# Prenatal screening for Down syndrome and for structural congenital anomalies in the Netherlands

## Information provision, informed decision-making and participation

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# Prenatal Screening for Down Syndrome and for Structural Congenital Anomalies in the Netherlands

## Information provision, informed decision-making and participation

# Prenatale screening op Downsyndroom en op aangeboren structurele afwijkingen in Nederland

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Voor mijn ouders

And when the hardest part is over we'll be here
and our dreams will break the boundaries of our fears

- Brandon Flowers Crossfire

# Contents

# Chapter 1 Introduction

# 1. Congenital anomalies

Congenital anomalies, i.e., malformations present at birth, are the leading cause of death and morbidity in children under 1 year of age [1]. In Europe, the reported prevalence of major congenital anomalies in the period 2003-2007 was 239 per 10,000 births. Eighty percent of major congenital anomalies occurred in live births; 2.5% of these babies died in the first week of life. Two percent were stillbirths or fetal deaths occurring after 20 weeks gestation or more. Of all affected pregnancies, 17.6% were terminated following prenatal diagnosis. Most babies with a major congenital anomaly survive the early neonatal period, but they have considerable medical, social and educational needs [2].
During the last decades, an increasing number of congenital anomalies have been diagnosed before birth by prenatal screening [3-5]. In this thesis, we will take a closer look at the information provision procedure, informed decision-making and participation in the prenatal screening program for Down syndrome and neural tube defects. Down syndrome and neural tube defects are chromosomal and structural congenital anomalies respectively, that can both be diagnosed before birth. Down syndrome and neural tube defects are the primary focus of the Dutch national prenatal screening program for congenital anomalies.

## 1.1 Down syndrome

In 1866, John Langdon Down published an essay presenting a phenotypic description of children with common features distinct from other children with mental retardation. This phenotype is now called Down syndrome. In his essay, Down referred to these children as 'Mongoloids', based on his feeling that these children phenotypically resembled people from Mongolia, who were erroneously thought to have an arrested development [6]. The typical facial characteristics of individuals having Down syndrome were described by Down as: *'The face is flat and broad, and destitute of prominence. The cheeks are roundish, and extend laterally. The eyes are obliquely placed, and the internal canthi, more than normally distanced from one another. The palpebral fissure is very narrow. The forehead is wrinkled transversely from the constant assistance, which the levatores palpebrarum derive from the occipitofrontalis muscle in the opening of the eyes. The lips are large and thick with transverse fissures. The tongue is long, thick, and is much roughened. The nose is small.'*

In 1959, Lejeune et al. discovered that Down syndrome results from the presence of an additional chromosome 21 [7]. Due to this extra copy of chromosome 21, the clinical condition Down syndrome is also called trisomy 21.
In addition to the typical facies (Figure 1), Down syndrome is clinically characterised by cognitive impairment. The severity of this impairment varies between individuals. Adults with Down syndrome have an increased risk of Alzheimer's disease in their early fifties [8]. In addition, about half of children with Down syndrome have a congenital heart disease, the most common being an atrioventricular septal defect (35%) [9].

In the past 50 years, survival beyond the first year of life among individuals with Down syndrome has improved remarkably: from below 50% to more than 90% [10]. In developed countries, medical interventions for the clinically life-threatening conditions have resulted in increased longevity, with an estimated life expectancy of individuals with Down syndrome increasing from an average of 12 years in the 1940s to an average of 57.8 years for women and 61.1 years for men [11-13].

**Figure 1:** Milan, a child with Down syndrome.
(With permission of E. Snoijink (www.fluitekruidje.nl))

It has been known for a long time that the probability of the fetus being affected by trisomy 21 increases with the age of the pregnant woman [14,15] (Table 1). Therefore, the birth prevalence of Down syndrome in the pregnant population at large depends on the maternal age distribution of the population being considered [16,17]. From 1979 to 2003, the birth prevalence of Down syndrome increased by 31%, from 9 to 12 per 10,000 live births in 10 regions of the USA. The number of infants born with Down syndrome was almost 5 times higher among births to older mothers (38.6 per 10,000) than among births to younger mothers (7.8 per 10,000) [18]. The birth prevalence of live born infants with Down syndrome also depends on the prenatal screening policies being present, and the readiness of women to have a pregnancy termination if Down syndrome is diagnosed [19-22]. The historical birth prevalence, excluding the potential effect of pregnancy termination for Down syndrome, is 1 in 800 [23].

