partner screen negative)	109	Women screen negative identified using 2-step method Women screen negative identified using couple method	113 179
Clausen *et al.*, 1996[100]	Denmark	To assess the psychological and social impact of carrier screening for CF in pregnant women	Carriers of CF	160	Negative test for CF	200
Hartley *et al.*, 1997[101]	Manchester, UK	To determine the uptake and acceptability of CF carrier testing when offered to women at the first antenatal booking appointment by their GP	Allocated to couple testing	262	Allocated to stepwise testing	267
Harris *et al.*, 1996[102]	Manchester, UK	To assess the acceptability of integrating CF carrier testing into antenatal care by general practitioners at the first booking appointment	All patients booking in before 14 weeks gestation	75		
Livingstone *et al.*, 1994[110]	Edinburgh, UK	To assess the delivery and acceptability of antenatal screening for CF	Couples screened for CF	300 couples	Individuals screened for CF Individuals not screened (screening not offered or couple ineligible)	1325 114
Loader *et al.*, 1996[123]	Rochester, NY, USA	To determine the receptivity of prenatal care providers and their patients to carrier testing for CF	Women who accepted CF screening	5120	Women who declined CF screening	1228
Fang *et al.*, 1997[124]	Los Angeles, USA	To examine the relations among psychosocial factors associated with pregnant women's attitudes toward genetic carrier testing for CF	Women in 1st or 2nd trimester, no family history of CF, non-Hispanic whites who received written education material leaflet	255	Women in 1st or 2nd trimester, no family history of CF, non-Hispanic whites who received video education material	256
Mennie *et al.*, 1994[125]	Edinburgh, UK	To investigate whether decisions of couples to accept prenatal CF carrier screening might be influenced by the advent of gene therapy	Couples who had accepted CF screening	135		
Mennie *et al.*, 1993[126]	Edinburgh, UK	To examine the reasons given by women who have not wanted CF screening in pregnancy	Accepted CF screening	1798	Declined CF screening	260
Haemoglobinopathies/Tay – Sachs carrier screening						
Rowley *et al.*, 1988[103]	Rochester, NY, USA	To determine whether haemoglobinopathy carrier screening should be part of routine prenatal care	Women who screened positive as haemoglobinopathy carrier and counselled	283		

continued

Authors, year	City, country	Stated aim of article	Study group 1	*N*	Comparison group(s)	*N*
Wallerstein *et al.*, 1994[104]	New Jersey, USA	To determine the rate of utilisation of Tay–Sachs disease screening by the Ashkenazi Jewish population and reasons for non-use	Ashkenazi Jewish women having genetic counselling for other reasons, who declined screening for Tay–Sachs	25		
Loader *et al.*, 1991[105]	Rochester, NY, USA	To describe learning as a result of genetic counselling of pregnant women identified as haemoglobinopathy carriers	Women identified as haemoglobinopathy carriers who came for counselling	551		
Green and France-Dawson, 1997[106]	West Midlands, UK	To examine women's knowledge and experiences of sickle-cell screening	Pregnant women of Afro-Caribbean descent	159		
Rowley *et al.*, 1991[107]	Rochester, NY, USA	To analyse the factors affecting decisions of pregnant women identified as haemoglobinopathy carriers, using the Health Belief Model	Women identified as haemoglobinopathy carriers	722		

Neonatal

Authors, year	City, country	Stated aim of article	Study group 1	*N*	Comparison group(s)	*N*
PKU (Guthrie test)						
Statham *et al.*, 1993[28]	9 sites in south-east England, UK	To investigate mothers' knowledge about newborn screening	Unselected new mothers who had taken part in the Cambridge Prenatal Screening Study	1387		
Holtzman *et al.*, 1983[140]	Maryland, USA	To determine if knowledge about PKU screening is improved by obtaining informed consent from mothers	Women randomised to be interviewed before having been through the neonatal screening consent procedure	210	Women randomised to be interviewed after giving consent	418
Faden *et al.*, 1982[141]	Maryland, USA	To evaluate parental consent as public policy for neonatal screening	Women randomised to be interviewed before having been through the neonatal screening consent procedure	210	Women randomised to be interviewed after giving consent	418

