Women's experiences of fetal screening for Down's syndrome by means of an early ultrasound examination

Susanne Georgsson Öhman

Stockholm 2005

Department of Nursing
Karolinska Institutet, Stockholm, Sweden

Women's experiences of fetal screening for Down's syndrome by means of an early ultrasound examination

Susanne Georgsson Öhman

Stockholm 2005

Cover: Painting by Rebecca Ramsey
Printed by Repro Print AB, Stockholm, 2005

ISBN: 91-7140-228-4

Det finns en enda känsla
som mäktig är att liv
åt livet ge,
och denna känsla
har jag kallat kärlek.

E.J. Stagnelius

Till Henrik & Mathilda

ABSTRACT

Women's experiences of fetal screening for Down's syndrome by means of an early ultrasound examination

Susanne Georgsson Öhman, Department of Nursing, Karolinska Institutet

The general aim of this thesis was to explore women's reactions to and experiences of fetal screening for Down's syndrome (DS) by means of an ultrasound examination, including measurement of fetal nuchal translucency (NT). The effect of this screening on maternal worry about the baby's health was investigated, as well as reactions to a false positive test and interpretation of information about risk. Also, an instrument measuring worry during pregnancy, the Cambridge Worry Scale, was translated into Swedish and tested on a sample of pregnant women.

A sub-sample of 2026 women was drawn from a larger randomised controlled trial including 39,572 women, which investigated medical outcomes of the new fetal screening policy. Of these women, 1030 were randomly allocated to the intervention group, and 996 to routine care. No statistically significant differences were found between the two groups regarding major worry about something being wrong with the baby, general anxiety and depressive symptoms in mid-pregnancy and two months postpartum.

Twenty-four women who had received information about an increased risk according to NT were interviewed during pregnancy and after birth. Twenty of these women had false positive tests, and for 16 the risk was higher than expected considering their age. These women expressed major worry, and many said they chose to reject their pregnancy, to take "time out", while waiting for the results of fetal karyotyping. Two months after the birth, most of these women seemed to have overcome the stressful situation.

In the intervention group of the above trial 796 women had a risk score for DS recorded in a clinical database. Of these women 620 said they had received information about the risk score, and 64 percent stated the figure almost correctly. The actual risk was associated with women's perception of the risk. Worry about the baby's health and depressive symptoms did not differ statistically between women who were at high risk (1:250 or higher) and at low risk. However, women who *perceived* that the risk was high were more worried about the baby's health and also seemed to have more depressive symptoms in mid-pregnancy compared with those who perceived the risk to be low. No differences were observed at two months after birth.

The translated version of the Cambridge Worry Scale was tested on 200 Swedish pregnant women in Stockholm. The three main sources of worry were about the baby's health, giving birth and miscarriage. The internal-consistency reliability was 0.81 (Cronbach's alpha). Three items were added to the original scale to capture women's worry about the maternity services.

In conclusion, the intervention with an early ultrasound examination including risk assessment for DS by measuring the NT did not affect maternal worry about the baby's health, general anxiety or depressive symptoms in mid-pregnancy or two months after birth. However, a false positive test could cause strong reactions of anxiety and rejection of the pregnancy for some weeks. Many had problems to recall and interpret a given risk score. An actual high risk score was not associated with major worry about the baby's health or depressive symptoms, whereas a woman's perception of being at high risk had such an association. The Swedish version of the Cambridge Worry Scale was considered to be useful and well suited for its purpose.

Keywords: fetal ultrasound screening, nuchal translucency, Down's syndrome, worry, depressive symptoms, false positive results, women's reactions, risk information

ORIGINAL PAPERS

The thesis is based on the following papers, which will be referred to in the text by their Roman numerals:

I Georgsson Öhman, S., Grunewald, C. & Waldenström U. (2003). Women's worries during pregnancy: testing the Cambridge Worry Scale on 200 Swedish women. *Scandinavian Journal of Caring Sciences, 17*, 148-152

II Georgsson Öhman, S., Saltvedt, S., Grunewald, C. & Waldenström, U. (2004). Does fetal screening affect women's worries about the health of their baby? A randomized controlled trial of ultrasound screening for Down's syndrome versus routine ultrasound screening. *Acta Obstetricia et Gynecologica Scandinavica, 83*, 634-640

III Georgsson Öhman, S., Saltvedt, S., Waldenström, U., Grunewald, C. & Olin-Lauritzen, S. Pregnant women's responses to information about an increased risk of carrying a baby with Down's syndrome. ***Submitted.***

IV Georgsson Öhman, S., Grunewald, C. & Waldenström U. Risk information after ultrasound screening for Down's syndrome and its association with maternal emotional well-being. ***Submitted.***

TABLE OF CONTENTS

LIST OF ABBREVIATONS

AC	Amniocentesis
AFP	Alpha Feto Protein
ANOVA	ANalysis Of VAriance
CI	Confidence Interval
CVS	Chorion Villus Sampling
CWS	Cambridge Worry Scale
DS	Down's Syndrome
EPDS	Edinburgh Postnatal Depression Scale
EUG	Early Ultrasound Group
HCG	Human Chorion Gonadotrophine
MFA	Maternal Fetal Attachment
NT	Nuchal Translucency
NUPP	NackUPPklarning (Swedish for nuchal translucency)
OR	Odds Ratio
PAPP-A	Pregnancy Associated Plasma Protein-A
QF-PCR	Quantitative Fluorescent-Polymeras Chain Reaction
RUG	Routine Ultrasound Group
SCWS	Swedish version of the Cambridge Worry Scale
STAI	State Trait Anxiety Inventory

INTRODUCTION

Swedish antenatal care

The primary aims of Swedish antenatal care are to detect deviations in growth and development of the fetus and to identify maternal diseases, which may affect the pregnancy or its outcome. Additional aims are to give psychosocial support including parenthood education. In the first trimester, genetic counselling has become an increasing part of the information given by the midwife. During pregnancy the recommended numbers of visits to the midwife are 8-9 for primiparas and 6-7 for multiparas and a single visit is recommended to the physician (Swedish National Board of Health and Welfare, 1996). Attendance is generally high. In a study of reasons for not attending antenatal care among 3278 women only 5 percent had registered late to the antenatal clinic or had fewer than three visits. This was mostly because of difficulties in speaking and understanding the Swedish language. Not attending the antenatal care at all or attending very occasionally is extremely unusual: a few per thousand (Darj & Lindmark, 2002).

Routine ultrasound examination

Pregnant women in Sweden are offered one ultrasound scan in the second trimester (gestational week 15-20) and this offer is accepted by the vast majority (97%). Midwives with special training in ultrasonography usually perform the examination. In 1996, the average number of ultrasound examinations per pregnancy in Sweden was 2.1. The current aims of the routine ultrasound examination are to estimate the gestational age, to localise the placenta, to screen for multiple pregnancy and to detect structural malformations. The possibility of detecting malformations has increased with the development of the ultrasound technique and the training and experience of the ultrasonographers (Swedish Council on Technology Assessment in Health Care, 1998).

Fetal screening

Fetal screening for chromosomal abnormalities is primarily aimed at detecting fetuses with Down's syndrome (DS) because this is the most common chromosomal abnormality. The incidence of DS in Sweden is 1 newborn baby in 750 (Swedish National Board of Health and Welfare, 2004). DS is always associated with different degrees of mental retardation (Carr, 1988), but invariably also with structural abnormalities such as congenital heart diseases and gastrointestinal atresia (Brookes & Alberman, 1996). DS is positively associated with maternal age. The risk of a 20-year-old woman giving birth to a baby with DS is 1 in 1527 while for a 40-year-old woman the risk is 1 in 97 (Snijders, Sundberg, Holzgreve, Henry & Nicolaides, 1999).

Current screening programme

According to the Swedish national guidelines, all pregnant women at early gestation should be given both verbal and written information about methods for fetal diagnosis and screening, including ultrasound examination with the emphasis on voluntary participation. Women at increased risk should be given detailed information by a physician (Swedish National Board of Health and Welfare, 1997). Women aged 35 years or older are routinely offered an amniocentesis (AC) in order to detect fetuses with DS. With maternal age-based screening the detection rate is limited to 20-30 percent (Nicolaides, Brizot & Snijders, 1994).

Second trimester maternal serum screening with analyses of alpha-fetoprotein (AFP) (Merkatz, Nitowsky, Macri & Johnson, 1984), often combined with HCG and unconjugated estriol (triple test) and also inhibin-A (quadruple test) (Benn, 2002), as well as first trimester serum screening with analyses of PAPP-A and β-HCG (Wald et al., 2003) are biochemical methods to estimate the risk of the fetus having DS. These methods are not routinely used for screening in Sweden but are available on request.

One of the latest non-invasive techniques for assessing the risk of DS is nuchal translucency (NT) screening at 11-14 weeks of gestation by means of an ultrasound examination. A fluid-filled space at the back of the fetal neck (nuchal translucency), which only exists in early pregnancy, is measured in millimetres. In combination with maternal age and length of gestation the NT gives the probability of the fetus having DS (Nicolaides et al., 1994). An increased NT is also associated with heart diseases or other fetal structural malformations (Nicolaides, Heath & Cicero, 2002; Snijders & Smith, 2002).

Fetal karyotyping

Amniocentesis is the most commonly used method for fetal karyotyping in Sweden and is usually performed at 15 gestational weeks. Under ultrasound guidance, amniotic fluid is aspirated and the cultivation that follows results in the fetal karyotype (Creasey & Reasnik, 2003). The analysis based on chromosomal cultivation takes two to three weeks. A new and quicker DNA-based method for analysing the fetal chromosomes, QF-PCR, has recently become available. With this method, usually only chromosomes 13, 18, 21 and the sex chromosomes are included for analysis (Swedish Council on Technology Assessment in Health Care, 2004). Chorion Villus Sampling (CVS), which is mostly performed transabdominally after 10 weeks of gestation, is an alternative method for fetal karyotyping. A catheter is inserted in the placental bed under ultrasound guidance. Villi is aspirated and further analysed (Creasey & Reasnik, 2003). The risk of miscarriage after an AC and CVS is estimated to be 0.5-1.0 percent (Tabor et al., 1986; Canadian Collaborative CVS-amniocentesis Clinical Trial Group, 1989).

Aspects of general screening

Before introducing a new screening programme some general issues related to screening have to be taken into account. The aims of a screening programme are to improve health, and to detect common diseases or an increased risk of a disease. Screening should be offered to a larger population in order to identify a smaller sample of people who are at high risk of the condition searched for. The screening procedure should thus detect individuals who have the abnormality (sensitivity) and exclude all individuals without the abnormality (specificity). Screening may give a false positive result, i.e. the condition seems to be present but in fact it is not. Further screening tests may follow, which can cause conflicting results and unnecessary worry. A diagnostic test, sometimes associated with risks, will rule out the alternatives. Another aspect is the false negative results, i.e. the disease occurs despite the fact that the screening confirms health, leading to false reassurance and psychological distress. Moreover, the condition which is screened for should ideally have an available, effective and acceptable treatment. The quality of the test must be high, and the relation between costs and benefits has to be taken into account (Mant & Fowler, 1990; Nielsen & Lang, 1999; Wilson & Jungner, 1968).

Ethical issues

The benefits of screening for the individual person have to outweigh the harm. However, benefits for the entire population do not necessarily imply benefits for each individual (Mant & Fowler, 1990; Wilson & Jungner, 1968). Another basic ethical principle is that of autonomy. Adequate information is a prerequisite for free choice (Posner, 1993). Refraining from a test is also a choice and puts pressure on the woman (Farrant, 1985; Green, 1990). The only available treatment for DS is termination of pregnancy; and this raises important ethical problems (Delholm & Olsen, 1992; Tymstra; 1991) such as questions about human dignity and the society's view of disabled children and handicapped people (Farrant, 1985).

Psychological changes and worry associated with pregnancy

Interventions during pregnancy, this unique time in a woman's life, have to be considered in the light of normal psychological changes. Pregnancy is characterised not only by physical and hormonal changes, but also by strong emotional reactions and ambivalent feelings. The first pregnancy is often described in terms of transition, and a period of important psychological adaptation. Many potential conflicts are involved in this complex process related to the relationship with the woman's partner, her own mother and friends (Bibring, Dwyer, Huntington & Valenstein 1961; Shereshefsky & Yarrow, 1975). Early pregnancy may be a vulnerable period when the woman accepts the fetus as an integral part of herself. During mid-pregnancy, the fantasy about the baby grows and may cause mixed feelings. Closer to the delivery there is a successive psychological separation from the fetus, as concern about the approaching birth and

also the preparation for parenthood take more of the woman's attention (Placek Lederman, 1990; Raphael-Leff, 1992).

The extent to which normal pregnancy affects everyday worry has been insufficiently studied (Green, Kafetsios, Statham & Snowdon, 2003). The causes of worry during pregnancy and how it is expressed may depend on personality, coping strategies and the social context (Affonso, Liu-Chiang & Mayberry, 1999). Ambivalent feelings about the pregnancy, a negative mood and previous negative pregnancy outcomes are factors associated with major worry. The most common sources of worry are concerns about the baby's health, miscarriage and the delivery (Placek Lederman, 1990; Light & Fenster, 1974; Statham, Green & Kafetsios, 1997). The degree of anxiety may vary during the course of pregnancy. During the first trimester many women experience increased emotional sensitivity. Anxiety often decreases in the second trimester when feeling the fetal movements are felt, but increases again as the time of the birth approaches (Placek Lederman, 1990; Shereshefsky, 1975; Statham et al., 1997). Nulliparas are usually more worried than women with a previous history of an uncomplicated pregnancy and a healthy child (Placek Lederman, 1990).

Attitudes towards prenatal screening and ultrasound examination

Prenatal screening has become a routine component of antenatal care and it has made irreversible changes to the view of pregnancy (Green, 1990). The focus on the unborn baby has become stronger, and the health of the baby is also crucial for expectant mothers. In a study of 3061 Swedish women's expectations of antenatal care the most important aspect was to check the baby's health (Hildingsson, Waldenström & Rådestad, 2002). This may explain why most women have a positive attitude towards prenatal screening (Green, Hewison, Bekker, Bryant & Cuckle, 2004). The strong desire for reassurance about the health of the fetus is frequently mentioned as a reason for participating in prenatal screening (Larsen, Nguyen, Munk, Svendsen & Teisner, 2000; Ekelin, Crang-Svalenius & Dykes, 2004; Santalahti, Aro, Hemminki, Helenius & Ryynänen, 1998). In a Swedish study by Crang-Svalenius and colleagues (1998), women had the opportunity to choose between the following methods of examining the fetus: a) no ultrasound screening other than for medical reasons, b) early ultrasound without inspection of fetal anatomy, c) routine ultrasound examination in the second trimester and d) amniocentesis and routine ultrasound examination. Most women (85.5%) chose alternative c), 13.4 percent chose alternative d) and no one chose alternative a). Factors that influenced women's choices were: interest in checking the health of the fetus, maternal age and knowledge of possible consequences of the method, e.g. miscarriage and detection of malformations. Local routines play an important role in women's decision. When ultrasound screening was not routinely offered to pregnant women, the examination was less likely to be considered reassuring compared with when it was part of routine care (Hyde, 1986). This can illustrate the phenomenon "what is must be best" discussed

by Porter and McIntyre in their study of satisfaction with antenatal care (Porter & McIntyre, 1984).