In the Netherlands, there is no formal registration of prevalence data of Down syndrome [24]. From Eurocat registrations in the Northern Netherlands it is shown that between 1981 and 1990 Down syndrome prevalences ranged from 10.6 per 10,000 live births to 12,8 per 10,000 pregnancies [25]. Mohangoo et al. reported Down syndrome prevalences for the period 1997-2007, with a prevalence of 14.9 per 10,000 births in 2007 [26]. This is in agreement with estimates based on a theoretical model, showing an upward trend from around 11 per 10,000 births in the early 1990s to around 14 per 10,000 in 2007 [27]. In a recent study, the estimated prevalence of Down syndrome in the Netherlands in 2003 was much higher, i.e., 16 per 10.000 live births [28]. This was in agreement with estimates from Cornel et al. in 1993, predicting that the prevalence of Down syndrome in the Netherlands would rise to approximately 17 per 10,000 births [29]. All of these birth prevalence data are based on different registrations, periods and calculations. Despite these different estimates, agreement exists that the birth prevalence of Down syndrome in the Netherlands tended to increase until 2003, and stabilised in the period until 2007 (personal communication, Michel Weijerman, Paediatrician Rijnland Ziekenhuis, Leiderdorp, The Netherlands).

**Table 1:** Expected prevalence's with 95% confidence intervals (CIs) of live born infants with Down syndrome by maternal age, as derived from Morris et al. [17].

| Maternal age at birth (years) | Expected birth prevalence | 95% CI | |
|---|---|---|---|
| | | Upper limit | Lower limit |
| 15 | 1:1514 | 1:1216 | 1:1885 |
| 16 | 1:1510 | 1:1221 | 1:1867 |
| 17 | 1:1505 | 1:1226 | 1:1848 |
| 18 | 1:1498 | 1:1228 | 1:1827 |
| 19 | 1:1489 | 1:1229 | 1:1803 |
| 20 | 1:1478 | 1:1228 | 1:1777 |
| 21 | 1:1462 | 1:1223 | 1:1747 |
| 22 | 1:1442 | 1:1214 | 1:1712 |
| 23 | 1:1416 | 1:1199 | 1:1671 |
| 24 | 1:1383 | 1:1178 | 1:1622 |
| 25 | 1:1341 | 1:1148 | 1:1563 |
| 26 | 1:1288 | 1:1108 | 1:1492 |
| 27 | 1:1222 | 1:1057 | 1:1408 |
| 28 | 1:1142 | 1:993 | 1:1310 |
| 29 | 1:1048 | 1:915 | 1:1196 |
| 30 | 1:940 | 1:824 | 1:1068 |
| 31 | 1:822 | 1:723 | 1:930 |
| 32 | 1:697 | 1:615 | 1:787 |
| 33 | 1:573 | 1:507 | 1:645 |
| 34 | 1:457 | 1:405 | 1:513 |
| 35 | 1:354 | 1:314 | 1:396 |
| 36 | 1:268 | 1:238 | 1:300 |
| 37 | 1:200 | 1:178 | 1:224 |
| 38 | 1:149 | 1:133 | 1:167 |
| 39 | 1:112 | 1:100 | 1:126 |
| 40 | 1:86 | 1:76 | 1:96 |
| 41 | 1:68 | 1:60 | 1:76 |
| 42 | 1:55 | 1:49 | 1:62 |
| 43 | 1:46 | 1:41 | 1:52 |
| 44 | 1:40 | 1:35 | 1:45 |
| 45 | 1:36 | 1:31 | 1:40 |

Maternal age has increased in almost all high-income countries; the same is true for terminations of pregnancies with Down syndrome [30]. Worldwide, the annual number of births of children with Down syndrome decreased or remained stable [30]. However, children with Down syndrome now have a better life expectancy, which makes it necessary to address the quality of this longer life span [28]. To promote the optimal development of individuals with Down syndrome, the Down syndrome Foundation (Stichting Downsyndroom [SDS]) was set up in the Netherlands, [31] which is member of the European Down Syndrome Association (EDSA [32]). The aim of the SDS is to promote activities that contribute to the optimal development of children and adults with Down syndrome, striving at integration in society and providing opportunities for living a normal life. To reach these goals, SDS collects knowledge about Down syndrome, provides relevant information to parents and others concerned with

individuals having Down syndrome and promotes contacts between them, and stimulates scientific research in this field [33].