continued

Authors, year	City, country	Stated aim of article	Study group 1	*N*	Comparison group(s)	*N*
Hypothyroidism						
Bodegard *et al*., 1983[145]	Stockholm, Sweden	To investigate if parents are worried by false-positive screening results, and how they cope with the threat and whether reactions triggered by false alarms have lasting effects	Parents whose baby screened false-positive for hypothyroidism	102		
Fyro and Bodegard, 1988[146]	Stockholm, Sweden	To assess the effects of a new screening programme	Parents whose baby screened false-positive for hypothyroidism	11		
Fyro and Bodegard, 1987[147]	Stockholm, Sweden	To examine long-term effects of false-positive screening results for congenital hypothyroidism	Parents whose baby screened false-positive for hypothyroidism showing distress 6–12 months later	16	Matched families showing no elevated distress	16
Fyro, 1988[148]	Stockholm, Sweden	To study life-stress factors in families who received a false-positive result for congenital hypothyroidism	Parents whose baby screened false-positive for hypothyroidism	102		
Tymstra, 1986[149]	3 northern provinces, The Netherlands	To determine the experiences of parents of children with a false-positive result screening result	Parents whose baby screened false-positive for hypothyroidism	31		
CF						
Al-Jader *et al*., 1990[111]	Wales, UK	To investigate the psychological impact of neonatal diagnosis of CF when the child is 'relatively well' and assess attitudes towards antenatal testing for CF	Parents of children with CF diagnosed following screening	36	Parents of children diagnosed with CF symptomatically	22
Baroni *et al*., 1997[137]	Wisconsin, USA	To investigate possible parenting stress associated with false-positive results or early diagnosis of an asymptomatic infant (a pilot study)	Parents whose baby screened false-positive for CF (IRT) (= group 1)	14	Parents of healthy children matched for age and gender with group 1 (= group 2) Parents of children diagnosed with CF symptomatically (= group 3) Parents of children diagnosed with CF following IRT screening (= group 4) Parents of healthy children matched for age, gender with groups 3 and 4 (= group 5)	14 17 20 33

continued

Authors, year	City, country	Stated aim of article	Study group 1	*N*	Comparison group(s)	*N*
Boland and Thompson, 1990[138]	New South Wales, Australia	To investigate whether screening decreases the time from first maternal concern about CF-related symptoms to diagnosis; whether length of delay is related to maternal protectiveness; whether absence of symptoms has an effect; whether strength of maternal denial is related to symptom delay	Parents of children diagnosed with CF symptomatically and unscreened (born before screening introduced)	29	Parents of children diagnosed with CF who were detected through screening but who were already symptomatic Parents of children diagnosed with CF who were detected through screening who had had no symptoms	13 16
Helton *et al*., 1991[139]	Colorado, USA	To investigate the attitude and emotional response towards neonatal screening of parents whose child is diagnosed following screening, or diagnosed traditionally after symptoms arise	Parents of children with CF diagnosed following screening	62	Parents of children diagnosed with CF symptomatically	30
Mischler *et al*., 1998[142]	USA	To evaluate the impact of newborn screening for CF in terms of reproductive knowledge/behaviour both of CF families and false-positives	Parents of children with CF detected through neonatal screening	100	Parents whose baby screened false-positive for CF (206 IRT only and 109 IRT/DNA)	315
Tluczec *et al*., 1992[143]	Wisconsin, USA	To investigate parental understanding, knowledge, anxiety and reproductive intentions in response to false-positive CF screening	Parents whose baby screened false-positive for CF (IRT)	104		
Tluczek *et al*., 1991[144]	Wisconsin, USA	To compare the psychological impact of false-positive results in those given results when infant 6 weeks or when child is 4 years	Parents of children who screened false-positive for CF (IRT) and were randomised to be given the IRT results at 4–6 weeks following birth	104	Parents of children who screened false-positive for CF (IRT) and were randomised to have disclosure of the IRT result delayed for 4 years	11
Dudding *et al*., 2000[164]	New South Wales, Australia	To document the reproductive choices made by women in New South Wales, Australia, after neonatal screening has identified CF	Mothers of children with CF detected through neonatal screening	87		
Sickle-cell disorders						
Grossman *et al*., 1985[154]	Baltimore, USA	To investigate the impact of counselling on knowledge levels and the characteristics of those accepting counselling	Parents whose baby screened positive for a sickle-cell disorder who received counselling	32	Parents whose baby screened positive for a sickle-cell disorder who were not counselled	59
Warren *et al*., 1982[155]	New York State, USA	To evaluate the responses of physicians and parents to the New York State-mandated newborn screening for sickle-cell disease	Parents of children with a sickle-cell disorder that had been detected through neonatal screening	18		