Ultrasound screening during pregnancy is described by expectant parents as a very positive, important, enjoyable and truly great experience (Baillie, Smith, Hewison & Mason, 2000; Bricker et al., 2000; Ekelin et al., 2004; Eurenius, Axelsson, Gällstedt-Fransson & Sjödén, 1997; Garcia et al., 2002; Villeneuve, Laroche, Lippman & Marrache, 1988). For many women and their partners it is a social rather than a medical event (Baillie et al., 2000, Sandelowski, 1994) and an offer that is not often refused (Crang-Svalenius, Dykes & Jörgensen, 1996a; Sandelowski, 1994). Attitudes towards screening differ between the practitioners who search for abnormalities and the patients who seek reassurance of a healthy baby (Farrant, 1985; Posner, 1993; Williams, Alderson & Farsides, 2002). Positive attitudes to NT measurement among women over 35 years of age have been reported, since immediate and early feedback about the risk of DS with reassuring NT results make the decision about an invasive test easier and decreases worry (Kaiser et al., 2004). Women seem to prefer screening in the first trimester instead of the second, since it gives an opportunity for earlier reassurance about the health of the fetus (Kornman, Wortelboer, Beekhuis, Morssink & Mantingh, 1997; DeGraaf, Tjimstra, Bleker & Van Lith, 2002), but not at the expense of less safety or a lower detection rate of malformations (Bishop et al., 2004).

Psychological aspects on fetal screening and diagnosis

Prenatal screening and diagnosis may affect women's worries and emotional well-being in different ways, depending on method, information, results and their own estimation of the fetal risk (Green, 1990). The ultrasound examination provides early visual confirmation of pregnancy and contact with the baby, but the evidence of effects on the attachment process is inconclusive (Bricker et al., 2000). For many parents the ultrasound scan has such an important confirmative role that they wait until after the examination before announcing the pregnancy (Ekelin et al., 2004). Communication with the examiner is an important factor for how the ultrasound examination is experienced and whether the parents are satisfied (Ekelin et al., 2004; Green, 1990). Worry may increase prior to the ultrasound scan (Garcia et al., 2002; Green, 1990) but if the results show a healthy baby, feelings of relief and reassurance will follow (Ayers & Pickering, 1997; Cox, Wittman et al., 1987; Eurenius et al., 1997; Green, 1990; Michelacci et al., 1988; Zlotogorski, Tadmor, Duniec, Rabinowitz & Diamant, 1995). An ultrasound examination with a reassuring outcome has a calming effect regardless of when it is being performed (Michelacci et al., 1988). In contrast, if something deviates from what is normal the great expectations shift to concern, shock and distress (Bricker et al., 2000).

Even if the woman has requested the procedure herself, she may experience worry and considerable stress in connection with the examination (Green, Statham & Snowdon, 1992;

Green & Statham, 1993). Lower levels of anxiety have been demonstrated by the end of pregnancy in women who have undergone antenatal tests or screening, as compared with women who have not (Marteu et al., 1989; Searle, 1996). The invasiveness of the procedure does not seem to affect the individual experience of prenatal diagnosis (Kowalcek, Mühlhoff, Bachmann & Gembruch, 2002). Waiting for the test results generates much worry and concern (Cederholm, Sjödén & Axelsson, 2001; Green & Statham, 1996; Santalahti, Latikka, Ryynänen & Hemminki, 1996). The risk of miscarriage following an invasive procedure also generates such worry (Cederholm et al., 2001).

Anxiety due to screen-positive and false positive results

The information of a screen-positive test result is negatively associated with emotional well-being (Marteau, 1995; Goel, Glazier, Summers & Holzapfel, 1998; Green, 2004, Santalahti et al., 1996) and high levels of anxiety reflected by increased worry about the baby's health are described (Marteau et al., 1992). Some residual anxiety may remain in women with screen-positive results even after a subsequent reassuring diagnostic test (Green et al., 2004). Remaining worry after false positive test results from ultrasound screening, including NT measurement and maternal serum screening, has been reported. Of 24 women who received false positive test results from an ultrasound scan, including risk assessment for DS, two thirds still described anxiety up to four weeks after a confirmatory normal diagnostic test. Not only worries about the health of the fetus but also a feeling that something unexpected could happen during pregnancy was described (Baillie et al., 2000). Weinans and colleagues (2004) compared anxiety in gestational week 20-32 in association with false positive results from NT screening and from serum screening in 20 women in the respective group. The risk was presented as numerical values in both groups. The women who had undergone NT screening were more worried about the health of the baby, and a possible explanation was the visualisation of the anomaly (NT) in this group. Another difference between the two methods is that positive results from NT screening may indicate other abnormalities than DS. Among 33 women with false positive results from maternal serum screening, one woman in five was still worried two months after having received confirmatory normal invasive test results (Santalahti et al., 1996). Ten years after receiving false positive results from maternal serum screening, feelings of worry could easily be recalled (Smedler & Bremme, 1992). In a study of false positive results of screening for congenital hypothyroidism, 78 of 102 families initially exhibited strong emotional reactions whereas after a period of 6 to 12 months, 18 families described persisting insecurity regarding the baby's health (Bodegård, Fyrö & Larsson, 1983). Contrary to these findings, others have reported short term worry due to false positive results (Watson, Hall, Langford & Marteau, 2002).

Information and the communication about risk

Giving adequate and comprehensive information about prenatal screening and tests is a challenge. The aim of the screening, the risks and benefits, the fact that participation is voluntary, the meaning of the results, the likelihood of false positive and false negative findings, the conceivable consequences and available alternatives all have to be included (Baillie et al., 2000; Marteau, 1995; Lowe, Pruitt, Smart & Dooley, 1998; Santalahti et al., 1998). Information has to be given long enough in advance in order to give the woman a chance to form an opinion (Kornman et al., 1997). Women often seem insufficiently informed about the available methods of prenatal screening or diagnosis, the purpose and the reliability of the test (Cederholm et al., 1999; Grewal et al., 1997; Lowe et al., 1998; Thorpe, Harker, Pike, & Marlow, 1993).

Understanding of the purpose of ultrasound screening varies, as well as how the women consider the information. In a study about opinions of antenatal care in 2109 women, Ladfors and colleagues (2001) showed that only 60 percent of the 1130 multiparous women understood that the routine ultrasound examination was voluntary, and 13 percent believed it was compulsory. One third of the 100 women in a study by Crang-Svalenius and colleagues (1996b) stated that they were not aware of the possibility that fetal malformations could be detected at the ultrasound screening. In a Norwegian trial of 891 women, 51 percent said they had not received any information about the ultrasound screening, and 37 percent did not realise it was voluntary (Sommerseth, 1993). However, later reports describe women who are satisfied with the information and are aware of the purpose of the ultrasound screening (Basama, Leonard & Leighton, 2004; Whynes, 2002). Women often seek and obtain information themselves. In a Swedish study by Eurenius and colleagues (1997), a majority of the women stated that they had received sufficient information about the examination but only 57 percent of 303 women had received this information from the antenatal clinic. Basama and co-workers (2004) reported that 21 percent of 385 women received information about the ultrasound screening from a non-medical medium.

The results of screening procedures are often presented in terms of probability as a risk figure, which may be difficult to understand and interpret (Rapp, 1988; Lobb, Butow, Kenny & Tattersall, 1999; Gifford, 1986). Previous life experiences, intuitive perception and psychological mechanisms, gender and socio-economic status may influence how to interpret risk information (Slovic, 1997; Slovic, Finucane, Peters & MacGregor, 2004). The pregnancy per se is associated with feelings of fear and being at risk (Searle, 1996) and this may affect the understanding of risk; making it more irrational, more sensitive and ambiguous (Darbyshire, Collins, McDonald & Hiller, 2003). The meaning of the screening results may also be influenced by the various, problematic interpretations of normality. There is seldom a clear distinction between normality and abnormality, and the definition may vary in different settings and contexts (Posner, 1993).

The Swedish randomised controlled study of early ultrasound screening including assessment for Down's syndrome with nuchal translucency versus routine ultrasound

Between 1999 and 2002 a multi-centre randomised controlled trial, the Swedish NUPP-trial (NackUPPklarning), was undertaken in order to establish whether a change in policy for fetal screening would result in fewer babies born with DS. Altogether, 39,572 women were randomised to an ultrasound scan at 12-14 gestational weeks including NT screening for DS, or to a routine scan at 15-20 gestational weeks with screening for DS only based on maternal age. Fetal karyotyping was offered if a risk according to NT was ≥ 1:250 in the intervention group and if maternal age was ≥ 35 years in the routine group.

In the intervention group the exact risk score was always given in writing and sometimes orally by the midwife after the ultrasound examination. In the case of the invasive test giving a positive result, i.e. the fetus had DS, the woman would be offered the option of termination. In the case of a negative result she was offered a follow-up scan at 18-20 gestational weeks. Women in the routine group with a scan at 15-20 gestational weeks served as controls. In both groups, the ultrasound examination included screening for fetal malformations, multiple pregnancy, assessment of gestational age and localisation of the placenta. The primary outcome of the NUPP trial was the number of babies born with DS. Secondary outcomes were other unbalanced chromosomal abnormalities, the number of terminations of DS and the number of invasive tests for fetal karyotyping (Saltvedt et al., submitted). Another focus was women's experiences; which constituted the general aim of this thesis.

AIMS

The general aim of this thesis was to explore women's reactions to and experiences of fetal ultrasound screening, including risk assessment for Down's syndrome.

The specific aims were:

(i) To test the translated version of Cambridge Worry Scale on pregnant women in the Stockholm region, to study possible variations in women's worries during pregnancy and to explore whether women expressed causes of worry other than those included in the original scale (Paper I);

(ii) To evaluate the effects of fetal ultrasound screening for DS on women's anxiety, specifically on women's worries about something being wrong with the baby in mid- pregnancy and two months after delivery (Paper II);

(iii) To explore women's reactions to information about being at risk of carrying a fetus with DS following an early ultrasound scan, particularly reactions to false positive tests (Paper III);

(iv) To explore how the risk information was understood, and if the actual risk and the woman's perception of the risk were associated with worry and depressive symptoms during and after pregnancy (Paper IV).

METHODS

General design of the studies

Paper I is an observational study with a methodological focus aiming at testing a translated version of the Cambridge Worry Scale (CWS) on a sample of Swedish pregnant women. Paper II is a randomised controlled trial including a sub-sample of a larger trial (the NUPP-trial) aiming at studying the effects of fetal screening for DS by means of an early ultrasound examination and measurement of NT, compared with routine care. When a woman had agreed to participate in the NUPP-trial, her name and personal data were faxed to the ultrasound unit where randomisation was performed in blocks by an Internet-based computer program. In the region where the present study was conducted, the midwives at the antenatal clinic who informed about the NUPP-trial gave information about the present study on the same occasion, but only to those who had agreed to participate in the NUPP-trial. Paper III is a qualitative study based on semi-structured interviews of women with false positive results of early ultrasound screening for DS. Paper IV is an observational study based on data from the intervention group in Paper II, and explores women's perception of risk information and the relation between actual and perceived risk respectively and worry and emotional well-being.

Study populations

Paper I

A sample of 200 Swedish-speaking pregnant women was recruited in 1999 during a period of 15 days, from the waiting rooms of three antenatal clinics that had been selected in order to represent a population of mixed socio-economic background. The researcher approached all women who attended the clinics during the given time frame, regardless of the length of pregnancy. The questionnaire was handed to the woman while she was waiting for her antenatal check-up. Fewer than ten women declined to participate.

Paper II

The sample of this study was drawn from the larger group of women who consented to participate in the NUPP-trial, which was a multi-centre trial including different regions in Sweden. For the purpose of this study, 22 antenatal clinics in the Stockholm region were selected. In total 8,717 women were booked at the included clinics during the recruitment period from March 2000 to April 2001. Of these women, those who were not sufficiently proficient in the Swedish language, or whose gestation was beyond 13 weeks and 2 days, were excluded from the NUPP-trial. Information about the exact number of these excluded women was not available in this study. In the larger NUPP-trial 80 percent of eligible women consented to participate. In this

study 2026 women agreed to participate, and this was 23.2 percent of all women admitted to antenatal care at the study clinics and a slightly higher percentage of all who were eligible. In all, 1030 women were randomised to the intervention group (EUG – Early Ultrasound Group) and 996 to the control group (RUG – Routine Ultrasound Group). The number of women who declined to participate in the study and their reasons for non-participation were not recorded. The women in the trial are illustrated in Figure 1.

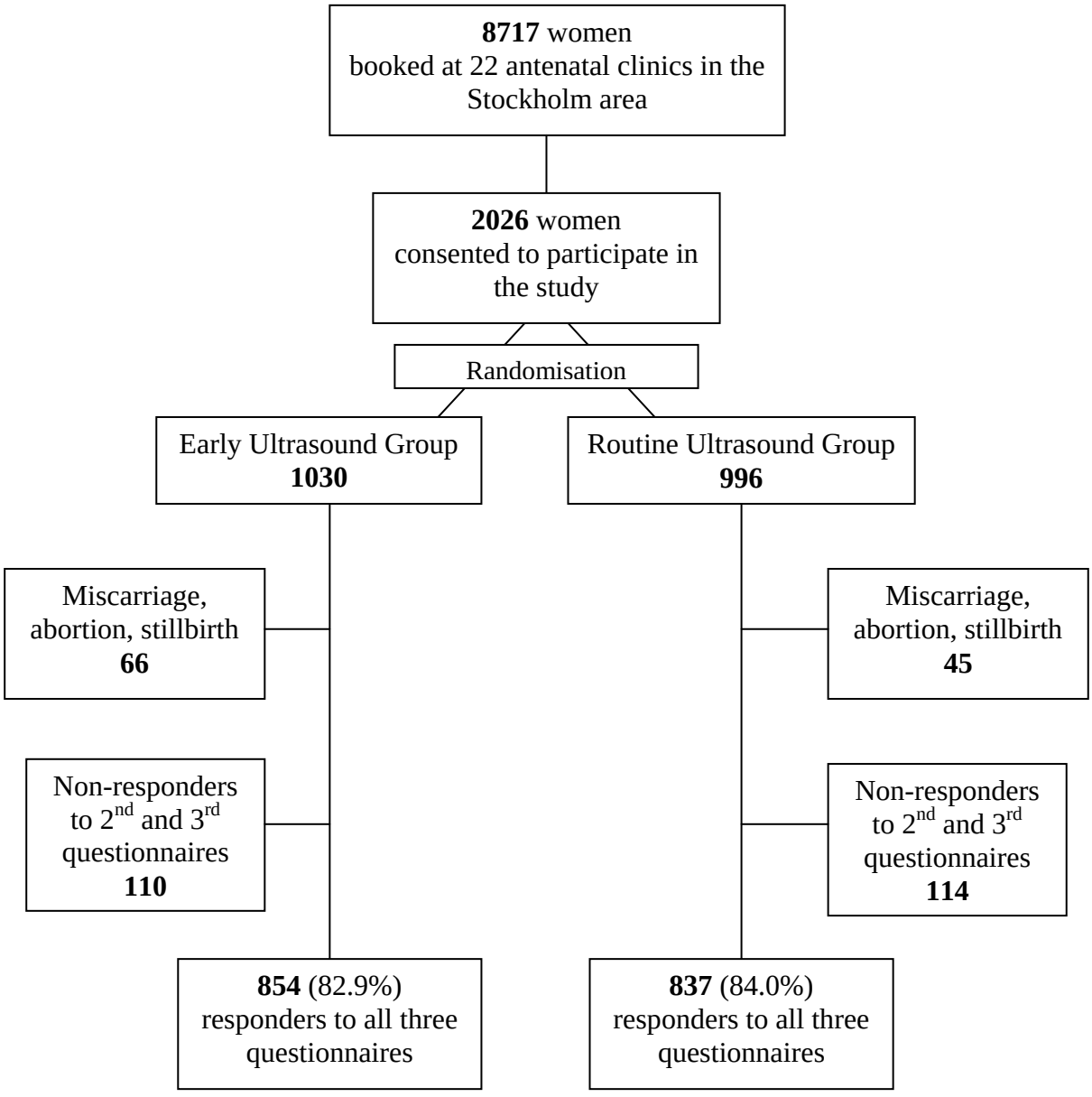

Figure 1. Flow Chart

From paper II with permission from Acta Obstetricia et Gynecologica Scandinavica

Paper III

Twenty-four women with an increased risk of carrying a fetus with DS, as estimated by NT measurement in the intervention group of the NUPP-trial, were consecutively recruited from four ultrasound units in Stockholm from April 2001 to October 2001. The midwife who performed the ultrasound scan gave written and oral information about this study at the same time, and obtained permission from the woman to give her name and telephone number to the researcher, who thereafter made an appointment for the first interview.

