Psychological consequences of prenatal screening

JH Kleinveld
The study presented in this thesis was performed at the Department of Public and Occupational Health within the EMGO Institute of the VU University Medical Center in Amsterdam (www.emgo.nl). The EMGO Institute participates in the Netherlands School of Primary Care Research (CaRe) which was re-acknowledged in 2005 by the Royal Netherlands Academy of Arts and Sciences (KNAW) for a second period of five years.

The study was part of a research project on risk perception, decision making, and psychological well-being of pregnant women who are offered prenatal screening for congenital defects. This project was funded by a grant of the Netherlands Organisation for Health Research and Development (ZonMw). Financial support for the printing of this thesis has been kindly provided by the EMGO Institute and the VU University, Amsterdam, the Netherlands, and by the J.E. Jurriaanse Stichting, Rotterdam.

For reasons of consistency within this thesis, some terms have been standardised throughout the text. As a consequence the text may differ in this respect from the articles that have been published.

ISBN: 978 90 8659 154 8

Design & typography: Digit@l Xpression, Bennekom, the Netherlands
Cover photo: J.H. Kleinveld
Cover design: Ponsen & Looijen B.V., Wageningen, the Netherlands
Printed by: Ponsen & Looijen B.V., Wageningen, the Netherlands

© J.H. Kleinveld, 2008
All rights reserved. No part of this thesis may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, without permission of the author.
Psychological consequences of prenatal screening

ACADEMISCH PROEFSCHRIFT

ter verkrijging van de graad Doctor aan
de Vrije Universiteit Amsterdam,
op gezag van de rector magnificus
prof.dr. L.M. Bouter,
in het openbaar te verdedigen
ten overstaan van de promotiecommissie
van de faculteit der Geneeskunde
op dinsdag 2 december 2008 om 10.45 uur
in de aula van de universiteit,
De Boelelaan 1105

doors

Johanna Hendrika Kleinveld

geboren te Hooglanderveen
promotoren: prof.dr. D.R.M. Timmermans
prof.dr. G. van der Wal
prof.dr. L.P. ten Kate
CONTENTS

1. General introduction 7

2. Does prenatal screening influence anxiety levels of pregnant women? 31

3. Prenatal screening for Down syndrome: Pregnant women's perceived risk and emotional well-being 47

4. Does offering and performing prenatal screening influence women’s attachment to their unborn child? 61

5. Does informed decision making influence psychological outcomes after receiving a positive screening outcome? 75

6. Does offering prenatal screening influence pregnant women's attitudes regarding prenatal testing? 83

7. The decision for or against prenatal screening in relation to pregnant women's values 97

8. General discussion 109

Summary 127

Samenvatting 135

List of publications 145

Dankwoord 147
1

General introduction
CONTENTS OF GENERAL INTRODUCTION

1. Preface 9
2. Prevalent congenital abnormalities 9
   2.1 Down syndrome 9
   2.2 Neural tube defects 10
3. Prenatal tests 11
   3.1 Diagnostic tests 11
     3.1.1 Amniocentesis 11
     3.1.2 Chorionic villus sampling 12
   3.2 Screening tests 12
     3.2.1 Maternal serum screening test 12
     3.2.2 Nuchal translucency measurement 13
     3.2.3 Combined test 13
     3.2.4 Standard anomaly scan 13
   3.3 Numbers of prenatal testing 13
4. Prenatal screening policy in the Netherlands 14
5. Psychological consequences of prenatal screening 16
   5.1 Anxiety 16
   5.2 Positive and negative emotions 17
   5.3 Attachment 18
6. Informed decision making 19
   6.1 Psychological consequences of informed decision making 19
   6.2 Attitudes towards prenatal testing 19
   6.3 Pregnant women’s preferences in pregnancy outcomes 20
7. Research questions 20
8. Research project 21
   8.1 Setting 21
   8.2 Design 21
   8.3 Participants 22
   8.4 Randomisation 22
   8.5 Intervention 22
   8.6 Questionnaires 22
9. Outline of the thesis 24
10. References 25
1. PREFACE

Ask a pregnant woman if she hopes for a boy or a girl and the chances are that she will answer: ‘I don’t care, as long as it’s healthy’. Unfortunately, the wish for a healthy child does not always materialise. Depending on the abnormality, this may seriously disturb the ideal image of the life parents had in mind for their child, and a process of mourning will be needed for them to accept the new image. In cases of severe physical defects and/or mental impairment, it may be necessary for the parents to care for their child for the rest of their lives. Even if their child is initially able to live at home with them, at some point in the future others may have to take responsibility for their child’s care.

In the past, parents had to wait till their child was born to know more about its condition. Over the last four decades however, several tests have become available to find out during the pregnancy whether or not the unborn child has a particular abnormality or an increased risk of having one. Although these tests were initially offered to women who were already at an increased risk, these tests are now being offered in more and more European countries to all pregnant women [1]. Offering these tests implies that women are confronted with the possibility that something may be ‘wrong’ with their unborn child. They have to decide whether or not they want to know more about its health, and ask themselves what they would do if the test result turns out to be abnormal. This raises the question of how the offer of prenatal tests influences a woman’s pregnancy experience. Does it make women anxious and worried? Or does it give them reassurance because they get to know more about the health of their child?

In this introduction section, we will first provide more background information about some common congenital abnormalities that can be tested for during pregnancy. Next, we will describe specific prenatal tests and then we will outline the history of prenatal screening in the Netherlands. Finally, we will review the literature on psychological aspects of prenatal screening, introduce the topics of the present thesis, and explain the methods that we used for conducting our research.

2. PREVALENT CONGENITAL ABNORMALITIES

Two prevalent congenital abnormalities that can be tested for during pregnancy are Down syndrome and neural tube defects.

2.1 Down syndrome

Down syndrome (DS) derives its name from dr. Langdon Down, who described it in 1866 [2]. In 95% of cases it is caused by a full trisomy 21, in 4% of cases by a translocation involving chromosome 21, and in 1% there is mosaicism of trisomy 21 (in which case the person is often less severely affected than in the full syndrome) [3].
Chapter 1

People with DS tend to develop at a slower rate, both physically and mentally. Yet, this development differs from person to person, as does the severity of the health problems [4]. People with DS are more likely to have problems that affect the breathing and respiratory functions, hearing, vision, speech, motor abilities, and immunity against infections. They are also at an increased risk for developing leukaemia and Alzheimer’s disease. In the absence of a severe cardiac anomaly, which leads to early death in 15-20% of cases, average life expectancy is 50-60 years [3]. People with DS show a broad range of intellectual ability with IQ scores ranging from 20 to 80 [3]. About 70 to 85% of adults with DS have a cognitive level that can be compared with that of children aged from 4 to 12 years old. The remainder have a cognitive level that is lower than that of a 4-year-old. Because of their mental handicap, almost all people with DS need care and supervision from others throughout the course of their lives. Approximately half of the children with DS start their education at a normal primary school, while the other half go straight into special education. After primary school, most transfer to special secondary education. Some can follow a simple vocational training, but most of the time they can only find a job as a volunteer. Some of the people with a mild mental disability can live independently, but under supervision. Most adults with DS live in sheltered accommodation [4].

Since approximately 1930 it has been known that having a child with DS is related to the age of the mother [5]. A 20-year-old woman has a chance of 1 in 1500, a 30-year-old a chance of 1 in 900, a 36-year-old a chance of 1 in 300, and a 44-year-old a chance of 1 in 40 [2]. Even though women over 35 years are at higher risk, more than half of the pregnancies involving DS are those of women under 36 years of age, because this group is larger [6].

2.2 Neural tube defects

The neural tube is a tube-like structure at the back of the embryo from which the spinal cord and brain develop. The term ‘neural tube defects’ (NTDs) refers to defective closure of the developing neural tube during the first month of embryonic life [2]. Common examples of NTDs are spina bifida and anencephaly. Spina bifida refers to a defect at the lower part of the neural tube, which can lead to a range of abnormalities that differ in severity. Children with spina bifida are generally physically disabled and sometimes also mentally. Their prognosis is determined by the nature, extent and location of the defect. Problems with walking are prevalent, although they vary from mild problems to such serious paralysis that a wheelchair is needed [7]. Other common problems concern bowel and bladder incontinence, and partial or complete loss of sensitivity in the lower half of the body. Although people with spina bifida can have a serious physical disability, they are able to live reasonably independent lives. However, social and emotional problems do occur regularly [7].

Anencephaly is the term used for defective closure of the neural tube at the location where the brains develop. It results in an absence of most of the skull and brains, and is therefore not compatible with life; infants die within a few hours of birth [2].
Most cases of NTDs have a multifactorial causation, meaning that many genetic factors as well as environmental factors (eating pattern, medication) play a role [8,9]. Maternal age has no influence. Folate deficiency during early pregnancy is a contributory factor for the failure of normal fusion of the foetal neural tube. Extra intake of folic acid (the synthetic form of folate) by women in the period around conception can prevent NTD in many cases [10]. Therefore in the Netherlands, as in various other countries, women are advised to take supplements as soon as they want to become pregnant [11-13]. Recently, the Dutch Health Council advised the Government to expand the informational activities for folic acid intake for women who wish to become pregnant, and to introduce a national program of preconception care [14]. In addition, it suggested enriching certain staple food products, like bread, with folic acid.

The birth prevalence of children with a neural tube defect differs strongly geographically and across time [15,16]. An estimate of the total mean prevalence in the Netherlands in the period of 2000–2004 was 6.6 per 10,000 live births and stillborns [14].

3. PREGNATAL TESTS

Prenatal tests in general, as well as tests for DS and neural tube defects, can be divided into prenatal diagnostic tests and prenatal screening tests. In virtually all cases, the diagnostic tests provide certainty about whether or not the foetus has the abnormality that it is being tested for, whereas screening tests may only give an estimation of the chance that the foetus has the abnormality. As these latter tests do not provide certainty about the presence or absence of a specific abnormality their outcomes are sometimes false-positive (i.e. an outcome that classifies the woman as being at high risk whereas her foetus does not have the disorder) or false-negative (i.e. an outcome that classifies the woman as being at no increased risk but whose foetus has the disorder). If prenatal screening tests indicate an increased risk, women are offered a prenatal diagnostic test to gain certainty.

3.1 Diagnostic tests

Commonly used prenatal diagnostic tests are the examination of foetal chromosomes or assessment of levels of alpha-fetoprotein in amniotic fluid, and the examination of foetal chromosomes in chorionic villi. The methods with which these samples can be obtained are called amniocentesis and chorionic villus sampling, respectively. In everyday use, at least in the Netherlands, these latter names are often used to refer to the diagnostic testing procedure.

3.1.1 Amniocentesis

In 1968 amniocentesis was used for the first time to diagnose DS prenatally [17]. This diagnostic test involves the aspiration of 10-20 ml of amniotic fluid through the abdominal wall under ultrasound guidance [2]. The earliest it can be performed is from a pregnancy duration of 15 weeks. The woman (and her partner) have to wait two to three weeks to receive the test outcome; by then sufficient cells have grown for chromosome analyses.
Chapter 1

In the beginning of the 1970s, it was discovered that an increased amount of the protein alpha-fetoprotein (AFP) in the amniotic fluid indicates the presence of a neural tube defect of the foetus [18]. Since then, amniocentesis is also offered for diagnosis of neural tube defects to pregnant women who have an indication for it. Because it is an invasive test, amniocentesis has a procedure-related risk of miscarriage of about 0.3% [19]. If the test result is abnormal parents can choose whether or not they wish to terminate the pregnancy. Termination occurs through the induction of labour.

3.1.2 Chorionic villus sampling

Chorionic villus sampling (CVS) has been performed since the 1980s [20]. This test involves transcervical or transabdominal aspiration of chorionic villi, which are foetal in origin [2]. CVS can be performed from the 10th week till, preferably, the 14th week of pregnancy. Depending on whether short-term or long-term cultures, or both, are used, women have to wait seven days to two weeks for the test outcome. The risk of a procedure-related miscarriage is about 0.5% [19]. If the result is abnormal, parents can choose whether or not they wish to terminate the pregnancy, which is done through curettage.

3.2 Screening tests

Over time, several screening tests have been developed. We will restrict ourselves here to the tests that were used in the study on which this thesis is based (maternal serum screening, nuchal translucency measurement) and those that are presently used in the prenatal screening policy of the Netherlands (combined test, standard anomaly scan)

3.2.1 Maternal serum screening test

In 1972 it was recognized that many pregnancies in which the baby had an open neural tube could be detected at 16 weeks gestation by the assaying of a protein in maternal serum; alpha-fetoprotein (AFP). If the foetus has an open NTD, the level of AFP is elevated in both the amniotic fluid and maternal serum as a result of leakage from the open defect [2]. Since the end of the 1970s, maternal serum screening for AFP has been introduced in various countries. In 1984 it emerged that the AFP concentration in maternal serum is also a suitable indicator for the risk of DS. Since that time, programmes have been offered in various countries that consist of combined screening for DS and NTD by means of a triple test [21]. The triple test consists of three markers: AFP, unconjugated oestradiol (uE3), and human chorionic gonadotrophin (hCG). Low AFP, low uE3, and high hCG are indicative of chromosomal abnormalities. High AFP indicates neural tube defects [3]. Combining this measure with other data like maternal age and pregnancy duration leads to an estimation of the chance that the foetus has DS or an NTD. After approximately a week, the test result is known.

The triple test is best performed between the 15th and 19th week of pregnancy (or from 14 weeks if screening is for DS only). If the test shows an increased risk of DS, women are offered an amniocentesis to gain certainty about the presence or absence of the abnormality. If the
test shows an increased risk of neural tube defects, women are offered an amniocentesis or an advanced ultrasound examination at 20 weeks to gain certainty. An increased risk can also indicate another chromosomal abnormality than DS. However, DS is the most frequent.

3.2.2 *Nuchal translucency measurement*

The term 'nuchal translucency' refers to a thin layer of subcutaneous fluid in the neck region of the foetus. In 1992 it was observed that this is increased in foetuses that are subsequently born with DS. The nuchal translucency can be measured by ultrasound, but it requires specialised costly equipment as well as a skilled and experienced operator [22]. The measurement is performed between the 10th and 14th week of pregnancy. Combining this measure with other data like maternal age and pregnancy duration, leads to an estimation of the chance that the foetus has DS (or another chromosomal abnormality). The test outcome is known directly after it has been performed. If it is found that the risk of DS is increased, pregnant women are offered chorionic villus sampling or amniocentesis to gain certainty about the presence or absence of DS. Especially when no indication of DS is found, parents can also choose to have an advanced ultrasound examination at around 20 weeks, to look for structural abnormalities that may have caused the increased nuchal translucency.

3.2.3 *Combined test*

In recent years the combined test has come into use to provide information about the chance that the foetus has DS. This test is a combination of a blood test (first-trimester serum screening) and a nuchal translucency measurement [23]. The blood test, performed between 9 and 14 weeks of pregnancy, uses pregnancy-associated plasma protein A (PAPP-A) and free beta-human chorionic gonadotropin (fβ-hCG) as markers. The test results of both tests are combined with the age of the mother and the pregnancy duration. From this the chance that the child has DS is derived. If the screening result is abnormal, parents can choose to have either a chorionic villus sampling or amniocentesis performed for confirmation of the outcome.

3.2.4 *Standard anomaly scan*

For screening for NTDs, the standard anomaly scan (SAS) has come into use. This is performed between 18 to 22 weeks of pregnancy duration. This screening looks for the structure and development of the organs of the child and whether the size of the child matches the pregnancy duration. If the SAS shows an NTD or other serious anatomical abnormality of the unborn child, parents can choose to have an advanced ultrasound examination for confirmation or further diagnosis [24].

3.3 *Numbers of prenatal testing*

In the period 1991-2000 the mean annual number of prenatal invasive diagnostic procedures was 11.839 [25]. As in the Netherlands around 200.000 children are life-born each year [26], this means that around 6% of all children underwent invasive prenatal diagnostic testing. On
average, maternal age was the indication for 72% of the amniocenteses and chorionic villi biopsies [25]. Maternal serum screening was the indication of 1.9% in 1991 and of 4.4% in 2000. For the indication ‘abnormalities on foetal ultrasound’ the percentage rose from 4.4% to 8.8%. The total number of abnormalities detected by invasive diagnostic procedures increased from 362 in 1991 to 638 in 2000. An average of 71% of the pregnancies with abnormal results was terminated. Since 2007, all pregnant women in the Netherlands are informed about prenatal screening. This will likely change the number of screening and invasive diagnostic tests that are performed each year.

4. PRENATAL SCREENING POLICY IN THE NETHERLANDS

The Health Council of the Netherlands defines prenatal screening in general as: ‘Screening among pregnant women or their partners, in order to systematically and at an early stage identify women or couples having an increased risk of a deviating pregnancy outcome as a consequence of disease, predisposition or carriersonship, regardless of the type of examination conducted’ [20]. The Health Council states that the goal of prenatal screening is to give all pregnant women (and their partners) who want it, timely information about the presence or absence of the disorder in question, thereby enabling them, in the case of an unfavourable outcome, to decide to terminate the pregnancy or to prepare for the birth of an affected child. It is not the purpose of screening to save costs by preventing as many births of children with certain serious abnormalities as possible [20,27,28].

Because of the risk of miscarriage, and for practical and financial reasons, prenatal diagnostic testing was, and is, not offered to all pregnant women in the Netherlands, but only to those who are at an increased risk. When prenatal diagnostic testing for DS was introduced, maternal age and having a previous child with DS were the only available criteria for defining an ‘increased risk’ group. In the Netherlands, prenatal testing for DS has been offered to pregnant women aged 38 and over since the 1970s. In 1985 this threshold was lowered to 36 years. The age-related threshold that has been adopted is relatively arbitrary [20]. Nowadays, screening tests have become available that can better indicate whether pregnant women are at an increased risk for having a child with DS than age alone [27,30].

Serum screening was already being performed in some places in the Netherlands since the end of the 1970s. Van Berkel and Stemerding described how the introduction of maternal serum screening in the Netherlands had been debated [31]. Some tension existed between the process of the medical technological introduction of maternal serum screening on the one hand, and political and public debate on the psychosocial, ethical, and legal acceptability of this screening on the other hand. While discussion in the Netherlands was focussed on whether or not serum screening should be offered to all pregnant women regardless of age, in many other European countries it was already part of standard prenatal care [1].
Arguments put forward by opponents of prenatal screening for all pregnant women included that it causes further medicalisation of the pregnancy and is a psychological burden for pregnant women, thereby reducing the enjoyment of the pregnancy period. In addition, pregnant women could feel pressurized to accept the test, threatening their freedom of choice. They would become more and more dependent on medical technologies, while feeling more and more the burden of the responsibility for the course and outcome of the pregnancy. In contrast, proponents argued that women should be able to decide for themselves whether or not they want to have prenatal screening performed, and that this should not be limited to women who come to know about these tests by chance. In addition, it was argued that screening is already being performed in practice and could not longer be stopped, and that it provides a better estimate of an individual woman’s risk than age alone. It would also drastically reduce the number of invasive tests and the number of associated miscarriages, since, if prenatal screening shows no increased risk, an invasive test is unnecessary.

In this period of debate, in 1996, the Population Screening Act (PSA) (WBO in Dutch) came into effect. The aim of this law is to protect the population against screening programmes that could be a threat to psychological and physical health [30]. It states that screening for serious disorders that can neither be treated nor prevented is such a threat, and is therefore prohibited without ministerial approval. Because termination of a pregnancy is considered as neither treatment nor prevention, and because there is no approval, population screening for DS and neural tube defects was prohibited. Midwives and gynaecologists were not allowed to take the initiative themselves to inform women under 36 years of age about the possibility of having a screening test. However, if the woman asked for the test herself, it would be allowed. The situation was different for women of 36 years and older. Because of the Dutch Medical Treatment Act (WGBO in Dutch), pregnancy counsellors had to offer women not only amniocentesis and chorionic villus sampling, but also the choice of maternal serum screening [33].

In 2001 and 2004, the Health Council of the Netherlands published reports in which it advised the Government to offer prenatal screening for DS and neural tube defects to all pregnant women [6,20]. This finally resulted in a change of policy in which the Government made a distinction between offering and informing pregnant women about prenatal tests. ‘Offering’ implies that the Government pays for the test, whereas ‘informing’ implies that women have to pay for the test themselves or can get reimbursed if they are insured. Women of 36 years and older are still offered the prenatal tests. Women younger than 36 years are informed about screening for Down syndrome if they wish for it. Women of all ages are offered the SAS. On 1 January 2007, new guidelines on prenatal screening were implemented: All pregnant women have to be given the opportunity to express the wish to be informed or not to be informed about screening for DS and the SAS. All pregnant women who wish to have screening for DS and/or a SAS have to have the possibility of informed choice.
Chapter 1

As a licence is still needed for prenatal screening, every region has one license holder, the so-called Regional Centre for prenatal screening. These Regional Centres correspond to the 8 Academic/University hospitals. Pregnancy counsellors, laboratories and sonographers need to collaborate on the basis of a collaborative contract with a Regional Centre to be allowed to be involved in prenatal screening. [34]. Currently, women who wish to be informed about screening for DS are given information about the combined test. Women whose pregnancy duration is too far advanced are offered the triple test.

5. PSYCHOLOGICAL CONSEQUENCES OF PRENATAL SCREENING

Guidelines for screening programmes state that the benefits of screening programmes should outweigh any harmful physical or psychological effect as a result of participating [35,36]. With the appearance of prenatal screening, the question arises as to whether offering prenatal screening has an effect on pregnant women’s psychological well-being. The pregnancy period involves physical and emotional changes, a change of future perspective, and having the responsibility for a life other than one’s own [37-39]. Fears and doubts may be evoked concerning the health of the baby, fear about the delivery, and uncertainty about the future and motherhood [40,41]. But there can also be feelings of joy and happiness about the growing child inside and pleasurable expectations of the future. We therefore aimed to gain more insight into the influence of prenatal screening on women’s general feelings of anxiety, anxiety specifically related to the health of their unborn child, attachment to their pregnancy and unborn child, and positive and negative emotions during pregnancy. In the following sections, a brief overview is given of what was already known about these topics at the time we conducted our research.

5.1 Anxiety

Offering prenatal screening confronts parents with the possibility that their child is disabled. Among health professionals and politicians, views differed on how this would affect pregnant women. Some were concerned that offering prenatal screening would unnecessarily burden women and their partners with doubts and anxiety about the health of their foetus [20,42-45]. However, others held the opinion that in general pregnant women are, to a greater or lesser extent, already concerned about the health of the foetus, regardless of information on, or the offer of, prenatal screening [43]. Gaining reassurance about the health of their unborn child is a frequently-mentioned reason by women who accept prenatal screening [46-51]. They perceive prenatal screening as being the most effective factor in reducing the levels of fear and anxiety experienced throughout pregnancy [52]. However, not much is known about whether receiving a negative screening outcome lessens anxiety, i.e. whether women do indeed get the reassurance they were looking for [53]. In contrast, it has been shown that women who received a negative screening outcome had doubts and worries because they did not know how to handle the risk numbers and how to interpret the screening outcome [54]. In addition,
it has repeatedly been shown that the impact of receiving a positive screening outcome leads to an increase in anxiety in pregnant women [51,53]. The effect of receiving a positive prenatal screening outcome on anxiety may depend on the kind of test that is offered. A study showed that an increased risk after having an NTM, in which an image of the unborn child is seen, has a greater impact on anxiety than an increased risk after an MST [51].

In their review study, Green et al. [53] concluded that limitations of studies concerning anxiety are that they concerned only women who accepted screening, not reported before-testing anxieties, or had an under-representation of women who declined the screening test compared to those who accepted it. Therefore, it was still unresolved whether or not anxiety differs between screening acceptors and decliners. In addition, not much research had been done on the effect of offering prenatal screening on anxiety. A study conducted 20 years ago, comparing women who lived in an area with a well-established screening programme and women who lived in an area without such a programme, showed no differences in anxiety in the period during which screening tests are offered [55]. One interpretation of this finding could be that offering prenatal screening does not influence levels of anxiety. But to gain insight into the effect of offering screening, this has to be clearly differentiated from the effect of undergoing the test. That was not the case in this study. In addition, when comparing women in different geographical areas there might be other differences between the groups that influence anxiety levels.

Studies concerning the influence of prenatal screening on anxiety have often used general scales of anxiety. However, these scales are not designed to assess anxieties and worries related specifically to pregnancy. Huizink et al. showed in their study that the fear of bearing a physically or mentally disabled child can be differentiated from general anxiety [56]. Child-related anxiety was highest during early pregnancy (measured at 15-17 weeks), lowest during mid-pregnancy (27-28 weeks) and increased from mid- to late pregnancy (37-38 weeks).

5.2 Positive and negative emotions

As mentioned earlier, pregnancy may influence women's emotional well-being. Therefore, in addition to anxiety, we wanted to gain insight into the influence of prenatal screening on a broader range of feelings, both positive and negative. Positive and negative affect are two distinct, relatively independent dimensions of emotional well-being [57-60]. High positive affect reflects the extent to which a person feels enthusiastic, active and alert. Low positive affect is characterized by sadness and lethargy. High negative affect reflects a variety of aversive emotional states, like anger, guilt, nervousness, while low negative affect is a state of calmness and serenity. Positive affect is related to social activity, while negative affect is related to perceived stress. As far as we know, no studies have been performed on these two emotional dimensions in the context of prenatal testing.
Chapter 1

5.3 Attachment

The relationship of a mother with her child has already begun during pregnancy [61]. A woman initially becomes attached to the idea of being pregnant and gradually develops an attachment to her unborn child [62]. This starts with an intellectual knowledge of her child, and is then followed by a physical and kinaesthetic awareness [63]. Cranley defined prenatal attachment as ‘the extent to which women engage in behaviours that represent an affiliation and interaction with their unborn child’ [63], while Muller emphasized the affiliative aspect: ‘The unique, affectionate relationship that develops between a woman and her foetus’ [64]. Feelings of attachment begin early in pregnancy [65] and increase significantly across time [61,65-69]. The prenatal bond between a woman and her foetus is important because it correlates with positive health practices during pregnancy, like paying attention to one’s food intake and adhering to prenatal care regimens [70-72]. Furthermore, prenatal attachment is predictive of postnatal attachment, like being more involved while interacting with one’s baby [73,74].

Some studies suggested that prenatal diagnostic testing influences prenatal attachment. Women were inclined to distance themselves emotionally from their pregnancy and from their foetus until after receiving a favourable outcome [69,75-78]. This has been called ‘tentative pregnancy’: ‘When pregnancy is probed for normality or defectiveness, the foetus itself becomes a tentative foetus, whose birth is conditional on certain quality parameters verified by expert interventions’ [79,80]. However, other studies could not find an effect of diagnostic testing on attachment [81,82].

Not much is known about the effect of prenatal screening tests on pregnant women’s feelings of attachment towards their pregnancy and unborn child. Undergoing prenatal screening may facilitate an emotional distancing from the pregnancy because women have to contemplate the health of their foetus and the implications it has for the future of their pregnancy in the same manner as with diagnostic testing [83]. But since screening test results do not give certainty, it may not provide the information that is necessary for women to move beyond the tentative pregnancy stage [83].