continued

Authors, year	City, country	Stated aim of article	Study group 1	*N*	Comparison group(s)	*N*
Multiple rare conditions						
Sorenson *et al.*, 1984[160]	Boston, USA	To assess parental understanding of the reason for repeat testing following a neonatal screening result outside normal range; assess response to repeat test as a function of understanding; assess frequency of concern arising from repeat testing	Parents of infants who required repeat blood/urine test following initial abnormal neonatal screening result	60		
Other single gene disorders						
Hildes *et al.*, 1993[151]	Manitoba, Canada	To assess the impact of genetic counselling after neonatal screening for DMD	Mother, aunts and sisters of baby boys with DMD detected through neonatal screening	11		
Parsons *et al.*, 1996[152]	Cardiff, UK	To assess parents' satisfaction with screening protocol for DMD that was designed to maximise parental choice and minimise distress (the main purpose of the paper is to describe the protocol)	Parents of children receiving positive DMD screening results by protocol	25	Families informed without protocol	16
Bradley *et al.*, 1993[153]	Wales, UK	To assess acceptability of screening newborn boys for DMD	Parents of children receiving positive DMD screening results	9		
Yu *et al.*, 1999[156]	Denver, Colorado, USA	To investigate whether the notification of high-risk status for type 1 diabetes in newborn infants results in greater parental stress compared with those with low-risk status	Mothers of children given a moderate or high risk of developing type 1 diabetes after screening	23	Mothers of children given a low risk of developing type 1 diabetes after screening	65
Senior *et al.*, 1999[157]	London, UK	To describe parents' perceptions of familial hypercholesterolaemia, following population-based neonatal screening	Parents whose child had screened positive for familial hypercholesterolaemia	24		
Thelin *et al.*, 1985[158]	Malmo, Sweden	To investigate the psychological and psychosocial consequences of neonatal identification of ATD 5–7 years after diagnosis	Parents of 61 children with ATD identified through neonatal screening	107		
Sveger and Thelin, 1981[159]	Malmo, Sweden	To compare children with and without ATD clinically; to assess psychological consequences of neonatal identification 4 years after diagnosis	40 parents of 26 4 year olds diagnosed with ATD as part of neonatal screening programme. These were a subgroup of 172 ATD children on whom other health/social information (including parental smoking) was also available	40	Health/social information (including parental smoking) was also available for a control group of 80 healthy 4 year olds, but not information directly from the parents	

continued

Authors, year	City, country	Stated aim of article	Study group 1	*N*	Comparison group(s)	*N*
Thelin *et al*., 1985[162]	Malmo, Sweden	To identify the possible long-term effects of having a child at high somatic risk on parents' attitudes towards themselves and toward having more children	Parents of 61 children with ATD identified through neonatal screening	108	Parents from 61 matched families with children without ATD	106
Thelin *et al*., 1985[163]	Malmo, Sweden	To test the hypothesis that the inherited antitrypsin deficiency matter had negatively influenced parents' views of their own health and current life situation	Parents of 61 children with ATD identified through neonatal screening	108	Parents from 61 matched families with children without ATD	106

HCG, human chorionic gonadotrophin; MSS, maternal serum screening.