Paper IV

Of the 1030 women who had been allocated to the EUG in Paper II, 908 had a risk score recorded in the NUPP-trial database. Of these, 101 had not filled in all three questionnaires and 11 had not answered the questions about risk in the second questionnaire. Consequently, 796 women provided data for this study.

Data collection

Paper I

Data were collected by means of a questionnaire including the translated version of the Cambridge Worry Scale. For the purpose of this study the scale had been translated into Swedish by one of the researchers and translated back to English by another person. Questions about parity, maternal age, gestational week and obstetric history such as infertility, previous miscarriage and adverse infant outcome (severe morbidity or stillbirth) in a previous pregnancy were included in the questionnaire, as well as an open-ended question about worries not included in the original scale. The completed questionnaire was returned in a sealed envelope.

Paper II

Data were collected by means of three questionnaires. The first was distributed in early pregnancy, before randomisation. The questionnaires were either filled in at the first visit at the antenatal clinic or at home and mailed to the researcher. In 1688 cases the questionnaire was filled in before and in 338 after randomisation. The latter group was equally distributed between the trial groups: 165 in the EUG and 173 in the RUG. The second questionnaire was sent by post to the women in gestational week 24. This point of time was chosen to ensure that all the women had undergone their ultrasound examinations, and in some cases even invasive tests, and had received information about the test results. Another reason choosing this time point was that mid-pregnancy is regarded as the calmest period during pregnancy, with less worry. Mid-pregnancy data would also allow comparisons with findings from other studies. The last questionnaire was posted two months after the birth. The average time when filling in the first

questionnaire was at 10.2 and 10.3 gestational weeks the EUG and the RUG respectively; the second questionnaire was filled in at 24.9 gestational weeks in both groups, and the third questionnaire at 9.8 and 9.5 weeks after delivery (p=0.02).

The first questionnaire included questions about socio-demographic background, such as age, marital status, native language and education; and questions about obstetric background, such as gestational week, parity, previous children, previous abortion, miscarriage, infertility and stillbirth. All three questionnaires included the same instruments: the Swedish version of the Cambridge Worry Scale as tested in Paper I, the State-Trait Anxiety Inventory (STAI) to measure anxiety of a more stable (Trait) and situational nature (State), and the Edinburgh Postnatal Scale (EPDS) to measure depressive symptoms.

Paper III

Data were collected in three interviews with each woman, conducted at about the same time points as the questionnaires in Paper II were distributed. The interviews were semi-structured and followed an interview guide with six themes: experience of the early ultrasound scan; reactions to the information about an increased risk; how the risk information was understood; the decision processes related to having an invasive test or not; attitudes towards the baby; and finally, support from closely related people and professionals. In the third interview an additional theme was retrospective reflections on having an early ultrasound scan.

Paper IV

This paper was based on data from the second questionnaire used in Paper II, which included questions about information related to the ultrasound examination, about the risk score and how the woman perceived the risk. The actual risk score was collected from the clinical database of the NUPP-trial. In order to assess the representativity of the sample, background characteristics were compared with the data on the total national birth cohort of 2000, retrieved from the Medical Birth Register (Swedish National Board of Health and Welfare).

Instrument description

The Cambridge Worry Scale - CWS

The original Cambridge Worry Scale measures women's worries during pregnancy, and was developed in the United Kingdom by Statham and colleagues (Statham, Green & Snowdon, 1993). The original scale has been tested at three time points during pregnancy. The reliability of the scale, as measured by the homogeneity was 0.79 at 16 and 22 weeks of pregnancy, and 0.76 in week 35 (Cronbach's alpha coefficient). Validity was considered satisfactory (Green et al., 2003).

The original version includes 16 items describing possible sources of worry during pregnancy. The response alternatives ranged from 0 to 5 with the anchors verbally described (0 = not a worry, 5 = major worry). The items of the scale are presented in Figure 2.

Item	**Not a worry**					**Major worry**
Your housing	0	1	2	3	4	5
Money problems	0	1	2	3	4	5
Problems with the law	0	1	2	3	4	5
Your relationship with your husband/partner	0	1	2	3	4	5
Your relationship with family and friends	0	1	2	3	4	5
Your own health	0	1	2	3	4	5
The health of someone close to you	0	1	2	3	4	5
Employment problems	0	1	2	3	4	5
The possibility of something being wrong with the baby	0	1	2	3	4	5
Going to hospital	0	1	2	3	4	5
Internal examinations	0	1	2	3	4	5
Giving birth	0	1	2	3	4	5
Coping with the new baby	0	1	2	3	4	5
Giving up work	0	1	2	3	4	5
Whether or not your partner will be with you for the birth	0	1	2	3	4	5
The possibility of miscarriage	0	1	2	3	4	5

Figure 2. The Cambridge Worry Scale (Green et al., 2003)

The testing of the translated scale (Swedish version of the Cambridge Worry Scale – SCWS) in Paper I showed that all items were well understood by Swedish pregnant women, but three new items were added and these were related to women's concerns about the maternity services in the Stockholm region. Some of the items (internal examinations, giving birth, the possibility of miscarriage, and if the partner would be present for birth) were not relevant to the postpartum period and were therefore excluded in the postnatal questionnaire.

State-Trait Anxiety Inventory – STAI

Women's general anxiety was studied by the State-Trait Anxiety Inventory (STAI), which includes two scales measuring trait anxiety, i.e. how the subject generally feels, and state anxiety, i.e. how the subject presently feels at present. Each scale includes 20 statements, and responses may range from 20 (minimum anxiety) to 80 (maximum anxiety) (Spielberger, 1970). STAI is considered to be well validated and one of the most widely used scales for the evaluation of anxiety in research. In stressful situations the state anxiety shows higher values than in non-stressful situations. The Cronbach's alpha coefficient was 0.93 in the first evaluation of the scale (Spielberger, 1970). The scale has not been specifically evaluated for pregnant women.

Edinburgh Postnatal Depression Scale – EPDS

The Edinburgh Postnatal Depression Scale (EPDS) was included in the questionnaires to measure depressive symptoms. It is a 10-item, self-report scale assessing common symptoms of depression, including anxiety. The EPDS has been validated for antenatal use in the United Kingdom where EPDS scores were compared with the results of psychiatric interviews in gestational week 24-38 (Murray & Cox, 1990). In Sweden the EPDS has been validated for postnatal use only, and the optimum cut-off for major depression postpartum was 11/12 (Wickberg & Hwang, 1996). Each item is scored on a 4-point scale (from 0 to 3), the minimum and maximum total scores being 0 and 30 respectively. The women rank how they have felt during the past week. Five of the items are concerned with dysphoric mood, two with anxiety, and one each with guilt, thoughts of harming oneself, and "not coping" (Cox, Holden & Sagovsky, 1987).

Analyses

All statistical analyses were conducted by using SPSS version 11.0 and 12.0 (Statistical Package for Social Science, Inc., Chicago, IL).

Paper I

Non-parametric statistics were used to analyse the 16 items of the Cambridge Worry Scale. Differences between women at different gestational ages were tested by one-way ANOVA. The exact median values were estimated using the computer program SPRISTAT, based on the database Paradox 4.5. Statistical significance was defined as $p < 0.05$. Internal-consistency reliability was estimated by using Cronbach's alpha coefficient. The open-ended question was analysed by listing and summarising additional sources of worry.

Paper II

The power calculation was based on figures from an English survey showing that 22 percent of the women were worried about the fetus in mid-pregnancy, and 23 percent were worried in late pregnancy (Statham et al., 1997). The primary outcome was based on the item "worry about the possibility of something being wrong with the baby" in the SCWS. To detect a clinically significant increase by 25 percent of women who were worried about the health of the fetus from the expected 23 percent in the RUG to 29 percent in the EUG (80% power, 95% CI), 840 women were required in each group. In each group, 700 women would be required to detect a reduction of the same size, from 23 percent to 17 percent. The sample was estimated to 2000 women with 1000 in each group, after taking non-responders into account.

The comparison of the trial groups and the analyses in mid-pregnancy and two months after delivery were based on the responders to all three questionnaires; 854 (82.9%) in the EUG and 837 (84.0%) in the RUG. The 6-point SCWS was dichotomised and women scoring 4 or 5 were defined as suffering from major worry. This made it possible to compare the findings with those of the English study on which the power calculation was based (Statham, 1997). A cut-off at 11/12 was used when analysing the EPDS, both during pregnancy and postpartum in order to allow comparison between the time points. Categorical data were analysed by χ^2 - test, odds ratio (OR) and associated 95 percent confidence intervals, and continuous data by Student t-test for normally distributed variables and Mann Whitney U-test when distributions were skewed. All statistical tests were two-sided, and a p-value < 0.05 was considered statistically significant.

Paper III

The interviews were audiotaped and transcribed verbatim. The qualitative analysis was performed in three steps with focus on the content of the women's responses (Kvale, 1996, Malterud, 1998).

1. All three interviews with each woman were read and re-read several times to form a comprehensive picture of each woman's responses.
2. Themes reflecting experiences expressed by each woman were identified and described, starting with the first interview and adding new themes as they emerged in the second and third interview.
3. The themes were categorised across all cases, and followed the chronological order of the screening and examination procedures throughout pregnancy.

During the process the senior researchers who independently described the content of the text validated the results and then all researchers discussed them until an agreement was reached.

Paper IV

Comparisons between groups were calculated by Student's t-test and paired samples t-test for continuous variables. For categorical variables, χ^2 - test and Friedman's analysis of repeated measures was used.

Table 1. Overview of the papers

Paper	Design	n	Data collection	Outcome measures	Data coll. period
I	Observational	200	1 questionnaire	Feasibility of filling in the Swedish version of CWS Scale properties Distribution of worry	April – May 1999
II	Randomised Controlled Trial *	2026	3 questionnaires: before randomisation, at 24 week of gestation, 2 months postpartum	Worry about the health of the baby Maternal emotional well-being	March 2000 - April 2001
III	Qualitative *	24	3 semi-structured interviews at same time points as in paper II	Reactions and responses to increased risk of having a baby with Down's syndrome	March 2001 – September 2002
IV	Observational *	796	3 questionnaires: same as in Paper II	Interpretation of risk information Actual and perceived risk in relation to worry and maternal emotional well-being	March 2000 - April 2001

*The women in the study sample also participated in the NUPP-trial

Ethical considerations

Screening for fetal malformations and abnormalities raises a number of complex ethical questions, specifically when the only "treatment" is termination of the pregnancy. Screening for DS has been established in Sweden for several decades. The NUPP-trial could be seen as a way of improving the technique by detecting a larger proportion of cases of DS, and possibly by reducing the risk of miscarriage if the number of "unnecessary" invasive test can be reduced. The evaluation of women's experiences of the new fetal screening method is a necessary component in order to make an overall evaluation of the method that can also be justified from an ethical point of view. The problem of false positive results and how information should be given are crucial in this context.

All participants in the randomised part of the study were given both written and oral information. The covering letter to the second questionnaire in gestational week 24 included a comment, and excuse that it could not be completely ruled out that the questionnaire was also sent to women who had had a miscarriage. In order to minimise this risk, the information available in the NUPP database was checked before mailing the questionnaires. In the end of the questionnaires, the women were also encouraged to talk with the midwife at the antenatal clinic if they had any questions or worries. To avoid reminder letters the women were asked to return the questionnaire empty if they wanted to break off their participation in the study.

Women in the qualitative study were asked about participation by the midwife at the ultrasound unit and they were also given written information. During the interviews the researchers tried to be sensitive to women's emotional reactions, and the women could choose what they wanted to talk about and to what extent they wanted to talk about sensitive topics. All women had an established contact with a midwife at the antenatal clinic who could provide support, and if necessary refer them to a psychologist or a physician.

The Regional Research and Ethical Committee at Karolinska Institutet approved the studies (Dnr. 99-394).

RESULTS

Testing the Cambridge Worry Scale *(Paper I)*

Women had no obvious problems filling in the translated version of the Cambridge Worry Scale, and all items seemed to be well understood. The three main sources of worry were related to pregnancy and delivery, and the four items associated with the least worry were about the partner's presence at the birth, the relationship with the partner and others, and problems with the law (Table 2).

Table 2. Items causing the most and the least worry

	Major worry (4+5)	
	%	**Median**
The possibility of something being wrong with the baby	32.0	2.81
Giving birth	28.2	2.69
The possibility of miscarriage	17.1	1.05
Whether your partner will be with you for the birth	3.5	0.11
Your relationship with your husband/partner	2.0	0.15
Problems with the law	1.0	0.07
Your relationship with your family and friends	0.5	0.12

Length of gestation was reported by 199 women, and these were divided into four groups: ≤15 weeks (n=41), 16-25 weeks (n=44), 26-33 weeks (n=54) and ≥34 weeks (n=60). When comparing women's worries in these groups, worry about the baby's health and about the approaching birth was less in mid-pregnancy and rose again closer to the delivery. However, these differences were no statistically significant.

The homogeneity of the scale was satisfactory. The Cronbach's alpha coefficient measuring the internal-consistency reliability for the total scale was 0.81. This value was also stable when items were deleted one by one, and for primiparas and multiparas separately. The item-total correlation varied from 0.27 (the health of someone close to you) to 0.55 (internal examination) with 7 items < 0.40, and 9 items ≥ 0.50.

Of the 200 women who participated in the study, 59 also filled in the open-ended question asking about whether they were worried about anything else, not previously listed. The most common concern was about the maternity services in the Stockholm area. Women worried about whether their hospital would be overbooked, and whether the staff would be too busy; they were also afraid that the medical safety would not be guaranteed. As a consequence, three new items were added to the scale to capture these concerns.

Effects of fetal screening for Down's syndrome by means of an ultrasound examination in early pregnancy including measurement of fetal nuchal translucency *(Paper II)*

No statistically significant differences were found in socio-demographic background or obstetric history between the trial groups at baseline before the randomisation (Table 3).

Table 3. Socio-demographic and obstetric background
(% unless stated otherwise)

	EUG n=854	**RUG** n=837
Mean age	30.3	30.4
Married or cohabiting	96.8	96.5
Swedish as native language	93.9	92.8
Education: College or university	52.7	51.3
Nullipara	54.7	53.9
Previous miscarriage	17.8	15.5
Previous abortion	27.8	27.6

Also, no statistically significant differences were found at baseline in general anxiety measured by STAI, and depressive symptoms measured by the EPDS. Neither were statistical differences found regarding women's worries about specific issues during pregnancy according to the SCWS, except worry about housing, where women in the EUG rated less worry (OR 0.6; 95% CI 0.4-0.9). The difference in worry about something being wrong with the baby between the EUG and the RUG was not statistically significant (39.1% vs. 36.0 %, OR 1.1; 95% CI 0.9-1.4).

In mid-pregnancy, 29.2 percent of the women in the EUG and 27.8 percent in the RUG worried that something might be wrong with the baby, and this difference was not statistically significant (OR 1.1; 95% CI 0.9-1.3) (Figure 3). At this time point, the only item of the SCWS that reached statistical significance was worry about the relationship with the partner (4.1% vs. 2.0%, OR 2.1; 95% CI 1.1-3.7). Women's general anxiety and depressive symptoms did not differ statistically between the trial groups.

Two months after delivery no statistical differences were observed in any of the outcomes measured by the SCWS, STAI and EPDS. Major worry about something being wrong with the baby had decreased to 5.2 percent and 6.6 percent (OR 0.8; 95% CI 0.5-1.2) in the EUG and the RUG respectively, and the decline in worry about the baby's health from early to mid-pregnancy, and from mid-pregnancy to two months after delivery was statistically significant in both groups.