In 1998, a guideline was developed by the working group Down syndrome of the section Inheritable and Congenital Conditions (Sectie Erfelijke en Aangeboren Aandoeningen [SEAA] of the Dutch Organisation of Pediatrics (Nederlandse Organisatie voor Kindergeneeskunde [NVK]) aiming at an optimal (para)-medical care of children with Down syndrome and their parents, by paediatricians and associated health care professionals. Most important aspects are a timely detection and treatment of related medical disorders, facilitation of an optimal cognitive and psychomotor development, and guidance to an active participation in society [34].

## 1.2 Neural tube defects

Neural tube defects are a group of heterogeneous and complex structural congenital anomalies of the central nervous system [35]. The development and closure of the human neural tube are normally completed within 28 days after conception [36,37]. Neural tube defects result from a failure of the neural tube to close, or by the reopening of an already closed tube [38,39].
Anomalies of the central nervous system are by far the most common birth defects, only congenital cardiovascular anomalies occur more often [40]. The estimated total mean prevalence of neural tube defects in the Netherlands in the period of 2002-2004 was 6.6 per 10,000 live births and stillbirths [41].

The majority of cases of neural tube defects can be categorised as either anencephaly (lack of closure in the region of the head) or spina bifida (lack of closure of the spine) [42]. The birth prevalence of these two categories of neural tube defects is approximately equal [38,43]. In addition to anencephaly and spina bifida, the clinical spectrum of neural tube defects also includes the less often occurring encephalocele, craniorachischisis, and iniencephaly [38]. Neural tube defects can also be classified as open, if neural tissue is exposed or covered only by membrane, or as closed, if the defect is covered by normal skin [44].
Most cases of neural tube defects have a multifactorial causation, including intrinsic (genetic, metabolic) and extrinsic (e.g. drugs, environmental toxins, temperature etc.) factors [43,45,46]. Approximately 20% of affected infants have additional congenital anomalies [38]. All infants with anencephaly are either stillborn or die shortly after birth, whereas many infants with spina bifida now survive (35% survival for infants affected by open spina bifida in the Netherlands [47]), usually as a result of extensive medical and surgical care[38]. Infants with open spina bifida who survive may have severe, life-long disabilities [48] and are at risk for psychosocial maladjustment [49].

Recently, a randomized clinical trial (MOMS; Management of Myelomeningocele Study) was performed in which prenatal repairment of a myelomeningocele (the most frequent form of spina bifida) was compared with postnatal repairment. It was concluded that prenatal repairment of myelomeningocele (rather than after birth) reduces the risk for fetal or neonatal death and the need for shunting by age 1 and substantially improves neurologic and motor outcomes. However, prenatal surgery was associated with an increased risk of preterm delivery and uterine dehiscence at delivery [50]. Although the potential benefits should be balanced against the risks, this finding is an important step in the development of prenatal surgery.

The risk of anencephaly and spina bifida may be reduced significantly by an increased intake of foliate before and during the first 28 days after conception [51]. This water-soluble B-vitamin is present in legumes, leafy green vegetables, such as spinach and turnip greens, and some fruits, such as citrus fruits. Folic acid is the synthetic and most stable form of foliate and the form often used in supplements and in fortified foods [52]. The results of randomised trials indicate that at least half the cases of neural tube defects could be prevented if women consume sufficient amounts of folic acid before conception and during early pregnancy [51,53]. Therefore, in the Netherlands, as well as in many other countries, women are advised to take supplements as soon as they wish to become pregnant [54]. In 2008, the Dutch Health Council advised the Government to expand the informational activities for folic acid intake for women wishing to become pregnant, and to introduce a national program of preconception care [41].