Only one study has been concerned with the relationship between maternal serum screening and attachment. In this study, women who had received a negative maternal serum screening result showed lower levels of attachment compared to women who had declined prenatal screening and diagnostic testing [83]. Since this study did not include a measure of attachment before screening was performed, it might be possible that women who felt more attached were less inclined to have screening done. It is unclear whether prenatal screening by means of an ultrasound would have a different impact on attachment than prenatal screening by means of serum screening. Some studies suggest that seeing the baby through ultrasound enhances feelings of attachment [65,84-86], but other studies did not find an effect [69,87-89].
6. INFORMED DECISION MAKING

Because a prenatal screening test can lead to decisions about invasive diagnostic testing and abortion, the decision about prenatal screening is associated with values about the abnormalities tested for and termination of pregnancy. Policy makers and health professionals therefore stress that parents should be able to make their own decision, involving what they consider to be advantages and disadvantages as seen from their personal perspective and values [90]. In other words, parents should be able to make an informed decision about whether or not to have prenatal screening performed.

There are several definitions of what constitutes an informed decision [91]. Two common attributes are that it is based on sufficient knowledge and that it is in accordance with the decision maker’s values.

In addition, some definitions include deliberation about the alternatives; thinking through their advantages and disadvantages. The latter criterion matches the view of the Health Council which states that women should be offered the necessary information to be able to make a deliberate decision about the prenatal screening test and about the other possible decisions that may follow in the screening trajectory [20]. This involves an active processing of the information instead of just having enough knowledge. Analyses on the same dataset as presented in this thesis showed that only about 50% of the participants made a decision that was value-consistent, knowledgeable, and based on deliberation [91]. Other studies also found low rates of informed decision making, which ranged from 40-70% [92-95].

6.1 Psychological consequences of informed decision making

Even though much research has been done on whether pregnant women do indeed make informed decisions, not much is known about whether informed decision making is associated with better psychological outcomes for the decision maker [53]. Some studies showed that women who made an informed decision and women who did not make an informed decision, did not differ in their levels of anxiety [92,96-98]. In addition, no difference in anxiety after receiving the screening result was found between these groups [98]. However, this study concerned women whose prenatal screening test result indicated a low risk. No studies have been performed on women who received a positive screening result, which generally has a big emotional impact [53,77]. In order to study this properly, a prospective design is required to prevent recall bias. This implies that a large group of women who decide on prenatal screening should be followed and their decision making assessed, in order to obtain enough persons who have the screening test and receive a positive screening outcome.

6.2 Attitudes towards prenatal testing

One component of an informed decision is that the choice is in line with the decision maker’s values. When studying informed decision making, attitudes are often used as a reflection of the values [91,92,97,98]. However, attitudes are not stable and can be influenced by behaviour
[99,100]. This raises the question as to whether attitudes towards prenatal testing change when women are actually offered screening, compared to women who are not offered screening. And what does this imply for measuring informed decision making?

6.3 Pregnant women’s preferences in pregnancy outcomes

Some health professionals and policy makers feared that because prenatal screening tests are safe for the child, women would very easily choose to have such a test done without considering what they would do in case of a positive screening outcome [20,54,101]. Women seek to be reassured by the screening test [48-50], but may be unprepared for an unfavourable outcome [20]. In addition, women may see the fact that the screening tests are offered as an indication that they are useful, which makes them prone to accept them without thinking the matter through [54]. The Dutch Health Council describes a potential disadvantage of the prenatal screening test: ‘Pregnant women who think they are undergoing a simple blood test without considering the possibility of receiving an abnormal result and the implications of it, could get into a so-called ‘multi-phased trap’. If the trap closes, there is no way back: the screening result cannot be undone and leads automatically further into the screening trajectory’ [20]. The Health Council states that to prevent this multi-phased trap, potential participants of screening should be informed at the beginning about the possible next steps and their implications [102].

So, ideally, when women have decided about accepting or declining a prenatal screening test, they should also have thought about whether or not they would want to have an invasive diagnostic test or an abortion. Of course, diagnostic testing after a positive screening result, and termination of pregnancy after an unfavourable diagnostic test outcome are not the only options. Parents can also choose to prepare themselves for the birth of a child with a congenital abnormality. But figures show that around 90% of women who receive a positive screening result choose to have diagnostic testing done [103]. And, in the Netherlands, around 71% of women who receive an abnormal diagnostic test result choose to terminate their pregnancy [25].

It would therefore be interesting to know what values are assigned to the various possible pregnancy outcomes by women who are deciding on prenatal screening: are these values in line with what may be expected in women who may opt for diagnostic testing and a chosen abortion in the case of unfavourable test results?

7. RESEARCH QUESTIONS

Ensuign from sections 6 and 7, are the following research questions that we aimed to answer in this thesis:

1. Psychological consequences on pregnant women of offering prenatal screening
   a) What is the effect of being offered prenatal screening on anxiety and attachment?
   b) What is the effect of receiving a screening result on anxiety, attachment and positive and negative emotions?
c) What are the longer-term effects of being offered prenatal screening and receiving a screening result on anxiety, attachment and positive and negative emotions?

2. Informed decision making
   a) Do women who made an informed decision and those who did not, differ in their emotional reaction when confronted with a positive screening outcome?
   b) What is the effect of offering prenatal screening on pregnant women’s attitudes towards prenatal testing?
   c) What are pregnant women’s preferences in pregnancy outcomes?

8. RESEARCH PROJECT

The data presented in this thesis were collected in the context of a larger research project aimed at studying risk perception, decision making, and psychological well-being of pregnant women when offered prenatal screening for DS and neural tube defects by a triple test and nuchal translucency measurement. Another thesis based on this project has appeared earlier: ‘Decision making on prenatal screening’, by Matthijs van den Berg. Topics in his thesis include: pregnant women’s reasons for accepting or declining the offer of a prenatal screening test, test uptake, the influence of counsellors’ attitudes on women’s decision making, and whether women make informed decisions [91,96,104-106]. Elisa Garcia is working on her thesis concerning the role of ethics in decision making on prenatal screening [107,108].

8.1 Setting
We collected our data in the period between May 2001 and May 2003. In the Netherlands, at this time, it was prohibited to offer prenatal screening to women younger than 36 years of age [32]. We received permission from the Minister of Health to offer prenatal screening in the context of this longitudinal randomised controlled trial at the EMGO institute. The Netherlands has a unique system of maternity care. The Dutch Government actively promotes birth at home under the care of primary caregivers: midwives and GPs [109]. In the Netherlands, women who expect a normal (‘physiological’) birth must receive their care from either a midwife or a GP [109]. Specialist care can be used only when complications occur.

8.2 Design
The research project is a longitudinal randomised controlled trial. Pregnant women were offered a nuchal translucency measurement or a maternal serum screening test (triple test), two screening tests that were commonly in use at the time this study was being conducted. The design of the study was approved by both the Minister of Health [110], and the Medical Ethics Committee of the VU University Medical Centre.
Chapter 1

8.3 Participants
Midwifery and gynaecology practices in various parts of the Netherlands were approached until a sufficient number (n=44) consented to participate. These practices consisted of group and individual practices and were located in rural and urban areas. Pregnant women attending one of these practices were asked permission to be sent a research information letter. Only women with a gestational age of at most 16 weeks and command of the Dutch language were approached. The first information letter invited women to participate in a study for evaluating different kinds of pregnancy care. We did not mention prenatal screening tests, otherwise women in the control group may have looked for more information about it, which would mean that they were no longer a proper control group. Of the 4077 women who were approached, 2986 women (73%) gave informed consent and filled in the first questionnaire. Figure 1 shows the number of women who filled in the subsequent questionnaires.

8.4 Randomisation
After informed consent was granted, women were randomised into three groups: a group that was given information about the NTM, a group that received information about the MST, and a group that was not offered screening (control group). Since the NTM can only be performed between the first 10 and 14 weeks of pregnancy, it was necessary to make sure that the pregnancy duration of women who would be offered this test did not fall outside this range. Consequently, women who gave consent after 10 weeks were randomised into either the MST group or the control group.

One of the aims of the study was to draw conclusions about the group of positively screened women. Since only approximately 5% of women who have screening performed receive a positive outcome, more women were randomised into the intervention groups than into the control group.

8.5 Intervention
Women received information about the prenatal screening test by means of a booklet sent to their home and a consultation by their midwife or gynaecologist. Depending on the screening test that was offered, the following topics were covered in the booklet: characteristics of people with DS/NTD, age-specific chances of having a child with DS, procedure of the NTM/MST, options available following an unfavourable screening result, procedure of the diagnostic tests including information about a procedure-related miscarriage, and the possibility of having to consider an abortion in the case of an unfavourable diagnostic test result. The booklet had previously been pilot-tested for comprehensibility. If women chose to accept the screening test, a separate visit was required to have the test performed.

8.6 Questionnaires
Participants were asked to fill in five postal questionnaires at various points in time. The first questionnaire was sent before any information about screening was given, i.e. before they had
Figure 1. Progress of the participants through the trial.

* Main reasons for dropping out were miscarriage or giving informed consent too late.
Chapter 1

to decide about accepting or declining prenatal screening (T1). The second questionnaire was filled in after women had been offered prenatal screening, or at a comparable point in time for the control group (T2). The third questionnaire was filled in after the screening test result was known, or at a comparable point in time for the control group and women who declined screening (T3). The fourth questionnaire was sent at 28 weeks of pregnancy (T4). The fifth questionnaire was sent two months after giving birth (T5).

9. OUTLINE OF THE THESIS

In Chapter 2 we aim to gain more insight into the effect of offering prenatal screening and receiving a negative or positive screening result on general anxiety and anxiety related to the health of the child.

Chapter 3 encompasses many topics, concerning both emotional well-being and informed decision making. For the discussion in the present thesis, we focus on the topic of positive and negative emotions.

Chapter 4 focuses on the effect of offering prenatal screening and receiving a negative screening result on pregnant women’s attachment towards their pregnancy and unborn child. In addition, we investigated whether attachment differs between women who had had an ultrasound screening test and women who had had a serum screening test.

In Chapter 5 we aim to gain more insight into whether informed decision making is associated with more favourable psychological outcomes. For these analyses we included only women who had received a positive screening result.

In Chapter 6 we investigate whether attitudes of pregnant women regarding prenatal testing change when they are offered prenatal screening, and what this implies for measuring informed decision making.

In Chapter 7 we investigate what values screening acceptors and decliners attach to the various pregnancy outcomes. These outcomes concern, among others: having a child with DS, having a procedure-related miscarriage of a healthy child, and having a chosen abortion of a child with DS.

Chapter 8 begins with a summary of the findings of the previous chapters, which are subsequently discussed. Finally, we address the strengths and limitations of the study, and the study’s implications for practice, policy and further research.
10. REFERENCES


19. VU Medical Center. [Onderzoek naar (erfelijke) afwijkingen bij het ongeboren kind]. Amsterdam: VU Medical Center, 2006.


General introduction


Does prenatal screening influence anxiety levels of pregnant women?

Johanna H Kleinveld
Daniëlle RM Timmermans
Denhard J de Smit
Herman J Adèr
Gerrit van der Wal
Leo P ten Kate

Prenatal Diagnosis, 2006; 26(4): 354-361
Chapter 2

ABSTRACT

Objective: Questions addressed are: (1) Does offering prenatal screening increase anxiety? (2) Does receiving a negative screening result make women less anxious and does a positive screening result make women more anxious? (3) What are the long-term consequences on anxiety of offering screening and receiving a screening result?

Methods: Women were offered prenatal screening or no screening in a randomised controlled trial. State anxiety (STAI) and child-related anxiety (PRAQ-R) were measured. Questionnaires were filled in before prenatal screening was offered (T1), after the offer (T2), after the test result (T3), and in the third trimester of pregnancy (T4).

Results: Child-related anxiety levels were higher in women who chose to be screened compared to women who declined screening. Offering prenatal screening did not lead to increased anxiety levels. General anxiety increased in positively screened women, but decreased later in pregnancy. Women who were negatively screened or declined screening scored lower than the control group.

Conclusion: For most women, offering prenatal screening and receiving the test result do not adversely affect anxiety. Giving pregnant women a choice to have prenatal screening done seems to have a small favourable effect on general feelings of anxiety.
INTRODUCTION

In many countries, prenatal screening tests are offered to pregnant women as part of the usual prenatal care. These tests give an estimation of the chance that the child has a particular abnormality. A frequently heard concern among opponents of prenatal screening is that offering information about screening makes women focus more on what can be wrong with the child and that this could cause anxiety. In contrast, proponents argue that screening gives women reassurance.

There has not been much research done on this topic. A study conducted 20 years ago comparing women who lived in an area with a well-established screening programme and women who lived in an area without such a programme showed no differences in anxiety in the beginning of pregnancy, i.e. in the period during which screening tests are offered [1]. One interpretation of this could be that offering prenatal screening does not influence levels of anxiety. But to gain insight into the effect of offering screening, this has to be clearly differentiated from the process of conducting the test. As far as we are aware, this has not been studied hitherto.

Although little attention has been paid to the effect of offering prenatal screening on anxiety, research has been done on the effect of screening outcomes on anxiety among pregnant women. Various studies have shown that women who receive a positive screening result have increased anxiety levels [2-7]. Another study, however, did not find heightened anxiety levels after a positive test result [8]. Conclusions about anxiety levels in positively screened women are mainly based on comparisons with women who were given a negative screening result, or women who were at risk through advanced age. Most of these studies do not report anxiety levels of women who declined screening or who were not offered screening, as Green et al. [6] concluded in their systematic review, and therefore give limited evidence for the effect of undergoing prenatal screening on anxiety levels of women.

An important reason for pregnant women to undergo prenatal screening is to gain reassurance [9,10]. Whether this is achieved after a negative screening result is still a topic of debate. Some researchers conclude that there is no reassuring effect [11,12], while others infer that there is [5,13]. In the latter studies, anxiety levels after the screening test were sometimes lower than before the test was done, but these differences were not rated as being significant.

When this study was performed, prenatal screening was not offered to pregnant women as standard practice in The Netherlands. This was against regulations as specified in the Population Screening Act (PSA). The aim of the PSA is to protect the population against screening programmes that could be a threat to psychological and physical health [14]. It can only be done if women ask for prenatal screening themselves. Because of this situation, we were able
to conduct a randomised controlled trial to study the effect on anxiety of an explicit offer of prenatal screening. A special license for offering prenatal screening within the framework of this study was obtained from the Minister of Health. Prenatal screening tests used in this study are the nuchal translucency measurement (NTM) and the maternal serum screening test (MST, Triple Test). Both give an estimation of the chance that the unborn child has Down syndrome. The MST also gives information about the chance on neural tube defects.

The present study is unique in that it is a longitudinal study that compares women who: (1) were not offered screening, (2) declined the offer, and (3) received a positive or negative screening result at various specific points in time during their pregnancy. The study forms part of a longitudinal randomised controlled research project (subsidised by The Netherlands Organization for Health Research and Development, project number 2200.0085), that aims to give a greater insight into the risk perception, informed decision making, and psychological well-being of pregnant women who are offered prenatal screening for congenital defects.

Questions addressed in this study are: (1) Does offering prenatal screening increase anxiety? (2) Does receiving a negative screening result make women less anxious and does a positive screening result make women more anxious? (3) What are the long-term consequences of offering screening and receiving a screening result on anxiety? General anxiety as well as child-related anxiety were measured.

**PATIENTS AND METHODS**

Midwifery and gynaecology practices in various parts of the Netherlands were approached; 44 consented to participate. Pregnant women attending these practices between May 2001 and May 2003 were asked permission to be sent a research information letter. Only women with a gestational age of at most 16 weeks and command of the Dutch language were approached. The first letter invited women to participate in a study for evaluating different kinds of pregnancy care without mentioning prenatal screening. The design of the study and the invitation were approved by both the Minister of Health, and the Medical Ethics Committee of the VU University Medical Centre.

**Randomisation**

After informed consent was granted, women were randomised by the researchers into three groups: the first was given information about the NTM, the second about the MST, and the third was the control group. The NTM can only be performed between 10 to 14 weeks of pregnancy. To make sure that the pregnancy duration of women who would be offered the NTM was not beyond this range, women who gave consent after 10 weeks were randomised into either the MST or control group. Because we wanted to draw conclusions
About the group of positively screened women, who constitute only approximately 5% of women who are screened, more women were randomised into the intervention than to the control group.

**Intervention**

Women received information about the prenatal screening test by means of a booklet sent to their home and a consultation with their midwife or gynaecologist. Women of 36 years and over received a booklet in which information was also given about the option of having an amniocentesis or chorionic villus sampling done directly. The booklets were previously pilottested for comprehensibility.

**Outcome measures**

Anxiety was assessed by the Dutch version of the State-Trait Anxiety Inventory version Y (STAI-form Y) [15] and the Pregnancy Related Anxieties Questionnaire-Revised (PRAQ-R) [16]. The STAI scales consist of 20 statements that ask the respondent to describe how she feels at a particular moment (State anxiety) or how she generally feels (Trait anxiety). State scales ranged from 1 (not at all) to 4 (very much), Trait scales ranged from 1 (almost never) to 4 (almost always). The PRAQ-R consists of three subscales: ‘fear of bearing a physically or mentally handicapped child’ (‘child-related anxiety’, 4 items), ‘fear of giving birth’ (3 items) and ‘concern about one’s appearance’ (3 items). Scales range from 1 (absolutely not relevant) to 5 (very relevant). Only data related to the first subscale will be presented in this article. Total scores on this subscale were divided by the number of items, so the minimum score on this subscale is 1 (low anxiety) and the maximum score is 5 (high anxiety).

**Questionnaires**

Participants were asked to fill in five postal questionnaires. All questionnaires included the State anxiety scales. The PRAQ-R was not included in the fifth questionnaire, because it was then no longer applicable. The first questionnaire was sent before any information about screening was given (T1) and included questions about demographic background such as age, education, and parity. The second questionnaire was filled in after women had read the booklet and had decided for or against prenatal screening (T2), but (if applicable) before they had received the test result. The control group received the second questionnaire at a comparable point in time. The third questionnaire was filled in after the test result was known or at a comparable point in time for women who chose not to be screened, or who were randomised into the control group (T3). This questionnaire contained the Trait anxiety scale and women were asked if they had had the screening test done and whether or not the test had shown an increased risk. The fourth questionnaire was sent at 28 weeks of pregnancy (T4), asking women whether or not they had had a prenatal diagnostic test done. The fifth questionnaire was sent after delivery (T5) and is not included in this study.
Participants
During the recruitment period 4077 women were asked permission to be sent a research information letter. A questionnaire that was sent to the midwifery and gynaecology practices showed that they approached nearly all women and that reasons for not approaching were lack of time or because it was forgotten. Two thousand nine hundred and eighty-six women (73%) gave informed consent and filled in the first questionnaire. Figure 1 shows the flow chart of the number of women who filled in the subsequent questionnaires. Of the women who had consented to participate, all questionnaires were filled in by 686 (62%) women in the NTM group, 512 (66%) in the control group and 648 (59%) in the MST group. Some of the women who did not want to participate and some who did not follow up were sent a questionnaire that showed that the main reason for not participating in the study or to stop participating was lack of time or interest. Sixteen percent (188 cases) of the loss to follow up was due to miscarriage.

Analyses
At T1 and T2, comparisons were made between women who had chosen to be screened, those who declined screening, and the control group. At T3 and T4, the group of women who had chosen to be screened was split up into a group that was negatively screened and a group that was positively screened. Because the group of women with an increased risk is very small compared to the other groups (n=20), they were compared with a matched sample of 20 persons from each of the other groups. Matching variables included background characteristics such as age, education, religion and number of children. Negatively screened women were compared to the total group of women who declined screening and the control group. Cross-sectional data analyses were performed with univariate analyses of variance with reversed Helmert contrasts. Separate univariate analyses of variance were performed at T3 and T4, with contrasts comparing positively screened women with the sample of 20 persons from each of the other groups; p-values were adjusted for multiple comparisons. Analyses were conducted using SPSS 11.0 (Statistical Package for Social Science, Inc., Chicago, IL).

RESULTS
Analyses were based on those participants who responded to all four STAI and PRAQ-R questionnaires during pregnancy. Owing to missing data, the final numbers used in these analyses are fewer than the ones shown in Figure 1. The NTM and MST groups differed only at T2 with respect to State anxiety (F=5.966; p=0.015); therefore data of these groups were combined. Analyses were performed on 20 women who were positively screened, 559 who were negatively screened, 694 who declined screening, and 503 in the control group. Six percent of women in the control group had prenatal screening done at their own request. On
Does prenatal screening influence anxiety levels of pregnant women?

the basis of the principle of intention to treat, they were analysed as part of the control group. Since groups differed at baseline on child-related anxiety, these values were taken as covariates in analyses of the next time points. To gain a better insight into the effect of receiving the test result (T3), scores at T2 were also used as a covariate if they differed significantly between groups.

There were no significant differences on STAI-Trait scores and background characteristics between the groups (Table 1), nor were there any significant differences between positively screened women and the samples of 20 persons. Women in the present study had higher levels of education than the general Dutch population of pregnant women (Table 1) [17].

Baseline scores (T1)
There were no differences at initial assessment in State anxiety between the groups (Figure 2(a)). Women who at T2 chose to be screened scored significantly higher on child-related anxiety than those who declined screening ($t=5.18, p=.000$) (Figure 3(a)).

The effect of offering prenatal screening on anxiety levels (T2)
No differences in State anxiety were observed after information had been offered (Figure 2(a)). After correction for baseline, women who had chosen to be screened scored higher on child-related anxiety than women who had chosen to decline screening ($t = 3.67, p < .001$) (Figure 3(a)).

The effect of a test result on anxiety levels (T3)
Women who were negatively screened and women who had declined screening scored significantly lower on State anxiety than the control group ($t = 3.56, p < 0.001$) (Figure 2(b)). Positively screened women scored significantly higher on State anxiety than the sample of negatively screened women and the sample of women who had declined screening ($t=2.48, p=0.048$ and $t=2.66, p=0.03$, respectively).

Table 1. Trait anxiety and background characteristics of the respondents and Dutch pregnant population

<table>
<thead>
<tr>
<th></th>
<th>Increased risk (n=20)</th>
<th>No increased risk (n=559)</th>
<th>No screening done (n=694)</th>
<th>Control group (n=503)</th>
<th>Dutch pregnant population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trait anxiety (mean)</td>
<td>37</td>
<td>35</td>
<td>36</td>
<td>36</td>
<td>31</td>
</tr>
<tr>
<td>Age (mean)</td>
<td>31</td>
<td>31</td>
<td>31</td>
<td>31</td>
<td>31</td>
</tr>
<tr>
<td>Educational level (%)</td>
<td>Low 10</td>
<td>15</td>
<td>9</td>
<td>13</td>
<td>37</td>
</tr>
<tr>
<td></td>
<td>Medium 65</td>
<td>44</td>
<td>46</td>
<td>45</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td>High 25</td>
<td>42</td>
<td>45</td>
<td>42</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td>Nulliparae (%)</td>
<td>50</td>
<td>46</td>
<td>43</td>
<td>44</td>
</tr>
</tbody>
</table>

37
Analyses with T1 and T2 as covariates showed that women who were negatively screened scored lower on child-related anxiety than women who had declined screening ($t=2.47$, $p=0.013$) (Figure 3(b)). The control group scored higher than both these groups ($t=2.76$, $p=0.005$). Positively screened women did not score significantly higher on child-related anxiety than the samples of the other groups.
Does prenatal screening influence anxiety levels of pregnant women?

**The long-term consequences of offering screening and receiving a test result (T4)**

In the last trimester of pregnancy, the control group had higher State anxiety scores than women who had declined screening and negatively screened women ($t=2.71, p=0.007$) (Figure 2(b)). No significant differences were observed between the positively screened women and the samples of the other groups.

No significant differences were seen in child-related anxiety between negatively screened women, women who had declined screening, and the control group (Figure 3(b)). No significant
difference was found between positively screened women and the samples of the other groups. Fifteen women from the positively screened group had had a prenatal diagnostic test done. All diagnostic test results were negative.
DISCUSSION

The aim of this study was to give more insight into the effect of offering prenatal screening on anxiety levels of pregnant women, and on the effect of receiving a test result on anxiety. Two different kinds of anxiety were measured; general feelings of anxiety and anxiety specifically relating to the health of the child.

Offering prenatal screening did not influence general anxiety. Women who chose to be screened were already more anxious about their child's health before screening was offered. However, after screening was offered and taking into account baseline differences, women who chose to screen still had more child-related anxiety compared to women who chose not to screen. After receiving the screening result, women who were positively screened had the highest levels of general anxiety. Women who were negatively screened or had declined screening scored lowest on general anxiety and child-related anxiety. In the last trimester of pregnancy, levels of general anxiety in positively screened women had returned to normal. Levels of general anxiety in negatively screened women and in women who had declined screening were lower than in women who had not been offered screening. Levels of child-related anxiety between these groups were the same.

After prenatal screening was offered, women who chose to screen had more child-related anxiety than women who chose not to screen. It might be the case that providing information about prenatal screening makes women who are already worried about their child focus even more on what may be wrong, and that they therefore stay more worried. Previous studies showed a reassuring effect of a negative screening test result comparing anxiety levels before and after screening, or with scores of women who had not had a test done [13]. The present study showed a reassuring effect of a negative test result compared to women who were not offered screening. However, women who had declined screening had the same general anxiety levels as women who were negatively screened. Possibly, in women who declined screening, post-decisional consolidation takes place to justify their decision not to be screened, causing their anxiety levels to decrease [18]. A lack of a difference in anxiety levels between negatively screened women and women who declined screening was previously established [12]. The present study also shows that the level of general anxiety in women who decline screening is lower than in women who were not offered screening at all.

Women who were screened were more anxious about the child's health at baseline, but after they had received a negative test outcome they showed lower levels of child-related anxiety than women who declined screening. Receiving good information about the child's health is apparently reassuring.
Chapter 2

Not surprisingly, positively screened women had higher general anxiety levels compared to the other women after they received the outcome. Although they had the highest levels of child-related anxiety, positively screened women did not differ significantly from women who were negatively screened, chose not to screen or the control group. An explanation for not reaching significance, might be the small size of the groups ($n=20$).

Although anxiety is not a pleasant state to be in, an increase in anxiety is not necessarily a bad thing. It is an appropriate response to a bad screening result. Moreover, moderately increased anxiety scores may reflect increased arousal that is, according to decision-making theory, necessary for actively engaging in making a choice between options with serious consequences [6]. Giving feedback and counselling could reduce anxiety associated with receiving a positive test result [19,20]. Another study, however, showed that personality characteristics might be a more important factor in relieving anxiety than giving feedback [21].

In the last trimester of pregnancy, the level of general anxiety of negatively screened women and women who had declined screening remained lower than the level of women who had not been offered screening. This points to an advantageous effect of offering screening. Opting out lessens anxiety and most women who opt in will get a negative, reassuring outcome. These results could be compared with the finding that women living in an area with a well-established screening programme had lower anxiety levels in mid- and late pregnancy than women from non-screened areas [1], suggesting that whether or not the test is done, it is beneficial to have the choice.

General anxiety levels of the positively screened women in the last trimester of pregnancy approached those of the other groups, probably because most women had undergone a prenatal diagnostic test, all of which had shown a good outcome [2,22].

A drawback of many studies on anxiety concerning prenatal screening relates to non-inclusion or non-response due to anxiety. This is assumed to be minimal in this study. At inclusion, women did not know that the study was about prenatal screening, and analyses of non-response showed that anxiety was not the main reason to stop participation. All differences, with the exception of greater general anxiety in positively screened women after receiving the screening result, were small. The practical relevance of these differences remains a point for discussion.