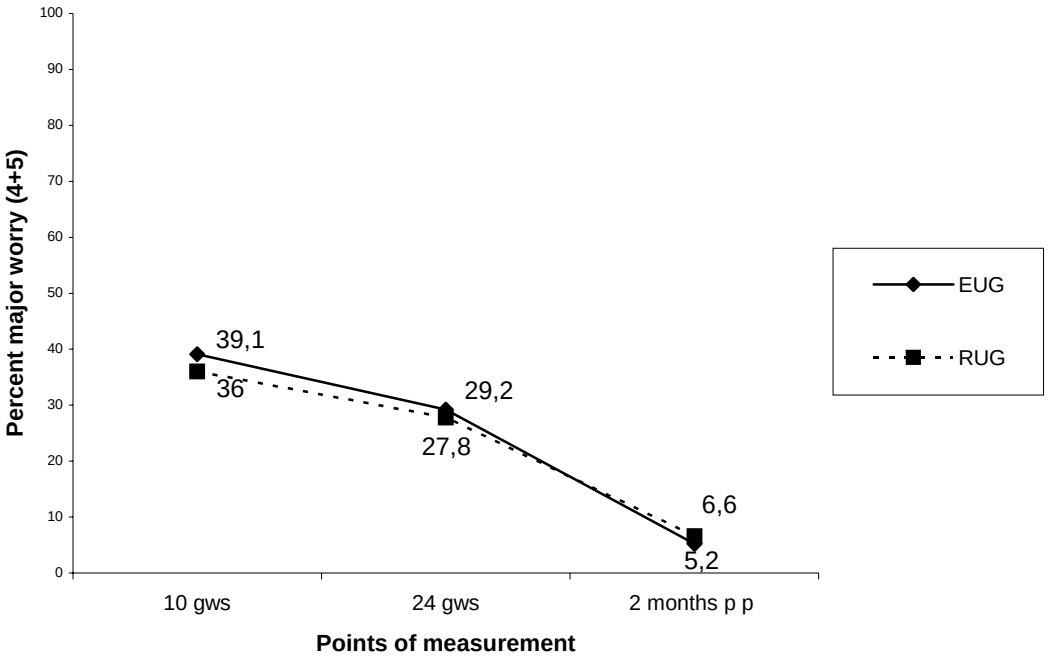

Figure 3. Worry about fetal health in women randomised to fetal screening by an early ultrasound vs. routine ultrasound screening

From paper II with permission from Acta Obstetricia et Gynaecologica Scandinavica.

There were no statistically significant differences between primiparas and multiparas regarding their worry about the health of the baby in mid-pregnancy. In the EUG, 28.7 percent of the primiparas and 29.6 percent of the multiparas expressed major worry and in the RUG the percentages were 27.6 and 28.0 respectively.

Of the 2026 women included in trial, 16.5 percent (335 women) did not complete all the three questionnaires. The frequency of non-responders was similar in both groups (EUG 17.1% and RUG 16.0%). Of the 335 non-responders, 111 completed the first and second questionnaire but not the third. Data on socio-demographic background, worries and general anxiety at baseline is presented in Table 4.

Table 4. Characteristics of the non-responders (% unless otherwise stated)

	Non-responders n=335	**EUG + RUG** n=1691	*p*
Mean age	30.5	30.3	0.45
Married or cohabiting	91.8	96.7	0.006
Education: College or university	46.7	52.0	< 0.001
Swedish as native language	85.6	91.1	0.001
Nullipara	45.7	54.0	0.006
SCWS at baseline (percentage major worry 4+5)			
The possibility of something being wrong with the baby at baseline	46.2	37.5	0.003
in mid-pregnancy	38.5	28.7	0.03
Going to hospital	13.8	7.6	< 0.001
Giving birth	36.0	29.2	0.01
Risk of miscarriage	39.6	31.0	0.001
Safety of medical care during labour	19.6	14.6	0.02
STAI (Mean)			
State	34.5	32.8	0.002
Trait	34.7	33.2	0.003
EPDS Scores > 11	19.5	11.8	< 0.001

Women's reactions to information about being at risk of carrying a fetus with Down's syndrome *(Paper III)*

After the early ultrasound scan the 24 women included were informed that they were at risk of carrying a fetus with DS. Eleven women were younger and 13 were older than 35 years, 7 were expecting their first baby and 17 were multiparas. The risk scores ranged from 1:3 to 1:250. All women were offered an invasive test for fetal karyotyping to confirm the diagnosis. Five women declined this offer, 17 had an amniocentesis and two a chorion villus sampling. The outcome of the invasive tests showed that 20 women had a false positive ultrasound test, and in four cases the fetus had DS. These four women all terminated their pregnancy.

The ultrasound examination as such was an event that the women had looked forward to, and the experience of this examination was mostly described in positive terms. When they received information about being at risk of carrying a baby with DS, many women seemed unprepared. They expressed strong feelings of anxiety and used expressions like *"it was a slap in the face", "I was deeply worried" and "everything went dark"*. The women often cried when talking about this experience, and some said it caused them loss of sleep and made it difficult to concentrate in daily life.

The predominant way of handling the risk information was to withhold or reject the pregnancy, take a "time out" while waiting for the outcome of the invasive test*: "It felt like a vacuum … I think we had a little break, so to speak, a time out"* (Ann, 30). The women said they avoided talking about their pregnancy and they tried to ignore physical signs of being pregnant. Some women prepared themselves for a worst-case scenario by thinking of the baby as damaged or unhealthy, *"I saw images showing it was completely deformed, extremely bad"* (Jenny, 32). However, some women tried to interpret the risk score in a more optimistic way, or looked for positive signs that could be interpreted as evidence of the baby's health and well-being.

For some women the decision about an invasive test seemed easy. They wanted to know as soon as possible if the baby had DS or not: *"I want to be 100 percent sure that the baby is okay"* (Greta, 24). However, other women described the decision as difficult, and were very concerned about the risk of miscarriage associated with the amniocentesis.

The two to three weeks of waiting for the results of the amniocentesis were described as long, hard and sometimes almost unbearable: *"It was a three-week nightmare"* (Jenny, 33). Immediately after the amniocentesis, the greatest concern was the risk of miscarriage. Different ways of coping with the stress were described, such as working hard or trying to ignore the worry. When they received a normal test result most of the women were relieved and very happy,

and they felt that the pregnancy could recommence. However, two women continued to be worried about something being wrong with the baby.

The follow-up scan in the second trimester was mostly described as a positive experience, but some women worried about the possibility of detecting new abnormalities that had not been found at the first examination. Most of the women were not aware of the purpose of this second ultrasound examination.

Two months after delivery, women in general were pleased with having had the early ultrasound screening for DS. They reflected on the pros and cons and came to the conclusion that they would also consider this type of examination in a future pregnancy. However, one woman clearly expressed that she regretted her participation in the NUPP-trial and another woman expressed strong psychological suffering due to the false positive results.

Six women aged over 35 years, who had a risk score lower than their age-related risk were not equally anxious, but they were very concerned about the risk of miscarriage associated with the amniocentesis.

The four women who chose to terminate their pregnancy because of the positive test result reacted to the risk information after the early ultrasound scan in a similar way to the other women; with very strong reactions and high levels of worry. They also obviously rejected their pregnancies. They had very high risk scores and when receiving the definite diagnoses, their strongest fears were confirmed.

Risk information and its association with maternal emotional well-being *(Paper IV)*

Some characteristics of the study group could be compared with the national birth cohort of 2000 (Swedish National Board of Health and Welfare) as shown in Table 5. The women in the study group were more often married or cohabiting with the expectant father, and were slightly older. More of these women were nulliparas and they were also better educated. The obstetric history of miscarriage and stillbirth was rather similar for both groups.

Table 5. Characteristics of the study group compared with the national birth cohort in 2000.

	Study group	**National Birth Cohort* 2000**
	n=796	n=88,208
	%	%
Age, years		
15-24	9.5	15.5
25-34	73.4	67.6
35-44	17.1	16.8
Mean age	30.3	29.6
Married or cohabiting	97.1	94.6
Native language		
Swedish	93.9	
Other than Swedish	6.1	18.2 (not born in Sweden)
Education: College or university	52.8	36.1 (Statistics Sweden, 2000, females 30 years of age)
Nullipara	55.8	44.0
Obstetric history		
Miscarriage	18.0	18.7
Stillbirth	0.5	0.8

* Data from the Medical Birth Register in 2000 (F. Lundgren, Centre of Epidemiology, Swedish National Board of Health and Welfare, personal communication, February, 2005).

In all, 620 women stated that they had received information about the risk score after the ultrasound examination, whereas 176 said they had not been informed (Figure 4). The latter group was younger and less well educated than those who said they were informed. Of the 620 women who received a risk score, 64 percent stated the figure almost correctly, whereas 36 percent did not. Most of the 620 women (63 percent) who said they had received a risk score were satisfied with the risk being presented as a numerical value.

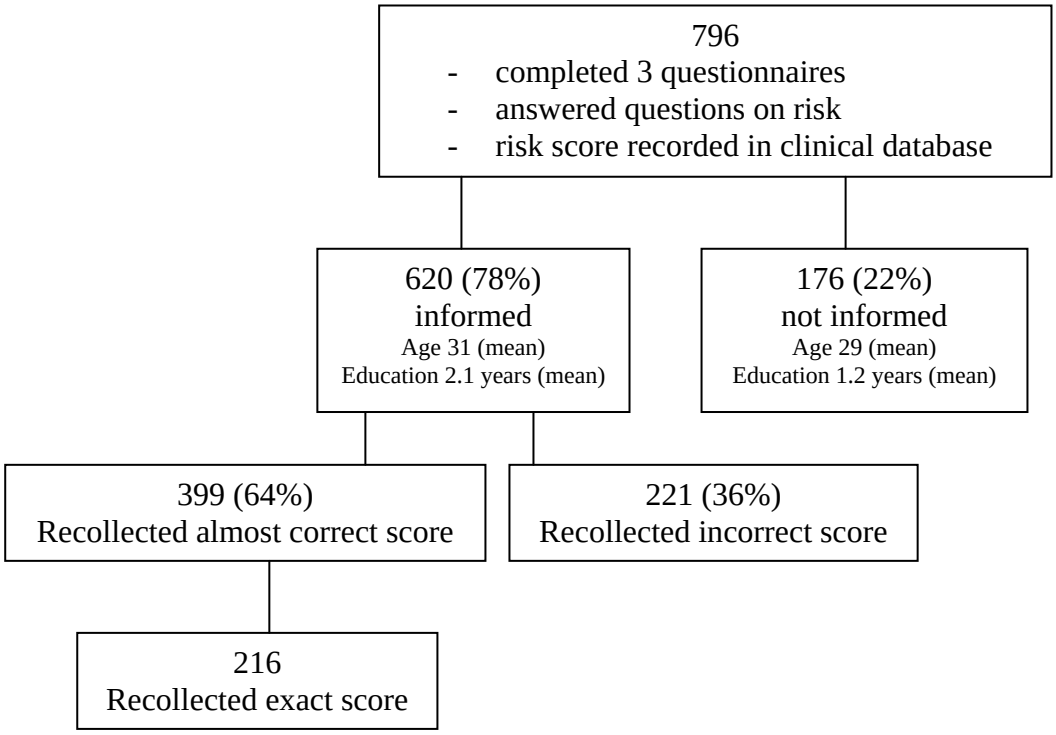

Figure 4. Illustration of women's recollection of the risk score

There was an association between the actual risk score and women's perception of the risk, expressed on a 5-point scale ranging from "very high" to "very low". Women who said their risk was very high had a median risk score of 1:157, while those who said it was very low had a median risk of 1:2706. However, of 26 women whose risk score was 1:250 or higher, only about half said the risk was high (very high + rather high), and out of the 31 women who perceived their risk as very high or rather high, 17 were actually at low risk. These 17 women tended to be younger (<25 years: 18% vs. 7%), more often primiparas (59% vs. 56%), of non-Swedish background (18% vs. 10%), and fewer had had a previous miscarriage (6% vs. 18%). However, none of these differences were statistically significant.

Actual risk and perceived risk in relation to maternal emotional well-being

Figures 5-8 show the proportions of women with depressive symptoms and worry about the baby's health at baseline, in mid-pregnancy and two months after birth, in relation to actual risk (1:250 or higher vs. lower than 1:250) and perceived risk (very + rather high vs. neither high nor low vs. very + rather low). The prevalence of depressive symptoms (Figure 5) and worry about the baby's health (Figure 6) were rather similar in women with a high and low actual risk, respectively. The proportion of women with depressive symptoms was about the same on all three occasions; except for a small non-statistical increase in mid-pregnancy in women with a high risk score (Figure 5). Worry about the baby's health abated almost continuously from baseline to postpartum, and the higher SCWS scores of women with a high risk score for DS were not statistically significant (Figure 6). Figures 7 and 8 show that a larger proportion of the women who perceived the risk as high had depressive symptoms and worried about the baby's health in mid-pregnancy, compared with the other women. However, even this difference was statistically non-significant.

Figures 5-8. Maternal emotional well-being at baseline, in mid-pregnancy and two months postpartum in relation to actual and perceived risk of carrying a fetus with DS

The same pattern was found when analysing the mean EPDS and SCWS scores in the same groups. The ***actual*** risk score was not associated with any worsening of maternal emotional well-being. All measures declined from baseline to postpartum, except for women with a high risk score, where a non-significant increase in mean EPDS scores was found in mid-pregnancy. However, whereas mean EPDS scores declined from baseline to postpartum in women with low perceived risk, this did not happen in women who ***perceived*** their risk to be high. The differences in mean SCWS scores were all statistically significant, with a continuous decline from baseline to postpartum in all women except those who perceived that their risk was high. These women were more worried in mid-pregnancy than at baseline but, as in the other groups, worry had abated after the birth (Table 6).

Table 6. Depressive symptoms and worry about the baby's health at baseline, in mid-pregnancy and two months after birth in relation to women's perception of the risk

Perception of risk	Number of women	Baseline	Mid-pregnancy	Two months postpartum	Paired-samples t-test	*p*
		Depressive symptoms: mean EPDS score				
Very high + Rather high	30	5.2	6.7	5.7	B*/M**	ns
					M/PP***	ns
					B/PP	ns
Neither low nor high	57	6.3	6.5	5.6	B/M	ns
					M/PP	ns
					B/PP	ns
Very low + Rather low	509	5.7	5.3	4.9	B/M	0.03
					M/PP	0.03
					B/PP	< 0.001
		Worry about the baby's health: mean SCWS score				
Very high + Rather high	31	2.7	2.9	1.1	B/M	< 0.001
					M/PP	< 0.001
					B/PP	< 0.001
Neither low nor high	56	3.4	2.9	1.5	B/M	0.003
					M/PP	< 0.001
					B/PP	< 0.001
Very low + Rather low	516	3.1	2.6	1.1	B/M	< 0.001
					M/PP	< 0.001
					B/PP	< 0.001

* = Baseline, ** = Mid-pregnancy, *** = Postpartum

DISCUSSION

The randomised controlled trial included in this thesis showed that fetal screening for Down's syndrome by an ultrasound examination in early pregnancy including measurement of fetal nuchal translucency did not cause more worry about the baby's health in mid-pregnancy or two months postpartum than in women who had a routine scan. However, a qualitative study of a smaller group of women who had a false positive test and were informed that they were at risk of carrying a baby with DS expressed strong feelings of anxiety. The most common coping strategy while waiting for the result of the subsequent chromosome analysis was to reject the pregnancy. Two months after the birth of a healthy baby, the worry about the baby's health had declined or disappeared in most of the women, but one regretted participating in the study and another was still suffering from the experience. Information about fetal risk is complicated and only two third of the women who stated they had received a risk score recalled it correctly. An actual high risk was not associated with worry in mid-pregnancy, but so was a woman's own perception that she was at high risk. More than half of the women who perceived their risk as high were actually at low risk.

Effect of fetal screening for Down's syndrome on maternal anxiety

The hypothesis of the randomised controlled study was that the new screening method could increase maternal worry, specifically about the baby, because of its focus on detecting fetal abnormality, such as DS. Previously, screening for DS was predominantly based on maternal age; which has increased the worry among women of 35 years and above who were routinely offered the option of having an amniocentesis.