## 2. Prenatal screening

In the Netherlands, different prenatal screening programs do exist. One of the purposes of prenatal screening in general is to increase the possibility of optimal management of the pregnancy in terms of antenatal management, referral for birth to an adequate level of specialist care where indicated, and planning of the postnatal management of the baby. In this thesis, we will focus on first-trimester prenatal screening for Down syndrome and second-trimester ultrasound screening for structural congenital anomalies.
Down syndrome and neural tube defects are congenital anomalies that may be diagnosed before birth using prenatal tests. Non-invasive prenatal screening tests (also called 'risk assessment tests') provide an estimation of the probability that a fetus has a certain condition. Invasive diagnostic tests (i.e., chorionic villus sampling or amniocentesis) provide certainty about the presence or absence of a specific condition in the unborn child. In most European countries parents may opt for termination if one or more malformations are diagnosed in the fetus [55]. However, European countries currently vary widely in the provision and uptake of prenatal screening and its quality, as well as in their 'culture' in terms of decisions to continue the pregnancy. This contributes to variation between countries in perinatal an infant mortality and in childhood prevalence of congenital anomalies [30,55].

In the Netherlands now, prenatal screening for Down syndrome and structural congenital anomalies is offered to every pregnant woman in the context of a nation-wide prenatal screening program. According to the national screening guidelines set by the Dutch National Institute for Public Health and the Environment (RIVM), prenatal screening for Down Syndrome and structural congenital anomalies is not meant for preventive or treatment purposes, but to timely inform prospective parents of the options available to them [56].

### 2.1. Prenatal screening for Down syndrome

The Dutch prenatal screening program for Down syndrome aims at informing pregnant women and their partners in a timely manner about the likelihood of having a child affected by this condition. If the fetus is diagnosed with Down syndrome, prospective parents have the opportunity to either prepare for the birth of a child with Down syndrome, or to opt for termination of the pregnancy [57].
A high prevalence of aneuploidy, particularly trisomy 21, and other abnormalities such as genetic syndromes and cardiac defects was reported in 1992 by Nicolaides and colleagues. He

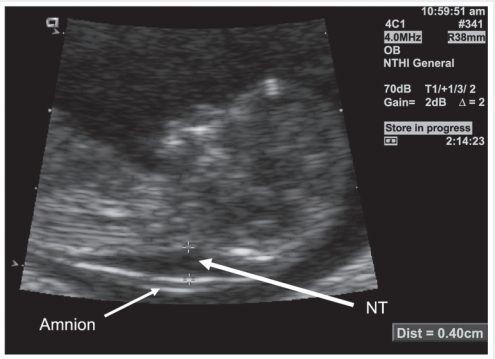


**Figure 2:** Increased NT. Transabdominal image of a fetus with nuchal edema [60].

coined the term 'nuchal translucency' to describe the echolucent space between the dorsal edge of soft tissue of the fetal neck and the linear echo of the skin as observed in a midline sagittal image. Linking this observation to Langdon Down's original description of the redundant skin of children with what is now known as Down syndrome, [6] the Nicolaides group pioneered the use of the NT- measurement as a screening method for fetal aneuploidy in the first-trimester (Figure 2) [58]. The reliability of NT as a risk assessment tool critically depends on the skill and accuracy of the sonographer. The Fetal Medicine Foundation (FMF) was the first to establish technical guidelines for NT-measurement, and these have been accepted as the standard in many countries [59].

Currently, the first-trimester combined test is typically used for prenatal calculation of the risk of carrying a child with Down syndrome. This risk is calculated from concentrations of pregnancy-associated plasma protein-A (PAPP-A) and the free ß-subunit of human chorionic gonadotropin (fß-hCG) in maternal serum, the sonographic fetal nuchal translucency (NT) measurement, and maternal age [61,62]. With an established algorithm, the false positive rate is set at 5%. With this 5% false-positive rate, the detection rate of the first-trimester combined test ranges from 64% to 87% [63].