Since participating women in the Netherlands were not used to standard prenatal screening and because overall it does not cause anxiety in them, it is to be expected that the same will apply in countries where the offer of screening is part of customary pregnancy care. This assumption is supported by other research [1,2], showing that the presence of a screening programme in a community does not raise the general level of anxiety among pregnant women.
Does prenatal screening influence anxiety levels of pregnant women?

In conclusion, offering prenatal screening and receiving the test result do not adversely affect anxiety. However, women with a positive screening result do show increased general anxiety levels, but these decrease again when the outcome of prenatal diagnosis is good. Giving pregnant women a choice to have prenatal screening done even seems to have a small favourable effect on general feelings of anxiety.
Chapter 2

REFERENCES


Does prenatal screening influence anxiety levels of pregnant women?


Prenatal screening for Down syndrome: Pregnant women’s perceived risk and emotional well-being

Daniëlle RM Timmermans
Johanna H Kleinveld
Matthijs van den Berg
John MG van Vugt
Gerrit van der Wal

Submitted
Chapter 3

ABSTRACT

Objective: According to screening guidelines pregnant women’s choice to undergo prenatal screening for Down syndrome should be an informed choice and should not lead to undue anxiety and worries. An important aspect of informed decision making is an individual woman’s perceived risk of bearing a child with Down syndrome. We performed a study with research questions: Does explicitly offering prenatal screening (1) has an effect on pregnant women’s accurate perception of the risk of bearing a child with Down syndrome and their decisions, (2) lead to a decreased emotional well-being of pregnant women?

Methods: A randomised controlled trial with two groups being offered one of two prenatal screening tests and a control group with one base-line and four follow-up measurements. 4077 pregnant women before 16 weeks gestation from 44 midwifery and gynecology practices in the Netherlands were invited to participate; 2877 (71%) women participated; 1779 (62%) women filled in all questionnaires. Main outcome measures were perceived risk of bearing a child with Down syndrome and emotional well-being.

Results: More women had an accurate risk perception of giving birth to a child with Down syndrome after as compared to before the prenatal screening offer (60% versus 50%) due to the received information, but the decision to screen or not had no relation to participants’ perceived risk. Offering prenatal screening did not lead to increased anxiety about giving birth to a child with Down syndrome, but resulted in a larger increase in positive feelings ($F(4,1722) = 4.3$, $p<.01$) as compared with the control group.

Conclusion: An explicit offer of prenatal screening positively affected emotional well-being. However, decisions are generally not well informed because they are not based on adequate risk perception.
Pregnant women's perceived risk and emotional well-being

INTRODUCTION

Although prenatal screening is generally accepted in many countries and does not seem to meet with many problems, there are also critical comments. Studies show that women’s understanding of the risks and their knowledge of prenatal screening is poor [1-7], they often did not feel fully informed when making the choice for prenatal screening or did not realize that they had a choice and thought the test was compulsory [1,5]. Few women take the decision to opt out, uptake in many countries is around 90% [8,9], suggesting that it concerns informed compliance rather than informed choice. While prenatal screening is assumed to offer reassurance to pregnant women that the foetus is healthy [9,10], and to reduce anxiety and worries [11,12], others argue that prenatal screening leads to undue anxiety and worry, and to medicalisation of the pregnancy—as though the pregnancy has been put ‘on hold’ until approved by tests. [13,14] Guidelines for screening programmes [15-17] state that the benefits of screening programmes should outweigh the physical and psychological harms, including anxiety or distress as a result of participating. Therefore, it is felt that the choice to undergo screening should be an informed choice based on a full understanding of the likely benefits, limitations and harms of screening [18,19]. It is the topic of this study whether the practice of prenatal screening complies with these guidelines.

Informed choice and prenatal screening has been the topic of study in several articles [6,20-23]. These articles show that many women do not make informed decisions. However, these studies do not explicitly study whether the risk information which is communicated is understood and taken into account when making a prenatal screening decision. Communicating this risk information about bearing a child with a handicap may lead to unrest or increased anxiety with pregnant women. Therefore we decided to study whether offering (information on) prenatal screening leads to distress with pregnant women and whether it has an impact on their informed decision making.

In the Netherlands, at the time of the study, only women with an increased risk of giving birth to a child with Down syndrome due to advanced maternal age or a medical indication were allowed to be explicitly offered prenatal testing. At the time of the study an offer to all pregnant women was against the regulations of the Population Screening Act (PSA), which is aimed at protecting the population against screening programs that could be a threat to psychological or physical health [24,25]. This situation in the Netherlands enabled us to conduct a randomised controlled trial to determine if an explicit offer of prenatal screening has negative effects on emotional well-being. In addition, we were able to study the decision making process of pregnant women who were offered prenatal screening in a situation where it was not usual care. A special permit for offering prenatal screening was granted by the Minister of Health. The study was also approved by the Medical Ethics Committee of the VU University Medical Centre.
Chapter 3

Research questions are: Does explicitly offering prenatal screening (1) have an effect on pregnant women’s accurate perception of the risk of bearing a child with Down syndrome (DS) and their decisions, (2) lead to a decreased emotional well-being of pregnant women?

MATERIALS AND METHODS

Setting
In a randomised controlled trial, pregnant women of the general population were offered prenatal screening. All women who made a first appointment with their midwife or gynaecologist of 44 participating midwifery and gynaecology practices in several urban and rural parts of the Netherlands were approached. After receiving informed consent, participants were randomised by the researchers into one control group and one of the two intervention groups. Two computer-generated randomisation tables were drawn up by a statistician. Women who contacted their midwife or obstetrician before 10 weeks of pregnancy were randomised in the group that was offered the nuchal translucency measurement which tests for DS (NTM), the group who was offered the second trimester maternal serum screening test which tests for DS and neural tube defects (MST) or the control group. Women who contacted their midwife or obstetrician after 10 weeks of pregnancy could not be randomised into the NTM group because not enough time would be left to perform the NTM after inclusion in the trial. These women were therefore only randomised in the MST or control group. The researchers allocated the next available number of one of the tables to a participant on entry into the trial. The ratio for allocation was 1.4: 1.4: 1 for MST, NTM and control group respectively because we needed a larger group of respondents in the intervention groups than in the control group (see sample size). See Figure 1.

The information letter invited women to participate in a study for evaluating different kinds of pregnancy care without mentioning prenatal screening. Therefore, women who would later on be randomised into the control group did not know that other women were offered prenatal screening. After the women were randomised, the researchers informed the woman’s midwife or gynaecologist about the condition the woman was allocated in order for them to be able to give the consultation.

Participants
When making their first appointment for pregnancy counselling, all women were asked by their midwife or gynaecologist whether they agreed to be sent information about a study on different methods of pregnancy counselling. Women who agreed were sent a letter by the researchers explaining the study and an informed consent form which was approved by the Medical Ethics Committee of the VU University Medical Center. Only women before 16 weeks gestation were invited to participate in the study, in order to be able to perform the prenatal screening tests. Only women with a command of the Dutch language were approached because they were
Pregnant women's perceived risk and emotional well-being

Figure 1. Progress of the participants through the trial.

requested to fill in Dutch questionnaires. Almost all women in the Netherlands attend prenatal care. Women aged 36 years and older who are eligible for invasive diagnostic testing were also offered amniocentesis. Pregnant women who were not offered screening, were mostly not familiar with prenatal screening and mostly did not request prenatal testing.
Chapter 3

Sample size
For the power analyses of this study, we performed an analysis on “child-related anxiety” in order to determine if the power is sufficient for the present study. In order to find a difference of 0.2 on the sum score of the items of this scale with a significance level of .05 and a power of .80 and assuming a standard deviation of 0.8 [27], \( n = 350 \) for each group is needed when comparing groups and \( n = 135 \) is needed for detecting a difference within one sample over two measurements.

Intervention
The test offer consisted of a booklet containing information about the particular test and a standardized oral explanation by the woman’s midwife or obstetrician (see Box 1). A separate visit to a hospital was needed for having prenatal screening performed. Participants in the control group were not offered prenatal screening and did not receive information.

Outcome measures
The participants received postal questionnaires at: (T1) before the prenatal screening offer; (T2) after the prenatal screening offer but before performing screening; (T3) after receiving the screening test result (similar point in time for women who were not tested); (T4) in the 7th month of pregnancy after all possible pregnancy tests had been done; (T5) two months after delivery after women were assumed to have recovered from delivery but before the end of their maternity leave, which is in the Netherlands generally 10-12 weeks after delivery. The control group received the questionnaires at similar points in time.
Main outcome measures were for research question (1) Perceived risk of bearing a child with DS before and after women made a decision (T1, T2) compared with a control group who did not receive the information and offer; (2) Emotional well-being over time before and after

<table>
<thead>
<tr>
<th>Box 1. Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>The test offer consisted of:</td>
</tr>
<tr>
<td>a booklet containing information about the particular test;</td>
</tr>
<tr>
<td>a standardized oral explanation by the woman's midwife or obstetrician.</td>
</tr>
<tr>
<td>The following subjects were covered:</td>
</tr>
<tr>
<td>characteristics of Down Syndrome and neural tube defects (the latter not for NTM),</td>
</tr>
<tr>
<td>age-specific risks of Down Syndrome,</td>
</tr>
<tr>
<td>population risk of neural tube defects (not for NTM),</td>
</tr>
<tr>
<td>procedure of the screening tests (including the cut-off point 1 in 200),</td>
</tr>
<tr>
<td>the meaning of a positive test result,</td>
</tr>
<tr>
<td>options after a positive test result,</td>
</tr>
<tr>
<td>procedure of amniocentesis and chorionic villus sampling,</td>
</tr>
<tr>
<td>a paragraph focusing the attention on advantages and disadvantages of the screening test to help pregnant women in making their decision.</td>
</tr>
<tr>
<td>The booklets were pilot-tested for comprehensibility among a group of 350 women who had given birth to a child in the previous year.</td>
</tr>
</tbody>
</table>

Note: NTM = Nuchal Translucency Measurement
Pregnant women’s perceived risk and emotional well-being

Box 2. Variables and items in questionnaires measured at five different measurement points.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Items</th>
<th>Cronbach’s α</th>
<th>Measured at</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRAQ-R: Pregnancy-related anxiety questionnaire – only items referring to a possible disability of the baby (i.e. child-related anxiety) [28,29] measured on a 5 point scale</td>
<td>“I am afraid the baby will be mentally disabled or will suffer from brain damage”</td>
<td>0.85</td>
<td>T1, T2, T3, T4</td>
</tr>
<tr>
<td></td>
<td>“I am afraid our baby will be stillborn, or will die during or immediately after delivery”</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>“I am afraid the baby will suffer from a physical defect or worry that something will be physically wrong with the baby”</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>“I sometimes think that our child will be in poor health or will be prone to illnesses”</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PANAS: Positive feelings during week before measurement [30], measured on a 5 point scale</td>
<td>Could you indicate to what extent you have experienced the following feelings in the past few days: interested, excited, strong, enthusiastic, proud, alert, inspired, determined, attentive, active.</td>
<td>0.87</td>
<td>T1, T2, T3, T4, T5</td>
</tr>
<tr>
<td>PANAS: Negative feelings during week before measurement [30], measured on a 5 point scale</td>
<td>Could you indicate to what extent you have experienced the following feelings in the past few days: distressed, upset, guilty, scared, hostile, irritable, ashamed, nervous, jittery, afraid.</td>
<td>0.83</td>
<td>T1, T2, T3, T4, T5</td>
</tr>
<tr>
<td>Attachment to the unborn child</td>
<td>“Could you indicate on a scale from 1 to 10 how strong you feel your attachment is to your unborn child at this moment?”</td>
<td>–</td>
<td>T1,T2,T3,T4</td>
</tr>
<tr>
<td></td>
<td>very weak – very strong</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perceived risk of giving birth to a child with Down Syndrome</td>
<td>“What do you think your chance is of giving birth to a child with Down Syndrome with this pregnancy?”</td>
<td>–</td>
<td>T1, T2</td>
</tr>
<tr>
<td></td>
<td>1 out of 50000</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 out of 10000</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 out of 5000</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 out of 2500</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 out of 1000</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 out of 750</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 out of 500</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 out of 100</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 out of 50</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>other …….</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

T1 = before the intervention; T2 = after the intervention or comparable time; T3 = after test result or comparable time; T4 = in 7th month of pregnancy; T5 = after delivery.

the offer of prenatal screening for the intervention groups or similar points in time for the control group (T1, T2, T3, T4, T5). Perceived risk and accuracy of perceived risk of getting a child with DS were measured before and after the intervention (T1, T2). Perceived risk of giving birth to a child with DS was measured with a numeric risk scale (see Box 2) recalculated into three categories: (1) a risk between 1 out of 2 and 1 out of 200, including 200 (as being the threshold of identifying a risk as increased); (2) a risk between 1 out of 200 and 1 out of 1000
Chapter 3

including 1000 (as the range in which false negative results mainly occur [27]); (3) a risk smaller than 1 out of 1000. Adequate knowledge of a pregnant woman about her own risk of giving birth to a child with DS was based on whether or not her risk estimate correctly fell into one of these three categories. Emotional well-being was measured by several scales measuring fear of bearing a physically or mentally handicapped child (PRAQ-R or ‘child-related anxiety’ [28,29]), positive and negative feelings during the previous week of measurement (PANAS) [30] and emotional experience of pregnancy (measured with a self-constructed item referring to emotional attachment to the unborn child). Variables used in the present study are shown in Box 2. The first questionnaire also included demographic variables.

Statistical methods
Multivariate analyses with repeated measures and t-tests were done to test differences over time of emotional well-being between the intervention group and the control group. Multivariate differences in test-uptake were analyzed by chi-square analysis. No further separate analyses were performed for the NTM and MST groups, since this is not the focus of this paper. Analyses showed no significant differences between these groups. For the same reason, no analyses were performed on women having received positive or negative test results. Analyses were performed on the data of women who filled in all questionnaires (n=1779).

RESULTS

Participants
Inclusion took place between May 2001 and May 2003. The last follow-up measurement was in April 2004. During the recruitment period, 4077 women were invited to participate in the study, and 2877 (71%) women agreed to participate. Of these women, 1779 (62%) women returned all questionnaires. Figure 1 shows the response rates of the questionnaires. Analysis of non-response based on a separate questionnaire study among a subgroup of women who were sent an information letter revealed that the main reasons for not consenting to participate in the study were lack of time or lack of interest. In total, 1098 (38%) women who were randomised were excluded or lost to follow-up. There were 188 cases (17%) lost due to miscarriage. 375 women (34%) were excluded because they did not fill in all five questionnaires. 443 women (40%) were lost to follow-up because of, for example, logistic reasons (e.g. moving away). No differences in background characteristics were found between women who were randomised into the intervention group (NTM, MST) or the control group, or into three (NTM, MST or control group) groups or two groups (MST or control group). Compared with the general pregnant population of the Netherlands, participants in our study were on average more highly educated (see Table 1).
Pregnant women’s perceived risk and emotional well-being

Table 1. Demographic characteristics of participants compared to the general pregnant female population in the Netherlands (percentages)

<table>
<thead>
<tr>
<th></th>
<th>General pregnant female population</th>
<th>Participants Intervention group (n=1285)</th>
<th>Participants Control group (n=494)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25</td>
<td>10</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>25-30</td>
<td>26</td>
<td>37</td>
<td>37</td>
</tr>
<tr>
<td>30-35</td>
<td>43</td>
<td>48</td>
<td>45</td>
</tr>
<tr>
<td>&gt;35</td>
<td>22</td>
<td>9</td>
<td>11</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>71</td>
<td>67</td>
<td>70</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower*</td>
<td>37</td>
<td>11</td>
<td>12</td>
</tr>
<tr>
<td>Medium</td>
<td>35</td>
<td>44</td>
<td>44</td>
</tr>
<tr>
<td>Higher**</td>
<td>19</td>
<td>42</td>
<td>40</td>
</tr>
<tr>
<td>Unknown</td>
<td>10</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Number of children</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>46</td>
<td>44</td>
<td>43</td>
</tr>
<tr>
<td>1</td>
<td>37</td>
<td>43</td>
<td>42</td>
</tr>
<tr>
<td>2</td>
<td>13</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>3 or more</td>
<td>5</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

* primary school, vocational training; ** college, university

Accuracy of perceived risk.

Participants generally perceived their risk of giving birth to a child with DS as rather low: about 77% of the women thought they had a risk lower than 1 out of 1000 before information was offered (T1) while this was about 43% of the women after test information was given (Table 2). Before the test offer, about 50% of women correctly classified their risk of giving birth to a child with DS. After the screening test offer this was 60%.

Of the women who were offered prenatal screening, 46% took the test (T3). This was 53% in the NTM group (n=348), and 38% (n=239) in the MST group (32).

Table 2. Percentages of pregnant women’s categorized perceived risk of giving birth to a child with Down syndrome.

<table>
<thead>
<tr>
<th></th>
<th>Before intervention (T1)</th>
<th>After decision (T2)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1:2 to 1:200</td>
<td>1:200 to 1:1000</td>
</tr>
<tr>
<td>Perceived risk on</td>
<td>Accepted test offer</td>
<td>0.1</td>
</tr>
<tr>
<td>Down syndrome</td>
<td>(n=587)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rejected test offer</td>
<td>0.4</td>
</tr>
<tr>
<td></td>
<td>(n=699)</td>
<td></td>
</tr>
</tbody>
</table>
Chapter 3

Table 3. Effects of offering prenatal screening on emotional well-being over time of pregnant women: intervention versus control group (means and standard deviations)

<table>
<thead>
<tr>
<th></th>
<th>Before intervention (T1)</th>
<th>After decision* (T2)</th>
<th>After test result* (T3)</th>
<th>7th month of pregnancy (T4)</th>
<th>After delivery (T5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child-related anxiety</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(PRAQ) Intervention group</td>
<td>2.6 (0.9)</td>
<td>2.4 (0.8)</td>
<td>2.3 (0.8)</td>
<td>2.2 (0.7)</td>
<td>–</td>
</tr>
<tr>
<td>Control group</td>
<td>2.5 (0.9)</td>
<td>2.4 (0.9)</td>
<td>2.3 (0.8)</td>
<td>2.2 (0.8)</td>
<td>–</td>
</tr>
<tr>
<td>Positive feelings</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(PANAS) Intervention group</td>
<td>30.9 (6.9)</td>
<td>32.3 (6.7)</td>
<td>33.1 (6.6)</td>
<td>33.1 (6.7)</td>
<td>36.6 (6.6)</td>
</tr>
<tr>
<td>Control group</td>
<td>30.8 (7.8)</td>
<td>31.1 (7.0)</td>
<td>32.7 (7.0)</td>
<td>32.3 (6.9)</td>
<td>35.6 (6.9)</td>
</tr>
<tr>
<td>Negative feelings</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(PANAS) Intervention group</td>
<td>17.3 (5.8)</td>
<td>16.4 (5.8)</td>
<td>15.6 (5.3)</td>
<td>15.9 (5.3)</td>
<td>14.8 (4.8)</td>
</tr>
<tr>
<td>Control group</td>
<td>17.2 (5.7)</td>
<td>15.8 (5.2)</td>
<td>16.4 (5.6)</td>
<td>16.2 (5.7)</td>
<td>15.2 (5.1)</td>
</tr>
<tr>
<td>Attachment to the fetus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention group</td>
<td>5.4 (2.1)</td>
<td>6.3 (1.9)</td>
<td>6.8 (1.6)</td>
<td>8.1 (1.2)</td>
<td>–</td>
</tr>
<tr>
<td>Control group</td>
<td>5.2 (2.2)</td>
<td>5.8 (1.9)</td>
<td>6.6 (1.6)</td>
<td>7.9 (1.2)</td>
<td>–</td>
</tr>
</tbody>
</table>

n=1285 women were offered prenatal screening and n=494 women were in the control group
* or similar point in time for control group

Table 4. Confidence intervals

<table>
<thead>
<tr>
<th>Intervention versus control group</th>
<th>Mean difference</th>
<th>Standard error</th>
<th>Significance</th>
<th>95% confidence interval for differences</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lower bound</td>
</tr>
<tr>
<td>Positive feelings (PANAS)</td>
<td>.729</td>
<td>.294</td>
<td>.013</td>
<td>.153</td>
</tr>
<tr>
<td>Attachment to the foetus</td>
<td>.275</td>
<td>.080</td>
<td>.001</td>
<td>.117</td>
</tr>
</tbody>
</table>

Confidence intervals for significant differences between means of the intervention versus the control group, and of respondents who accepted versus who rejected screening.

Emotional well-being: child-related anxiety, positive and negative feelings, attachment to the foetus.

Child-related anxiety was not very high and this decreased during pregnancy from 2.6 to 2.2 \((F(3,1789) = 132.7, p<.001; \text{Table 3})\). There were no differences between the intervention and control group. Positive feelings increased during pregnancy especially after delivery \((F(4,1722) = 264.7, p<.001)\). Over time, the control group showed a lower increase in positive feelings than the intervention group (interaction effect \((F(4,1722)=4.3, p<.01)\). Negative feelings decreased for all women during pregnancy especially after delivery \((F(4,1722) = 66.1, p<.001)\), and especially for the intervention group \((F(4,1725) = 6.7, p<0.001)\). Emotional attachment to the foetus increased during pregnancy \((F(3,1658) = 1358.9, p<.001)\). Women in the control group reported a lower emotional attachment than the others \((F(3,1660) = 11.7, p<.001)\), especially at T2 and T3.
DISCUSSION

At the time of the study prenatal screening was not usual care in the Netherlands. Therefore, we were able to conduct a randomised controlled longitudinal trial on the effects of explicitly offering prenatal screening on pregnant women’s emotional well-being and perceived risk. Unlike other studies [1], our study was conducted with an unselected population of pregnant women, largely representative for the general (Dutch) pregnant population, and unlike other studies risk perception, attitude toward screening and emotional well-being were also measured before women knew they would be offered prenatal screening.

Offering prenatal screening did not lead to increased anxiety levels about giving birth to a disabled child, nor did it have a negative effect on women’s emotional well-being in general and emotional attachment of women to their unborn child. There was some evidence of a lower emotional attachment to the foetus and less positive feelings during pregnancy in the group that was not offered screening compared with the group that was offered prenatal screening. After receiving information about the screening test, more women correctly identified their risk of giving birth to a child with DS than before although still 40% lacked adequate knowledge about their risk. Although perceived risk of getting a child with DS became more accurate after the information and the screening offer, this did not influence women’s decision to screen or not.

Our results do not support opinions that offering prenatal screening may lead to undue anxiety and worries [1], or to barriers in the emotional attachment of the future mother to her unborn child [13,14]. Moreover, being able to choose for prenatal screening and make up one’s mind even seems to have a positive effect on women’s feelings and emotional attachment to their unborn child. Our results further show that an explicit offer of prenatal screening only partly resulted in informed choices. As an accurate perception of one’s risk of getting a child with DS is seen as relevant knowledge for a prenatal screening decision, our study confirms the studies that show that many women do not make well-informed decisions [1-6].

A possible limitation of this study was that the average educational level of our sample was somewhat higher than the average educational level of the population. Therefore, results might be somewhat biased. In particular, it has been show that higher educated women have a lower uptake than lower educated women which is also the case in our sample [31]. Also, only women with a command of the Dutch language were included, thereby partly excluding women from several ethnic groups.

What do these results mean for prenatal screening in other countries? The Dutch practice of prenatal screening was different from that in many other countries. Performing prenatal screening was not standard practice and the offer of prenatal screening took place in a research context and women filled in several questionnaires, which might have made them more aware of the information given. However, it is worrisome that a large minority still does not have an
accurate perception of their risk of getting a child with DS after information is given and that this information does not seem to play a role in the decision of most women. In a care context where screening is part of usual care, it is likely that pregnant women who are offered prenatal screening might even be less knowledgeable about their own risk of giving birth to a child with DS, and it would thus be less likely that they make informed screening choices. Important is that offering prenatal screening had no negative effects on women's emotional well-being or attachment to their unborn child. This effect likely applies to women being offered prenatal screening in other countries, where prenatal screening is standard care, and for newer prenatal screening tests.

All in all, our results showed that explicitly offering prenatal screening was partly successful in promoting informed choice while there was no negative effect on emotional well-being. Whether or not the latter applies to other public health screening programs needs to be studied [19,30]. Participants' knowledge, i.e. their perception of the risk of disease or a congenital defect, is likely to be inaccurate in other screening programs as well [30,34]. As informed choice is seen as important within public health screening [15-19,30,34], it will become more important to develop methods which stimulate informed decision making. Further research should be done on how to present risks in a screening context in such a way that it is relevant for decisions. It is advisable to offer decision aids in order to help participants understand the risks [35].

Name of trial registry and registration number: Nederlands Trialregister; ISRCTN24427684; Link: http://www.trialregister.nl/trialreg/admin/rctsearch.asp?Term=risk%20perception
Pregnant women’s perceived risk and emotional well-being

REFERENCES


Does offering and performing prenatal screening influence pregnant women’s attachment to their unborn child?

Johanna H Kleinveld
Daniëlle RM Timmermans
Matthijs van den Berg
Jacques ThM van Eijk
Leo P ten Kate

Prenatal Diagnosis, 2007; 27(8): 757-64
ABSTRACT

Objective: The question addressed was: Does offering prenatal screening and receiving a negative screening outcome influence women's attachment to their unborn child?
Methods: Women were offered a nuchal translucency measurement, maternal serum screening, or no screening at all in a randomised controlled trial. Attachment was measured by a self-developed questionnaire at four points in time: before screening was offered, after the offer, after receiving the negative screening result (or at comparable points in time) and in the last trimester of pregnancy. In the last trimester, the Prenatal Attachment Inventory was also filled in.
Results: Women who had been offered screening \( (n=1031) \) showed more attachment \( F(1,1415)=19.42, p<.001 \) compared to women who had not been offered screening \( (n=387) \). This difference disappeared later in pregnancy. At all points in time, negatively screened women \( (n=466) \) had equal levels of attachment compared to screening decliners \( (n=565) \). No difference was observed between women who received a negative result of the ultrasound screening \( (n=285) \) as compared to the blood test screening \( (n=162) \).
Conclusion: Offering prenatal screening seems to temporarily increase attachment. However, this difference is very small. Attachment is not influenced by whether a blood screening or an ultrasound screening is performed.
INTRODUCTION

In order to survive, infants must be cared for by more mature human beings for many years [1]. Therefore, the bond between an infant and its mother is very important. This bond already starts to develop before birth and begins with the woman’s intellectual awareness that she is carrying a child inside her. It is followed later in pregnancy by a physical and kinaesthetic awareness of her unborn child [2]. This bond is referred to as ‘prenatal attachment’. Cranley defined it as ‘the extent to which women engage in behaviours that represent an affiliation and interaction with their unborn child’ [2], while Muller [3] emphasized the affiliative aspect: ‘The unique, affectionate relationship that develops between a woman and her foetus’. Prenatal attachment differs from postnatal attachment in that there are no opportunities for reciprocal interactions between a pregnant woman and her foetus [4].

The prenatal bond between a woman and her foetus is important because it is correlated with positive health practices during pregnancy like paying attention to one’s food intake and adhering to prenatal care regimens [5]. Furthermore, prenatal attachment is predictive of postnatal attachment, like being more involved while interacting with one’s baby [6,7].