The conclusion that the intervention had no effect on maternal worry about the baby's health was supported by the non-statistical difference in one of the items of the SCWS, i.e. worry about something being wrong with the baby. Only women who completed all the three questionnaires were included in the final analysis in Paper II. When the 111 women (EUG n= 57, RUG n = 54) who filled in the two pregnancy questionnaires, but not the postpartum questionnaire, were included in the analysis, the difference between the two groups regarding maternal worry about the baby's health in mid-pregnancy remained statistically non-significant (EUG 30.0%; RUG 28.3%; p=0.44). The conclusion about the intervention having no effect was further supported by the finding that no statistical differences between the trial groups were observed in general anxiety (measured by the STAI), or in depressive symptoms (measured by the EPDS).

Even if the intervention as such did not affect women emotionally, it cannot be excluded that the focus of the trial on something being wrong with the baby did affect women, but equally so in

both groups, since worry about the health of the baby was greater in both groups than in other studies. In the British study, on whose data the power calculation was based (Statham, 1997), only 22 percent of the women reported major worry about the baby's health in gestational week 22, compared with 29 percent in the EUG and 28 percent in the RUG in the current study. A Swedish observational study based on a national sample, using the same scale, found a prevalence of major worry about the baby's health of 25 percent in gestational week 16 (Hildingsson, Rådestad, Rubertsson & Waldenström, 2002).

On the other hand, the larger percentage of worried women in the trial could be explained by a selection of women who were more worried about their baby at baseline. Women were recruited to the trial by two steps. First, the women agreed to participate in the larger medical study, and then some of these women were invited, and agreed, to participate in this study of psychological outcomes. It cannot be excluded that the participants in the medical study were more interested in being reassured that the baby did not have DS than women who declined to participate, and participants in the current study may have had a greater need to express their feelings and concerns. The assumption that women who participated in this trial were more worried than other women is further supported by the analysis of non-responders to the questionnaires. Altogether 335 women did not provide complete data, and this was 17 percent in the EUG and 16 percent in the RUG. These women differed from the responders not only by being older, less educated, more often single multiparas, and non-native Swedes, but also by being more anxious at baseline. A larger percentage expressed major worry about the baby's health, a larger percentage had depressive symptoms, and the average STAI score was higher than that of the responders. If these women had been included in the final sample the percentage of worried women would have been even higher. However, the difference between the trial groups would probably still not have been statistically significant.

Even if women who chose to participate in the trial may have been more worried about their baby's health at baseline, their general emotional well-being seemed to be better than the total population of Swedish new mothers. Compared with data from the previously mentioned study of a Swedish national sample, where 12.3 percent had depressive symptoms (EPDS score > 11) at two months after the birth, the rates of the current trial were lower (8.2% in the EUG and 9.0% in the RUG) (Rubertsson, 2004). This finding can be explained by the fact that even if the antenatal clinics were selected with the aim of representing a socio-economically mixed population, clinics located in more affluent areas were slightly over-represented. Compared with the national birth cohort of 88,208 women, year 2000, the women in the trial were more often married or cohabiting with the expectant father (97.1% vs. 94.6%), slightly older (mean: 30.4 vs. 29.6 years), more often primiparas (54.3% vs. 44.0%) (Swedish National Board of Health and Welfare) and better educated, compared with Swedish females aged 30 years old (college or university: 52% vs. 36%) (Statistics Sweden, 2004). However, the proportion of older women

(≥35 years) in the trial was about the same as in the national birth cohort (17.1% vs. 16.8%). In contrast to previous presentations of figures from the Medical Birth Register in the papers of this thesis, these national figures were from year 2000, which was the year when most of the data of the thesis were collected.

Altogether, the women in the trial constituted a positive selection of the childbearing population concerning social background, and maybe also in terms of general emotional wellbeing. However, they may have been more anxious about their baby's health and more interested in being reassured that nothing was wrong. The findings of the trial can be generalised to this group of women. However, a number of background variables differed between the women in the trial and the women in the national birth cohort. Only one of these, maternal age of 35 years and older, was associated with increased baby worry in mid-pregnancy. the only variable associated with increased baby worry in mid-pregnancy that differed between women in the trial and those in the national birth cohort, was the maternal age of 35 years and older. Since the proportion of these women was the same in the trial as in the national population, the findings of our trial may thus be generalised to the larger population.

The power calculation of the trial was based on the view that a difference between the two groups of 25 percent would be of clinical significance. It could be questioned whether it would not be important to detect even smaller effects, considering that studies have found associations between maternal anxiety during pregnancy and fetal developmental disturbances. Studies have suggested that maternal anxiety during pregnancy may reduce blood circulation in the placenta, and influence the development of the central nervous system (Teixeira, Fisk & Glover, 1999), leading to long-term effects on the child's neurobehavioural development (O'Connor, Heron, Holding & Glover, 2003; Van Den Bergh, Munner, Menne & Glover, 2005). However, detecting small differences require large samples. In order to detect a difference of 1.4 percent in major worry about the baby's health in mid-pregnancy as reported in Paper II, or a difference of 1.7 percent as found when including also the 111 women who completed the second but not the third questionnaire, a sample of more than 29,000 and 20,000 women respectively would have been required.

To my knowledge, this is the first randomised controlled trial of fetal screening for DS, or any other form of fetal screening, which has aimed at studying the psychological effects on the mothers-to-be and new mothers. An Australian trial including 648 women reported less worry about the pregnancy in women randomised to an early ultrasound scan at their first antenatal visit, compared with those who did not have a scan on this occasion, but in this study the aim of the scan was assessment of gestational age (Crowther, Kornman, O'Callaghan, George, Furness & Willson, 1999). A number of studies demonstrated a decrease in maternal anxiety, usually

measured by the STAI, when comparing measures immediately before an ultrasound examination with those obtained after the scan (Baillie, Hewison & Mayson, 1999; Bricker et al., 2000). This difference between the two time points was probably explained by increased anxiety in anticipation of the scan, rather than an expression of a reassuring effect of the ultrasound examination. In the present study, anxiety was not measured in connection with the ultrasound scan, and the reduction in mid-pregnancy cannot be explained as a reassuring effect of the examination. The reason for distributing the second questionnaire in mid-pregnancy was to ascertain a reasonable interval from the time of the fetal test, in order to allow women to adapt to the response of the test. Also, worry during pregnancy has been described as peaking during the first and last trimester, with a decrease in mid-pregnancy (Shereshefsky & Yarrow, 1975; Placek Lederman, 1990; Statham et al., 1997). This pattern was confirmed by the lower rates of worry in mid-pregnancy in both trial groups.

Even if this trial did not show any differences in maternal worry, long-term effects cannot be completely ruled out. The follow-up was scheduled at two months after the birth. A study of women's experience of childbirth showed that some women had become more critical at one year after the birth than they were ten months earlier (Waldenström, 2004). These findings suggest that some traumatic experiences in relation to childbirth may take a long time to work through.

False positive tests

In contrast to the finding of the randomised controlled trial, the qualitative study showed strong reactions of anxiety and great distress among some women, namely those who had a false positive test result and a risk higher than expected considering their age. The most common way of coping with this information was to "withhold" the pregnancy until the result of the subsequent invasive test confirmed normal chromosomes. Withholding the pregnancy must be regarded as a strong reaction. However, two months after birth most women seemed to have overcome the stress experienced during pregnancy, except one woman who said she regretted her participation in the study and another woman who was still suffering from the experience. These findings were not reflected in the randomised controlled trial, probably because the number of women with false positive tests was small. Only 3.3 percent of the women in the EUG (27 women) who completed all questionnaires, and where a risk score was noted, had a false positive test. This percentage was the same as in the NUPP-trial (Saltvedt et al., submitted). Further studies are needed to investigate the prevalence of these reactions in a representative sample of pregnant women and new mothers.

The women's reaction of withholding the pregnancy must have affected their emotional involvement with the fetus during the period when they were waiting for the outcome of the

chromosome analysis. Baillie et al., (2000) reported similar responses in a qualitative study of 24 women who were also waiting for the result of an amniocentesis, which was performed following a similar ultrasound screening for DS as in this study. Also, Rothman Katz (1988) described the same phenomenon in relation to the waiting for the outcome of an amniocentesis, and labelled it "the tentative pregnancy". These descriptions raise the question whether fetal screening as described in these studies may have an adverse effect on maternal fetal attachment (MFA) and bonding to the newborn child. The general research on MFA is limited by methodological and construct problems (Salisbury, Law, LaGasse & Lester, 2003; Shieh, Kravitz & Wang, 2001). In a study of MFA in relation to invasive prenatal tests, the attachment between the pregnant woman and the fetus started as early as the 10^{th} gestational week, increased continuously during pregnancy and intensified when a normal test result was received (Caccia, Johnson, Robinson & Barna, 1991). In the current interview study, the women did not indicate any difficulty in bonding with their baby, but the association between fetal screening and bonding needs further investigation.

Not all women reacted by withholding their pregnancy. Some tried to interpret the situation in a more positive way, for instance by regarding it as a learning experience, or an expression of high quality care, since the baby was well examined. Another way of reasoning was that everything was decreed by fate. People's adaptation to disruptive life events is not a matter of rational calculation but rather actions taken to mobilise resources and to strive for a favourable outcome (Williams, 2000). The women may strive for new ways of understanding their situation and try to create a way to handle it (Becker, 1997). By finding useful coping strategies the situation can be made less stressful and anxiety can be reduced (Brisch et al., 2003).

Most of the women in this study seemed to be satisfied at two months after the birth and would consider undergoing this kind of ultrasound examination in a future pregnancy. However, a few expressed that they regretted participating in the study. This finding is important to follow up in order to explore the prevalence of long-lasting strong reactions in a representative sample.

Information about risk

Paper IV showed that many women had difficulty in recalling their risk score and interpreting it correctly. The most worrying was the finding was that about half of the 31 women who interpreted the risk as very or rather high were in fact at low-risk, especially when considering that a woman's own perception of being at high risk was associated with anxiety and depressive symptoms, but not the actual risk. These findings confirm the complexity and difficulty of giving information about the risk of carrying a fetus with DS. From this study no explanation can be given as to why some women misunderstood the information and interpreted the risk as high when in fact it was low. These responses may be related to aspects of the information, but may

also be related to the woman herself, regardless of how the information was given. Depressive symptoms and worry about the baby's health abated two months postpartum to almost the same levels, regardless of the perception of risk. Even if these findings are reassuring by suggesting no long-term adverse effects of a perceived high risk on maternal emotional health, the duration of the maternal worry and depressive symptoms in mid-pregnancy was unknown.

The midwives performing the ultrasound scans were instructed to provide information about the risk. The finding that women who stated they had not received a risk figure were younger and less educated may be attributed to a lack of interest in knowing, presumably because young age is known to be associated with low risk. They may therefore not have requested the information, or had difficulty in understanding the risk score. Another explanation may be selective behaviour on the part of the midwives, who may have informed women in different ways.

The women interviewed in Paper III expressed a need for more information in order to understand the risk score, a finding that supports the difficulties related to the risk information observed in Paper IV. The complexity of risk interpretation is well documented (Renn, 2004; Slovic, 1987), and risk presented as a percentage may, for instance, be interpreted differently from the same risk being presented as a numerical value of probability (Slovic, 2004). Lay people make their own interpretations of information about threats to their health based on their life experiences (Adelsvärd & Sachs, 1996; Olin Lauritzen & Sachs, 2001; Slovic et al., 2004). An interpretation by some women in our study was that the baby definitely was affected. Interpreting risk in a binary way and not as a relative risk is common (DeSwaan, 1990; Baillie et al., 2000; Green, Statham & Snowdon, 1992).

Interpretation of risk is dependent on maternal age, and this was obvious in Paper III. Women older than 35 years of age were more aware of possible risks and expressed less worry. In an Italian study, 46 women were informed both about the numerical risk, based on a serum screening test, and the baseline risk associated with maternal age. The greater the increase from baseline, the higher the degree of anxiety. Three out of seven women with a negative test (lower than 1:270), but with an increased risk in relation to age, chose to have an amniocentesis (Quagliarini, Betti, Brambati & Nicolini, 1998). In our study, 63 percent said that they were satisfied with receiving the risk information as a numerical value. Mulvey and colleagues (2002) investigated women's preferences regarding how to report DS screening results and concluded that 82 percent of the 115 women preferred to have the risk expressed numerically.

Women in our study often commented on ***how*** the midwife informed them about the risk. Watson et al., (2002) showed that women who were told during the scan that their baby would probably be all right, in spite of the fact that small ultrasound abnormalities were detected, were significantly less anxious about their baby compared with women who had similar fetal findings,

but received no such information. Similarly to our study, others have reported that many women are confused over the results from fetal screening, both in relation to DS screening with ultrasound and NT measurement (French, 2000) and serum screening (Smith, Shaw & Marteau, 1994). Practitioners interviewed about their experiences of fetal screening by NT measurement have also expressed that they find it difficult to know how to inform their patients about the results, and are uncertain whether they should view pregnancy as a normal or a risky condition (Williams et al., 2002). These findings contrast with those of Pilnick, Fraser & James (2004), who found that low-risk women who had undergone fetal screening for DS with NT measurement felt well informed about the test results, probably depending on the emphasis on high quality information in this study.

The participants in the study in paper IV were not representative of all childbearing women in Sweden, as the sample was drawn from the intervention group of a randomised controlled trial of a new method for fetal screening which was only available for women invited to participate in the NUPP-trial. The NUPP-trial was conducted in different parts of Sweden but the sample for the study in paper IV was drawn only from centres in the Stockholm region. When comparing the study sample with all women who gave birth in Sweden in 2000, the year when most data for the study were collected, we found that they were slightly older, more often nulliparas, better educated and that women with a Swedish background were over-represented. Risk information is probably even more problematic in the general childbearing population, where there is a larger proportion of women who do not understand the Swedish language or who may have another attitude to fetal screening.

The issue of risk information is a great challenge for the practitioners. Pregnant women's knowledge and need for information vary to a great extent. The Internet has opened new ways to easily access information, and consumers of today are more aware of their rights. Some women may ask for detailed information and can easily understand a numerical risk score, whether it is presented as a probability or in some other way. Others may need more time and explanation, and some women may even not want to hear about risk. The findings of this thesis indicate that the issue of information needs great attention, and research evaluating different ways of providing information is needed.

The concept "worry"

In studies of women's reactions to prenatal screening and diagnostic tests, the words "worry" and "anxiety" are both used to describe the same phenomenon and usually refer to non-pathological reactions. However, the two concepts may be regarded as separate constructs (Bruhn, 1990, Davey, Hampton, Farrell & Davidson, 1992), describing pathological as well as non-pathological reactions (Tallis, Eysenck & Mathews, et al., 1991; Kelly, 2001). The concept worry has been

described as related to problem-solving and a way of coping with unpleasant situations, whereas anxiety has been referred to as an emotional signal of imminent danger (Bruhn, 1990). Measurements of worry have been performed in the general population (Davey et al., 1992; Joorman & Stöber, 1997; Tallis et al., 1991) but not specifically in the pregnant population (Green, 2003). In this thesis, the two words have been used more or less synonymously

The instruments

The Cambridge Worry Scale – CWS

To my knowledge, the Cambridge Worry Scale is the only instrument developed to measure worry specifically during pregnancy. The scale was developed for use in a large trial to measure worry about the health of the baby (Green et al., 2003). The aim was to develop an instrument measuring both the extent and content of worry in everyday life during pregnancy, as opposed to pathological anxiety. A dialogue with women and researchers formed the 16 items included in the original scale. When the scale was tested in Sweden (Paper I), three new items related to the maternity services were added. These were based on concerns expressed by the women in the study, and they were probably mostly related to the specific situation at the Stockholm area at the time of the study. Two of the maternity units had been closed down in 1996 for financial reasons. After this, the birth rate increased, and two years later there was a shortage of delivery beds. In 1999, approximately 8 percent of the women were referred to another hospital than the hospital of their choice. Since then the maternity services have expanded with new delivery beds, and in 2004 only 1.7 percent of the women at one of the delivery wards in the Stockholm region (Huddinge) were referred to another hospital (S. Wallin, personal communication, February, 2005). These changes have probably resulted in less worry about shortage of delivery beds and associated problems, and this should be considered when using the Swedish version of the scale in the future, or in other places in Sweden. The measurement of psychometric properties of the scale was based on the translated version of the original version even if the internal consistency, Cronbach's alpha, was also satisfactory when the three new items about delivery care were added (0.81 in early pregnancy, 0.83 in mid-pregnancy).