Appendix 4

Papers with overlapping samples

Authors, year	Disorder	Context
Holtzman *et al*., 1983[140] Faden *et al*., 1982[141]	PKU (and others)	Maryland, 1978, women were randomised to be interviewed either before or after having been through the screening consent procedure. Same sample
Thelin *et al*., 1985[158] Thelin *et al*., 1985[162] Thelin *et al*., 1985[163]	ATD	61 families 5–7 years after testing, all the same sample
Sveger and Thelin, 1981[159] and the above	ATD	Sveger and Thelin (1981)[159] report 4 years after testing. It is not made explicit to what extent the samples overlap with the papers by Thelin *et al*.,[158,162,163] but it seems inevitable that they do given the limited numbers of the target families. However, findings are oddly disparate in places
Bodegard *et al*., 1983[145] Fyro and Bodegard, 1987[147] Fyro, 1988[148]	Hypothyroidism	Part of a Swedish integrated pilot neonatal screening programme for congenital hypothyroidism with a meticulous protocol. Same sample
Fyro and Bodegard, 1988[146]	Hypothyroidism	Not the same study as the above. These were 11 families who had had a false-positive result in the period 1979–81 when the neonatal screening programme had just been introduced into routine practice
Tluczek *et al*., 1992[143] Tluczek *et al*., 1991[144]	CF	Wisconsin trial (ran from 1985 to 1994). 104 false-positives (IRT) during the first 40 months of the project. Same parents (and many of the same results reported) in these two papers
Baroni *et al*., 1997[137]	CF	Wisconsin trial: the false-positive group were those who got their results between July 1992 and September 1992 (therefore IRT/DNA), therefore **not** the same parents as in Tluczek *et al*. (1992,)[143] and Tluczek *et al*. (1991)[144] because those papers were published in 1991 and 1992
Mischler *et al*., 1998[142]	CF	This paper is the clearest account of the Wisconsin trial: based (potentially) on all participants throughout the trial. Therefore will potentially include all the parents in Tluczek *et al*. (1992),[143] Tluczek *et al*. (1991)[144] and Baroni *et al*. (1997)[137] but also others (NB: testing method changed in 1989 to IRT/DNA)
Boland and Thompson, 1990[138] Dudding *et al*., 2000[164]	CF	Different authors. Both concerned with true-positives in the New South Wales screening programme. Dudding *et al*. 2000[164] = 87 mothers whose children screened 1981–96; Boland and Thompson, (1990)[138] = mothers of children with CF born 1977–85 – 29 of these had been screened and therefore were potentially part of the Dudding *et al*. (2000)[164] sample [but Dudding *et al*. (2000)[164] do not reference Boland and Thompson (1990)[138]]

Health Technology Assessment Programme

Prioritisation Strategy Group

Members

Chair,
Professor Tom Walley,
Director, NHS HTA Programme, Department of Pharmacology & Therapeutics, University of Liverpool

Professor Bruce Campbell, Consultant Vascular & General Surgeon, Royal Devon & Exeter Hospital

Professor Shah Ebrahim, Professor in Epidemiology of Ageing, University of Bristol

Dr John Reynolds, Clinical Director, Acute General Medicine SDU, Radcliffe Hospital, Oxford

Dr Ron Zimmern, Director, Public Health Genetics Unit, Strangeways Research Laboratories, Cambridge

HTA Commissioning Board

Members

Programme Director,
Professor Tom Walley,
Director, NHS HTA Programme, Department of Pharmacology & Therapeutics, University of Liverpool

Chair,
Professor Shah Ebrahim,
Professor in Epidemiology of Ageing, Department of Social Medicine, University of Bristol

Deputy Chair,
Professor Jenny Hewison,
Professor of Health Care Psychology, Academic Unit of Psychiatry and Behavioural Sciences, University of Leeds School of Medicine

Dr Jeffrey Aronson
Reader in Clinical Pharmacology, Department of Clinical Pharmacology, Radcliffe Infirmary, Oxford