Feelings of attachment begin early in pregnancy and increase with pregnancy duration [8,9]. However, its development might be influenced by prenatal testing. Caccia et al. [9] found that attachment increased significantly between pre- and postdiagnostic testing. However, since no control group was included, it cannot be left out of consideration that mothers undergoing diagnostic testing showed lower levels of prenatal attachment prior to testing, compared to those who were not.

An interview study with women who underwent amniocentesis showed that they distanced themselves emotionally from their pregnancies until the health of the foetus was confirmed by the test result [10]. Another study also showed that women who had had an amniocentesis done felt less attached both before the procedure and before the test results were made known, suggesting that women are putting their pregnancy ‘on hold’ until they receive a good test result [8]. These reactions may be adaptive; if the test result is unfavourable, women will have to choose whether or not to have an abortion.

Nowadays, prenatal screening tests are offered routinely in many countries. These tests give an estimation of the chance that the child has a certain abnormality. If the test shows an increased risk, women can choose to have a prenatal diagnostic test done to gain certainty about the presence or absence of the abnormality. Not much is known about the influence of offering prenatal screening and receiving a screening outcome on the development of attachment. Up till now, only one study has been concerned with this topic. In that study, women who had received a negative maternal serum screening result showed lower levels of attachment compared to women who had declined prenatal screening and diagnostic testing [11]. Since this study did not include a measure of attachment before screening was performed, it might
be possible that women who felt more attached were less inclined to have screening done. The present study aims to gain more insight into this.

Two prenatal screening tests that were often used at the time the present study was performed are the nuchal translucency measurement (NTM) and the maternal serum screening test (MST, triple test). Both give an estimation of the chance that the unborn child has Down syndrome. In addition, the MST gives information about the chance of neural tube defects. The NTM is an ultrasound test, while the MST is a blood test. Since seeing the baby through ultrasound might enhance feelings of attachment [9], it may be hypothesized that the NTM has a beneficial influence on attachment compared to the MST. However, another study did not find an effect of ultrasound scans [8]. One of the aims of the present study is to gain insight into whether there are differences in attachment depending on whether a woman undergoes an ultrasound (NTM) or a blood test (MST).

The present study includes a baseline measure and a control group consisting of women who were not offered screening. The formation of the control group was possible because at the time this study was performed, offering prenatal screening to pregnant women in the Netherlands who are not at increased risk of giving birth to a child with congenital defects was prohibited [12]. A special license for offering screening within the framework of this study was obtained from the Minister of Health, based on a positive advice of the Health Council of the Netherlands [13].

Questions addressed in this study are as follows:
1. Do women who choose to accept prenatal screening already have different attachment levels compared to women who decline screening before the screening test is offered?
2. Does offering prenatal screening influence attachment to the unborn child?
3. Does receiving a negative screening result influence attachment to the unborn child?
4. What is the longer term influence of having been offered prenatal screening and having received a negative screening result on attachment to the unborn child?

**PATIENTS AND METHODS**

This study is part of a larger research project that aims to give more insight into the risk perception, informed decision-making, and psychological well-being of pregnant women who are offered prenatal screening for congenital defects. The design of the study was approved by both the Minister of Health and the Institutional Review Board of the VU University Medical Center.

**Participants**

Midwifery and gynaecology practices in various parts of the Netherlands were approached, of which 44 consented to participate. These practices consisted of group and individual practices.
Does prenatal screening influence pregnant women’s attachment?

and were located in rural and urban areas. Pregnant women attending one of these practices from May 2001 to May 2003 were asked permission to be sent a research information letter. Only women with a gestational age of at most 16 weeks and command of the Dutch language were approached. The first information letter invited women to participate in a study for evaluating different kinds of pregnancy care without mentioning prenatal screening. A questionnaire that was sent to the midwifery and gynaecology practices showed that they approached nearly all women and that if any were not approached, this was due to lack of time or forgetfulness. Of the 4077 women who were approached, 2986 women (73%) gave informed consent and filled in the first questionnaire. Figure 1 shows the number of women who filled in the

Figure 1. Progress of the participants through the trial.
* Main reasons for dropping out were miscarriage or giving informed consent too late.

4077 women were invited to participate

2986 (73%) women gave IC and filled in the 1st questionnaire

Randomisation 2877

1091 (27%) women declined participation

109 (4%) women dropped out*

NTM

1066 offered NTM

844 (79%) women filled in the 1st and 2nd questionnaire

735 (69%) women filled in the 3rd and previous questionnaires

686 (64%) women filled in the 4th and previous questionnaires

MST

1061 offered MST

806 (76%) women filled in the 1st and 2nd questionnaire

686 (65%) women filled in the 3rd and previous questionnaires

648 (61%) women filled in the 4th and previous questionnaires

Control

750 not offered screening

627 (84%) women filled in the 1st and 2nd questionnaire

547 (73%) women filled in the 3rd and previous questionnaires

512 (68%) women filled in the 4th and previous questionnaires
subsequent questionnaires. Sixteen percent (188 cases) of the loss to follow-up (n=1140) was due to miscarriage. For analysis of nonresponse, all women who were asked to participate between September 2002 and January 2003 were sent a short questionnaire. Of these 259 women, 130 (50%) replied. The main reason for not participating in the study, or ceasing to participate, was lack of time or interest.

**Randomisation**

The NTM can only be performed between 10 and 14 weeks of pregnancy. To make sure that the pregnancy duration of women who were to be offered the NTM was not outside this range, we used two randomisation lists. Women with a gestational age of at most 10 weeks were randomised by us into three groups: a group that was given information about the nuchal translucency measurement (NTM), a group that received information about the maternal serum screening test (MST), or the control group. Women with a gestational age between 11 and 16 weeks were randomised into the MST or control group. One of the aims of the larger study was to draw conclusions about the group of positively screened women. Since only approximately 5% of women who have screening done receive a positive outcome, more women were randomised into the intervention groups than into the control group.

**Intervention**

Women in the intervention groups received information about prenatal screening by means of a booklet sent to their home and a consultation by the woman’s midwife or gynaecologist. The booklets had previously been pilot-tested for comprehensibility.

**Outcome measures**

We started measuring attachment very early in pregnancy. Therefore, existing instruments like the Prenatal Attachment Inventory (PAI) [3] and the Maternal Fetal Attachment Scale (MFAS) [2] were not sufficient since they include items that are not yet applicable at that time (e.g. item about quickening). We therefore developed our own questionnaire (see Appendix 1), based on the sort of items that were used in these existing questionnaires. These items are: ‘I look forward to the birth of my child’, ‘I try to imagine what my child will look like’, ‘I look after my health more now that I’m pregnant’, ‘I’m looking for things for the baby’, ‘I think about how I will bring up my child’. Since attachment to the pregnancy and development of a child are related [14] we also constructed items that we thought would capture the involvement with the pregnancy, especially because these items are applicable from the first moment a woman finds out she is pregnant. These items are: ‘I read information about pregnancy’, ‘Being pregnant makes me feel beautiful’, ‘I talk to other people about my pregnancy’, ‘I’m proud of my pregnancy’ and ‘I’m preoccupied with my pregnancy’. Factor analyses showed that these 10 items loaded on 1 factor. We therefore decided to use them as a one-dimensional scale: the Pregnancy Involvement List (PIL). Women could answer on a 5-point Likert scale ranging from 1 (‘absolutely not applicable’) to 5 (‘very applicable’). Mean scores were calculated.
Does prenatal screening influence pregnant women’s attachment?

Table 1. Background characteristics of the respondents

<table>
<thead>
<tr>
<th>Screening offered, (NTM or MST), declined (n=565)</th>
<th>NTM offered, accepted, negative screening result (n=285)</th>
<th>MST offered, accepted, negative screening result (n=162)</th>
<th>No screening offered, no screening done (n=359)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (M (SD))</td>
<td>30.28 (1.59)</td>
<td>30.30 (1.55)</td>
<td>30.31 (1.61)</td>
</tr>
<tr>
<td>Educational level (%) *</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>9</td>
<td>15</td>
<td>14</td>
</tr>
<tr>
<td>Medium</td>
<td>45</td>
<td>45</td>
<td>41</td>
</tr>
<tr>
<td>High</td>
<td>46</td>
<td>40</td>
<td>45</td>
</tr>
<tr>
<td>Nulliparae (%)</td>
<td>47</td>
<td>52</td>
<td>42</td>
</tr>
<tr>
<td>Gestational age in weeks (M (SD))</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>9.30 (2.24)</td>
<td>8.52 (1.82)</td>
<td>9.81 (2.35)</td>
</tr>
<tr>
<td>T2</td>
<td>12.61 (1.99)</td>
<td>11.47 (1.43)</td>
<td>13.39 (2.16)</td>
</tr>
<tr>
<td>T3</td>
<td>18.40 (3.29)</td>
<td>14.16 (1.35)</td>
<td>20.05 (1.95)</td>
</tr>
<tr>
<td>T4</td>
<td>30.28 (1.59)</td>
<td>30.30 (1.55)</td>
<td>30.19 (1.38)</td>
</tr>
</tbody>
</table>

* Low= comparable with primary school, lower secondary vocational education, junior general secondary education. Middle= comparable with senior secondary vocational education, ‘A’ levels (university or equivalent entrance). High= comparable with first degree level (university or equivalent).

Questionnaires were filled in at T1 (before screening was offered), T2 (after screening was offered or at a comparable point in time), T3 (after the screening result was received or at a comparable point in time) and T4 (last trimester of pregnancy).

NB: The data presented in this table are of the groups that were used for analyses at T3 and T4.

Cronbach’s alpha coefficient ranged between .79 and .81 at the various points in time. The item-scale correlations fell between .30 and .70. These data indicate that the PIL is a reliable measure.

According to the literature, attachment increases with pregnancy duration [8,9]. This increase is also reflected in the scores on the PIL, thereby giving some support to its construct validity. To assess the concurrent validity of the PIL, the PAI was administered at T4, when all its items are applicable. Cronbach’s alpha for the PAI in our study was .88. The PIL correlated reasonably well with the PAI ($r(1369)=.62, p<.001$), meaning that, for a large part, they measure the same construct. Since the PAI is an instrument that has been shown to reliably and validly measure attachment [3,15], this implies that the PIL also measures attachment for a large part.

Questionnaires

Participants were asked to fill in four postal questionnaires. All questionnaires included the Pregnancy Involvement List. The first questionnaire was sent before any information about screening was given, in other words, before women had to make a decision about whether or not to have screening done (T1). It included questions about demographic background such as age, education, and parity. The second questionnaire was filled in after women had read the booklet and had decided for or against prenatal screening (T2), but (if applicable) before they had received the screening result. The control group received this questionnaire at a comparable point in time. The third questionnaire was filled in after the screening result was
known or at a comparable point in time for women who chose not to be screened, or who were randomised into the control group (T3). In this questionnaire the women were asked whether they had had screening done and whether or not it had shown an increased risk. The fourth questionnaire was sent at 28 weeks of pregnancy (T4).

**Analyses**

The data were analysed cross-sectionally. Table 2 shows which groups are compared with each other to answer the research questions. For analysing question 1 ('Do screening acceptors already have different attachment levels compared to decliners before screening is offered?'), comparisons were made between screening acceptors and screening decliners. Question 2 ('Does offering prenatal screening influence attachment to the unborn child?') was analysed comparing the intervention group (i.e. screening acceptors and screening decliners) with women who had not been offered screening (the control group). For analysing questions 3 ('Does receiving a negative screening result influence attachment to the unborn child?') and 4 ('What is the longer-term influence of having been offered prenatal screening and receiving a negative screening result on attachment to the unborn child?') comparisons were made between women who were negatively screened on the NTM, women who were negatively screened on the MST, screening decliners, and an adapted control group. The adapted control group consists of women who were randomised into the control group excluding those who had screening done at their own request. So the 'control group' refers to a representative sample of Dutch pregnant women, while the 'adapted control group' refers to women who had not been offered screening and had not had screening done.

Table 2. Groups that were compared to each other to answer the research questions

| Do women who choose to accept prenatal screening have different attachment levels compared to women who decline screening before screening is offered? |
|---|---|
| T1 | Screening offered (NTM or MST), accepted (NTM or MST), declined |

| Does offering prenatal screening influence attachment to the unborn child? |
|---|---|
| T2 | Screening offered (NTM or MST) |

| Does receiving a negative screening result influence attachment to the unborn child? |
|---|---|
| T3 | Screening offered, NTM offered, MST offered, accepted, negative screening result |

| What is the longer term influence of having been offered prenatal screening and receiving a negative screening result on attachment to the unborn child? |
|---|---|
| T4 | Screening offered, NTM offered, MST offered, accepted, negative screening result |

NB: Questionnaires were filled in at T1 (before screening was offered), T2 (after screening was offered or at a comparable point in time), T3 (after the screening result was received or at a comparable point in time) and T4 (last trimester of pregnancy).
Does prenatal screening influence pregnant women’s attachment?

Data analyses were performed using ANOVAs. Post hoc tests with Bonferroni correction showed which groups differed statistically significantly. To gain a better insight into the effect of receiving a screening result, scores at T2 were used as a covariate when analysing data at T3. Analysis of background characteristics were performed by ANOVAs and chi-Square tests. Analyses were conducted using SPSS 11.0 (Statistical Package for Social Science, Inc., Chicago, Illinois, USA).

RESULTS

Analyses were based on those participants who had filled in the Pregnancy Involvement List at all points in time; 686 women in the NTM group, 648 women in the MST group, and 512 women in the control group (see Figure 1). Of these women, those of 36 years and older were excluded from the analyses since they could have opted to have a diagnostic test done directly (numbers excluded are: 66 (11%) women in the NTM group, 69 (12%) women in the MST group and 62 (14%) women in the control group). Approximately 9% of the remaining women had missing data and were therefore excluded. At T3 and T4, two additional groups were excluded from the analyses. The group of positively screened women was considered too small to include (n=19). And women in the control group who had screening done at their own request (7%) were excluded since they could confound the effect of receiving a screening result. The final numbers of the groups that were used for the analyses of the various research questions are shown in Table 3(a) and 3(b).

Table 3(a). Scores on the Pregnancy Involvement List of the groups that were compared at T1 and T2

<table>
<thead>
<tr>
<th>Screening offered (NTM or MST), screening offered (NTM or MST),</th>
<th>Screening offered (NTM or MST), screening offered (NTM or MST),</th>
<th>No screening offered (n=387)</th>
</tr>
</thead>
<tbody>
<tr>
<td>declined (n=565)</td>
<td>accepted (n=466)</td>
<td>(not included in these analyses )</td>
</tr>
<tr>
<td>M (SD)</td>
<td>M (SD)</td>
<td>M (SD)</td>
</tr>
<tr>
<td>T1 3.59 (.03)</td>
<td>3.60 (.03)</td>
<td></td>
</tr>
<tr>
<td>T2 3.78 (.02)</td>
<td>3.63 (.03)</td>
<td></td>
</tr>
</tbody>
</table>

NB: T1=before screening was offered, T2= after screening was offered or at a comparable point in time. At T2 the groups of women who declined or accepted screening were combined into one group; the group of women who were offered screening. Scores are corrected for pregnancy duration.

Table 3(b). Scores on the Pregnancy Involvement List of the groups that were compared at T3 and T4

| Screening offered, NTM offered, MST offered, No screening offered, no screening done |
|---------------------------------------------------------------|---------------------------------------------------------------|--------------------------------|
| (NTM or MST), accepted, negative screening result accepted, negative screening result (n=359) |
| (n=565)                                                       | (n=285)                                                       | (n=162)                         |
| M (SD)                                                        | M (SD)                                                        | M (SD)                               |
| T3* 3.86 (.02)                                                | 3.83 (.02)                                                    | 3.79 (.03)                        |
| T4 4.11 (.02)                                                 | 4.13 (.03)                                                    | 4.05 (.04)                        |

NB: T3=after the screening result was received or at a comparable point in time, T4=last trimester of pregnancy. Scores are corrected for pregnancy duration.

* Scores at T3 are also corrected for scores at T2.
Chapter 4

The number of negatively screened women in the NTM and MST groups differ because test uptake in the NTM group was higher [16]. The small number of positively screened women may be due to the way in which the NTM was performed in this study [17]. There were no significant differences between the groups in age, educational level or having children (Table 1). However, the pregnancy duration differed between the groups at the various points in time and was therefore included in the analyses as a covariate.

1. Do women who choose to accept prenatal screening already have different attachment levels compared to women who decline screening before screening is offered? (see Table 3(a))
   At baseline, no difference in attachment level was observed between screening acceptors and screening decliners ($F(1,1028)=0.14, p=.71$, partial eta squared=.000).

2. Does offering prenatal screening influence attachment to the unborn child? (see Table 3(a))
   After women had been offered prenatal screening, they had significantly higher attachment levels compared to women who had not been offered screening ($F(1,1415)=19.42, p<.001$, partial eta squared =.014).

3. Does receiving a negative screening result influence attachment to the unborn child? (see Table 3(b))
   After the screening result was received, when correcting for differences at T2, no significant difference was seen in attachment between negatively NTM screened women, negatively MST screened women, and screening decliners. Women who had not been offered screening (and had not had screening done at their own request) had significantly higher attachment scores compared to negatively MST screened women ($t(1365)=3.47$, Bonferroni $p=.003$, partial eta squared=.011), but not compared to negatively NTM screened women or screening decliners.

4. What is the longer-term influence of having been offered prenatal screening and receiving a negative screening result on attachment to the unborn child? (see Table 3(b))
   In the last trimester of pregnancy, no significant difference was observed in attachment scores between negatively NTM screened women, negatively MST screened women and screening decliners. Women who had not been offered screening (and had not had screening done at their own request) had significantly lower attachment levels compared to negatively NTM screened women ($t(1366)=-3.39$, Bonferroni $p=.004$,) and compared to screening decliners ($t(1366)=-3.29$, Bonferroni $p=.006$), but not compared to negatively MST screened women ($t(1366)=-1.15$, Bonferroni $p=1.0$) (partial eta squared=.011).

   Prenatal attachment as measured by the PAI did not differ significantly between negatively NTM screened women ($M=52.00, SD=.57$), negatively MST screened women ($M=52.11, SD=.75$), screening decliners ($M=51.56, SD=.41$) and women who had not been offered screening and had not had screening done at their own request ($M=52.28, SD=.51$) ($F(3,1296)=.446, p=.72$, partial eta squared=.001).
DISCUSSION

At baseline, when no prenatal screening test had been offered yet, women who would accept prenatal screening had the same level of attachment as women who would decline it as measured with the Pregnancy Involvement List. After women had been offered prenatal screening, they showed more attachment compared to women who had not been offered screening. After the test was performed, no differences were observed between women who had received a negative NTM result, women who had received a negative MST result, and screening decliners. Women who had not been offered screening and had not had screening done at their own request showed more attachment compared to women who had just received a negative MST result. In contrast, in the last trimester of pregnancy, women who had not been offered screening showed less attachment compared to women who had received a negative NTM result and screening decliners. However, no differences between the groups were observed in the last trimester on the PAI.

After having been offered a prenatal screening test, women felt more attached to their unborn child compared to women who had not been offered screening. Possibly, having to decide on accepting or declining screening made them more aware of their unborn child and might therefore have enhanced attachment. However, the effect size was very small. Therefore, the implications of these differences for the actual pregnancy experience could be considered negligible.

The only other study we are aware of on the influence of prenatal screening on attachment has been conducted by Lawson and Turiff-Jonasson [11]. In their study, women who received a negative screening outcome had lower levels of attachment compared to women who had an amniocentesis performed or who had declined screening and testing. This contrasts with our finding that negatively screened women had the same attachment level as screening decliners. Because Lawson & Turiff’s study did not include a baseline measure, it can not be excluded that some differences in attachment already existed before the test result was known.

A difference between Lawson & Turiff’s study and ours is the age of the participants. Lawson & Turiff hypothesize that since their study involved women at high age-related risk for foetal anomaly, these women need more definitive reassurance than younger women. Because of its probabilistic nature, a screening outcome is less reassuring than a diagnostic outcome and may therefore result in lower levels of attachment. Presuming that women with a lower age-related risk need less reassurance and that this would result in a smaller difference between screening acceptors and decliners, the result of our study is not necessarily in contradiction with that of Lawson and Turiff. It would imply that when offering prenatal screening special attention should be paid to women who are at higher risk for foetal anomaly.

Earlier research has shown that prenatal diagnostic testing may cause women to distance themselves emotionally from their pregnancy [8,10]. The bonding is restored only after a
negative diagnostic test result has been received. However, our study showed no evidence 
that a similar phenomenon would be applicable to prenatal screening; screening acceptors 
had the same level of attachment as screening decliners.

Even though there are some differences in attachment between women who had not been 
offered screening (and had not had screening done at their own request) and women who 
had received a negative screening result or who declined screening, the effect sizes of these 
differences are very small. We would therefore like to withhold ourselves from drawing practical 
implications based on these differences and would prefer to conclude that offering prenatal 
screening and receiving a negative screening result do not seriously influence attachment.

Research has shown contradictory findings of the effect of seeing images of the foetus (via 
ultrasound imaging); one study suggests that it facilitates bonding [9], while another suggests 
it has no effect on attachment [8]. In our study, having prenatal screening done in which 
the foetus is visible (NTM) did not lead to different attachment levels compared to having 
screening done in which the foetus is not visible (MST). However, the comparison might have 
been blurred a little because women who underwent an MST also had an ultrasound, although 
its purpose was to determine pregnancy duration.

A limitation of this study might be the self-developed questionnaire, which has not yet been 
validated. However, based on our analyses we suggest that our questionnaire measures 
attachment reasonably well. Literature reports that attachment increases with pregnancy 
duration [8,9] and this is reflected in our outcome measure. In addition, our instrument 
correlates reasonably well with a validated instrument - the PAI [3]. The reason the correlation 
between the PIL and the PAI is not stronger may be explained by their slightly different focus. 
The PAI focuses mainly on the here and now, while our child-related items are more future-
oriented (e.g.: ‘I wonder what the baby looks like now’, versus ‘I try to imagine what my child 
will look like’). In addition, the PIL includes items that concern involvement with the pregnancy, 
while the PAI does not.

We decided not to include positively screened women in the analyses due to their small 
number. It would however be interesting to observe what happens to the development of 
attachment in this group: these women are the ones who receive worrying news about the 
health of the foetus. Future research should investigate this.

In conclusion, offering prenatal screening seems to temporarily increase attachment. However, 
because this difference is very small, it is not considered to have an impact on the actual 
pregnancy experience. In addition, attachment seems not to be influenced by whether a blood 
screening or an ultrasound screening is performed.
Does prenatal screening influence pregnant women's attachment?

ACKNOWLEDGEMENT

This study was subsidised by the Netherlands Organization for Health Research and Development, project number 2200.0085. We would like to thank an anonymous reviewer for the valuable comments.

APPENDIX 1

Pregnancy Involvement List (PIL)
1. I'm looking forward to the birth of my child
2. I try to imagine what my child will look like
3. I read information about pregnancy
4. Being pregnant makes me feel beautiful
5. I talk to other people about my pregnancy
6. I look after my health more now that I’m pregnant
7. I’m looking for things for the baby
8. I’m proud of my pregnancy
9. I think about how I will bring up my child
10. I’m preoccupied with my pregnancy
REFERENCES

Does informed decision making influence psychological outcomes after receiving a positive screening outcome?

Johanna H Kleinveld
Leo P. ten Kate
Matthijs van den Berg
John M.G. van Vugt
Daniëlle R.M. Timmermans

Submitted
RESEARCH LETTER

Health care professionals and policy makers find it important that women are able to make an informed decision on whether or not to have prenatal screening performed [1]. Guidelines for screening programmes state that the benefits should outweigh any harmful psychological effect as a result of participating [2]. It is not yet clear, however, whether making an informed decision has a beneficial or unfavourable effect on pregnant women's psychological well-being [3]. Michie et al. [4] found that women who made an informed decision and those who did not make an informed decision did not differ in their anxiety levels after receiving a negative screening outcome. No studies have been performed on women who received a positive screening outcome. As receiving a positive screening outcome has a large emotional impact [3,5], it is relevant to know if women's reactions are affected by whether or not they had made an informed decision. This could have consequences for the way in which women should be counselled about screening.

We have collected data in the context of a large longitudinal study in which women were offered prenatal screening, and aimed to answer the following questions: Do women who made an informed decision and those who made an uninformed decision (1) differ in their emotional reaction when confronted with a positive screening test outcome? (2) differ in how much they feel pressurized, and feel able to decide on consecutive prenatal diagnostic testing?

In this large longitudinal study, midwifery and gynaecology practices in various parts of the Netherlands were approached of which 44 consented to participate. Pregnant women attending these practices between May 2001 and May 2003 were asked to participate in the study. Women were offered the nuchal translucency measurement (NTM) or the maternal serum screening test (MST, also called triple test). Both give an estimation of the chance that the unborn child has Down syndrome. The MST also gives information about the chance of neural tube defects. Women were sent a booklet with information about the prenatal screening test and a consultation with their midwife or gynaecologist. For more information about the larger study see Kleinveld et al. [6]. The design of the study was approved by both the Minister of Health and the Medical Ethics Committee of the VU University Medical Centre. For the present report, data were used of women who received a positive prenatal screening result.

The data were collected by questionnaires at various points in time. Before the screening test was performed, informed decision making was measured by an extended Multidimensional Measure of Informed Choice (MMIC, [7])[(8)]. According to this measure, an informed decision is based on deliberation and sufficient knowledge about the screening test, and is value-consistent, i.e.: to have screening performed when one has a positive attitude and to reject screening when one has a negative attitude. The women in the present study were classified as having made an informed decision if their attitude towards screening was positive, if
they possessed sufficient knowledge, and if they had deliberated upon the advantages and disadvantages of having screening performed. The knowledge-scale consisted of 7 (NTM group) or 10 (MST group) ‘yes’/’no’ questions. It was dichotomised at the guess-corrected midpoint. The deliberation-scale consisted of 6 5-point Likert items and was dichotomised at the midpoint of the scale. For more information about these scales, see Van den Berg et al. [8]. Since the number of respondents in the present study is small, we chose to dichotomise the attitude scale so as to be able to include as many women as possible for the analyses. Women whose score was at the midpoint of the attitude scale (n=2) were categorised as being value-inconsistent, as was also done by Michie et al. [4].

The outcomes were measured by a questionnaire after women had received the positive screening outcome. The emotional reaction to the screening outcome was measured by 4 items: ‘I felt disappointed by the test outcome’, ‘I regretted having had the (MST/NTM) done’, ‘I was shocked by the test outcome’ and ‘I became/stayed insecure by the test outcome’. The variables were measured on a 5-point Likert scale, ranging from ‘not at all applicable’ to ‘very applicable’. Cronbach’s alpha coefficient was 0.61, which is sufficient. Perceived pressure was measured by the item ‘When making the decision, I felt pressurized by others’. Feeling able to decide about diagnostic testing was measured by the item ‘I thought I was very well able to decide whether or not to have the amniocentesis or chorionic villus sampling done’. These variables were measured on a 5-point Likert scale, ranging from ‘absolutely disagree’, to ‘totally agree’.

The data were analysed by means of independent T-tests. Comparison of background characteristics was performed by Fischer’s exact tests. Analyses were conducted using SPSS 14.0 (Statistical Package for Social Science, Inc., Chicago, Illinois, USA).