Since the testing of the CWS in the Swedish context, the original producers of the scale have tested it further by factor analysis (Green et al 2003). The following four factors were identified: Factor 1: socio-medical; Factor 2: socio-economic; Factor 3: health; and Factor 4: relations. The item "The possibility of something being wrong with the baby" was included in Factor 3 together with "Worry about own health", "Health of someone close" and "The possibility of miscarriage".

State Trait Anxiety Inventory – STAI

The STAI is commonly used in studies of reactions to prenatal screening. The frequent use of the scale allows comparisons between studies, including different samples. The scale is fairly short and easy to administer, and it is appropriate for self-administration. Green (1990) questioned the STAI instrument for use during pregnancy in a review about reactions to prenatal screening and diagnosis. Several arguments about its weaknesses were stated, such as the scale only catching feelings of anxiety at the time of filling in the scale. It is often administrated immediately before and after an examination, but not during waiting periods. Also, there are no studies investigating whether the scale is independent of the way it is administered, for instance if it is filled in face to face in a hospital setting or in the subject's own home, or if it is sent by post. Green presumed that STAI-values might be lower when the STAI was sent by post because women might choose to fill it in during a calmer moment. Recent reports also suggest that the scale may be unstable during pregnancy, especially around the time of delivery (Hundley, Gurney, Graham & Rennie, 1998). This is confirmed by our results, where the Trait scale, which is supposed to measure general anxiety, was not stable over time.

Edinburgh Postnatal Depression Scale – EPDS

The EPDS was developed for postnatal use, and the Swedish validation of the instrument, two and three months after birth, led to a recommended cut-off at 11/12 (Wickberg & Hwang, 1996). This cut-off was used in this thesis, both antenatally and postnatally in order to allow comparisons. However, the scale has not been validated for antenatal use in Sweden, only in the UK, where the recommended cut-off was 14/15 (Murray & Cox, 1990). The lower cut-off used in this thesis may therefore have overestimated the prevalence of depressive symptoms during pregnancy. The EPDS has been questioned for antenatal use, since it may not discriminate between depressive symptoms and worry that is a natural part of pregnancy. The principal aim of this thesis was, however, not to study depressive symptoms per se, but rather differences between groups, and the limitation of the instrument may therefore not be equally important in this context.

Response rates to instruments

The numbers of internal missing values in the SCWS were low. The STAI and EPDS scales were only analysed if women had completed all items of the scales. In the STAI instrument, the frequency of completed answers was 96.8 percent in the Trait component in the EUG and 97.2 in the RUG, and 95.4 percent and 95.6 percent respectively in the State component. In the EPDS, 99.4 percent in the EUG and 98.7 percent in the RUG completed the scale.

The qualitative study

In order to achieve the aim of the study presented in Paper III, to elucidate women's experiences of receiving a false positive test, an in-depth study of a limited number of women was conducted. The participants in this study were recruited by the midwives at four of the ultrasound units in Stockholm. These midwives did not have any further involvement in the study. The criteria for recruitment were having an increased risk of DS (≥ 1:250) and being fluent in Swedish. When a woman had the diagnosis of DS confirmed, another woman was recruited in order to ascertain at least 20 women in the study with a false positive test. This number was regarded as reasonable to achieve the aim of the study. Exactly how many women declined participation and the reasons why they did so were unknown, but according to the recruiting midwives there was great interest in participating. The participants in the study were mostly Swedish-born (except for three women). Their degrees of worry when included in the study were unknown. However, this was less important considering that the study aimed at exploring patterns of reactions and experiences. In order to answer the question about how common the observed patterns of reactions were, another study with a larger representative sample is required.

In order to minimise possible effects of the interviewers, their role as researchers and not professional caregivers was emphasized. However, given that the interviewers were a midwife and obstetrician it cannot be excluded that this influenced the women's responses, even if neither of them was involved in a woman's care or the conducting of the ultrasound examination. Several steps were taken to create an interview situation that would allow the women to speak freely about their experiences. The interviewers were trained in interview technique and were supervised by an experienced researcher in qualitative methodology. The interviews were mostly carried out in the women's homes. The aim of the interviews was pointed out clearly, and if questions of a medical nature were raised, these were discussed after the interview. Nevertheless, it cannot be excluded that the clinical backgrounds of the interviewers may have affected the woman's understanding of interview situation. Even if the women criticised the health professionals and aspects of the care during the interviews, they might have been more inclined to be critical if interviewed by someone with no connection to the health services. However, the interviewers' impressions were that women were open about their experiences and feelings. On the other hand, it may be an advantage to have clinical knowledge in the research area, in order to be able to recognise the described situations and follow up interesting issues (Kvale, 1996). The women were interviewed several times, under different conditions and over a long period of time. The first interview was performed in an acute situation after recently having received the risk information; the second when all examinations had been carried out; and finally the third after the delivery at some distance from the event and having a healthy newborn baby. This process promoted a deeper relation to the women, and provided an opportunity to follow up themes and in this way obtain in-depth material.

The interviews were audiotaped and transcribed verbatim in order to allow a detailed analysis of the material, independent of the experience of the interviewers in the interview situation. This also allowed the other members of the research group to participate in the process of analysis. The content analysis was performed in three steps (Kvale, 1996; Malterud, 1998) in order to identify major patterns in women's reactions to a false positive test. The first and second steps included repeated reading to form a whole, followed by identifying and describing themes reflecting experiences expressed by each woman. In the third step, when themes were categorised across the cases, the senior researchers analysed parts of the data independently of the interviewers. The interpretations were then discussed among all five authors. Different professional backgrounds, midwifery, medicine and psychology, were represented among the authors. The analyses of the interviews were thus first close to the data, with descriptions of the themes in each case, and then gradually more and more analytical with categorising of patterns over all cases. The main findings were similar to those of a British study (Baillie, 2000), suggesting that the qualitative study captured the most common ways of reacting to a false positive test of fetal screening by ultrasound examination and fetal NT measurement.

GENERAL CONCLUSIONS

The intervention with fetal screening for Down's syndrome by means of an early ultrasound examination including measurement of fetal nuchal translucency did not affect maternal worry about the baby's health, general anxiety or depressive symptoms in mid-pregnancy and two months postpartum. The percentage of women who were worried about the baby's health was higher in both the intervention and the control group compared with data from a national Swedish sample of pregnant women. This finding may be explained by either a selection into the trial of women who were more worried about the baby at baseline, or by the information to all women in the trial which focused on the possibility that something might be wrong with the baby.

A false positive test of fetal screening by ultrasound examination may cause strong reactions of anxiety, and even rejection of the pregnancy, during the period of waiting for a reassuring result of a subsequent chromosome analysis. Most women recover from this experience and are prepared to undergo a similar examination in a future pregnancy. The prevalence of strong reactions and possible long-term effects need further investigation.

Information in relation to fetal screening for DS is problematic. Many women do not remember a given risk score, and some interpret it incorrectly. An actual high risk score was not associated with increased maternal worry about the baby's health or depressive symptoms, whereas a woman's perception of being at high risk had such an association.

The Cambridge Worry Scale could easily be translated into Swedish, and was well understood by Swedish pregnant women. However, three new items had to be added to capture women's worries about the maternity services in the Stockholm region. The SCWS had satisfactory scale properties. The issues causing most worry during pregnancy were "The possibility of something being wrong with the baby", "Giving birth" and "The possibility of miscarriage".

CLINICAL IMPLICATIONS

The findings of this thesis need to be taken into account when making an overall evaluation of fetal screening for Down's syndrome by means of ultrasound screening including measurement of NT. Before introducing this screening method into routine care it is necessary to take into account the different pros and cons obtained from the medical evaluation; current studies on psychological outcomes; financial considerations; and not least, the ethical problems associated with this method, where termination of pregnancy is an option offered to women diagnosed as carrying a fetus with DS.

The findings of the randomised controlled trial suggest that the fetal screening method did not cause increased maternal worry, but the qualitative study showed that a false positive test may cause strong reactions and a break in maternal-fetal attachment. The magnitude of this problem, and its possible long-term effects, needs further investigation in order to make a comprehensive assessment of the method. The issue of false positive tests is important, considering that this is an intervention involving a very large part of the population during an important life event.

This thesis has elucidated the difficulty of understanding and interpreting risk information in association with fetal screening. It is obvious that information in relation to fetal screening needs great attention. The information prior to the scan is important in order to allow an informed choice, and prevent the procedure from being seen as more or less compulsory. The most important factor is the information given to women who are at increased risk. Since women's reactions to information vary, the most important thing may be to allow sufficient time for the woman to ask her own questions, and also for the care provider to check how the woman has understood the information. Furthermore, different forms of information need to be evaluated in randomised controlled trials.

FUTURE RESEARH

Suggestions for topics to be studied in future research:

- The prevalence of strong reactions of anxiety and rejection of the pregnancy in a larger sample of women who have a false positive test;
- Possible long-term effects of false positive tests on maternal emotional well-being;
- Possible effects of maternal anxiety during pregnancy on fetal and infant development;
- Different ways of providing information about fetal screening and risk;
- Ethical aspects of fetal screening for Down's syndrome.

SVENSK SAMMANFATTNING – SWEDISH SUMMARY

Gravida kvinnor i Sverige erbjuds undersökning med ultraljud i graviditetsvecka 15-20 i syfte att fastställa graviditetslängd, diagnostisera flerbörd, lokalisera moderkakan och bedöma fostrets anatomi. Ultraljudteknikens utveckling och ökad kunskap och färdighet hos dem som utför undersökningen har gjort att möjligheterna att diagnostisera fostermissbildningar ökat. Idag erbjuds vanligen screening för Down's syndrom (DS) genom fostervattenprov (amniocentes) till alla kvinnor som är 35 år eller äldre. Med denna metod upptäcks endast ca 20-30 procent av fallen med DS, eftersom de flesta barn föds till mödrar yngre än 35 år. Risken för missfall vid fostervattenprov är 0.5-1 procent.

Samband har visats mellan ökad vätskespalt i fostrets nacke (nackuppklarning, NUPP), synlig i graviditetsvecka 11-14, och kromosomavvikelser samt även andra missbildningar hos fostret. Genom ultraljudsundersökning kan vätskespalten mätas och tillsammans med moderns ålder och graviditetsvecka kan en riskbedömning för att fostret har DS göras. Med denna metod kan möjligen fler foster med DS upptäckas och det totala antalet fostervattenprov minska. Denna metod utvärderas nu i Sverige genom en randomiserad kontrollerad studie, den så kallade NUPP-studien. I denna studie har 39 572 kvinnor deltagit och lottats till antingen tidigt ultraljud med mätning av nackuppklarning eller till dagens rutin. Den nya metoden har starkare fokus mot fosterdiagnostik än dagens rutin och kan tänkas väcka andra tankar och känslor än den hittills gängse undersökningen och detta var bakgrunden till studierna i denna avhandling.

Det övergripande syftet med denna avhandling var att undersöka kvinnors reaktioner och upplevelser av fosterdiagnostik i form av ultraljudsundersökning i tidig graviditet med bedömning av fostrets risk för Down's syndrom genom mätning av nackuppklarning. Effekten på kvinnans oro för barnets hälsa undersöktes liksom reaktioner på falskt positiva test och erfarenheter av information om risk. Dessutom översattes en skala som mäter oro under graviditet, The Cambridge Worry Scale, till svenska och testades på en grupp gravida kvinnor.

Delstudie I: The Cambridge Worry Scale (CWS) är den enda kända skalan som mäter oro specifikt under graviditet och den innehåller 16 tänkbara orsaker till oro. Svaren graderas på en skala från 0 (ingen som helst oro) till 5 (mycket stor oro). Den översattes till svenska och testades på 200 gravida kvinnor som rekryterades i väntrummet vid tre mödravårdscentraler i Stockholm. Frågeformuläret som delades ut innehöll, förutom skalan och frågor om kvinnans bakgrund, en öppen fråga om ytterligare tänkbara källor till oro. Skalan föreföll vara lätt att fylla i och att förstå. Det som oroade kvinnorna mest var risken för missfall, att det skulle vara något fel på barnet och förlossningen. Skalans psykometriska egenskaper bedömdes som goda (Cronbach's alpha 0.81). På den öppna frågan svarade ett flertal kvinnor att de oroade sig för att de inte skulle få plats på

det sjukhus de ville föda på, eller få bristfällig vård på grund av tidsbrist hos personalen. Till följd av detta kompletterades skalan med tre frågor relaterade till förlossningsvården.

Delstudie II: En undergrupp med 2026 kvinnor från den större NUPP-studien deltog i utvärderingen av effekterna av den nya metoden på oro och kvinnans psykiska välbefinnande. Av dessa lottades 1030 kvinnor till interventionsgruppen och 996 till en kontrollgrupp som fick ordinarie vård med rutinmässiga ultraljud. Kvinnorna besvarade enkäter vid tre tillfällen, i tidig graviditet före randomiseringen, i mitten av graviditeten (graviditetsvecka 24) och två månader efter förlossningen. Huvudfrågan för studien var om den tidiga ultraljudsundersökningen påverkade oron för barnets hälsa i mitten av graviditeten, mätt med CWS. I mitten av graviditeten angav 29.2 procent i försöksgruppen och 27,8 procent i kontrollgruppen stark oro för barnets hälsa, en icke statistiskt signifikant skillnad. Inga statistiska skillnader kunde heller påvisas mellan andelen kvinnor som var generellt oroliga (mätt med STAI) eller hade depressiva symptom (mätt med EPDS).

Delstudie III: Tjugofyra kvinnor som fick besked om ökad risk för att fostret hade DS intervjuades vid tre tillfällen, vid samma tidpunkter som enkäterna delades ut i delstudie II. Tjugo hade falskt positiva svar och 16 av dem hade en risk som var högre än den för åldern förväntade. De resterande fyra avbröt graviditeten. Besked om ökad risk gav upphov till starka reaktioner. Kvinnorna var oförberedda på beskedet som av många upplevdes som chockartat. De flesta följde upp ultraljudsundersökningen med ett invasivt prov med kromosomanalys. Väntetiden på beskedet från denna undersökning beskrevs som mycket plågsam, ibland nästan outhärdligt. Många kvinnor sa sig stänga av graviditeten, de tog ”time-out”. När de sedan fick svar att barnet inte hade DS fortsatte de att vara gravida. Två månader efter barnets födelse hade minnet av den jobbiga tiden bleknat. De flesta kunde tänka sig en likadan undersökning vid en kommande graviditet, men två kvinnor var fortfarande påverkade av den negativa upplevelsen.

Delstudie IV: I denna delstudie deltog 796 kvinnor ur interventionsgruppen i delstudie II, som hade en risksiffra noterad i NUPP-studiens databas och som hade svarat på den andra enkätens frågor om riskinformation. 620 kvinnor uppgav att de hade fått en risksiffra, medan 176 uppgav att de inte fått någon. Av de 620 kvinnorna mindes 64 procent siffran nästan korrekt medan 36 procent inte kom ihåg den. Det fanns ett samband mellan den faktiska risken och hur kvinnan själv uppfattade risken. Oro för barnets hälsa och depressiva symtom skiljde sig inte signifikant mellan de kvinnor som hade hög risk (1:250 eller högre) jämfört med dem som hade låg risk. Däremot var fler kvinnor som ***upplevde*** risken som hög oroliga för barnets hälsa i mitten av graviditeten jämfört med dem som uppfattade sig ha en låg risk. Drygt hälften av de kvinnor som upplevde att de hade en hög risk hade i verkligheten låg risk. Två månader efter förlossningen var det inga skillnader i oro mellan kvinnor med hög respektive låg risk.