Professor Ann Bowling, Professor of Health Services Research, Primary Care and Population Studies, University College London

Professor Andrew Bradbury, Professor of Vascular Surgery, Department of Vascular Surgery, Birmingham Heartlands Hospital

Professor John Brazier, Director of Health Economics, Sheffield Health Economics Group, School of Health & Related Research, University of Sheffield

Dr Andrew Briggs, Public Health Career Scientist, Health Economics Research Centre, University of Oxford

Professor Nicky Cullum, Director of Centre for Evidence Based Nursing, Department of Health Sciences, University of York

Dr Andrew Farmer, Senior Lecturer in General Practice, Department of Primary Health Care, University of Oxford

Professor Fiona J Gilbert, Professor of Radiology, Department of Radiology, University of Aberdeen

Professor Adrian Grant, Director, Health Services Research Unit, University of Aberdeen

Professor F D Richard Hobbs, Professor of Primary Care & General Practice, Department of Primary Care & General Practice, University of Birmingham

Professor Peter Jones, Head of Department, University Department of Psychiatry, University of Cambridge

Professor Sallie Lamb, Research Professor in Physiotherapy/Co-Director, Interdisciplinary Research Centre in Health, Coventry University

Professor Julian Little, Professor of Epidemiology, Department of Medicine and Therapeutics, University of Aberdeen

Professor Stuart Logan, Director of Health & Social Care Research, The Peninsula Medical School, Universities of Exeter & Plymouth

Professor Tim Peters, Professor of Primary Care Health Services Research, Division of Primary Health Care, University of Bristol

Professor Ian Roberts, Professor of Epidemiology & Public Health, Intervention Research Unit, London School of Hygiene and Tropical Medicine

Professor Peter Sandercock, Professor of Medical Neurology, Department of Clinical Neurosciences, University of Edinburgh

Professor Mark Sculpher, Professor of Health Economics, Centre for Health Economics, Institute for Research in the Social Services, University of York

Professor Martin Severs, Professor in Elderly Health Care, Portsmouth Institute of Medicine

Dr Jonathan Shapiro, Senior Fellow, Health Services Management Centre, Birmingham

Ms Kate Thomas, Deputy Director, Medical Care Research Unit, University of Sheffield

Professor Simon G Thompson, Director, MRC Biostatistics Unit, Institute of Public Health, Cambridge

Ms Sue Ziebland, Senior Research Fellow, Cancer Research UK, University of Oxford

Current and past membership details of all HTA 'committees' are available from the HTA website (www.ncchta.org)

Diagnostic Technologies & Screening Panel

Members

Chair,
Dr Ron Zimmern, Director of the Public Health Genetics Unit, Strangeways Research Laboratories, Cambridge

Ms Norma Armston, Freelance Consumer Advocate, Bolton

Professor Max Bachmann Professor Health Care Interfaces, Department of Health Policy and Practice, University of East Anglia

Professor Rudy Bilous Professor of Clinical Medicine & Consultant Physician, The Academic Centre, South Tees Hospitals NHS Trust

Dr Paul Cockcroft, Consultant Medical Microbiologist/Laboratory Director, Public Health Laboratory, St Mary's Hospital, Portsmouth

Professor Adrian K Dixon, Professor of Radiology, Addenbrooke's Hospital, Cambridge

Dr David Elliman, Consultant in Community Child Health, London

Professor Glyn Elwyn, Primary Medical Care Research Group, Swansea Clinical School, University of Wales Swansea

Dr John Fielding, Consultant Radiologist, Radiology Department, Royal Shrewsbury Hospital

Dr Karen N Foster, Clinical Lecturer, Dept of General Practice & Primary Care, University of Aberdeen

Professor Antony J Franks, Deputy Medical Director, The Leeds Teaching Hospitals NHS Trust

Mr Tam Fry, Honorary Chairman, Child Growth Foundation, London

Dr Edmund Jessop, Medical Adviser, National Specialist Commissioning Advisory Group (NSCAG), Department of Health, London