Results of the study were as follows. 1650 women were offered screening, 1421 of whom returned the questionnaires. Of these women, 625 (44%) had the test done and had returned the questionnaires. Of the 625 women who chose to have prenatal screening done, 21 received a positive screening result. After women received the positive screening outcome, they were given the choice whether or not to have a diagnostic test performed to gain certainty about the presence or absence of the abnormality. Fifteen women chose to have a diagnostic test done. All of these outcomes were favourable.

Because of missing values, we have data of 19 out of the 21 women concerning the reaction to the screening outcome, and of 18 women concerning the items about diagnostic testing (the extra missing value was of a woman who had not made an informed decision). Seven women (35%) made an informed decision. Two women did not make an informed decision because of value inconsistency, 3 women because of lack of deliberation, 4 women were not value-consistent and had not deliberated, 2 women had insufficient knowledge, 1 woman had both insufficient knowledge and lack of deliberation. Table 1 shows the background characteristics of women who made an informed decision and women who made an uninformed decision.
Does informed decision making influence psychological outcomes?

Table 1. Background characteristics of women who had received an increased screening outcome divided into women who made an informed decision (n=7) and women who had not made an informed decision (n=12).

<table>
<thead>
<tr>
<th></th>
<th>Informed decision</th>
<th>No informed decision</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 26</td>
<td>0 (0)</td>
<td>1 (8)</td>
</tr>
<tr>
<td>26-30</td>
<td>1 (14)</td>
<td>4 (33)</td>
</tr>
<tr>
<td>31-35</td>
<td>6 (86)</td>
<td>7 (58)</td>
</tr>
<tr>
<td>&gt;35</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Educational Level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>0 (0)</td>
<td>1 (8)</td>
</tr>
<tr>
<td>Middle</td>
<td>4 (57)</td>
<td>8 (67)</td>
</tr>
<tr>
<td>High</td>
<td>3 (43)</td>
<td>3 (25)</td>
</tr>
</tbody>
</table>

The Fischer’s exact tests did not show any significant difference on these items between the groups.

Women who made an informed decision seemed to have a less adverse emotional reaction when confronted with the positive screening outcome compared to women who did not make an informed decision ($M=3.7$, $SD=0.76$ and $M=4.4$, $SD=0.62$ respectively, $t(17)=2.18$, $p=.043$). They also seemed to feel more able to make a decision about whether or not to have a prenatal diagnostic test done ($M=4.7$, $SD=0.49$ and $M=3.8$, $SD=0.87$, respectively, $t(16)=-2.46$, $p=.026$). No significant difference was found between women who made an informed decision and those who did not, concerning feeling pressurized by others when deciding about prenatal diagnostic testing ($M=1.4$, $SD=0.54$ and $M=1.8$ and $SD=0.60$, respectively, $t(16)=1.39$, $p=.183$).

In conclusion, compared to women who had not made an informed decision, those who had made an informed decision about prenatal screening seemed to have a less adverse emotional reaction when confronted with the screening outcome and seemed to feel more able to make a decision about prenatal diagnostic testing. This implies that from a psychological point of view, women should be stimulated to make an informed decision. Pregnancy counsellors could play a role in helping women to make value-consistent decisions, based on sufficient knowledge and deliberation. In addition, decision aids have been shown to be a useful tool in enhancing informed decision making [9], and could be used more in prenatal counselling.

The strength of the present study is its longitudinal design. This allowed us to measure informed decision making at the time the decision was made, and to prevent a recall bias that could have occurred if measuring had taken place after the test result was known. As we measured the outcome variables within a few days after the screening result had been received, this also limits a recall bias.

A limitation of this study is the small number of women who received a positive screening result, which makes the results less reliable. Furthermore, as our results might be sensitive to
Chapter 5

development issues. In the framework of the local context, the scattered typing in
can be expected. However, the randomized design, the sample selection,
and the data collection methods all contributed to the internal validity of the
study. The study population was representative of the general population
in terms of age, gender, and educational level. The response rate was
sufficiently high to ensure the external validity of the study. The study
procedures were standardized and monitored to maintain the internal
validity of the study. The study findings have implications for
healthcare providers, policymakers, and the general public. The
findings suggest the need for further research to develop
interventions that are effective in improving the mental
development of children in the local context.

ACKNOWLEDGEMENT

This study was subsidized by the Netherlands Organization for Health Research and
Development, project number 2200.0085.
Does informed decision making influence psychological outcomes?

REFERENCES

Does offering prenatal screening influence pregnant women’s attitudes regarding prenatal testing?

Johanna H Kleinveld
Matthijs van den Berg
Jacques TM van Eijk
John MG van Vugt
Gerrit van der Wal
Daniëlle RM Timmermans

Community Genetics 2008; 11: 368-374
Chapter 6

ABSTRACT

**Objective**: This study aims to find out whether offering prenatal screening for Down syndrome and neural tube defects influences pregnant women’s attitudes toward having a screening test.

**Methods**: Women were randomised into a group that was offered prenatal screening and a group that was not offered screening (controls). Both groups completed questionnaires before screening was offered, after the offer, and in the last trimester of pregnancy.

**Results**: Women with a neutral attitude at baseline who accepted the screening test had a more positive attitude, decliners became more negative and the attitude of the control group did not change.

**Conclusion**: Offering prenatal screening triggers a change in some pregnant women’s attitude regarding prenatal testing. This instability of women’s attitudes may pose a problem for determining whether some women made an informed choice.
INTRODUCTION

The decision of whether or not to have prenatal screening can have important consequences. If the screening test shows an increased risk, a decision has to be made concerning diagnostic testing, which involves a risk of unintended foetal loss [1]. In the case of an unfavourable diagnostic outcome, parents have to make a decision concerning abortion. Policy makers and health professionals find it important that parents are able to make an informed decision about whether or not to screen [2]. A requirement for making an informed decision is that the choice is consistent with the decision maker’s values [3-5]. When studying informed decision making, values are measured by attitudes [3,6,7], which can be defined as ‘a psychological tendency that is expressed by evaluating a particular entity with some degree of favour or disfavour’ [8]. Research shows that attitudes are not stable and can be influenced by behaviour [8,9]. This raises the question of how attitudes change when a decision has to be made on whether to accept or decline prenatal screening, and what this implies for measuring informed decision making.

In the Netherlands, at the time this study was performed, offering prenatal screening to pregnant women who are not at increased risk of giving birth to a child with congenital defects was prohibited [10]. A special license for offering prenatal screening within the framework of this study was therefore obtained from the Minister of Health [11]. Because of this unique situation, it was possible to study the effect of offering a prenatal screening test on attitudes regarding prenatal testing, since we were able to measure the attitudes before women were aware they would have to make a choice between accepting and declining prenatal screening. In addition, we were able to compare attitudes between women who have, and women who have not been offered prenatal screening.

The questions addressed in this study are: (1) Does offering prenatal screening influence attitudes regarding prenatal testing? (2) Does having prenatal screening influence attitudes regarding prenatal testing? (3) What do these changes in attitude imply for informed decision making?

METHODS

Setting
This study is part of a longitudinal randomised controlled research project, aiming to give more insight into the risk perception, informed decision making, and psychological well-being of pregnant women who are offered prenatal screening for congenital defects. In this study, women were offered the nuchal translucency measurement (an ultrasound test) or a maternal serum screening test (a blood test, also called triple test).
Midwifery and gynaecology practices in various parts of the Netherlands were approached until a sufficient number (n=44) consented to participate to provide a representative sample of both group and individual practices in rural and urban areas.

Participants
Pregnant women attending one of these practices from May 2001 till May 2003 were asked permission to be sent a research information letter. Only women with a gestational age of at most 16 weeks and command of the Dutch language were approached. The first information letter invited women to participate in a study for evaluating different kinds of pregnancy care. Prenatal screening was not mentioned.

Randomisation
After informed consent was granted, women were randomised into three groups: a group that was given information about the nuchal translucency measurement (NTM), a group that received information about the maternal serum screening test (MST), and a control group that was not offered screening. The NTM can only be performed between 10 to 14 weeks of pregnancy. To make sure that the pregnancy duration of women who would be offered the NTM was not beyond this range, women who gave consent after 10 weeks were randomised into either the MST group or the control group.

Intervention
The women received information about the prenatal screening test by means of a booklet sent to their home and a consultation by their midwife or gynaecologist. The booklets had been pilot-tested for their comprehensibility. If women chose to accept the screening test, a separate visit was required to have the test performed.

Questionnaires
Participants were asked to fill in four postal questionnaires at several points in time. Attitudes of the intervention groups were measured in all questionnaires except the third. Attitudes of the control group were only measured in the first and fourth questionnaire. The first questionnaire was sent before any information about screening was given, i.e. before they had to decide about accepting or declining prenatal screening (T1). The second questionnaire was filled in after women had been offered prenatal screening (T2). The third questionnaire was filled in after the test result was known, or at a comparable point in time for women who chose not to be screened or who had been randomised into the control group (T3). Women were asked if they had had the screening test done, and whether or not the test had shown an increased risk. The fourth questionnaire was sent at 28 weeks of pregnancy (T4).
Does prenatal screening influence pregnant women’s attachment?

Outcome measures
Attitude regarding having a prenatal test done was measured by a self-developed Attitude Scale [12]. It consisted of the statement ‘In my opinion, testing for congenital defects during my pregnancy is…’, which was followed by 4 items consisting of opposite word pairs (bad/good, frightening/not frightening, not reassuring/reassuring, not self-evident/self-evident). Women had to answer on 5-point semantic differential scales. The internal consistency of the scale was high at all time points (Cronbach’s alpha around 0.79). Mean scores on the Attitude Scale were calculated, so the final scores ranged from 1 (negative attitude) to 5 (positive attitude).

Analyses
We divided the women into groups with a negative attitude (total scores for all four attitude items 1 through 10), a neutral attitude (total scores 11 through 13), and a positive attitude (total scores 14 through 20) at baseline (see also [13]). These three groups were then each divided into subgroups that either accepted the screening test or declined it. To analyse question 1 (‘Does offering prenatal screening influence attitudes regarding prenatal testing?’), we compared attitudes at T1 and T2. To analyse question 2 (‘Does having screening influence attitudes regarding prenatal testing?’), we compared attitudes at T2 and T4. Because we did not have attitude scores of the control group at T2, we conducted separate analyses comparing scores of the control group with screening acceptors and decliners at T1 and T4. Difference scores were calculated and compared between groups using ANOVAs. Post-hoc tests with Bonferroni correction were used in the analyses with three groups. T-tests were used to analyse within-group differences. Results of the NTM and MST groups did not differ, therefore data of these groups were combined. Gestational age did not influence attitudes and was therefore not included in the analyses.

Screening acceptors with a positive attitude and screening decliners with a negative attitude were categorised as value-consistent. Screening acceptors with a negative attitude and screening decliners with a positive attitude were categorised as value-inconsistent.

Analyses were conducted using SPSS 14.0 (Statistical Package for Social Science, Inc., Chicago, Illinois, USA).

RESULTS
Of the 4,077 women approached, 2,986 (73%) gave informed consent and filled in the first questionnaire. Analyses were based on those participants who had filled in the questionnaires at all points in time (n=1,846): 686 women in the NTM group, 648 women in the MST group and 512 women in the control group (Figure 1). Of these women, 46 had did not fill in the Attitude Scale completely and were therefore excluded. Women who had received a positive screening result (n=20) was too small to be included in the analyses. Women whose screening result was unknown (n=39) were also excluded. Women of 36 years and older were excluded as they could have opted to have a diagnostic test done directly (n=169). In addition, women in the
Chapter 6

Figure 1. Progress of the participants through the trial.

* Main reasons for dropping out were miscarriage or giving informed consent too late.
control group who had screening done at their own request were excluded \((n=43)\). The total number of women included in the analyses is 1,529.

**Does offering prenatal screening influence attitudes regarding prenatal testing? (T1-T2)**

**Negative attitude group** (Table 1). Attitudes of both screening acceptors \(t(74)=-9.21, p<.001\) and decliners \(t(297)=-6.43, p<.001\) became more positive. However, acceptors became more positive than decliners \(F(1,372)=50.17, p<.001\).

**Neutral attitude group** (Table 2). Attitude change differed between screening acceptors and decliners \(F(1,326)=88.43, p<.001\). Attitudes of acceptors became more positive \((t(138)=-5.86, p<.001)\), while those of decliners became more negative \(t(187)=7.55, p<.001\).

**Positive attitude group** (Table 3). Both screening acceptors \(t(264)=5.99, p<.001\) and decliners \(t(162)=15.39, p<.001\) became more negative. However, decliners became more negative than acceptors \(F(1,427)=106.92, p<.001\).

---

**Table 1. Mean attitude scores and standard deviations of women with a negative attitude at baseline.**

<table>
<thead>
<tr>
<th>Attitude Score</th>
<th>T1</th>
<th>T2</th>
<th>T4</th>
<th>T1-T2</th>
<th>T2-T4</th>
<th>T1-T4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accepted</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>screening</td>
<td>2.2 (VI)</td>
<td>3.0 (NL)</td>
<td>3.1 (NL)</td>
<td>-0.8</td>
<td>-0.1</td>
<td>-0.9</td>
</tr>
<tr>
<td></td>
<td>(.35)</td>
<td>(.71)</td>
<td>(.72)</td>
<td>(.71)</td>
<td>(.66)</td>
<td>(.74)</td>
</tr>
<tr>
<td>Declined</td>
<td>2.0 (VC)</td>
<td>2.2 (VC)</td>
<td>2.3 (VC)</td>
<td>-0.2</td>
<td>-0.1</td>
<td>-0.3</td>
</tr>
<tr>
<td></td>
<td>(.44)</td>
<td>(.58)</td>
<td>(.61)</td>
<td>(.57)</td>
<td>(.61)</td>
<td>(.61)</td>
</tr>
<tr>
<td>Controls</td>
<td>2.1</td>
<td>2.4</td>
<td>.1</td>
<td>-0.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(.44)</td>
<td>(.68)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(n=75)</td>
<td>(n=298)</td>
<td>(n=154)</td>
<td>(n=154)</td>
<td>(n=154)</td>
<td>(n=154)</td>
</tr>
</tbody>
</table>

**NB:** T1: before screening was offered, T2: after screening was offered, T4: at 28 weeks of pregnancy. VI= Value-inconsistent, NL=Neutral, VC= Value-consistent.

**Table 2. Mean attitude scores and standard deviations of women with a neutral attitude at baseline.**

<table>
<thead>
<tr>
<th>Attitude Score</th>
<th>T1</th>
<th>T2</th>
<th>T4</th>
<th>T1-T2</th>
<th>T2-T4</th>
<th>T1-T4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accepted</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>screening</td>
<td>3.1 (NL)</td>
<td>3.4 (VC)</td>
<td>3.6 (VC)</td>
<td>-0.3</td>
<td>-0.2</td>
<td>-0.5</td>
</tr>
<tr>
<td></td>
<td>(.34)</td>
<td>(.69)</td>
<td>(.70)</td>
<td>(.68)</td>
<td>(.59)</td>
<td>(.69)</td>
</tr>
<tr>
<td>Declined</td>
<td>3.0 (NL)</td>
<td>2.7 (VC)</td>
<td>2.7 (VC)</td>
<td>0.3</td>
<td>-0.1</td>
<td>0.3</td>
</tr>
<tr>
<td></td>
<td>(.19)</td>
<td>(.62)</td>
<td>(.65)</td>
<td>(.61)</td>
<td>(.64)</td>
<td>(.66)</td>
</tr>
<tr>
<td>Controls</td>
<td>3.0</td>
<td>2.9</td>
<td>.1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(.18)</td>
<td>(.69)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(n=139)</td>
<td>(n=188)</td>
<td>(n=112)</td>
<td>(n=112)</td>
<td>(n=112)</td>
<td>(n=112)</td>
</tr>
</tbody>
</table>

**NB:** T1: before screening was offered, T2: after screening was offered, T4: at 28 weeks of pregnancy. NL=Neutral, VC=Value-consistent.
Chapter 6

Table 3. Mean attitude scores and standard deviations of women with a positive attitude at baseline.

<table>
<thead>
<tr>
<th>Attitude Score</th>
<th>T1</th>
<th>T2</th>
<th>T4</th>
<th>T1-T2</th>
<th>T2-T4</th>
<th>T1-T4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accepted screening</td>
<td>4.2 (VC)</td>
<td>3.9 (VC)</td>
<td>3.9 (VC)</td>
<td>0.2</td>
<td>-0.0</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td>(.52)</td>
<td>(.65)</td>
<td>(.65)</td>
<td>(.64)</td>
<td>(.69)</td>
<td></td>
</tr>
<tr>
<td>n=265</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Declined screening</td>
<td>4.0 (VI)</td>
<td>3.0 (NL)</td>
<td>3.1 (NL)</td>
<td>1.0</td>
<td>-0.0</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>(.46)</td>
<td>(.80)</td>
<td>(.78)</td>
<td>(.78)</td>
<td>(.87)</td>
<td></td>
</tr>
<tr>
<td>n=163</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Controls</td>
<td>4.0</td>
<td>3.3</td>
<td>0.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(.46)</td>
<td>(.82)</td>
<td>(.82)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=135</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NB: T1: before screening was offered, T2: after screening was offered, T4: at 28 weeks of pregnancy.
VI= Value-inconsistent, NL=Neutral, VC= Value-consistent.

Table 4. Value-consistency of women (n=1128)

<table>
<thead>
<tr>
<th></th>
<th>T1</th>
<th>T2</th>
<th>T4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value-consistent</td>
<td>563 (50%)</td>
<td>685 (61%)</td>
<td>644 (57%)</td>
</tr>
<tr>
<td>Value-inconsistent</td>
<td>238 (21%)</td>
<td>133 (12%)</td>
<td>121 (11%)</td>
</tr>
<tr>
<td>Neutral</td>
<td>327 (29%)</td>
<td>310 (28%)</td>
<td>363 (32%)</td>
</tr>
</tbody>
</table>

NB: T1: before screening was offered, T2: after screening was offered, T4: at 28 weeks of pregnancy.

Does having screening influence attitudes regarding prenatal testing? (T2-T4)

Negative attitude group (Table 1). The attitude of screening acceptors did not change ($t(74)=-1.50, p=.139)$, while the attitude of decliners became more positive ($t(297)=-3.00, p=.003$). However, attitude change did not differ significantly between acceptors and decliners ($F(1,372)=0.01, p=.924$).

Neutral attitude group (Table 2). The attitude of screening acceptors became more positive ($t(138)=-3.46, p=.001$), while the attitude of decliners did not change ($t(187)=-1.08, p=.283$). Attitude change did not differ significantly between acceptors and decliners ($F(1,326)=3.09, p=.080$).

Positive attitude group (Table 3). The attitude of screening acceptors ($t(264)=0.17, p=.866$) and decliners did not change ($t(162)=-0.03, p=.980$). Attitude change did not differ between acceptors and decliners ($F(1,427)=.01, p=.907$).

Does offering prenatal screening and actually having screening influence attitudes regarding prenatal testing? Comparisons with control group. (T1-T4).

Negative attitude group (Table 1). The control group became more positive ($t(153)=-6.40, p<.001$). Women became less positive compared to screening acceptors ($t(228)=5.94, p<.001$), but changed as much as decliners ($t(225)=0.30, p>.999$).

Neutral attitude group (Table 2). Attitudes of the control group did not change ($t(111)=0.82, p=.415$). Attitude change of the control group differed from that of acceptors ($t(250)=-6.57, p<.001$) and decliners ($t(299)=2.89, p=.012$).
Does prenatal screening influence pregnant women's attachment?

*Positive attitude group* (Table 3). The control group became more negative ($t(134)=9.09, p<.001$). Attitude change of the control group differed from that of screening acceptors ($t(399)=-4.84, p<.001$) and decliners ($t(297)=3.65, p=.001$).

*What do these changes in attitude imply for informed decision making? (Table 4)*

Before screening was offered, 50% of the women were value-consistent. After screening was offered, this number had risen to 61%. At 28 weeks of pregnancy, 57% of the women had an attitude in line with their decision.

Before screening was offered, 21% of the women were value-inconsistent. After screening was offered, this number fell to 12%. At 28 weeks of pregnancy, 11% of the women were value-inconsistent.

The number of women with a neutral attitude stayed approximately the same at all points in time (29%, 28%, and 32%).

**DISCUSSION**

Offering prenatal screening to pregnant women may trigger a change in their attitude regarding prenatal testing for congenital anomalies. Women with a neutral attitude at baseline became more positive when accepting the screening test and more negative when declining the test. Attitudes of both acceptors and decliners with a negative attitude at baseline became more positive, although acceptors became more positive than decliners. Both acceptors and decliners with a positive attitude at baseline became more negative, but decliners became more negative than acceptors. After the screening test was performed, no difference in attitude change was observed between screening acceptors and decliners. Attitudes of women who had not been offered screening, and who had a neutral attitude at baseline, did not change over time. Attitudes of women who had a negative or positive attitude at baseline, and who had not been offered screening, became less extreme. After screening was offered, more women were value-consistent than before screening was offered.

After prenatal screening was offered, attitudes of women who were neutral at baseline changed in the direction of their choice. This may be explained by Differentiation and Consolidation (Diff Con) Theory [14,15]. According to Diff Con Theory a decision is made once the differences in attractiveness between the alternatives are big enough. In other words, when the attractiveness of having prenatal screening (which we measured by means of attitude) is sufficiently positive (or negative) compared to not having screening, the decision is made. This process is called differentiation. In line with this theory, women with a neutral attitude at baseline who were not offered screening, and therefore did not have to make a decision, showed no change in attitude over time.

Even though attitude is a strong predictor of uptake [7,16], other factors which may lead women to make a value-inconsistent decision play a role. A study of Dormandy *et al*. showed...
that more women with a positive attitude declined the test when a separate visit was required compared to when it was part of a routine visit [17]. In our study a separate visit was required to have the test performed, which may have been a practical barrier for some women. Cognitive Dissonance Theory states that when someone can not change or revoke a decision, dissonance is reduced by selectively favouring information that is congruent with the decision [18]. This might explain why attitudes became more consistent with the behaviour of women who, for some reason, acted against their baseline attitude. A change in attitude such that it fits the decision, has also been found in other studies [9].

Another possibility for a change in attitudes may be the information women received about the screening tests, e.g. learning that prenatal screening is safe for the unborn child, but does not give certainty. A previous study of ours has shown that a main reason for accepting the screening test is that it does not involve a risk for the unborn child, while a main reason for declining the screening test is that it does not provide certainty [19]. The present study cannot distinguish between an effect of decision making or an effect of knowledge. In order to be able to make such a distinction, one would have to offer prenatal screening without giving any information about the test. Apart from the question of whether this is possible at all (offering screening involves giving at least some information), it would raise ethical difficulties, as an important aspect of informed decision making is that women have sufficient knowledge about the test [3]. A study on the relationship between knowledge about the screening test and attitude suggested that these are not associated with each other [7]. However, this study concerned women who had already been offered screening and the results might therefore not be generalisable to our study in which women were not familiar with prenatal screening.

Average scores of women with a positive or negative attitude became less extreme. This cannot be ascribed to the offer of prenatal screening, since the same pattern was visible in women who had not been offered screening. Possibly, the phenomenon of extreme scores becoming less extreme is due to the effect of regression to the mean.

Having a prenatal screening test done does not seem to influence attitudes; no difference in attitude change was observed between acceptors and decliners of screening. The present study, however, concerned women who had received a favourable screening result. Results might be different for women who had received an unfavourable screening result.

The group of women who had not been offered screening could be considered to consist of potential acceptors and decliners. Therefore, one would expect their scores to lie in between those of the intervention groups. This is indeed the case in women with a neutral or positive attitude at baseline. However, in women with a negative attitude at baseline, the control group showed a similar change in attitude compared to women who declined screening. This implies that offering prenatal screening does not have an effect on attitude in women with a negative
Does prenatal screening influence pregnant women’s attachment?

attitude who decline the screening test. Since people have a preference for attitudinally consistent information [20,21], it might be hypothesized that these women put away the leaflet immediately and did not make a deliberate decision on accepting or declining screening.

Before screening was offered, there was a group of women with a neutral attitude, who, after the offer, became either positive or negative, depending on whether they had accepted or declined the test. In the last trimester of pregnancy, the group of women with a neutral attitude, consisted of initially positive women who had declined the screening test, and initially negative women who had accepted the screening test. So even though at all points in time, there was a group of women with a neutral attitude, the composition of this group differs.

Future parents should be able to make informed decisions about whether or not to have a screening test[2]. A key component of making informed decisions is that women act according to their values. Attitudes can be considered to be a reflection of one’s values and are used as such in research [3,6,7]. However, as the present study implies, when making a decision about whether or not to have prenatal screening, attitudes change. If attitude is measured before the decision is made, some women would be incorrectly defined as having made an uninformed choice. So, in order to measure informed choice, attitudes should be assessed at the moment the decision is made.

In conclusion, our results suggest that when women are offered prenatal screening, their attitudes on prenatal testing may change. This instability of women’s attitudes regarding prenatal screening poses a problem when determining whether some women really made an informed decision in accordance with their own values.

ACKNOWLEDGEMENT

This project was subsidized by the Netherlands Organization for Health Research and Development, project number 2200.0085
Chapter 6

REFERENCES

Does prenatal screening influence pregnant women’s attachment?


The decision for or against prenatal screening in relation to pregnant women’s values

Johanna H Kleinveld
Gerrit van de Wal
Dirk L Knol
John MG van Vugt
Daniëlle RM Timmermans

Submitted
Chapter 7

ABSTRACT

Objective: In many western countries prenatal screening tests are offered to pregnant women to give an indication of the risk that their unborn child has Down syndrome. In cases where there is an increased risk, women are offered invasive diagnostic testing to gain certainty. However, these tests involve the risk of a procedure-related miscarriage. Some health professionals and policy makers fear that women decide too easily to accept the risk-free screening test without considering the possible consequences. It is therefore particularly important that pregnant women make decisions in accordance with their values. We aimed to gain insight into what values women who accept and women who decline prenatal screening assign to various pregnancy outcomes.

Methods: Values assigned to various pregnancy outcomes were measured by a Visual Analogue Scale (VAS) at the time women had to take a decision concerning prenatal screening (a nuchal translucency measurement). Pregnancy outcomes were: having a healthy child or a child with Down syndrome (DS), losing a healthy child or a child with DS through a spontaneous or procedure-related miscarriage, losing a child with DS through a chosen abortion.

Results: Acceptors of screening (n=303) assigned a lower value to having a child with DS than to a procedure-related miscarriage or an abortion of a child with DS (t(560)=−5.24, \( p_{adj}<.001 \) and \( t(560)=-4.21, \ p_{adj}<.001 \), respectively), whereas this is the reverse in women who declined screening (n=266) (t(560)=4.96, \( p_{adj}<.001 \) and \( t(560)=5.37, \ p_{adj}<.001 \), respectively.) Both acceptors and decliners assigned the lowest value to having a procedure-related miscarriage of a healthy child.