Slutsatser:

Interventionen med tidigt ultraljud med riskbedömning för Downs syndrom genom mätning av fostrets nackuppklarning påverkade inte moderns oro för barnets hälsa, generell oro eller depressiva symtom i mitten av graviditeten eller två månader efter förlossningen. Falskt positiva svar orsakade däremot starka reaktioner och en period av förnekande av graviditeten i väntan på svar från det invasiva provet. Information i samband med screening för DS är komplicerat. Många kvinnor hade problem att minnas och tolka sin risk. En faktiskt förhöjd risk var inte förenad med högre grad av oro för barnets hälsa eller depressiva symtom men det var däremot uppfattningen av att ha förhöjd risk.

TILLKÄNNAGIVANDEN – AKNOWLEDGEMENTS

Tack alla kvinnor som har besvarat frågeformulären, tack till er som har ställt upp på intervjuer och på detta sätt bidragit till ny kunskap. Tack alla barnmorskor på de mödravårdscentraler och ultraljudsavdelningar som hjälpte till med rekryteringen. Utan er hade inte denna studie varit genomförbar.

Mitt innerliga tack till min huvudhandledare, Ulla Waldenström. Tack för att du gav mig chansen till denna utbildning, och att delta i detta projekt. Du har lärt mig massor. Du har alltid varit tillgänglig för små och stora frågor och din gästfrihet är fantastisk.

Min bihandledare, Charlotta Grunewald, varmt och hjärtligt tack för all uppmuntran, alla vikitga synpunkter, snabba svar på e-mail och din optimism.

Sissel Saltvedt, det har varit jättekul att jobba ihop med dig. Lycka till med din avhandling!

Sonja Olin-Lauritzen på Stockholms Universitet, tack för utmärkt guidning genom den kvalitativa delen av studien.

Tack alla ni andra som arbetar med NUPP-studien, speciellt Harald Almström, Roger Bottinga och Lil Valentin, för att ni intresserat följt detta arbete.

Stefan Eriksson, f d prefekt vid Institutionen för omvårdnad, tack för ditt stöd.

Tack Petter Gustavsson för statistikhjälp och goda råd.

Rebecca Ramsey, jag är så glad för den fina omslagsbilden.

Ann Rudman, tack för ditt engagemang och många goda råd, inte bara om forskning. Jag ser fram emot fortsatt vänskap. Ett speciellt tack och kram till Karin Gottvall för alla kloka ord.

Varmt tack till mina doktorandkollegor och forskare för trevliga luncher, givande seminarier och uppmuntran under doktorandutbildningen: Annica Örtenstrand, Erica Schytt, Helena Fabian, Anette Forss, Catarina Widmark, Anna Christensson, Agneta Wennman-Larsen, Joacim Larsen, Jenny Larsson, Malin Bruce, Ulrika Östlund, Kerstin Nilsson-Kajermo, Johanna Hök, Ulrika Schüldt Håård, Eva Broberger Wiberg, Christina Johnsson, Ethel Ramfeldt, Carina Persson, Ingrid Wännström, Anna Carin Wahlberg, Lars Eriksson, Claes Cederfjäll, Ullaliina Lehtinen, Barbro Gustavsson, Regina Wredling och flera andra.

Hilary Hocking, tack för språkgranskning. Din flexibilitet och service var enastående.

Barbro Karlsson, tack för små pratstunder och det viktiga jobb du gör. Anita Johansson, tack för allt du fixar.

Stort tack alla mina vänner: Elisabeth Välme, Pernilla Danielsson, Therese Fredriksson, Lotta Blomberg, Thomas Casswall, Johanna Ulfvarson och ni andra som jag inte så ofta umgås med men desto oftare tänker på. Tack för er ovärderliga vänskap.

Jag vill alldeles särskilt tacka min mamma, Gunilla, vi vet att vi alltid har varandra, i vått och torrt, och min pappa, Olle, för allt stöd och för att du gav mig min vetgirighet och kunskapstörst. Tack också till min bror Mats, Laila, Ludvig och William, ni betyder mycket för mig. Mina svärföräldrar, Birgit och Jan, tack för att ni har tänkt på mig.

Henrik, tack för din kärlek, ditt tålamod och för allt du har gjort för mig. Äskade fina lilla Mathilda, du ger mig nya perspektiv på livet och obeskrivligt mycket glädje.

Funding for this study has been gratefully received from The Swedish Foundation for Health Care Sciences and Allergy Research (Vårdalstiftelsen) and The Centre for Health Care Sciences, Karolinska Institutet.

REFERENCES

Adelswärd, V. & Sachs, L. (1996). The meaning of 6.8: numeracy and normality in health information talks. *Social Science & Medicine, 43*(8), 1179-87.

Affonso, D., Liu-Chiang, S.Y. & Mayberry, L.J. (1999). Worry: conceptual dimensions and relevance to childbearing women. *Health Care for Women International, 20*, 227-36.

Ayers, S. & Pickering, A.D. (1997). Psychological factors and ultrasound: differences between routine and high-risk scans. *Ultrasound in Obstetrics & Gynecology,* 9, 76-9.

Baillie, C., Hewison, J. & Mayson, G. (1999). Should ultrasound scanning in pregnancy be routine? *Journal of Reproductive and Infant Psychology, 17*, 149-57.

Baillie, C., Smith, J., Hewison, J. & Mason, G. (2000). Ultrasound screening for chromosomal abnormality: women's reactions to false positive results. *British Journal of Health Psychology, 5*, 377-94

Basama, F.M., Leonard, B. & Leighton, M. (2004). Audit: women's perception and knowledge of the 20 weeks anomaly scan. *Journal of Obstetrics and Gynaecology, 24*, 44-6.

Becker, G. (1997). *Disrupted lives. How people create meaning in a chaotic world.* Berkley: University of California Press.

Benn, P.A. (2002). Advances in prenatal screening for Down syndrome: I. General principles and second trimester testing. *Clinica Chimica Acta, 323*(1-2), 1-16.

Bibring, G., Dwyer, T., Huntington, D.S. & Valenstein, A.F. (1961). A study of the psychological processes in pregnancy and of the earliest mother-child relationship: some propositions and comments. *Psychoanalytic Study of the Child, 16*, 9-27.

Bishop, A.J., Marteau, T.M., Armstrong, D., Chitty, L.S., Longworth, L., Buxton, M.J. & Berlin, C. (2004). Women and health care professionals' preferences for Down's syndrome screening tests: a conjoint analysis study. *British Journal of Obstetrics and Gynaecology, 111(*8), 775-9.

Bodegård, G., Fyrö, K. & Larsson, A. (1983). Psychological reactions in 102 families with a newborn who has a falsely positive screening test for congenital hypothyroidism. *Acta Paediatrica, 304*, 1-21.

Bricker, L., Garcia, J., Henderson, J., Mugford, M., Neilson, J., Roberts, T. & Martin, M.A. (2000). Ultrasound screening in pregnancy: a systematic review of the clinical effectiveness, cost-effectiveness and women's views. *Health Technology Assessment, 4*(16), 1-193.

Brisch, K., Munz, D., Bemmerer-Mayer, K., Terinde, R., Kreienberg, R. & Kächele, H. (2003). Coping styles of pregnant women after prenatal ultrasound screening for fetal malformation. *The Journal of Psychosomatic Research, 55*(2), 91-7.

Brookes, M.E. & Alberman, E. (1996). Early mortality and morbidity in children with Down's syndrome diagnosed in two regional health authorities in 1989. *Journal of Medical Screening, 3*(1), 7-11.

Bruhn, J.G. (1990). The two sides of worry. *Southern Medical Journal, 83*(5), 557-62.

Caccia, N., Johnson, J.M., Robinson G.E. & Barna, T. (1991). Impact of prenatal testing on maternal-fetal bonding: chorionic villus sampling versus amniocentesis. ***American Journal of Obstetrics and Gynecology,*** 165, 1122-5.

Canadian Collaborative CVS-Amniocentesis Clinical Trial Group. (1989). Multicentre randomised clinical trial of chorion villus sampling and amniocentesis. First report. ***The Lancet,*** *1*(8628), 1-6.

Carr, J. (1988). Six weeks to twenty-one years old: a longitudinal study of children with Down's syndrome and their families. Third Jack Tizard memorial lecture. ***Journal of Child Psychology and Psychiatry and Allied Disciplines,*** *29*(4), 407-31.

Cederholm, M., Axelsson, O. & Sjöden, P-O. (1999). Women's knowledge, concerns and psychological reactions before undergoing an invasive procedure for prenatal karyotyping. ***Ultrasound in Obstetrics and Gynecology,*** *14*, 267-72.

Cederholm, M., Sjöden, P-O. & Axelsson, O. (2001). Psychological distress before and after prenatal invasive karyotyping. ***Acta Obstetricia et Gynecologica Scandinavica,*** *80*(6), 539-45.

Cox, D.N., Wittman, B.K., Hess, M., Ross, A.G., Lind, J. & Lindahl, S. (1987). The psychological impact of diagnostic ultrasound. ***Journal of Obstetrics and Gynecology,*** *70*(5), 673-6.

Cox, J.L., Holden, J.M. & Sagovsky, R. (1987). Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. ***British Journal of Psychiatry,*** *150*, 782-6.

Crang-Svalenius, E., Dykes, A-K. & Jörgensen, C. (1996a). Women's informed choice of prenatal diagnosis: early ultrasound examination-routine ultrasound examination-age-independent amniocentesis. ***Fetal Diagnosis and Therapy,*** *11*(1), 20-5.

Crang-Svalenius, E., Dykes, A-K. & Jörgensen, C. (1996b). Organized routine ultrasound in the second trimester - one hundred women's experiences. ***Journal of Maternal-Fetal Investigation,*** *6*, 219-22.

Crang-Svalenius, E., Dykes, A-K., & Jörgensen, C. (1998). Factors influencing informed choice of prenatal diagnosis: women's feelings and attitudes. ***Fetal Diagnosis and Therapy,*** *13*(1), 53-61.

Creasy, R. & Resnik, R. (2003). ***Maternal-Fetal Medicine,*** 4th ed. Philadelphia: WB Saunders Company.

Crowther, C.A., Kornman, L., O'Callaghan, S., George, K., Furness, M. & Willson, K. (1999). Is an ultrasound assessment of gestational age at the first antenatal visit of value? A randomised clinical trial. ***British Journal of Obstetrics and Gynaecology,*** *106* (12), 1273-9.

Darbyshire, P., Collins, C., McDonald, H.M. & Hiller, J.E. (2003). Taking antenatal group B Streptococcus seriously: women's experiences of screening and perceptions of risk. ***Birth,*** *30*(2), 116-23.

Darj, E. & Lindmark, G. (2002). Mödravården utnyttjas inte av alla gravida kvinnor. Språksvårigheter och rädsla för undersökningen vanliga orsaker. [Not all women use maternal health services. Language barriers and fear of the examination are common]. In Swedish. ***Läkartidningen,*** *99*(1-2), 41-4.

Davey, G., Hampton, J., Farrell, J. & Davidson, S. (1992). Some characteristics of worrying: evidence for worrying and anxiety as separate constructs. ***Personality and Individual Differences,*** *13*, 133-47.

DeGraaf, I.M., Tijmstra, T., Bleker, O.P. & Van Lith, J.M. (2002). Womens' preference in Down syndrome screening. ***Prenatal Diagnosis,*** *22*(7), 624-9.

Delholm, G. & Olsen, J. (1992). Ethical and psychological aspects of screening. Screening why, when and how. National Board of Health in Denmark.

DeSwaan, A. (1990). ***The management of normality. Critical essays in health and welfare.*** London: Routledge.

Ekelin, M., Crang-Svalenius, E. & Dykes, A-K. (2004). A qualitative study of mothers' and fathers' experiences of routine ultrasound examination in Sweden. ***Midwifery,*** *20*(4), 335-44.

Eurenius, K., Axelsson, O., Gällstedt-Fransson, I. & Sjödén, P-O. (1997). Perception of information, expectations and experiences among women and their partners attending a second-trimester routine ultrasound scan. ***Ultrasound in Obstetrics and Gynecology,*** *9*, 86-90.

Farrant, W. (1985).Who is for Amniocentesis*?* The Politics of Prenatal Screening. In H. Homans (ed.): ***The sexual Politics of Reproduction*** (pp. 96-122). Hants: Gower Publishing Comp Ltd.

French, S. (2000). Perceptions of routine nuchal translucency screening. ***British Journal of Midwifery,*** *8*, 632-8.

Garcia, J., Bricker L., Henderson, J., Martin, M.A., Mugford, M., Nielson, J. & Roberts, T. (2002).Women's views of pregnancy ultrasound: a systematic review. ***Birth,*** *29*(4), 225-50.

Gifford, S.M. (1986).The meaning of lumps: a case study of the ambiguities of risk. In C. R. Janes (ed.): ***Anthropology and Epidemiology: Interdisciplianry Approaches to the study of Health and Disease*** (pp. 213-46). Dordrecht: Riedel Publishing Company.

Goel, V., Glazier, R., Summers, A. & Holzapfel, S. (1998). Psychological outcomes following maternal serum screening: a cohort study. ***Canadian Medical Association Journal,*** *159*, 651-6.

Green, J.M. (1990). ***Calming or harming? A critical review of psychological effects of fetal diagnosis on pregnant women***. London: The Galton Institute Occasional papers.

Green, J.M., Statham, H. & Snowdon, C. (1992). ***Screening for fetal abnormality: attitudes and experiences.*** In Chard (ed.), ***Obsterics in the 1990's*** (pp 65-89). London: MacKeith.

Green, J.M. & Statham, H. (1993). Testing for fetal abnormality in routine antenatal care. (Clinical review). ***Midwifery,*** *9*, 124-35.

Green, J.M. & Staham, H. (1996). *Psychological aspects of prenatal screening and diagnosis*, in M. Marteau & M. Richards (eds.), *The troubled helix: social and psychological implications of the new human genetics* (pp 140-163). Cambridge: University Press.

Green, J.M., Kafetsios, K., Statham, H.E. & Snowdon, C. (2003). Factor structure, validity and reliability of the Cambridge Worry Scale in a pregnant population. *Health Psychology, 8*(6), 753-64.

Green, J.M., Hewison,J., Bekker, H.L., Bryant, L.D. & Cuckle, H.S. (2004). Psychosocial aspects of genetic screening of pregnant women and newborns: a systematic review. *Health Technology Assessment, 8*(33), 1-109.

Grewal, G.K., Moss, H.J., Aitken, D.A., Bjornsson, S., Camerin, A.D. & Pell, J.P. (1997). Factors affecting women's knowledge of antenatal serum screening. *Scottish Medical Journal, 42*(4), 111-3.

Hildingsson, I., Waldenström, U. & Rådestad, I. (2002) Women's expectations on antenatal care as assessed in early pregnancy: number of visits, continuity of caregiver and general content, *Acta Obstericia et Gynecologica Scandinavica, 81*, 188-25

Hildingsson, I., Rådestad, I., Rubertsson, C. & Waldenström, U. (2002). Few women wish to be delivered by caesarean section. *British Journal of Obstetrics and Gynaecology, 109*(6), 618-23.

Hundley, V., Gurney, E., Graham, W. & Rennie, A.M. (1998). Can anxiety in pregnant women be measured using the State-Trait Anxiety Inventory. *Midwifery, 14*(2), 118-21.

Hyde, B. (1986). An interview study of pregnant women's attitudes to ultrasound scanning. *Social Science & Medicine, 22*(5), 587-92.

Joormann J. & Stöber, J. (1997). Measuring facets of worry: A LISREL analysis of the worry domains questionnaire. *Personality and Individual differences, 23*, 827-37.

Kaiser, A.S., Ferris, L.E., Katz, R., Pastuszak, A., Llewellyn-Thomas, H., Johnson, J.A. & Shaw B.F. (2004). Psychological responses to prenatal NTS counseling and the uptake of invasive testing in women of advanced maternal age. *Patient Education and Counseling, 54*(1), 45-53.