Dr Jennifer J Kurinczuk, Consultant Clinical Epidemiologist, National Perinatal Epidemiology Unit, Oxford

Dr Susanne M Ludgate, Medical Director, Medical Devices Agency, London

Dr William Rosenberg, Senior Lecturer and Consultant in Medicine, University of Southampton

Dr Susan Schonfield, CPHM Specialised Services Commissioning, Croydon Primary Care Trust

Dr Margaret Somerville, Director of Public Health, Teignbridge Primary Care Trust

Professor Lindsay Wilson Turnbull, Scientific Director, Centre for MR Investigations & YCR Professor of Radiology, University of Hull

Professor Martin J Whittle, Head of Division of Reproductive & Child Health, University of Birmingham

Dr Dennis Wright, Consultant Biochemist & Clinical Director, Pathology & The Kennedy Galton Centre, Northwick Park & St Mark's Hospitals, Harrow

Pharmaceuticals Panel

Members

Chair,
Dr John Reynolds, Clinical Director, Acute General Medicine SDU, Oxford Radcliffe Hospital

Professor Tony Avery, Professor of Primary Health Care, University of Nottingham

Professor Stirling Bryan, Professor of Health Economics, Health Services Management Centre, University of Birmingham

Mr Peter Cardy, Chief Executive, Macmillan Cancer Relief, London

Dr Christopher Cates, GP and Cochrane Editor, Bushey Health Centre

Professor Imti Choonara, Professor in Child Health, University of Nottingham, Derbyshire Children's Hospital

Mr Charles Dobson, Special Projects Adviser, Department of Health

Dr Robin Ferner, Consultant Physician and Director, West Midlands Centre for Adverse Drug Reactions, City Hospital NHS Trust, Birmingham

Dr Karen A Fitzgerald, Pharmaceutical Adviser, Bro Taf Health Authority, Cardiff

Mrs Sharon Hart, Managing Editor, *Drug & Therapeutics Bulletin*, London

Dr Christine Hine, Consultant in Public Health Medicine, Bristol South & West Primary Care Trust

Professor Stan Kaye, Professor of Medical Oncology, Consultant in Medical Oncology/Drug Development, The Royal Marsden Hospital

Ms Barbara Meredith, Project Manager Clinical Guidelines, Patient Involvement Unit, NICE

Dr Frances Rotblat, CPMP Delegate, Medicines Control Agency, London

Professor Jan Scott, Professor of Psychological Treatments, Institute of Psychiatry, University of London

Mrs Katrina Simister, New Products Manager, National Prescribing Centre, Liverpool

Dr Richard Tiner, Medical Director, Association of the British Pharmaceutical Industry

Dr Helen Williams, Consultant Microbiologist, Norfolk & Norwich University Hospital NHS Trust

Therapeutic Procedures Panel

Members

Chair,
Professor Bruce Campbell,
Consultant Vascular and General Surgeon, Royal Devon & Exeter Hospital

Dr Mahmood Adil, Head of Clinical Support & Health Protection, Directorate of Health and Social Care (North), Department of Health, Manchester

Dr Aileen Clarke,
Reader in Health Services Research, Public Health & Policy Research Unit,
Barts & the London School of Medicine & Dentistry,
Institute of Community Health Sciences, Queen Mary,
University of London

Mr Matthew William Cooke,
Senior Clinical Lecturer and Honorary Consultant,
Emergency Department,
University of Warwick, Coventry & Warwickshire NHS Trust,
Division of Health in the Community, Centre for Primary Health Care Studies, Coventry

Dr Carl E Counsell, Senior Lecturer in Neurology,
University of Aberdeen

Dr Keith Dodd, Consultant Paediatrician, Derbyshire Children's Hospital

Professor Gene Feder, Professor of Primary Care R&D, Barts & the London, Queen Mary's School of Medicine and Dentistry, University of London

Professor Paul Gregg,
Professor of Orthopaedic Surgical Science, Department of Orthopaedic Surgery,
South Tees Hospital NHS Trust