Conclusion: Women who accept prenatal screening seem less averse to taking action to prevent having a child with Down syndrome. However, both groups prefer having a child with DS to having a procedure-related miscarriage of a healthy child. This is not in accordance with some cut-off scores for offering invasive diagnostic testing that imply that these outcomes are valued equally. Therefore, it is important that women who have received an increased screening result are aware of their own values, and understand that the decision to have diagnostic testing done is not a self-evident next step.
INTRODUCTION

In many western countries, pregnant women are offered prenatal screening tests [1]. These tests provide an estimation of the chance that the unborn child will have a certain abnormality, like Down syndrome (DS). When an increased chance is indicated, women are offered a prenatal diagnostic test to gain certainty. Two widely-used diagnostic tests are the chorionic villus sampling and the amniocentesis. However, these diagnostic tests induce a miscarriage in 0.3-0.5% of cases [2]. Therefore, in most countries, they are only offered to pregnant women of 35 years or older. In this group, the chance of having a procedure-related miscarriage is the same as, or lower than, the age-related chance of having a child with Down syndrome.

So, women who choose to have a prenatal screening test performed may be confronted with a choice of accepting or declining invasive prenatal diagnostic testing, and may even have to decide about whether or not to terminate their pregnancy. Some politicians and health professionals fear that, because prenatal screening tests are safe for the unborn child, women have this test performed without thinking through the possible consequences [3,4]. In case of an increased screening outcome, women may feel drawn further into the screening trajectory and make choices that do not correspond to their values. We tried to gain insight into whether or not this fear is justified. We investigated what values pregnant women who are deciding about a prenatal screening test, attach to the various pregnancy outcomes (e.g. having a child with DS, having a procedure-related miscarriage). Do these values correspond to what may happen further in the trajectory? If that is the case, one would expect screening acceptors to value having a child with DS less than a procedure-related miscarriage and an abortion of a child with DS. Among screening decliners, the opposite would be expected. Of course, termination of pregnancy after an unfavourable diagnostic test outcome is not the only option. Parents can also choose to prepare themselves for the birth of a child with a congenital abnormality. But numbers show that around 90% of women who receive an increased screening test result choose to have diagnostic testing done [5]. And around 71% of women who receive an unfavourable diagnostic test result for Down syndrome or a neural tube defect choose to terminate their pregnancy [6].

Although research has been conducted on values that pregnant women assign to pregnancy outcomes, hardly any research has differentiated clearly between screening acceptors and decliners. Kuppermann et al. found that, among women under 35 years of age, both acceptors and decliners of prenatal testing assigned a higher value to a procedure-related miscarriage compared to having a child with DS [7]. However, the group of acceptors in Kupperman et al.’s study consisted not only of women who had screening done, but also of women who had diagnostic testing performed. Chan et al. compared women who had prenatal screening done with women who had no screening performed [8]. Both groups preferred having a procedure-related miscarriage to having a child with DS. Yet, some of the women who had no screening done may not have been offered it or may not have been able to afford it.
Chapter 7

As our aim is to determine how women who have to make a decision about accepting or declining prenatal screening value different pregnancy outcomes, we also looked at other possible outcomes, i.e. having a healthy child, losing a healthy child or a child with DS through a spontaneous miscarriage, and having a chosen abortion. In order to find out whether the values of women who decide about prenatal screening already reflect the consequences of the possible follow-up trajectory, the present study addresses the following questions: (1) What values are assigned to pregnancy outcomes by women who accept prenatal screening?, (2) What values are assigned to pregnancy outcomes by women who decline prenatal screening?

METHODS

Design
This study is part of a larger research project that aims to provide more insight into the risk perception, informed decision-making, and psychological well-being of pregnant women who are offered prenatal screening for congenital defects. The project concerns a randomised controlled trial in which women were offered a nuchal translucency measurement (NTM), a maternal serum screening test (MST) or no screening. The NTM is an ultrasound screening which is performed between 10-14 weeks of pregnancy and indicates the chance that the child has DS. The MST estimates both the chance of having a child with DS and the chance of having a child with a neural tube defect. Because the possible pregnancy outcomes of the MST group differed from that of the NTM group, their values were not comparable. We decided to restrict ourselves in this study to the NTM group. The study was approved by both the Minister of Health and the Institutional Review Board of the VU University Medical Center. For more information about the study, see: Kleinveld et al. [9].

Participants
From May 2001 till May 2003, forty-four midwifery and gynaecology practices in various parts of the Netherlands asked pregnant women permission to be sent a research information letter. Only women with a command of the Dutch language were approached. Of the 4077 women who were approached in the main project, 2986 women (73%) gave informed consent and filled in the first questionnaire. Based on randomisation, 844 women were offered the NTM.

NTM offer
Women received information about the NTM by means of a booklet sent to their home and a consultation by the women's midwife or gynaecologist. The following topics were covered in the booklet: characteristics of people with DS, age-specific chances of having a child with DS, procedure of the NTM, options available following an unfavourable screening result, procedure of the diagnostic tests (amniocentesis and chorionic villus sampling) including information about a procedure-related miscarriage, and the possibility of having to consider an abortion.
The decision for or against prenatal screening in relation to pregnant women’s values in the case of an unfavourable diagnostic test result. The booklet had previously been pilot-tested for comprehensibility.

**Outcome measures**
Values for pregnancy outcomes were measured by means of a Visual Analogue Scale (VAS) [10]; one line 10 cm in length on which women had to order the pregnancy outcomes. This way of measuring values was chosen because it is easily administrable in postal questionnaires. Respondents were asked to place the pregnancy outcome they thought worst at the left end of the line, and the outcome that they valued best at the right end. They had to place the remaining five pregnancy outcomes in between the ends of the scale according to the value they assigned to them. Table 2 shows the items that respondents were given to order.

**Questionnaires**
Data were collected by means of three postal questionnaires. Participants filled in the first questionnaire before any information about screening was given (T1). It included questions about demographic background such as age, education, and parity. The second questionnaire was filled in after women had read the booklet and had decided for or against prenatal screening (T2), but (if applicable) before they had received the screening result. This questionnaire included the VAS. The third questionnaire was sent after the screening result was known, or at a comparable point in time (T3). It included the question of whether or not screening had been undergone.

**Analyses**
The values were calculated by measuring the distances of the pregnancy outcomes from the left end of the line to the point indicated by the respondent, as is also done in other studies [11]. The scores of the VAS provide more than simple rank-ordering, although they are not clearly interval values [12-14], and literature on psychological testing supports the use of parametric techniques for analysing the VAS [15].

We used a repeated measures design with ANOVAs to see whether the values assigned to the pregnancy outcomes differed from each other within the group of screening decliners and within the group of acceptors. We used contrasts to find out which items differed from each other. Bonferroni corrections were used to correct the p-values for multiple comparisons by multiplying them with the number of comparisons that were made (i.e. 21). Comparisons of categorical background variables were performed using $\chi^2$ tests. A T-test was used for comparing age. Analyses were conducted using SPSS 14.0 (Statistical Package for Social Science, Inc., Chicago, Illinois, USA)
Chapter 7

RESULTS

Inclusion criteria for the analyses were, respectively: having filled in the 1st, 2nd and 3rd questionnaires ($n=735$), having placed all variables on the VAS ($n=654$), giving the highest value to having a healthy child ($n=643$) and being younger than 36 years of age ($n=571$). Two of the remaining women had not filled in whether or not they had had screening done and were therefore not included. We excluded women who did not assign the highest value to having a healthy child; we thought it would be unlikely that someone would not consider this as the best of all options and we therefore assumed that they had not understood the question. Women aged 36 years and older were excluded because they could also have opted to have a diagnostic test done immediately without first undergoing prenatal screening.

Analyses were performed on 303 women who accepted the NTM and 266 women who declined the NTM. Table 1 shows their background characteristics. No significant difference between acceptors and decliners was observed between the educational level, whether or not they had children, had had a previous miscarriage or a previous pregnancy termination. Women who accepted screening were on average six months older and less religiously active compared to women who declined screening ($F(1,567)=3.98$, $p=.047$ and $\chi^2(2)=1.64$, $p=.44$, respectively).

Table 2 shows the mean values of the pregnancy outcomes of the screening acceptors and screening decliners.

Table 1. Background characteristics of the respondents ($n=569$)

<table>
<thead>
<tr>
<th></th>
<th>Screening acceptors</th>
<th>Screening decliners</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>$M=30.50$ ($SD=3.02$)</td>
<td>$M=29.99$ ($SD=3.11$)</td>
</tr>
<tr>
<td><strong>Educational level</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>45 (16)</td>
<td>32 (12)</td>
</tr>
<tr>
<td>Middle</td>
<td>131 (45)</td>
<td>114 (44)</td>
</tr>
<tr>
<td>High</td>
<td>115 (40)</td>
<td>114 (44)</td>
</tr>
<tr>
<td>Degrees of religiosity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active</td>
<td>2 (1)</td>
<td>16 (6)</td>
</tr>
<tr>
<td>Somewhat active</td>
<td>45 (15)</td>
<td>52 (20)</td>
</tr>
<tr>
<td>Not active</td>
<td>100 (33)</td>
<td>68 (26)</td>
</tr>
<tr>
<td>Not religious</td>
<td>156 (52)</td>
<td>130 (49)</td>
</tr>
<tr>
<td><strong>No children</strong></td>
<td>153 (52)</td>
<td>124 (48)</td>
</tr>
<tr>
<td>Previous miscarriage</td>
<td>59 (20)</td>
<td>46 (17)</td>
</tr>
<tr>
<td>Previous pregnancy termination</td>
<td>14 (5)</td>
<td>10 (4)</td>
</tr>
</tbody>
</table>

NB: The numbers of respondents given for each demographic variable do not add up to 569 because of missing values on these questions. $M=$ mean, $SD=$ standard deviation.
The decision for or against prenatal screening in relation to pregnant women's values

Table 2. Mean value scores of possible pregnancy outcomes of screening acceptors and screening decliners

<table>
<thead>
<tr>
<th>Pregnancy outcomes</th>
<th>Acceptors (n=303) mean value in mm (SD) (ranking number)</th>
<th>Decliners (n=266) mean value in mm (SD) (ranking number)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Having a healthy child 9.7 (0.68) (7) 9.8 (0.43) (7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. Having a child with Down syndrome 2.9 (2.51) (3) 4.3 (2.73) (5,6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>c. Losing a healthy child through a spontaneous miscarriage 1.9 (1.84) (2) 2.1 (2.1) (2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>d. Losing a healthy child through a miscarriage as a consequence of an amniocentesis or chorionic villus sampling 1.2 (1.4) (1) 0.9 (1.27) (1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>e. Losing a child with Down syndrome through a spontaneous miscarriage 4.9 (2.49) (6) 4.5 (2.46) (5,6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>f. Losing a child with Down syndrome as a consequence of an amniocentesis or chorionic villus sampling 4.1 (2.20) (4,5) 3.1 (2.18) (3,4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>g. Losing a child with Down syndrome through a chosen abortion 3.8 (2.23) (4,5) 3.0 (2.34) (3,4)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NB: ranking number: lowest value assigned =1, highest value assigned= 7.

(1) What values are assigned to pregnancy outcomes by women who accept prenatal screening?

Within the group of screening acceptors, the mean scores of the items differed ($F(6,562)=2385.55, p<.001$). All values differed significantly from each other (see Table 3) except for the values of losing a child with DS by means of a procedure-related miscarriage and losing such a child through a chosen abortion ($t(560)=2.14, p_{adj}=.693$). The order of mean values from lowest through highest is: losing a healthy child through a procedure-related miscarriage, losing a healthy child through a spontaneous miscarriage, having a child with DS, losing a child with DS by means of a chosen abortion or a procedure-related miscarriage, and losing a child with DS by means of a spontaneous miscarriage. By definition, having a healthy child was valued highest.

(2) What values are assigned to pregnancy outcomes by women who decline prenatal screening?

Within the group of screening decliners, the mean scores of the items differed ($F(6,562)=2180.27, p<.001$). No difference was found between losing a child with DS by means of an abortion and by means of a procedure-related miscarriage ($t(560)=0.44, p_{adj} >.999$), and between having a child with DS and having a spontaneous miscarriage of such a child ($t(560)=-0.80, p_{adj} >.999$). The values of the other items were significantly different from each other (see Table 3). The order of values from lowest through highest is: losing a healthy child by means of a procedure-related miscarriage, losing a healthy child by means of a spontaneous miscarriage, losing a child with DS by means of a chosen abortion or a procedure-related miscarriage, having a child with DS or losing such a child through a spontaneous miscarriage. By definition, having a healthy child was valued highest.
DISCUSSION

Both decliners and acceptors most preferred a spontaneous miscarriage of a child with Down syndrome (DS) after having a healthy child. Within screening decliners this value did not differ from that of having a child with DS. Screening decliners preferred having a child with DS to a procedure-related miscarriage or a chosen abortion of such a child, while for screening acceptors this was the reverse. Both decliners and acceptors attached the lowest value to losing a healthy child by means of a procedure-related miscarriage.

Some politicians and health professionals fear that, because prenatal screening tests are safe for the unborn child, women have this test performed without thinking through the possible consequences [3,4]. If women subsequently receive an increased screening outcome, they may feel drawn further into the screening trajectory and make choices that do not correspond to their values. With respect to these worries, the results of our study are twofold. On the one hand, screening acceptors assigned a lower value to having a child with DS than to a chosen abortion of such a child. This is in line with what could be expected if one considers the decision to have prenatal screening done as the first step of a trajectory that may end

Table 3. Statistics of the differences between mean preference scores of the various pregnancy outcomes

<table>
<thead>
<tr>
<th>Item</th>
<th>a. Having a healthy child</th>
<th>b. Having a child with Down syndrome</th>
<th>c. Losing a healthy child through a spontaneous miscarriage</th>
<th>d. Losing a healthy child through a procedure-related miscarriage of an amniocentesis or chorionic villus sampling</th>
<th>e. Losing a child with Down syndrome through a spontaneous miscarriage</th>
<th>f. Losing a child with Down syndrome through a procedure-related miscarriage of an amniocentesis or chorionic villus sampling</th>
<th>g. Losing a child with Down syndrome through a chosen abortion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>t</strong></td>
<td><strong>t</strong></td>
<td><strong>t</strong></td>
<td><strong>t</strong></td>
<td><strong>t</strong></td>
<td><strong>t</strong></td>
<td><strong>t</strong></td>
<td><strong>t</strong></td>
</tr>
<tr>
<td>a. Having a healthy child</td>
<td>–</td>
<td>44.31</td>
<td>66.76</td>
<td>98.78</td>
<td>33.37</td>
<td>43.72</td>
<td>44.05</td>
</tr>
<tr>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
</tr>
<tr>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
</tr>
<tr>
<td>c. Losing a healthy child through a spontaneous miscarriage</td>
<td>61.03</td>
<td>10.50</td>
<td>–</td>
<td>6.16</td>
<td>20.31</td>
<td>13.42</td>
<td>10.97</td>
</tr>
<tr>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
</tr>
<tr>
<td>d. Losing a healthy child through a procedure-related miscarriage of an amniocentesis or chorionic villus sampling</td>
<td>97.65</td>
<td>17.69</td>
<td>10.57</td>
<td>–</td>
<td>24.12</td>
<td>22.13</td>
<td>17.93</td>
</tr>
<tr>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
</tr>
<tr>
<td>e. Losing a child with Down syndrome through a spontaneous miscarriage</td>
<td>34.51</td>
<td>0.80</td>
<td>14.74</td>
<td>21.78</td>
<td>-</td>
<td>7.39</td>
<td>6.98</td>
</tr>
<tr>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
</tr>
<tr>
<td>f. Losing a child with Down syndrome through a procedure-related miscarriage of an amniocentesis or chorionic villus sampling</td>
<td>48.97</td>
<td>4.96</td>
<td>5.23</td>
<td>15.56</td>
<td>12.23</td>
<td>2.14</td>
<td>6.93</td>
</tr>
<tr>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
</tr>
<tr>
<td>g. Losing a child with Down syndrome through a chosen abortion</td>
<td>47.64</td>
<td>3.77</td>
<td>4.54</td>
<td>13.51</td>
<td>8.96</td>
<td>0.44</td>
<td>9.99</td>
</tr>
<tr>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
<td><strong>p</strong></td>
</tr>
</tbody>
</table>

NB: The letters in the upper row refer to the same items of the corresponding letters in the first column. Statistics of women who accepted the screening test are printed in bold (n=303). The other statistics are of women who declined screening (n=266). The p-values are adjusted for multiple comparisons.
The decision for or against prenatal screening in relation to pregnant women’s values

with a decision about termination of the pregnancy. This result seems to imply that women who accept screening are aware of the possible consequences following their decision. On the other hand, acceptors assigned the lowest value to losing a healthy child by means of a procedure-related miscarriage.

Our finding that women who accept screening prefer having a child with DS compared to losing a healthy child by means of a procedure-related miscarriage is in contrast with many other studies that found that women prefer a procedure-related miscarriage above having a child with DS [7,8,16-18]. Grobman et al. found that women who desire prenatal diagnosis assign a lower value to having a child with DS than to having a miscarriage, although in women who did not want prenatal diagnostic testing this difference was not significant [19]. An almost equal valuation of these pregnancy outcomes was found by Kupperman et al. among women who were eligible for prenatal diagnostic testing but declined [20]. A study of Deverill and Robson among women who had had screening performed during pregnancy, and had already given birth, also suggests that the value assigned to having a child with DS was comparable to a procedure-related miscarriage [21].

An explanation for the differences between our study and that of some others may be that our respondents involved women who made a decision on prenatal screening instead of on diagnostic testing. The decision for screening is different from the decision to have invasive diagnostic testing performed in which the risk of a procedure-related miscarriage is imminent instead of related to a possible next step.

In the Netherlands the cut-off for labelling a screening outcome as ‘increased’ is set at a chance of 1:200 at 12 weeks of pregnancy [22]. This cut-off is equal to the risk of a procedure-related miscarriage for the chorionic villus sampling, implying that having a child with DS has an equal value to having a procedure-related miscarriage (which in most cases will be the miscarriage of a healthy child). However, our study showed that screening acceptors do not value these outcomes as equal. The risk of a procedure-related miscarriage of an amniocentesis is 0.3%, implying that a miscarriage is worse than having a child with DS. This is more a reflection of the preferences of screening acceptors.

Our findings imply that it is important that women, after they have received an increased screening result, understand that prenatal diagnostic testing is not a self-evident next step for them to take. During counselling, special attention should be paid to the values an individual woman attaches to the possible pregnancy outcomes. In addition, it is important that women are clearly informed about, and understand, their chances of having these pregnancy outcomes, as outcomes and their chances of occurring are crucial elements of the decision making process [23].

Results of our study further seem to reflect a difference between acting and not acting. On average, women in our study assigned the lowest value to losing a healthy child by means of a
procedure-related miscarriage. Apparently, it is not just about losing a healthy child, since losing it by means of a spontaneous miscarriage is also evaluated negatively, but not as negatively as losing it because of a diagnostic procedure. Possibly, the latter outcome may be considered worse because women feel that it could have been prevented, and therefore feel guilty [24,25]. This is also applicable to losing a child with DS; both screening acceptors and decliners would rather lose a child with DS through a spontaneous miscarriage than as a consequence of their own action, as would be the case in a procedure-related miscarriage and an abortion. This line of thinking may also explain why, within both the group of acceptors and within the group of decliners, no difference in value is found between having a procedure-related miscarriage of a child with DS and having an abortion of such a child; in both cases it concerns losing a child with DS through one's own action.

CONCLUSION

The preferences in pregnancy outcomes imply that women who accept prenatal screening are less averse to taking action to prevent having a child with DS compared to screening decliners. This is in accordance with the possible trajectory after receiving an increased screening outcome. However, both acceptors and decliners prefer having a child with DS to having a procedure-related miscarriage of a healthy child. This may not be in accordance with some cut-off scores for offering invasive diagnostic testing that imply that these outcomes are valued equally. Therefore, it is important that pregnant women are aware that the decision to have diagnostic testing done is not self-evident after an unfavourable screening result. When counselling women about diagnostic testing, special attention should be paid to the values an individual woman attaches to the possibly pregnancy outcomes and her chances of having these outcomes.
The decision for or against prenatal screening in relation to pregnant women’s values

REFERENCES


General discussion
Chapter 8

CONTENTS OF GENERAL DISCUSSION

1. Introduction 111
2. Main findings 111
   2.1 Psychological consequences 111
      2.1.1 What is the effect of being offered prenatal screening? 112
      2.1.2 What is the effect of receiving a screening result? 112
      2.1.3 What are the longer term effects of being offered prenatal screening and receiving a screening result? 112
   2.2 Informed decision making 112
      2.2.1 Do women who made an informed decision and those who did not, differ in their emotional reaction when confronted with a positive screening outcome? 112
      2.2.2 What is the effect of offering prenatal screening on pregnant women’s attitudes towards prenatal testing? 112
      2.2.3 What are pregnant women’s preferences in pregnancy outcomes? 113
3. Discussion of main findings 113
   3.1 Is prenatal screening psychologically harmful or beneficial? 113
   3.2 Informed decision making 115
   3.3 Attitudes 115
   3.4 Preferences 116
   3.5 Current and future prenatal tests 117
4. Strengths and limitations 118
   4.1 Strengths 118
   4.2 Limitations 119
5. Implications of the findings 120
   5.1 Implications for practice 120
   5.2 Implications for policy 120
   5.3 Implications for further research 121
6. Conclusions 122
7. References 123
1. INTRODUCTION

This thesis is divided into two parts: (1) psychological consequences of offering prenatal screening, and (2) informed decision making. In the first part we looked at the effect of offering prenatal screening and receiving a screening outcome on general feelings of anxiety, fear of bearing a physically or mentally disabled child (child-related anxiety), positive and negative emotions, and attachment to the pregnancy and unborn child. In the second part we looked at the effect of informed decision making on psychological outcomes after receiving an increased screening outcome. An important criterion for informed decision making is that women act in line with their values [1]. When studying informed decision making, attitudes are often used as a reflection of peoples values [1-4]. But attitudes are not stable [5,6]. We therefore looked at the effect of offering prenatal screening on pregnant women's attitudes. In addition, we explored what women's values are concerning various pregnancy outcomes, and whether these are in line with the decision women made about accepting or declining screening.

Women were randomised into a group that was offered a nuchal translucency measurement (NTM), or maternal serum screening (MST), or into a group that was not offered prenatal screening (control group). Women filled in questionnaires before the screening test was offered, after the test was offered (or at a comparable point in time for the control group), after the screening test had been performed (or at a comparable point in time), in the last trimester of pregnancy, and two months after delivery. The inclusion of a control group was possible because at that time in the Netherlands, it was prohibited to offer prenatal screening to pregnant women under 36 years of age [7]. We had received a license from the Minister of Health to offer these tests [8]. Women in the intervention group could choose whether or not they wanted to have the screening test done.

We will now present a short overview of the main findings of this thesis. We will then discuss these findings in the context of other literature and present-day practices. Finally, we will outline the strengths and limitations of our study and the implications of the findings for practice, policy, and future research.

2. MAIN FINDINGS

2.1 Psychological consequences (Chapter 2,3,4)

2.1.1 What is the effect of being offered prenatal screening?

Compared to screening decliners, screening acceptors were already more anxious about bearing a disabled child before screening was offered, but offering screening increased their child-related anxiety. In contrast, offering prenatal screening did not influence women’s general feelings of anxiety.

After having been offered screening, women felt more attached to their pregnancy and unborn child than women who had not been offered screening.
Chapter 8

2.1.2 What is the effect of receiving a screening result?
Receiving a favourable screening outcome lessened anxieties of bearing a disabled child, but did not influence general feelings of anxiety. The intervention group (excluding women who had received an unfavourable screening result) showed less general anxiety than the control group. There was no difference in child-related or general anxiety between women who received a favourable MST or NTM outcome. Women who received an unfavourable outcome (but had not yet had received a diagnostic outcome) showed an increase in general anxiety, but not in child-related anxiety.
Receiving a favourable screening outcome did not influence positive or negative emotions compared to not having screening performed, nor did it influence attachment. Attachment was not influenced by whether women had screening done in which the foetus was visible (NTM) or whether women had screening done in which the foetus was not visible (MST).

2.1.3 What are the longer-term effects of being offered prenatal screening and receiving a screening result?
In positively screened women, the increased levels of general anxiety had declined (most women had by then had a diagnostic test done, all results in this study were normal). In the last trimester of pregnancy, the intervention group showed less general anxiety than the control group. These groups did not differ in child-related anxiety. During pregnancy, positive emotions increased and negative emotions decreased. The control group showed a lower increase in positive emotions than the intervention group, and a smaller decrease in negative emotions. Women in the control group felt less attached to their unborn child and pregnancy compared to women in the intervention group.

2.2 Informed decision making
2.2.1 Do women who made an informed decision and those who did not, differ in their emotional reaction when confronted with a positive screening result? (Chapter 5)
Compared to women who did not make an informed decision, women who made an informed decision had a more favourable emotional reaction when confronted with a positive screening outcome (variables that were measured: regret, shock, disappointment, feeling insecure), and felt better able to decide about invasive diagnostic testing.

2.2.2 What is the effect of offering prenatal screening on pregnant women's attitudes towards prenatal testing? (Chapter 6)
Offering prenatal screening triggered a change in pregnant women's attitudes regarding prenatal testing for congenital anomalies. Women who had a neutral attitude at baseline became more positive when accepting the screening test and more negative when declining it. Women who had a neutral attitude at baseline and who were not offered screening remained neutral.
2.2.3 What are pregnant women’s preferences in pregnancy outcomes? (Chapter 7)
The choice that women made to accept or decline prenatal screening is reflected in their values for specific pregnancy outcomes. Screening decliners preferred having a child with Down Syndrome (DS) to a procedure-related miscarriage or a chosen abortion, whereas screening acceptors preferred a miscarriage or chosen abortion of a child with DS rather than to having it. Both decliners and acceptors assigned the lowest value to losing a healthy child by means of a procedure-related miscarriage.

3. DISCUSSION OF MAIN FINDINGS

3.1 Is prenatal screening psychologically harmful or beneficial?
Offering prenatal screening influenced certain psychological outcomes. After the screening offer, women showed more attachment towards their pregnancy and their unborn child compared to women who were not offered screening (Chapter 4), and some of the women became more anxious about the health of their unborn child (Chapter 2). Possibly, offering prenatal screening increases women’s awareness of their pregnancy and unborn child.

Overall, during pregnancy, women who had been offered screening seemed to have more favourable psychological outcomes than women who had not had the offer (Chapters 2, 3, 4). They showed a higher increase in positive feelings over time, a larger decrease of negative feelings, more attachment and less general anxiety. Other studies also found that women who had been offered screening had more favourable psychological outcomes than those who had not been offered screening. Müller et al. found they reported less general anxiety and less depression [9]. And a study of Burton et al. showed that women who had screening done (and had received normal results) had similar or lower levels of anxiety compared to women who did not have access to screening [10].