Kelly, W.E. (2002). Some evidence for nonpathological and pathological worry as separate constructs: an investigation of worry and boredom. *Personality and Individual Differences, 33*, 345-54.

Kornman, L., Wortelboer, M.J., Beekhuis, J.R., Morssink, L.P. & Mantingh, A. (1997). Women's opinions and the implications of first- versus second-trimester screening for fetal Down's syndrome. *Prenatal Diagnosis, 17*(11): 1011-8.

Kowalcek, I., Mühlhoff, A., Bachmann, S. & Gembruch, U. (2002). Depressive reactions and stress related to prenatal medicine procedures. *Ultrasound in Obstetrics and Gynecology, 19*, 18-23.

Kvale, S. (1996). *Interviews: an introduction to qualitative research interviewing*. California: SAGE publications.

Ladfors, L., Eriksson, M., Mattsson, L-Å., Kylebäck, K., Magnusson, L. & Milsom, I. (2002). A population based study of Swedish women's opinions about antenatal, delivery and postpartum care. *Acta Obstetricia et Gynecologica Scandinavica, 80*(2), 30-6.

Larsen, T., Nguyen, T.H., Munk, M., Svendsen, L. & Teisner, L. (2000). Ultrasound screening in The 2nd trimester. The pregnant woman's background, knowledge, expectations, experiences and acceptances. *Ultrasound in Obstetrics and Gynecology, 15*, 383-6.

Light, K. & Fenster C. (1974). Maternal concerns during pregnancy. *American Journal of Obstetrics and Gynecology, 118*, 46-50.

Lobb, E.A., Butow, P.N., Kenny, D.T. & Tattersall, M.H. (1999). Communicating prognosis in early breast cancer: do women understand the language used? *Medical Journal of Australia, 171*(6), 290-4.

Lowe, S.W., Pruitt, R.H., Smart, P.T. & Dooley, R.L. (1998). Routine use of ultrasound during pregnancy. *The Nurse Practitioner, 23*(10), 60, 63-6, 71.

Malterud, K. (1998). *Kvalitativa metoder i medicinsk forskning.* (In Swedish). Lund: Studentlitteratur.

Mant, D. & Fowler, G. (1990). Mass screening: theory and ethics. *British Medical Journal, 300*(6729), 916-8.

Marteau, T.M., Johnston, M., Shaw, R.W., Michie, S., Kidd, J. & New, M. (1989). The impact of prenatal screening and diagnostic testing upon the cognitions, emotions and behaviour of pregnant women. *The Journal of Psychosomatic Research, 33*(1), 7-16.

Marteau, T. M., Cook, R., Kidd, J., Michie, S., Johnston, M., Slack, J. & Shaw, R. (1992). The psychological effects of false-positive results in prenatal screening for fetal abnormality: a prospective study. *Prenatal Diagnosis,12*, 205-214.

Marteau, T. (1995). Towards informed decisions about prenatal testing: a review. *Prenatal Diagnosis, 15,* 1215-26.

Merkatz, I.R., Nitowsky, H.M., Macri, J.N. & Johnson, W.E. (1984). An association between low maternal serum alpha-fetoprotein and fetal chromosomal abnormalities. *American Journal of Obstetrics and Gynecology, 148*(7), 886-94.

Michelacci, L., Fava, G.A., Grandi, S., Bovicelli, L., Orlandi, C. & Trombini, G. (1988). psychological reactions to ultrasound. *Psychoterapy Psychosomatic, 50*, 1-4.

Mulvey, S., Pham, T., Tyzack, K. & Wallace, E.M. (2002). Women's preferences for reporting of Down syndrome screening results. *Australian and New Zealand Journal of Obstetrics and Gynaecology, 42*(5), 504-7.

Murray, D. & Cox, J.L. (1990). Screening for depression during pregnancy with the Edinburgh Depression Scale (EPDS). *Journal of Reproductive and Infant Psychology, 8*, 99-107.

Nicolaides, K.H., Brizot, M.L. & Snijders, R.J. (1994). Fetal nuchal translucency: ultrasound screening for fetal trisomy in the first trimester of pregnancy. *British Journal of Obstetrics and Gynaecology, 101*(9), 782-6.

Nicolaides, K.H., Heath, V. & Cicero, S. (2002). Increased fetal nuchal translucency at 11-14¨ weeks. *Prenatal Diagnosis, 22*(4), 308-15.

Nielsen, S. & Lang, R.S. (1999). Principles of screening. In R. Lang & J.H. Isaacson (eds.), *Screening* (p. 1323-1337). Ohio: Medical Clinics of North America.

O'Connor, T., Heron, J., Golding, J. & Glover, V. (2003). Maternal antenatal anxiety and behavioural/emotional problems in children: a test of a programming hypothesis. *Journal of Child Psychology and Psychiatry and allied disciplines, 44*(7), 1025-36.

Olin Lauritzen, S. & Sachs L. (2001). Normality, risk and the future: implicit communication of threat in health surveillance. *Sociology of Health and Illness, 23*, 497-516.

Pilnick, A.M., Fraser, D.M. & James, D.K. (2004). Presenting and discussing nuchal translucency screening for fetal abnormality in the UK. *Midwifery, 20(*1), 82-93.

Placzek Lederman, R. (1990). Anxiety and stress in pregnancy: significance and nursing assessment. *NAACOG's Clinical Issue Perinatal Women's Health Nursing, 1*(3), 279-88.

Polit, D. & Beck C.T. (2004). *Nursing research Principles and methods*. 7th ed. Philadephia: Lippincott Wiliams & Wilkins.

Porter, M. & MacIntyre, S. (1984). What is must be best: a research note on conservative or deferential responses to antenatal care provision. *Social Science & Medicine, 19*(11), 197-200.

Posner, T. (1993). Ethical issues and the individual woman in cancer sreening prgrammes. *Journal of Advances in Health and Nursing Cares, 2*, 55-69.

Quagliarini, D., Betti, S., Brambati, B. & Nicolini, U. (1998). Coping with serum screening for Down syndrome when the results is given as a numeric value. *Prenatal Diagnosis, 18*(8), 816-21.

Raphael-Leff, J. (1992). *Psychological processes of childbearing.* London: Chapman & Hall.

Rapp, R. (1988). Chromosomes and communication: the discourse of genetic counselling. *Medical Anthropology Quarterly, 2*, 143-57.

Renn, O. (2004). Perception of risk. *Toxocology Letters*, 149, 405-13.

Rothman Katz, B. (1988). *The tentative pregnancy. Prenatal Diagnosis and the Future of Motherhood.* Vol. 2. London: Pandora Press.

Rubertsson, C. (2004). *Depression and partner violence before and after childbirth*, Doctoral thesis. Stockholm: Karolinska Institutet.

Salisbury, A., Law, K., LaGasse, L. & Lester, B. (2003). Maternal-fetal attachment. *The Journal of the American Medical Association,* 289(13), 1701.

Saltvedt, S., Almström, H., Kublickas, M., Valentin, L., Bottinga, R., Bui, T.H. et al. Comparison of two methods of counselling women with regard to their risk of carrying a fetus with Down´s syndrome: a randomized controlled trial in 39,572 pregnancies. *Submitted.*

Sandelowski, M. (1994). Channel of desire: fetal ultrasonography in two use-contexts. *Qualitative Health Research, 4*, 262-80.

Santalahti, P., Latikka, A-M., Ryynänen, M. & Hemminki, E. (1996). Women's experiences of prenatal serum screening. ***Birth,*** *23*(2), 101-7.

Santalahti, P., Aro, A.R., Hemminki, E., Helenius, H. & Ryynänen, M. (1998). On what grounds do women participate in prenatal screening? ***Prenatal Diagnosis,*** *18*, 153-65.

Searle, J. (1996). Fearing the worst- why do pregnant women feel 'at risk'? ***Australian and New Zealand Journal of Obstetrics and Gynaecology,*** *36*(3), 279-86.

Shereshefsky, P. & Yarrow, L. (1975). ***Psychological aspects of a first pregnancy and early postnatal adaptation.*** New York: Raven Press.

Shie, C., Kravitz, M. & Wang, H-H. (2001). What do we know about maternal-fetal attachment? ***The Kaohsiung Journal of Medical Sciences,*** *17*, 448-54.

Slovic, P. (1987). Perception of risk. ***Science,*** *236*(4799), 280-5.

Slovic, P. (1997). Trust, emotion, sex, politics and science. Surveying the battlefield. In M.H. Bazerman, D.K. Messick, A.E. Tenbrunsel & K.A.Wade-Benzoni (eds.): ***Environment, ethichs and behaviour*** (pp. 277-313). San Fransisco; The New Lexington Press.

Slovic, P., Finucane, M.L., Peters, E. & MacGregor, D.G. (2004). Risk as analysis and risk as feelings: some thoughts about affect, reason, risk, and rationality. ***Risk Analysis,*** *24*(2), 311-22.

Smedler, A. & Bremme, K. (1992). Screeningundersökta gravida måste få hjälp att bearbeta oroande besked. [Pregnant women participating in screening must be helped with anxiety generated by alarming information]. In Swedish. ***Läkartidningen,*** *59*, 652-3.

Smith, D.K., Shaw, R.W. & Marteau, T.M. (1994). Informed consent to undergo serum screening for Down's syndrome: the gap between policy and practice. ***British Medical Journal,*** *309*(6957), 776.

Snijders, R.J., Sundberg, K., Holzgreve, W., Henry, G. & Nicolaides, K.H. (1999). Maternal age- and gestation-specific risk for trisomy 21. ***Ultrasound in Obstetrics and Gynecology,*** *13*(3), 167-70.

Snijders, R.J. & Smith, E. (2002). The role of fetal nuchal translucency in prenatal screening. ***Current Opinion in Obstetrics & Gynecology,*** *14*(6), 577-85.

Sommerseth, E. (1993). Gravides erfaringer med informasjonsrutinene ved rutinmessige ultralydsundersøkelser [Experiences of pregnant women with information procedures in routine ultrasound examinations]. In Norwegian. ***Tidsskrift Norsk Laegeforening,*** *113*(10), 1218-20.

Spielberger, B., Gorush, R.L. & Lushene, R. (1970). ***Manual for the State-Trait Anxiety Inventory (STAI).*** Palo Alto California: Consulting Psychologists' press.

Statham, H., Green J. & Snowdon, C. (1993). ***Psychological and social aspects of screening for fetal abnormality during routine antenatal care,*** in A. Thomson, S. Robinson & V. Tickner (eds.): ***Proceedings of the 1992 Research and the Midwife Conference.*** (pp 44-62). Manchester: School of Nursing, University of Manchester.

Statham, H., Green, J.M. & Kafetsios, K. (1997). Who worries that something might be wrong with the baby? A prospective study of 1072 pregnant women. ***Birth,*** *24*(4), 223-33.

Statistics Sweden (2004). Statistiska Centralbyrån. ***Befolkningsstatistik. Befolkningens utbildning.*** Internet-publication. (In Swedish). http://www.scb.se.

Swedish Council on Technology Assessment in Health Care. (1998). ***Rutinmässig ultraljudsundersökning under graviditet*** [Routine ultrasound screening during pregnancy] (SBU-rapport nr 139). In Swedish. Stockholm: SB Offset AB.

Swedish Council on Technology Assessment in Health Care. (2004). ***QF-PCR för bestämning av kromosomavvikelser hos foster.*** [QF-PCR in fetal diagnosis of chromosomal abnormalities] (Alert-report). http://www.sbu.se

Swedish National Board of Health and Welfare. (1996). ***Hälsovård före, under och efter graviditet,*** *1996:7.* (In Swedish). Stockholm: Socialstyrelsen.

Swedish National Board of Health and Welfare. (1997). Socialstyrelsens författningssamling, *SOSFS 1997:20.* (In Swedish). Stockholm: Socialstyrelsen

Swedish National Board of Health and Welfare. (2002). Fakta om mammor, förlossningar och nyfödda barn. Medicinska födelseregistret 1973-2000. Stockholm: Socialstyrelsen.

Swedish National Board of Health and Welfare (2004). Statistics Health and diseases, 2004:3. ***Medical birth Registration in 2002.*** Internet-publication. http://www.sos.se. Stockholm: Centre for Epidemiology.

Tabor, A., Philip, J., Madsen, M., Bang, J., Obel, E.B. & Norgaard-Pedersen, B. (1986). Randomised controlled trial of genetic amniocentesis in 4606 low-risk women. ***The Lancet,*** *1*(8493), 1287-93.

Tallis, F., Eysenck, M. & Mathews A. (1991). Elevated evidence requirements and worry. ***Personality and Individual Differences,*** *12*, 21-7.

Teixeira, J.M., Fisk, N.M. & Glover, V. (1999). Association between maternal anxiety in pregnancy and increased uterine artery resistance index: cohort based study. ***British Medical Journal,*** *318* (7177), 153-7.

Thorpe, K., Harker, L., Pike, A. & Marlow, N. (1993). Women's views of ultrasonography. A comparison of women's experiences of antenatal ultrasound screening with cerebral ultrasound of their newborn infant. ***Social Science & Medicine,*** *36*(3), 311-5.

Tymstra, T. (1991). Prenatal diagnosis, prenatal screening and the rise of the tentative pregnancy. ***International Journal of Technology Assessment in Health Care.*** *7*(4), 509-16.

Van Den Bergh, B.R.H., Mulder, E.J.H., Mennes, M. & Glover, V. (2005). Antenatal maternal anxiety and stress and the neurobahvioural development of the fetus and child: links and possible mechanisms. A review. ***Neuroscience and Biobehavioral Reviews.*** In press.

Villeneuve, C., Laroche, C., Lippman, A. & Marrache, M. (1988). Psychological aspects of ultrasound imaging during pregnancy. ***Canadian Journal of Psychiatry,*** *33*(6), 530-6.

Wald, N.J., Rodeck, C., Hackshaw, A.K., Walters, J., Chitty, L. & Mackinson, A.M. (2003). First and second trimester antenatal screening for Down's syndrome: the results of the Serum, Urine and Ultrasound Screening Study (SURUSS). *Journal of Medical Screening, 10*(2), 56-104.

Waldenström, U. (2004). Why do some women change their opinion about childbirth over time? *Birth, 31*(2), 102-7.

Watson, M.S., Hall, S., Langford, K. & Marteau, T.M. (2002). Psychological impact of the detection of soft markers on routine ultrasound scanning: a pilot study investigating the modifying role of information. *Prenatal Diagnosis, 22*(7), 569-75.

Weinans, M.J.N., Kooij, L., Müller, M.A., Bilardo, K.M., Van Lith, J. & Tymstra T. (2004). A comparison of the impact of screen-positive results obtained from ultrasound and biochemical screening for Down syndrome in the first trimester: a pilot study. *Prenatal Diagnosis, 24*(5), 347-51.

Whynes, D. (2002). Receipt of information and women's attitudes towards ultrasound scanning during pregnancy. *Ultrasound in Obstetrics and Gynecology, 19*, 7-12.

Wickberg, B. & Hwang, C. P. (1996). The Edinburgh Postnatal Depression Scale: validation on a Swedish community sample. *Acta Psychiatrica Scandinavica, 94*(3), 181-4.

Williams, C., Alderson, P. & Farsides, B. (2002). Dilemmas encountered by health practitioners offering nuchal translucency screening: a qualitative case study. *Prenatal Diagnosis, 22*(3), 216-20.

Williams, S. (2000). Chronic illness as biographical disruption or biographical disruption as chronic illness? Reflections on a core concept. *Sociology of Health and Illness, 22*, 40-67.

Wilson J.M.G. & Jungner, G. (1968). *Principles and practice of screening for disease,* Public Health Papers 34. Geneva: World Health Organization:

Zlotogorski, Z., Tadmor, O., Duniec, E., Rabinowitz, R. & Diamant, Y. (1995). Anxiety levels of pregnant women during ultrasound examination: coping styles, amount of feedback and learned resourcefulness. *Ultrasound in Obstetrics and Gynecology, 6*, 425-9.