Ms Bec Hanley, Freelance Consumer Advocate,
Hurstpierpoint

Ms Maryann L. Hardy,
Lecturer,
Division of Radiography,
University of Bradford

Professor Alan Horwich,
Director of Clinical R&D, The Institute of Cancer Research,
London

Dr Phillip Leech, Principal Medical Officer for Primary Care, Department of Health,
London

Dr Simon de Lusignan,
Senior Lecturer, Primary Care Informatics, Department of Community Health Sciences,
St George's Hospital Medical School, London

Dr Mike McGovern, Senior Medical Officer, Heart Team,
Department of Health, London

Professor James Neilson,
Professor of Obstetrics and Gynaecology, Dept of Obstetrics and Gynaecology,
University of Liverpool,
Liverpool Women's Hospital

Dr John C Pounsford,
Consultant Physician, North Bristol NHS Trust

Dr Vimal Sharma,
Consultant Psychiatrist & Hon Snr Lecturer,
Mental Health Resource Centre,
Victoria Central Hospital,
Wirrall

Dr L David Smith, Consultant Cardiologist, Royal Devon & Exeter Hospital

Professor Norman Waugh,
Professor of Public Health,
University of Aberdeen

Expert Advisory Network

Members

Professor Douglas Altman,
Director of CSM & Cancer Research UK Med Stat Gp, Centre for Statistics in Medicine, University of Oxford, Institute of Health Sciences, Headington, Oxford

Professor John Bond,
Director, Centre for Health Services Research, University of Newcastle upon Tyne, School of Population & Health Sciences, Newcastle upon Tyne

Mr Shaun Brogan,
Chief Executive, Ridgeway Primary Care Group, Aylesbury

Mrs Stella Burnside OBE,
Chief Executive, Office of the Chief Executive. Trust Headquarters, Altnagelvin Hospitals Health & Social Services Trust, Altnagelvin Area Hospital, Londonderry

Ms Tracy Bury,
Project Manager, World Confederation for Physical Therapy, London

Mr John A Cairns,
Professor of Health Economics, Health Economics Research Unit, University of Aberdeen

Professor Iain T Cameron,
Professor of Obstetrics and Gynaecology and Head of the School of Medicine, University of Southampton

Dr Christine Clark,
Medical Writer & Consultant Pharmacist, Rossendale

Professor Collette Mary Clifford,
Professor of Nursing & Head of Research, School of Health Sciences, University of Birmingham, Edgbaston, Birmingham

Professor Barry Cookson,
Director, Laboratory of Healthcare Associated Infection, Health Protection Agency, London

Professor Howard Stephen Cuckle,
Professor of Reproductive Epidemiology, Department of Paediatrics, Obstetrics & Gynaecology, University of Leeds

Professor Nicky Cullum,
Director of Centre for Evidence Based Nursing, University of York

Dr Katherine Darton,
Information Unit, MIND – The Mental Health Charity, London

Professor Carol Dezateux,
Professor of Paediatric Epidemiology, London

Mr John Dunning,
Consultant Cardiothoracic Surgeon, Cardiothoracic Surgical Unit, Papworth Hospital NHS Trust, Cambridge

Mr Jonothan Earnshaw,
Consultant Vascular Surgeon, Gloucestershire Royal Hospital, Gloucester

Professor Martin Eccles,
Professor of Clinical Effectiveness, Centre for Health Services Research, University of Newcastle upon Tyne

Professor Pam Enderby,
Professor of Community Rehabilitation, Institute of General Practice and Primary Care, University of Sheffield

Mr Leonard R Fenwick,
Chief Executive, Newcastle upon Tyne Hospitals NHS Trust

Professor David Field,
Professor of Neonatal Medicine, Child Health, The Leicester Royal Infirmary NHS Trust

Mrs Gillian Fletcher,
Antenatal Teacher & Tutor and President, National Childbirth Trust, Henfield

Professor Jayne Franklyn,
Professor of Medicine, Department of Medicine, University of Birmingham, Queen Elizabeth Hospital, Edgbaston, Birmingham