Overall, our study did not find a difference in psychological outcomes between screening acceptors (who received a negative screening outcome) and decliners. This finding is consistent with other studies that showed no difference between screening acceptors and decliners in anxiety levels or depression [9,11]. However, a study of Lawson and Turiff-Jonasson found that women who received a negative screening outcome had lower levels of attachment compared to women who had declined screening and testing [12]. A difference between Lawson & Turiff’s study and ours is the age of the participants. They hypothesize that since their study involved women at high age-related risk for foetal anomaly, these women need more definitive reassurance than younger women. Because of its probabilistic nature, a screening outcome is less reassuring than a diagnostic outcome and may therefore result in lower levels of attachment. Presuming that women with a lower age-related risk need less reassurance and that this would result in a smaller difference between screening acceptors and decliners, the result of our study, which included women younger than 36 years of age, is not necessarily in contradiction with that of Lawson and Turiff.
Chapter 8

The kind of screening test also does not seem to matter; i.e. whether or not an image of the child is visible. Our study found no difference in impact on anxiety or attachment in negatively screened women who received an NTM result or an MST result. Results might be different, however, in women who receive an unfavourable screening result. Weinans et al. found that an unfavourable screening result after NTM had a greater impact than an unfavourable outcome after serum screening [13].

So, it seems as though offering prenatal screening is psychologically beneficial for most women, compared to not being offered screening, regardless of whether or not women choose to accept the test, and regardless of the specific test offered. Possibly, giving women the possibility to decide themselves about the course of the pregnancy and pregnancy outcome makes them feel more in control. It has been shown that a sense of control is related to higher emotional well-being [14], whereas women who experience the course of their pregnancy as uncontrollable have an increased fear of bearing a physically or mentally disabled child [15].

Even though the differences in our study were statistically significant, the differences between the groups in our study were small. Therefore, at the population level, offering prenatal screening may have some beneficial influence for pregnant women, whereas the clinical significance of these differences for an individual pregnant woman can be questioned.

It is important to note that positively screened women do experience negative consequences of the prenatal screening trajectory. Our study found that after an increased screening outcome, general anxiety rises. This has also been shown in other studies [13,16]. In this thesis, we did not look at the consequences of receiving an increased risk on attachment. But a report about the results of interviews with positively screened women in our study gives some information about it [17]. The women were interviewed after delivery about how they looked back on their pregnancy period. Some women mentioned that, before receiving the diagnostic test result, they distanced themselves from their pregnancy, e.g. they delayed buying things for the baby and talked less about their pregnancy. These findings seem to be in line with other studies that found that women put their pregnancy on hold until a favourable diagnostic outcome is received [18-22].

In our questionnaire study, anxiety levels had decreased later in pregnancy (Most women who had received a positive screening outcome had had a diagnostic test done. All results were favourable). Some studies also report normal anxiety levels after receiving a favourable diagnostic test result, whereas other studies found that anxiety levels stay high in some women [13,16]. It has been hypothesized that part of the remaining anxiety may be due to incorrect understanding of the screening outcome and/or insufficient preparation for an unfavourable screening outcome [23]. Interviews of Visser et al. suggest that some women thought that the increased screening outcome was an indication for an underlying medical problem [17]. So,
possibly, part of the residual anxiety may be removed or may even have been prevented by adequate counselling.

So, it is suggested that receiving a positive screening outcome enhances anxiety and decreases attachment. But are these psychological consequences unfavourable? This question has no straightforward answer. For example, even though feelings of anxiety may be unpleasant, moderately increased anxiety scores may be necessary for actively engaging in making a choice between options with serious consequences [16]. And even though attachment of a mother to her unborn child is considered to be important, lower levels of attachment can be seen as adaptive because women may decide to terminate the pregnancy after a series of unfavourable outcomes. Concluding then, these emotions may not be pleasant to experience, but they may be adaptive reactions considering possible subsequent actions.

In conclusion, prenatal screening causes (temporary) emotional unrest in positively screened women, but is not psychologically harmful for most women.

### 3.2 Informed decision making

Policy makers and health professionals find it important that pregnant women are able to make an informed decision about prenatal screening [24]. Two frequently-mentioned attributes of an informed decision are that the choice is based on sufficient knowledge and that it is in accordance with the decision maker’s values [1]. In addition, some definitions include deliberation about the alternatives; thinking through their advantages and disadvantages. Studies show that many women do not make an informed decision [1,4,25-27]. Michie et al. found that, after receiving a negative screening result, anxiety levels in women who had made an informed decision were not different from those who had not made an informed decision [3]. Our study, outlined in Chapter 6, suggests that, when confronted with a positive screening outcome, women who had made an informed decision have a more favourable emotional reaction.

From our study, we cannot draw a conclusion on the direction of the association between informed decision making and emotional outcome. It could be hypothesized that women who are more emotionally stable are the ones that make an informed decision. However, concerning levels of anxiety, studies have shown that before the test outcome is known, there was no difference between women who made an informed decision and those who did not [2-4,28]. Therefore, we tentatively conclude that from a psychological point of view it is more favourable to make an informed decision.

### 3.3 Attitudes

One component of an informed decision is that it is value-consistent. When studying informed decision making, attitudes are often used as a reflection of the decision maker’s values [1-4]. Chapter 7 describes that attitudes towards prenatal testing may change when women are
Chapter 8

offered information about prenatal screening; they came more into line with the decision women made. Two hypotheses were mentioned to explain this change in attitudes. The first is that because women had gained more knowledge about prenatal testing, their ideas about it changed. The second hypothesis is that the attitude change is a cognitive mechanism that is associated with making a choice. According to Differentiation and Consolidation Theory, a decision is made once the differences in attractiveness between the alternatives are big enough [29,30]. In other words, when the attractiveness of having prenatal testing done (which we measured by means of attitude towards prenatal testing) is sufficiently positive (or negative) compared to not having screening done, the decision is made. This process is called differentiation.

Possibly, both explanations play a role. However, the first may be unfavourable concerning the presently-used guidelines for prenatal screening in the Netherlands. These guidelines state that the health professional first has to check whether the woman wishes to be informed about screening for abnormalities. If that is the case, she receives more information. So, it may be that a woman declines information about screening because she does not hold a positive attitude towards it, whereas, if she had known more about screening, she might have chosen to have the test performed. In the future however, this situation is probably less likely to occur. Now that all women have the option to be informed about prenatal screening, knowledge about prenatal testing will become more widespread among the population as a whole.

3.4 Preferences

Some health professionals and policy makers feared that because prenatal screening tests are safe for the child, women would very easily choose to have such a test done without considering what they would do in the case of a positive screening outcome [24,31,32]. When the screening outcome is positive, women may feel drawn further into the screening trajectory and make choices that do not correspond to their values. In Chapter 7 we tried to gain insight into whether or not this fear is justified. The results of our study are twofold. On the one hand, screening acceptors assigned a lower value to having a child with DS than to a chosen abortion of such a child. This is in line with what could be expected if one considers the decision to have prenatal screening done as the first step in a trajectory that may end with a decision about termination of the pregnancy. This result implies that women who accept screening are aware of the possible consequences following their decision. On the other hand, acceptors assigned the lowest value to losing a healthy child by means of a procedure-related miscarriage.

More than 90% of women who receive a positive screening result choose to have diagnostic testing done [33], and around 71% of women who have been found to be carrying a foetus with Down syndrome or an NTD choose to terminate their pregnancy [34]. Therefore, the finding that women who have screening done, on average, prefer having a child with DS compared to losing a healthy child as a result of a miscarriage needs attention when considering the cut-off that is used for offering invasive prenatal diagnostic testing. In the Netherlands the cut-off for labelling a screening outcome as ‘increased’ is set at a chance of 1:200 at 12 weeks of
pregnancy. This cut-off is equal to the risk of a procedure-related miscarriage for the chorionic villus sampling, implying that having a child with DS has the same value as having a procedure-related miscarriage (which in most cases will be the miscarriage of a healthy child). However, our study showed that screening acceptors do not value these outcomes as equal. Therefore, after women receive an increased screening result, it is important that they understand that it is not self-evident to have prenatal diagnostic testing. Special attention should be paid to the values an individual woman attaches to the possible pregnancy outcomes.

Our finding that women prefer having a child with DS to loosing a healthy child by means of a procedure-related miscarriage, is in contrast with most other studies that found that women prefer a miscarriage to having a child with DS [35-39]. Yet, some studies found similar valuations of these pregnancy outcomes. Grobman et al. found that women who desire prenatal diagnosis assign a lower value to having a child with DS than to having a miscarriage, though in women who did not want prenatal diagnostic testing this difference was not significant [40]. An almost equal valuation of these pregnancy outcomes was found by Kupperman et al. among women who were eligible for prenatal diagnostic testing but declined [41]. A study of Deverill and Robson among women who had had screening performed during pregnancy, and had already given birth, also suggests that the value assigned to having a child with DS was comparable to a procedure-related miscarriage [42].

An explanation for the differences between our study and that of some others may be that our respondents involved women who made a decision on prenatal screening instead of on diagnostic testing. The decision for screening is different from the decision to have invasive diagnostic testing performed as the risk of a procedure-related miscarriage is imminent instead of related to a possible next step.

3.5 Current and future prenatal tests

The screening tests that were offered in our study concerned mainly specific abnormalities like DS and NTD. If these tests showed an increased risk, women could gain certainty about the presence or absence of the abnormality through diagnostic testing. Chapter 2 and other studies suggest that receiving a favourable diagnostic outcome decreases the anxiety that was caused by the positive screening result [16]. Nowadays, women are ‘offered’, among others, the standard anomaly scan (SAS), which can indicate a wide range of abnormalities. Disadvantages of this screening test are that: not all abnormalities are (already) visible, the significance of an abnormality is not always clear, and the findings may be false positives. Another disadvantage of the SAS is that it is performed late in pregnancy – at around 20 weeks [43]. When an abnormal result is found, certainty has to be gained about the signs. And then parents have little time to decide about termination of the pregnancy, which is officially allowed until a pregnancy duration of 24 weeks. The test characteristics of the SAS raise questions concerning its psychological effects. How do women respond to an abnormal finding if the consequence of the anomaly is not clear? How do they deal with an abnormal result during the rest of their
pregnancy if diagnostic testing cannot give certainty? And what is the psychological impact of the time pressure of abortion? These questions remain to be answered.

Traditionally, prenatal diagnosis of chromosome abnormalities involved analysis of banded chromosomes obtained from cultured amniotic fluid or chorionic villus cells. Because sufficient cells had to be grown, it took 1-3 weeks to have the test outcome. The study outlined in Chapter 2, and other studies [16], imply that receiving a favourable diagnostic test outcome can lessen the worries caused by a positive screening outcome. It would therefore be beneficial for women to receive the diagnostic test result more quickly. Currently, MLPA (multiplex ligation-dependent probe amplification) is being implemented as a prenatal screening technique. This method enables a diagnosis of aneuploidy in 2-4 days [44]. It can be used as a supplement, with which especially the diagnostic result for the most frequent trisomies can be known within a few days, followed by a karyogram result after some weeks. Or it can be used as a stand-alone test, something which is currently being investigated and debated [44]. So, the period of tension between receiving a positive screening result and receiving a diagnostic test outcome is likely to be shortened in the future.

New knowledge about the genetic background of many diseases is increasingly quickly available. Recently, a report of the Dutch Health Council was published concerning screening in various parts of life, describing the state of affairs and possible future developments [45]. One future perspective mentioned for prenatal screening is that of sequencing the foetus's whole genome. This would give pregnant couples information about a broad variety of disorders that the foetus may develop, and about risk factors for its future-health. It can be questioned whether it is possible for pregnant women to handle this information and to make an informed decision about whether or not to have this type of screening performed. In paragraph 3.1 it was hypothesized that the beneficial emotional effect of prenatal screening is a consequence of women feeling more in control over the course of their pregnancy. But will women still feel more in control when they are ‘overloaded’ with information, of which the consequences for the child’s health are not always certain? Therefore, it remains to be seen whether such screening tests are also favourable for pregnant women's emotional well-being.

4. STRENGTHS AND LIMITATIONS

4.1 Strengths

Most studies concerning the psychological effect of prenatal screening were performed in regions where screening is already offered as part of standard practice [16]. This means that no comparisons can be made with a group in the same region that had not been offered screening, thereby introducing a bias when wanting to draw conclusions on the effect of offering screening. Therefore, a first strength of our research project is that we had a group of women that were offered screening and a group that was not offered screening, based
on randomisation. The inclusion of such a control group was possible because of the unique situation in the Netherlands, where offering prenatal screening to women who did not have an indication for prenatal diagnosis was prohibited. We had received a license from the Minister of Health to be allowed to offer it in the context of our research project [7].

A second strength is the longitudinal, prospective design of the study. Psychological variables were measured before screening was offered, after the offer (or at a comparable point in time), after the screening outcome was known (or at a comparable point in time), in the last trimester of pregnancy, and two months after delivery. This design makes it possible to study the development of psychological outcomes over time, preventing any hindsight bias that may occur when performing a retrospective study.

A third strength is the large, unselected sample of pregnant women that participated, and the high response rate. We had included women from various parts of the Netherlands, who were counselled by a midwife or gynaecologist, in group or one-person practices, in rural and urban areas. The percentages of women who filled in all five questionnaires are: 60% in the intervention group and 66% in the control group. For analysis of non-response, all women who were asked to participate between September 2002 and January 2003 were sent a short questionnaire. Of these 259 women, 130 (50%) replied. The main reason for not participating in the study, or ceasing to participate, was lack of time or interest. This implies that it is not likely that our results are biased because specifically women with adverse psychological reactions stopped participating.

A survey among the participating midwifery and gynaecology practices, showed that they approached nearly all women and that if any had not been approached, this was due to lack of time or forgetfulness. Therefore, it is also unlikely that our results are biased because of selective inclusion by the midwifery or gynaecology practices.

4.2 Limitations

A first limitation is that we were not able to draw solid conclusions about the psychological consequences for positively screened women; their number was smaller than expected. This is partly because, based on other research, we had expected a higher test uptake [46,47]. In addition, the percentage of positively screened women for the nuchal translucency measurement was also smaller than known from literature [48].

A second limitation is that we did not include the partners of the pregnant women. The goal of prenatal screening is to give those women and their partners who want it, timely information about the presence or absence of the disorder in question, thereby enabling them, in the case of an unfavourable outcome, to decide to terminate the pregnancy or to prepare for the birth of an affected child [24]. Even though the partners role is acknowledged in this description, when studying the psychological consequences of prenatal testing the partners have largely been ignored. The few studies that have been performed on this topic, suggest that prenatal screening also influences the partner’s emotional well-being. E.g. it has been shown that after receiving an increased screening outcome concerning a foetal developmental disturbance,
Chapter 8

men had higher anxiety levels compared to norm groups, though not as high as their female partners [49].

5. IMPLICATIONS OF THE FINDINGS

5.1 Implications for practice
Chapters 5 and 7 suggest that it is important that pregnant women make an informed decision on prenatal screening, and that special attention should be paid to the values that women attach to the various possible pregnancy outcomes. Enhancing informed decision making could be accomplished by using decision aids. These are interventions designed to help people understand the probable outcomes of options by providing information relevant to the decision, and to consider the personal value they place on benefits versus harms by helping clarify preferences [50]. A review on decision aids concluded that they are better than standard care interventions in improving people's knowledge regarding options, enhancing realistic expectations about the benefits and harms of options, feeling more comfortable with their choices, and feeling clearer regarding their personal values [50]. Nagle et al. showed that a decision aid is more effective than a pamphlet in improving women's informed choice [51]. Decision aids could be used as supplements to counselling.

A Dutch example of a decision aid for deciding about DS is the website www.kiesbeter.nl. This decision aid has been developed by TNO Quality of Life and the Department of Medical Decision Making of the Leiden University Medical Center. It gives information about DS, the age-related chance of having a child with DS, information about prenatal screening tests and their advantages and disadvantages. In addition, it gives issues to think about when deciding and helps to list arguments for and against prenatal screening. The website does not give advice about the best choice for women, but prepares women for their consultation with their GP, midwife or gynaecologist.

If preconception care is implemented in the Netherlands, this could be used to point out to couples who are thinking about having children where they can find information about prenatal screening, and to point out the various kinds of decision aids they can use. Thereby, parents have enough time to consider the various reproduction strategies.

5.2 Implications for policy
After years of discussion, the Health Council advised the Government to offer prenatal screening to all pregnant women [24,52]. But under the Population Screening Act (PSA) it is prohibited to offer screening tests to women younger than 36 years of age who do not have a medical indication. Therefore, in 2004, the Secretary of State of the Ministry of Health proposed that all pregnant women have to be informed about prenatal screening. She reasoned as follows. Caregivers should give proper counselling about the patients' health question. In the case of pregnant women, this concerns information about the course of the pregnancy, life style rules, and risks. According to the Dutch Medical Treatment Act, a patient has a right
to information and because prenatal screening has become more well-known in the Dutch society, the Secretary of State found it self-evident that pregnant women are informed about prenatal screening as well [53]. The distinction she makes between offering and informing has been criticized. De Wert argues that she gives a faulty interpretation of the PSA; the term ‘offer’ has always been interpreted broadly, including systematically giving unrequested information that leads to requests for a screening test [54].

Despite differing opinions in society on ‘informing’ and ‘offering’, the practice guidelines have been changed. Currently, it is first checked whether the woman wants to be informed about screening. If so, she is given information about these tests. This is different from the approach in our study, in which women were sent a leaflet about the screening test without being asked whether or not they wanted this information. Our procedure could be defined as an offer of prenatal screening. Of course, we emphasized that it was the woman’s own decision to accept or decline the test. And even though we gave women information about prenatal screening, they were not compelled to read it. So, women who did not appreciate receiving this information, may not have read the leaflet at all. We therefore think that there is no practical difference between the ‘offering’ in our study, and the ‘informing’ in the current Dutch pregnancy care. And we think that the results of our study are generalisable to the currently used combination test: no harmful psychological consequences for most women.

5.3 Implications for further research

The present study showed no unfavourable effect of offering and performing prenatal screening on pregnant women’s attachment towards their pregnancy and unborn child. However, we have not investigated the effects in positively screened women. Our interview study suggests that receiving a positive screening result may negatively affect attachment in some women [17]. Further research should give more insight into this.

Women who received a positive screening result in our study, knew for which anomaly the risk was increased, and had the choice to gain certainty about its presence by means of diagnostic testing. Nowadays, with the standard anomaly scan, women may be confronted with a finding about which no certainty can be gained of its consequences; whether it is normal or abnormal. Therefore, another question that should be answered is what effect an uncertain screening result has on pregnant women's emotional well-being.

It is emphasized that parents should be able to make an informed decision [52]. However, hardly any research has been done concerning the effects of informed decision making on the parents’ psychological well-being. Chapter 5 gives a preliminary indication that it is beneficial. But results have to be replicated in a broader sample and for a wider variety of outcome measures before firm conclusions can be drawn. In addition, it would be relevant to know which components of informed decision making have the strongest relationship with the outcome measures; e.g. what is the influence of deliberation.
Chapter 8

In the future, it is likely that parents will be able to have access to even more information about the foetuses (future) health. Therefore, it should be investigated how women can be facilitated to make an informed decision when a screening test can give information about a wide variety of, sometimes uncertain, outcomes.

6. CONCLUSION

The present thesis suggests that prenatal screening is not psychologically harmful for most women; it does not cause anxiety, nor decrease attachment to the pregnancy and unborn child, nor lead to less positive, or more negative emotions. There are adverse effects, however, in women who receive an increased screening result, although these seem to reduce after a favourable diagnostic test result is received. The thesis presents preliminary findings that making an informed decision is associated with a more favourable emotional outcome when confronted with a positive screening result.
7. REFERENCES

Chapter 8

41. Kuppermann M, Nease RF, Learman LA, Gates E, Blumberg B, Washington AE. Procedure-related mis-


Summary

Psychological consequences of prenatal screening
INTRODUCTION

Prenatal screening tests are being offered in more and more European countries to all pregnant women. Guidelines for screening programmes state that the benefits of those programmes should outweigh any harmful physical or psychological effect as a result of participating. Therefore, the question arises concerning whether offering prenatal screening has an effect on pregnant women’s psychological well-being.

The thesis is divided into two parts: (1) psychological consequences of offering prenatal screening, and (2) informed decision making. In the first part we looked at the effect of offering prenatal screening and receiving a screening outcome on general feelings of anxiety, fear of bearing a physically or mentally disabled child (child-related anxiety), positive and negative emotions, and attachment to the pregnancy and the unborn child. In the second part we looked at the effect of informed decision making on the emotional reaction after receiving an increased screening outcome. An important criterion for informed decision making is that women act in line with their values. When studying informed decision making, attitudes are often used as a reflection of people’s values. As attitudes are not stable, we looked at the effect of offering prenatal screening on pregnant women’s attitudes towards prenatal testing. In addition, we explored what women’s values are concerning various pregnancy outcomes, and whether these are in line with the decisions women made about accepting or declining screening.

In this thesis we aimed at answering the following research questions:

1. Psychological consequences
   a) What is the effect of being offered prenatal screening on anxiety (Chapter 2) and attachment (Chapter 4)?
   b) What is the effect of receiving a screening result on anxiety (Chapter 2), attachment (Chapter 4), and positive and negative emotions (Chapter 3)?
   c) What are the longer-term effects of being offered prenatal screening and receiving a screening result on anxiety (Chapter 2), attachment (Chapter 4), and positive and negative emotions (Chapter 3)?

2. Informed decision making
   a) Do women who made an informed decision and those who did not, differ in their emotional reaction when confronted with a positive screening outcome? (Chapter 5)?
   b) What is the effect of offering prenatal screening on pregnant women’s attitudes towards prenatal testing (Chapter 6)?
   c) What are pregnant women’s preferences in pregnancy outcomes (Chapter 7)?

Prenatal tests can be divided into prenatal diagnostic tests (e.g. amniocentesis and chorionic villus sampling) and prenatal screening tests (e.g. nuchal translucency measurement, maternal
Summary

serum screening test, and the combination test). In virtually all cases, diagnostic tests provide certainty about whether or not the foetus has the abnormality being tested for, whereas screening tests may only give an estimation of the chance that the foetus has the abnormality. If the prenatal screening test indicates an increased risk, women are offered a prenatal diagnostic test to gain certainty.

Invasive prenatal diagnostic testing has a procedure-related risk of miscarriage. Therefore, and for practical and financial reasons, these tests are not offered to all pregnant women in the Netherlands, but only to those who are at an increased risk (women of 36 years and older, and women with a medical indication).

Two prevalent congenital abnormalities that can be tested for during pregnancy are Down syndrome (DS) and neural tube defects.

METHODS

The data presented in this thesis were collected in the context of a larger research project; a longitudinal randomised controlled trial, aimed at studying risk perception, decision making, and psychological well-being of pregnant women when offered prenatal screening for DS and neural tube defects.

Setting

We collected our data in the period between May 2001 and May 2003. In the Netherlands, at that time, it was prohibited to offer prenatal screening to women younger than 36 years of age who had no medical indication. We received permission from the Minister of Health to offer prenatal screening in the context of this study.

Participants

Midwifery and gynaecology practices in various parts of the Netherlands were approached until a sufficient number ($n=44$) consented to participate. These practices consisted of group and individual practices and were located in rural and urban areas. Pregnant women attending one of these practices were asked permission to be sent a research information letter. Only women with a gestational age of at most 16 weeks, and with a command of the Dutch language were approached. The first information letter invited women to participate in a study for evaluating different kinds of pregnancy care. We did not mention prenatal screening tests, since there is a risk that women in the control group might look for more information about it, which would mean that they were no longer a proper control group. Of the 4077 women who were approached, 2986 women (73%) gave informed consent. Sixty percent of these women filled in the questionnaires at all points in time.
Randomisation
After informed consent was granted, women were randomised into three groups: a group that was given information about the nuchal translucency measurement (NTM), a group that received information about the maternal serum screening test (MST), and a group that was not offered screening (control group). Since the NTM can only be performed between the first 10 and 14 weeks of pregnancy, it was necessary to make sure that the pregnancy duration of women who would be offered this test did not fall outside this range. Consequently, women who gave consent after 10 weeks were randomised into either the MST group or the control group.

Intervention
Women received information about the prenatal screening test by means of a booklet sent to their home and a consultation by their midwife or gynaecologist. The booklet had previously been pilot-tested for comprehensibility.

Questionnaires
Participants were asked to fill in five postal questionnaires at various points in time: (1) before any information about screening was given; (2) after they had been offered prenatal screening, or at a comparable point in time for the control group; (3) after the screening result was known, or at a comparable point in time for the control group and women who declined screening; (4) at 28 weeks of pregnancy; and (5) two months after giving birth.

RESULTS AND DISCUSSION
Psychological consequences
Offering prenatal screening influenced certain psychological outcomes. After the screening offer, women showed more attachment towards their pregnancy and the unborn child compared to women who were not offered screening (Chapter 4), and some of the women became more anxious about the health of their unborn child (Chapter 2). Possibly, offering prenatal screening increases women’s awareness of their pregnancy and their unborn child.

Overall, during pregnancy, women who had been offered screening seemed to have more favourable psychological outcomes than women who had not been offered screening (Chapters 2, 3, 4). They showed a higher increase in positive feelings over time, a larger decrease of negative feelings, more attachment and less general anxiety. Overall, our study did not find a difference in psychological outcomes between screening acceptors (who received a negative screening outcome) and decliners, nor a difference between women who had had a screening test in which the child was visible (NTM) and women who had had a screening test in which the child was not visible (MST). So, it seems as if offering prenatal screening is psychologically beneficial for most women, compared to not being offered screening, regardless of whether
Summary

or not women choose to accept the test, and regardless of the specific test offered. Possibly, giving women the possibility to decide themselves about the course of the pregnancy and pregnancy outcome makes them feel more in control. Other studies have shown that a sense of control is related to higher emotional well-being, whereas women who experience the course of their pregnancy as uncontrollable have an increased fear of bearing a physically or mentally disabled child.

Even though the differences in our study were statistically significant, the differences between the groups in our study were small. Therefore, at the population level, offering prenatal screening may have some beneficial influence for pregnant women, whereas the clinical significance of these differences for an individual pregnant woman can be questioned.

Even though for most women prenatal screening does not seem harmful, positively screened women do experience negative consequences. Our study found that after women received a positive screening outcome, their level of general anxiety rose. However, their anxiety decreased later in pregnancy (most women had had a diagnostic test done, with all results being favourable).

Women who received a positive screening result in our study knew for which anomaly the risk was increased, and were given the choice to gain certainty about its presence by means of diagnostic testing. Currently, women are offered, among others, the standard anomaly scan (SAS), which can indicate a wide range of abnormalities, the clinical significance of which is not always clear. The test characteristics of the SAS raise questions concerning its psychological effects. How do women respond to an abnormal finding if the consequence of the anomaly is not clear? How do they deal with an abnormal result during the rest of their pregnancy if diagnostic testing cannot give certainty? These questions remain to be answered.

The study outlined in Chapter 2 implies that receiving a favourable diagnostic test outcome can lessen the worries caused by a positive screening outcome. It would therefore be beneficial for women to receive the diagnostic test result more quickly. Traditionally, prenatal diagnostic testing of chromosome abnormalities took 1-3 weeks before producing the test outcome. Currently, MLPA (multiplex ligation-dependent probe amplification) is being implemented as a prenatal screening technique, which enables a diagnosis of aneuploidy in 2-4 days. Therefore, the period of tension between receiving a positive screening result and receiving a diagnostic test outcome is likely to be shortened in the future.

**Informed decision making**

Our study outlined in Chapter 5 suggests that, when confronted with a positive screening outcome, women who had made an informed decision have a more favourable emotional reaction (variables that were measured: regret, shock, disappointment, feeling insecure), and felt better able to decide about invasive diagnostic testing. Because only a few women in our
study had received a positive screening outcome, this is a preliminary conclusion. Results will have to be replicated in a broader sample and for a wider variety of outcome measures before firm conclusions can be drawn.

Chapter 6 describes that attitudes towards prenatal testing may change when women are offered information about prenatal screening; these attitudes came more into line with the decision women made. It is possible that, because women had gained more knowledge about prenatal testing, their ideas about it changed. This may be unfavourable concerning the presently-used guidelines for prenatal screening in the Netherlands. These guidelines state that the health professional first has to check whether the woman wishes to be informed about screening for DS. If that is the case, she will receive more information. So it may be that a woman declines information about screening because she does not hold a positive attitude, whereas, if she had known more about screening, she might have chosen to have the test performed. In the future however, this situation is probably less likely to occur. Now that all women have the option to be informed about prenatal screening, knowledge about prenatal testing will become more widespread among the population as a whole.

Some health professionals and policy makers feared that because prenatal screening tests are safe for the child, women would very easily choose to have such a test done without considering what they would do in the case of a positive screening outcome. After receiving a positive outcome, women may feel drawn further into the screening trajectory and make choices that do not correspond to their values. In Chapter 7 we tried to gain insight into whether or not this fear is justified. The results of our study are twofold. On the one hand, screening acceptors assigned a lower value to having a child with DS than to a chosen abortion of such a child. This is in line with what could be expected if one considers the decision to have prenatal screening done as the first step in a trajectory that may end with a decision about termination of the pregnancy. This result implies that women who accept screening are aware of the possible consequences of their decision. On the other hand, acceptors assigned the lowest value to losing a healthy child by means of a procedure-related miscarriage. This finding requires attention when considering the cut-off that is used for offering invasive prenatal diagnostic testing. In the Netherlands, the cut-off for labelling a screening outcome as ‘increased’ is set at a chance of 1:200 at 12 weeks of pregnancy. This cut-off is equal to the risk of a procedure-related miscarriage for the chorionic villus sampling, implying that having a child with DS has the same value as having a procedure-related miscarriage (which in most cases will be the miscarriage of a healthy child). However, our study showed that screening acceptors do not value these outcomes as equal. Therefore, after women receive an increased screening result, it is important that they understand that prenatal diagnostic testing is not a self-evident next step. During counselling, special attention should be paid to the values an individual woman attaches to the possible pregnancy outcomes.
Summary

Chapters 5 and 7 suggest that it is important that pregnant women make an informed decision on prenatal screening, and that special attention should be paid to the values women attach to the various possible pregnancy outcomes. With the future development of screening techniques, parents will probably be able to have access to more, and sometimes uncertain, information about the (future) health of their foetus. Facilitating informed decision making will therefore become even more important. Decision aids are a useful supplement to counselling.

CONCLUSION

The present thesis suggests that prenatal screening is not psychologically harmful for most women; it does not cause anxiety, nor decrease attachment to the pregnancy and unborn child, nor lead to less positive, or more negative emotions. There are adverse effects, however, in women who receive an increased screening result, although these seem to reduce after a favourable diagnostic test result is received. The thesis presents the preliminary findings that making an informed decision is associated with a more favourable emotional outcome when confronted with a positive screening result.
Samenvatting

Psychologische gevolgen van prenatale screening
INLEIDING

In steeds meer Europese landen wordt prenatale screening voor aangeboren afwijkingen aangeboden. Volgens de richtlijnen voor screeningsprogramma’s moeten de voordelen ervan opwegen tegen mogelijke nadelige lichamelijke en psychologische effecten als gevolg van deelname. Een van de vragen die dit oproept is of prenatale screening effect heeft op het psychologisch welzijn van zwangere vrouwen. Deze vraag staat centraal in dit proefschrift.

Het proefschrift bestaat uit twee delen: (1) psychologische gevolgen, en (2) geïnformeerde besluitvorming. Met geïnformeerde besluitvorming wordt bedoeld dat vrouwen een beslissing nemen die gebaseerd is op voldoende kennis en die in overeenstemming is met hun waardes. In het eerste deel keken we naar het effect van het aanbieden van prenatale screening en het krijgen van een screeningsuitslag op algemene gevoelens van angst, angst voor afwijkingen bij het kind, positieve en negatieve emoties, en hechting aan de zwangerschap en het ongeboren kind. In het tweede deel keken we o.a. naar het effect van het maken van een geïnformeerde beslissing op de emotionele reactie na het ontvangen van een verhoogde screeningsuitslag. Een belangrijk criterium voor een geïnformeerde beslissing is dat vrouwen een keuze maken die in overeenstemming is met hun waardes. In onderzoek worden waardes vaak gemeten door middel van attitudes. Maar aangezien attitudes niet stabiel zijn, onderzochten we het effect van het aanbieden van prenatale screening op de attitude van zwangere vrouwen t.o.v. prenataal testen. Daarnaast bekeken we welke waarde zwangere vrouwen hechten aan de verschillende mogelijke zwangerschapsuitkomsten en of deze in overeenstemming waren met hun keuze om wel of niet de screeningstest te laten doen.

In dit proefschrift willen wij de volgende vragen beantwoorden:

1. Psychologische gevolgen
   a) Wat is het effect van het aangeboden krijgen van prenatale screening op angst (hoofdstuk 2) en hechting (hoofdstuk 4)?
   b) Wat is het effect van het krijgen van een screeningsuitslag op angst (hoofdstuk 2), hechting (hoofdstuk 4), en positieve en negatieve emoties (hoofdstuk 3)?
   c) Wat is het effect op de lange termijn van het aangeboden krijgen van prenatale screening en het krijgen van een screeningsuitslag op angst (hoofdstuk 2), hechting (hoofdstuk 4) en positieve en negatieve emoties (hoofdstuk 3)?

2. Geïnformeerde besluitvorming
   a) Is er een verschil in emotionele reactie na het krijgen van een verhoogde screeningsuitslag tussen vrouwen die een geïnformeerde beslissing hebben genomen en vrouwen die geen geïnformeerde beslissing hebben genomen? (hoofdstuk 5)?
   b) Wat is het effect van het aanbieden van prenatale screening op de attitudes van zwangere vrouwen ten opzichte van prenataal testen (hoofdstuk 6)?
Samenvatting

c) Welke waarde hechten zwangere vrouwen aan de verschillende mogelijke zwangerschapsuitkomsten (hoofdstuk 7)?

Prenatale testen kunnen onderscheid worden in prenatale diagnostische testen (b.v. de vruchtwaterpunctie en de vlokkentest) en prenatale screeningstesten (b.v. de nekplooimeting, de maternale serumtest, en de combinatietest). In bijna alle gevallen geven diagnostische testen zekerheid over of de foetus wel of niet de betreffende afwijking heeft. Screeningstesten daarentegen geven doorgaans slechts een schatting van de kans dat de foetus de betreffende afwijking heeft. Als prenatale screeningstesten een verhoogd risico aangeven, wordt vrouwen een prenatale diagnostische test aangeboden om zekerheid te krijgen.

Bij invasief prenataal diagnostisch testen is er een risico op een procedurele miskraam. Daarom, en om financiële redenen, worden deze testen in Nederland niet aan alle zwangeren aangeboden, maar alleen aan degenen die een verhoogd risico hebben (vrouwen van 36 jaar en ouder en vrouwen met een medische indicatie).

Twee veel voorkomende aangeboren afwijkingen waarop tijdens de zwangerschap getest kan worden zijn het syndroom van Down (DS) en neuralebuisdefecten.

**METHODE**

Deze studie was onderdeel van een groter onderzoeksproject. Dit project betrof een gerandomiseerde gecontroleerde trial, en was erop gericht om de risicoperceptie, de besluitvorming, en het psychisch welbevinden van zwangere vrouwen die prenatale screening aangeboden krijgen, te onderzoeken.

**Setting**

We verzamelden de data in de periode van mei 2001 tot mei 2003. In die periode was het in Nederland niet toegestaan om prenatale screening aan te bieden aan vrouwen die jonger zijn dan 36 jaar en geen medische indicatie hebben. Wij kregen een vergunning van de Minister van VWS om prenatale screening aan te bieden in de context van ons onderzoek.

**Deelnemers**

Verloskundige en gynaecologische praktijken in verschillende delen van Nederland werden benaderd tot een voldoende aantal (n=44) instemde om mee te doen. Deze praktijken bestonden uit groeps- en individuele praktijken in zowel landelijke als stedelijke gebieden. Aan de vrouwen die zich bij een van deze praktijken melden, werd toestemming gevraagd voor het opsturen van een informatiebrief over het onderzoek. Alleen vrouwen met een zwangerschapsduur van maximaal 16 weken en die de Nederlandse taal beheersten (de vragenlijsten waren Nederlandstalig), werden benaderd. De eerste informatiebrief nodigde vrouwen uit om mee te doen aan een onderzoek voor het evalueren van verschillende
soorten zwangerschapsbegeleiding. De prenatale screeningstesten werden niet genoemd, om te voorkomen dat vrouwen hier al meer informatie over zouden zoeken, en er daardoor geen geschikte controle groep mogelijk zou zijn. Van de 4077 vrouwen die werden benaderd, stemden 2986 (73%) vrouwen in met deelname (gaven informed consent). Zestig procent van deze vrouwen vulden de vragenlijsten in op alle tijdstippen.

**Randomisatie**

Nadat de vrouwen informed consent hadden gegeven, werden ze gerandomiseerd in een van drie groepen: een groep die informatie kreeg over de nekplooimeting (NTM), een groep die informatie ontving over de maternale serumtest (MST) of een groep die geen screeningstest aangeboden kreeg (controle groep). De NTM kan alleen gedaan worden bij een zwangerschapsduur tussen 10 en 14 weken. We wilden voorkomen dat vrouwen die de NTM aangeboden kregen te lang zwanger zouden zijn om de test te laten doen. Daarom werden vrouwen met een zwangerschapsduur die langer was dan 10 weken bij het geven van informed consent gerandomiseerd in de MST of controle groep.

**Interventie**

Het aanbod van prenatale screening bestond uit een folder met informatie over de NTM of MST die de vrouwen thuisgestuurd kregen, en een consult bij hun zwangerschapsbegeleider.

**Vragenlijsten**

De deelnemers werd gevraagd om vijf vragenlijsten in te vullen. Deze werden op verschillende tijdstippen per post verstuurd, en ingevuld (1) voordat informatie over screening was gegeven; (2) nadat prenatale screening aangeboden was, of op een vergelijkbaar tijdstip voor de controle groep; (3) nadat de uitslag van de screeningstest bekend was, of op een vergelijkbaar tijdstip voor de controle groep en de vrouwen die de test niet hadden laten doen; (4) bij een zwangerschapsduur van 28 weken; (5) twee maanden na de bevalling.

**RESULTATEN EN DISCUSSIE**

**Psychologische gevolgen**

Het aanbieden van prenatale screening beïnvloedde bepaalde psychologische uitkomsten. Na het aanbod toonden vrouwen een sterkere hechting aan hun zwangerschap en hun ongeboren kind vergeleken met vrouwen die geen screening aangeboden hadden gekregen (hoofdstuk 4). Daarnaast maakten sommige vrouwen zich na het aanbod meer zorgen over de gezondheid van hun ongeboren kind (hoofdstuk 2). Een mogelijke verklaring hiervoor zou kunnen zijn dat het aanbieden van prenatale screening het bewustzijn van vrouwen voor hun zwangerschap en ongeboren kind verhoogt.
Samenvatting

Ook later in de zwangerschap hadden vrouwen die screening aangeboden hadden gekregen, positievere psychologische uitkomsten dan vrouwen die dit aanbod niet hadden gekregen (hoofdstuk 2, 3, 4). Zij toonden een grotere toename in positieve emoties over tijd, een grotere afname in negatieve emoties, meer hechting en minder algemene gevoelens van angst. Wij vonden geen verschil in psychologische uitkomsten tussen vrouwen die de screeningstest niet hadden laten doen en degenen die het wel hadden laten doen (en een gunstige screeningsuitslag kregen). Wij vonden ook geen verschil tussen vrouwen die een screeningstest hadden laten doen waarin het kind zichtbaar was (NTM) en waarin het kind niet zichtbaar was (MST). Het lijkt er dus op alsof het aanbieden van prenatale screening psychologisch gunstiger is voor de meeste vrouwen dan het niet aanbieden. Een mogelijke verklaring is dat het hebben van de mogelijkheid om zelf te beslissen over het verloop van de zwangerschap en de zwangerschapsuitkomsten, ervoor zorgt dat de vrouwen er meer controle over voelden. Uit ander onderzoek blijkt namelijk dat een gevoel van controle gerelateerd is aan een beter emotioneel welzijn, terwijl vrouwen die hun zwangerschap als oncontroleerbaar ervaren, meer angst hebben voor afwijkingen bij het ongeboren kind.

Ook al lijkt het erop dat voor de meeste vrouwen prenatale screening geen nadelige invloed heeft op het psychologisch welzijn, er was een kleine groep vrouwen die wel negatieve gevolgen ervaart. Uit ons onderzoek bleek dat na een verhoogde screeningsuitslag algemene gevoelens van angst toenemen. Later in de zwangerschap waren deze angstniveaus gedaald (de meeste vrouwen hadden een diagnostische test gedaan, alle resultaten waren goed).

De screeningstesten die in ons onderzoek werden aangeboden betroffen voornamelijk specifieke afwijkingen zoals Down syndroom en neuralebuisdefecten. In het geval van een ongunstige screeningsuitslag, konden vrouwen ervoor kiezen om zekerheid te krijgen over de aanwezigheid van de afwijking door diagnostisch testen. Tegenwoordig krijgen vrouwen o.a. structureel echoscopisch onderzoek (SEO) aangeboden. Hiermee kan een grote variëteit aan afwijkingen geïndiceerd worden, waarvan de klinische betekenis niet altijd duidelijk is. Dit roept vragen op wat betreft de psychologische effecten. Hoe reageren vrouwen op een abnormale bevinding als de gevolgen van die afwijking niet duidelijk is? Hoe gaan zij om met een abnormale bevinding gedurende de rest van de zwangerschap wanneer geen zekerheid over de aanwezigheid ervan verkregen kan worden met diagnostisch testen? Deze vragen moeten nog beantwoord worden.

In hoofdstuk 2 wordt geïmpliceerd dat een gunstige diagnostische testuitslag, de angst kan verminderen die het gevolg is van een verhoogde screeningsuitslag. Dus zou het gunstig zijn voor vrouwen om de diagnostische testuitslag sneller te krijgen. Voorheen duurde het bij prenataal diagnostisch testen van chromosoomafwijkingen 1 tot 3 weken om de testuitslag te krijgen. Tegenwoordig wordt MLPA (multiplex ligation-dependent probe amplification) geïmplementeerd als een prenatale screeningstechniek. Dit maakt het mogelijk om een
Samenvatting
diagnose van aneuploïdie in 2 tot 4 dagen te krijgen. Dat betekent dat de periode van spanning tussen het krijgen van een verhoogde screeningsuitslag en het ontvangen van een diagnostische testuitslag in de toekomst korter wordt.

Geïnformeerde besluitvorming
In hoofdstuk 5 wordt gesuggereerd dat, wanneer zij een verhoogde screeningsuitslag krijgen, vrouwen die een geïnformeerde beslissing namen, een gunstiger emotionele reactie hadden (variabelen die gemeten waren: spijt, shock, teleurstelling, onzekerheid), en dat zij zich beter in staat voelden om een beslissing te nemen over invasief diagnostisch testen. Omdat deze studie slechts een klein aantal vrouwen betrof, is dit een voorlopige conclusie. De resultaten moeten gerepliceerd worden in een grotere steekproef en voor een groter aantal uitkomstmaten, voordat sterke conclusies getrokken kunnen worden.

Hoofdstuk 6 beschrijft dat attitudes ten opzichte van prenataal testen kunnen veranderen wanneer vrouwen informatie aangeboden krijgen over prenatale screening. Wij vonden dat de attitudes meer in overeenstemming kwamen met de beslissing die de vrouwen hadden genomen. Vrouwen die de test hadden laten doen, hadden een positievere attitude gekregen en de attitude van vrouwen die de test niet hadden laten doen was negatiever geworden. Wellicht is hun attitude veranderd, doordat zij meer kennis hadden gekregen over prenatale testen. Dit kan een nadeel betekenen van de huidige Nederlandse richtlijnen voor prenatale screening. Volgens deze richtlijnen moet een zwangerschapsbegeleider eerst nagaan of de vrouw geïnformeerd wil worden over screening voor DS. Pas indien dat het geval is, krijgt zij meer informatie. Het zou dus kunnen dat een vrouw de informatie over de screeningstest afwijst omdat ze er geen positieve attitude over heeft, terwijl, als zij meer had geweten over screening, zij misschien wel gekozen zou hebben om de test te laten doen. In de toekomst zal deze mogelijke situatie waarschijnlijk minder vaak voorkomen. Nu alle vrouwen de mogelijkheid hebben gekregen om geïnformeerd te worden over prenatale screening, zal de kennis over screeningstesten groter worden in de populatie.

Omdat de screeningstest veilig is voor het ongeboren kind, waren sommige professionals in de gezondheidszorg en beleidsmakers bang dat vrouwen erg makkelijk zouden besluiten om de test te laten doen zonder erover na te denken wat ze zouden doen in het geval ze een verhoogde screeningsuitslag zouden krijgen. Hierdoor zouden vrouwen, na het krijgen van een verhoogde screeningsuitslag, het gevoel kunnen hebben dat zij verder het screeningstraject worden ingezogen en dat zij keuzes maken die niet overeenkomen met hun waardes. In hoofdstuk 7 probeerden we inzicht te krijgen in of deze angst gerechtvaardigd is. De resultaten van onze studie zijn tweeledig. Aan de ene kant prefereerden screeners een gekozen abortus van een kind met DS boven het krijgen van zo’n kind. Dit is overeenkomstig wat je zou verwachten als je er van uit gaat dat prenatale screening een eerste stap is in een traject dat kan leiden tot een beslissing over het wel of niet beëindigen van de zwangerschap. Deze bevinding betekent
dat vrouwen die er voor kiezen om screening te laten doen, zich bewust zijn van de mogelijke gevolgen van hun beslissing. Aan de andere kant, gaven vrouwen die screening lieten doen de laagste waarde aan het verliezen van een kind door middel van een procedurele miskraam. Dit resultaat verdient aandacht gezien de afkapkans die wordt gebruikt voor het aanbieden van invasieve prenatale diagnostische testen. In Nederland ligt deze afkapkans op 1:200 bij een zwangerschapsduur van 12 weken. Deze afkapkans is gelijk aan het risico op een procedurele miskraam door een vlokkentest. Dat impliceert dat vrouwen dezelfde waarde hechten aan het krijgen van een kind met DS als het krijgen van een procedurele miskraam (welke in de meeste gevallen een gezond kind zal betreffen). Ons onderzoek laat echter zien dat vrouwen die screening laten doen deze zwangerschapsuitkomsten niet gelijk waarderen. Het is daarom belangrijk dat, na het krijgen van een verhoogde screeningsuitslag, vrouwen begrijpen dat het niet vanzelfsprekend is om een prenatale diagnostische test te laten doen. Bij het counselen na een verhoogde screeningsuitslag zou extra aandacht besteed moeten worden aan de waardes die de vrouw hecht aan de verschillende mogelijke zwangerschapsuitkomsten.

In hoofdstuk 5 en 7 wordt beargumenteerd dat het belangrijk is dat vrouwen een geïnformeerde beslissing nemen over prenatale screening; een beslissing op basis van voldoende kennis en overeenkomstig hun eigen waardes. Met de verdere ontwikkeling van screeningstechnieken krijgen ouders waarschijnlijk toegang tot meer, en soms onzekere, informatie over de (toekomstige) gezondheid van hun ongeboren kind. Daardoor wordt het nog belangrijker om het maken van een geïnformeerde beslissing te faciliteren. Keuzehulpen (b.v. folders, computerprogramma’s) kunnen hierbij een goede aanvulling zijn op de counselling.

**CONCLUSIE**

Uit dit proefschrift blijkt dat prenatale screening niet psychologisch schadelijk is voor de meeste zwangere vrouwen; het veroorzaakt geen angst, geen verminderte hechting aan de zwangerschap en het ongeboren kind, het leidt niet tot minder positieve en meer negatieve emoties. Er zijn wel nadelige psychologische effecten voor vrouwen die een verhoogde screeningsuitslag krijgen, maar deze lijken af te nemen na het ontvangen van een gunstige diagnostische testuitslag. In dit proefschrift wordt ook een voorzichtige conclusie getrokken dat het maken van een geïnformeerde beslissing, geassocieerd is met een gunstiger emotionele reactie op een verhoogde screeningsuitslag.
List of publications


Kleinveld JH, ten Kate LP, van den Berg M, van Vugt JMG, Timmermans DRM. Does informed decision making influence psychological outcomes after receiving a positive screening outcome? Submitted.

Kleinveld JH, van der Wal G, Knol DL, van Vugt JMG, Timmermans DRM. The decision for or against prenatal screening in relation to pregnant women’s values. Submitted.

Dankwoord
Dankwoord

Ik ben tijdens de jaren van mijn promotieonderzoek veel mensen tegengekomen die mij hebben geholpen bij de totstandkoming van mijn proefschrift. Ik wil hen allemaal bedanken. Een aantal wil ik hieronder noemen.


Debora van Dam en Carolien van Geest, toen ik kwam waren jullie al bezig met de voorbereidingen van het onderzoek. Debora, jammer dat je wegging, succes met je nieuwe promotietraject. Carolien, we hebben toen een tijd met z’n tweeën aan het onderzoek gewerkt. Ook al gingen er dingen mis (b.v.‘de fax’), we konden er gelukkig de slappe lach om krijgen. Matthijs, toen kwam jij het team versterken. Ik vergeet nooit jouw eerste werkdag. Je vroeg ‘Wat doet een AIO?’ en was enigszins verontwaardigd toen bleek dat je postzegels moest plakken. Matthijs, jij werd mijn maatje. Jij wist dingen heel simpel te benaderen als ik te ingewikkeld aan het denken was en dat was erg prettig. Humor, basketballen en “stok”gevechten, als afwisseling van het computerwerk. Ik vond het jammer dat je elders ging werken. Fijn dat je mijn paranimf wil zijn.


Mijn dank gaat ook uit naar de vele honderden vrouwen die onze vragenlijsten hebben ingevuld, een hele klus. En zonder de inzet van de verloskundigen, praktijkassistentes, gynaecologen, poliassistentes en echoscopisten was het ons niet gelukt om de data te verzamelen. Charlotte Kruizinga-Welling bedankt voor je hulp bij het ontwikkelen van het materiaal voor de echoscopisten. Peter Schielen van het Laboratorium voor Infectieziekten en Screening van het RIVM, dankzij jou ontvingen wij de uitslagen van de maternale serumtest, bedankt hiervoor. En gelukkig kregen wij ook hulp van onderzoekassistentes en stagiaires: Carolien, Berniek, Marissa Kok, Maartje van Wulfften Palthe, Kim van Rooy, Edith Woldring, Maartje Sander en Joanneke Visscher. De vragenlijsten werden ingevoerd door DESAN Research Solutions (Han
Dankwoord

van Dongen). Secretaresses Rita Verdurmen, Manigeh Ershadi en Inge van der Leden, dank voor jullie praktische ondersteuning.

Nadat de data verzameld waren begon het analyseren en schrijven. Dirk Knol, fijn dat ik altijd zo snel bij je terecht kon voor hulp bij de analyses. Kumar Jamdagni (Language Matters), thank you for correcting my English.

En toen kwam mijn promotiedip. Dag in dag uit achter de computer, alleen maar analyseren en schrijven, dat brak mij op. Ik miste het regelwerk en ik miste de interactie met mensen. Gerrit, ik had het gevoel dat je mij begreep toen ik zei dat ik afstand wilde nemen van mijn promotietraject, en dat was erg fijn. Gerrit, Daniëlle, bedankt dat jullie me de ruimte gaven om zonder druk een beslissing te nemen over het wel of niet afmaken van mijn promotieonderzoek. Lidewij Henneman, in deze periode kreeg ik van jou een hele lieve e-mail, die ik niet zal vergeten. Liesbeth, dank voor je geduld en luisterend oor.

Martina, dankzij jou kreeg ik werkzaamheden die in mijn behoeften voorzagen: het keniscentrum erfelijkheid en het onderwijs. Hierdoor kreeg ik ook weer energie om verder te gaan met mijn proefschrift. Mijn “nieuwe” collega’s bij community genetics waren voor mij een warm bad, dank voor jullie hartelijkheid en gezelligheid. Lidewij en Anne Marie Plass, toen ik besloten had om door te gaan, hebben jullie mij regelmatig aangemoedigd, bedankt daarvoor.

Vervolgens verhuisde ik van de afdeling sociale geneeskunde naar de polikliniek klinische genetica. Ook hier kreeg ik leuke collega’s. Annet van Hagen, jou wil ik nog even bij naam noemen. Toen ik kwam, zaten wij in hetzelfde schuitje: het afmaken van ons proefschrift. Je deur stond figuurlijk altijd open voor mij en ik ben dan ook regelmatig binnengekomen met nieuws over de vorderingen van mijn proefschrift. En jij kwam mij ’s avonds nog even een hart onder de riem steken. Phillis Lakeman, jou wil ik ook bedanken voor het fijne ‘lotgenotencontact’ en voor je praktische tips.

Hanne, bedankt voor de ruimte die je me hebt gegeven om aan de laatste loodjes van mijn proefschrift te werken. Dat heeft het voor mij een stuk makkelijker gemaakt om het af te krijgen. En ik waardeer het zeer dat je met me meedenkt over mijn toekomst en dat je me hierin stimuleert.

Gerrit, jij bent al weer enige tijd Inspecteur-Generaal voor de Gezondheidszorg. Ondanks deze drukke baan elders wilde je toch mijn promotor blijven en gaf je me feedback op mijn teksten en stuurde je me opbeurende e-mails. Dankjewel.

Leo, dank voor je kritische blik bij het lezen van mijn teksten en voor je suggesties. Ik vind het leuk dat onze samenwerking nog niet voorbij is. En je bent voor mij een mooi voorbeeld van iemand die passie heeft voor zijn werk en er gewoon volop mee doorgaat na zijn pensioen.
Dankwoord

Daniëlle, ik vond het erg prettig dat jij zo'n laagdrempelige begeleider was. Fijn dat je met zoveel verschillende onderzoeksprojecten onder je hoede, je toch altijd hebt verdiept in mijn artikelen. Bedankt voor het meedenken. En gefeliciteerd met je professoraat.

John, Melanie Engels en Aggie Nieuwint, jullie hebben me bijgepraat op het gebied van de prenatale testen, bedankt daarvoor.


Een belangrijke groep mensen die ik wil bedanken kende ik reeds vóór ik mijn promotie onderzoek begon; mijn vrienden en familie. Karin Ansing, onze lange wandelingen en leuke gesprekken waren een welkome afwisseling met het werken achter de computer. Ik vind het leuk dat je nu mijn paranimf bent. ‘De meiden’, vrienden, ooms, tantes, neven, nichten, pa, ma, Willem en Bertine, dank voor jullie nimmer aflopende interesse en steun. Het heeft wat jaarjes geduurd, maar nu klopte mijn planning echt.

Tot slot:
Yaron, jij vertrouwde me laatst toe dat je destijds dacht dat ik het niet af zou maken. Ziehier; het is klaar.