Ms Grace Gibbs,
Deputy Chief Executive, Director for Nursing, Midwifery & Clinical Support Servs, West Middlesex University Hospital, Isleworth

Dr Neville Goodman,
Consultant Anaesthetist, Southmead Hospital, Bristol

Professor Alastair Gray,
Professor of Health Economics, Department of Public Health, University of Oxford

Professor Robert E Hawkins,
CRC Professor and Director of Medical Oncology, Christie CRC Research Centre, Christie Hospital NHS Trust, Manchester

Professor F D Richard Hobbs,
Professor of Primary Care & General Practice, Department of Primary Care & General Practice, University of Birmingham

Professor Allen Hutchinson,
Director of Public Health & Deputy Dean of ScHARR, Department of Public Health, University of Sheffield

Dr Duncan Keeley,
General Practitioner (Dr Burch & Ptnrs), The Health Centre, Thame

Dr Donna Lamping,
Research Degrees Programme Director & Reader in Psychology, Health Services Research Unit, London School of Hygiene and Tropical Medicine, London

Mr George Levvy,
Chief Executive, Motor Neurone Disease Association, Northampton

Professor James Lindesay,
Professor of Psychiatry for the Elderly, University of Leicester, Leicester General Hospital

Professor Rajan Madhok,
Medical Director & Director of Public Health, Directorate of Clinical Strategy & Public Health, North & East Yorkshire & Northern Lincolnshire Health Authority, York

Professor David Mant,
Professor of General Practice, Department of Primary Care, University of Oxford

Professor Alexander Markham,
Director, Molecular Medicine Unit, St James's University Hospital, Leeds

Dr Chris McCall,
General Practitioner, The Hadleigh Practice, Castle Mullen

Professor Alistair McGuire,
Professor of Health Economics, London School of Economics

Dr Peter Moore,
Freelance Science Writer, Ashtead

Dr Andrew Mortimore,
Consultant in Public Health Medicine, Southampton City Primary Care Trust

Dr Sue Moss,
Associate Director, Cancer Screening Evaluation Unit, Institute of Cancer Research, Sutton

Professor Jon Nicholl,
Director of Medical Care Research Unit, School of Health and Related Research, University of Sheffield

Mrs Julietta Patnick,
National Co-ordinator, NHS Cancer Screening Programmes, Sheffield

Professor Robert Peveler,
Professor of Liaison Psychiatry, University Mental Health Group, Royal South Hants Hospital, Southampton

Professor Chris Price,
Visiting Chair – Oxford, Clinical Research, Bayer Diagnostics Europe, Cirencester

Ms Marianne Rigge,
Director, College of Health, London

Dr Eamonn Sheridan,
Consultant in Clinical Genetics, Genetics Department, St James's University Hospital, Leeds

Dr Ken Stein,
Senior Clinical Lecturer in Public Health, Director, Peninsula Technology Assessment Group, University of Exeter

Professor Sarah Stewart-Brown,
Director HSRU/Honorary Consultant in PH Medicine, Department of Public Health, University of Oxford

Professor Ala Szczepura,
Professor of Health Service Research, Centre for Health Services Studies, University of Warwick

Dr Ross Taylor,
Senior Lecturer, Department of General Practice and Primary Care, University of Aberdeen

Mrs Joan Webster,
Consumer member, HTA – Expert Advisory Network

Feedback

The HTA Programme and the authors would like to know your views about this report.

The Correspondence Page on the HTA website (http://www.ncchta.org) is a convenient way to publish your comments. If you prefer, you can send your comments to the address below, telling us whether you would like us to transfer them to the website.

We look forward to hearing from you.

The National Coordinating Centre for Health Technology Assessment,
Mailpoint 728, Boldrewood,
University of Southampton,
Southampton, SO16 7PX, UK.
Fax: +44 (0) 23 8059 5639 Email: hta@soton.ac.uk
http://www.ncchta.org

ISSN 1366-5278