In the Netherlands, one study reported a detection rate of 76%, for a false positive rate of 3.3% at a cut-off risk of 1 in 250 at term [64]. In another study, data on first-trimester prenatal screening with the combined test were analyzed (from January 2004 until december 2009, in the province of North-Holland in the Netherlands) to evaluate the performance of this test in different maternal age groups. In this study, the detection rate was 95.2% at a cut-off level of 1:200 at mid-term with a 6.6% false-positive rate based on follow-up data of 80%. Lowering the cut-off level for increased risk demonstrated an excellent screening performance with good balance between detection rate and false positive rate at the cut-off levels of 1:150 (detection rate 94.2%, false positive rate 5.2%) and 1:100 (detection rate 92.6%, false positive rate 3.7%). The authors argue that their results support the idea that the choice of cut-off level should be based on the best test characteristics of the screening center instead of a nationwide used cut-off level. In addition, it is stated that, although the false positive rate in women of advanced maternal age (women aged 36 years or older) is higher, screening performance of the combined test in this age group (detection rate 95.8% at 13.0 false positive rate) is definitely more effective than screening based on maternal age alone [65].

Chorionic villus sampling is typically performed between 10 and 14 weeks' gestation and amniocentesis at 15-18 weeks' gestation [66]. These tests are invasive, implying they may result in an iatrogenic miscarriage; chorionic villus sampling is associated with an excess risk of miscarriage of approximately 0.8%; amniocentesis gives an excess risk of miscarriage of approximately 0.3% [67].

In the Netherlands, a national screening program for Down syndrome, open to all pregnant women, exists as of 2007 [68]. Before 2007, offering a pregnant women information on a risk estimation test for Down syndrome was only allowed upon her explicit request. Invasive diagnostic testing was actively offered to women aged 36 years or over, in high-risk genetic categories, or with medical indications, such as type-1 and type-2 diabetes [69]. An important disadvantage of this 'age based diagnostic testing' is the exclusion of younger women (who overall have higher total numbers of pregnancies with Down syndrome); with the offer of diagnostic tests based on age, only 25-30% of fetuses with Down syndrome were identified prenatally [70]. Another major disadvantage of this approach is the risk of iatrogenic miscarriage induced by testing. Invasive diagnostics resulted in an iatrogenic miscarriage of a healthy fetus in approximately 1 of 100 to 300 women in the Netherlands in 2001 [69]. By providing an individual risk assessment, the combined test provides the opportunity for more accurate selection of candidates for invasive testing than maternal age [71]. This implies that, by offering the combined test to all pregnant women, the same number of fetuses with Down syndrome can be diagnosed by fewer invasive tests and hence a decrease of the number of iatrogenic miscarriages [72]. Furthermore, offering the combined test provides all women equal access to screening. If the combined test results in a probability exceeding an a priori specified threshold (≥1:200 in the Netherlands) at the time of screening, diagnostic testing is offered to obtain certainty.

Future improvements in Down syndrome screening performance may be obtained by drawing two serum samples during the first-trimester: one sample before 11 weeks to measure PAPP-A and one sample after 11 weeks to measure fß-hCG. At these points in time, the biochemical screening markers are most distinctive between Down syndrome and unaffected pregnancies. In clinical practice, it would be best to draw the second serum sample at the time of the NT-measurement [73]. Furthermore, other potential biochemical markers (e.g. ADAM metallopeptidase domain 12 and Epidermal growth factor) may be added to the first-trimester combined test, in order to increase the detection rate [74]. The use of fetal DNA and fetal cells in maternal blood is a promising new tool to diagnose Down syndrome non-invasively early in pregnancy [75-80]. Recently, non-invasive prenatal detection of Down syndrome, using the methylated DNA immunoprecipitation (MeDiP) methodology in combination with real-time quantitative PCR (qPCR), was reported with both a sensitivity and a specificity of 100% [81].

## 2.2 Prenatal screening for neural tube defects

In the Netherlands, second-trimester ultrasound screening for fetal anomalies, also known as the fetal anomaly scan or the 20-week scan, primarily aims at the detection of fetal neural tube defects at a time when termination of pregnancy is still legal [82]. Due to rapid developments in technology, structures in fetal anatomy which could not be visualised previously are also revealed and women receive detailed information about structural anomalies other than neural tube defects. This creates new reproductive dilemmas which women and their partners have to address [83,84].

Fetal anomaly scans are very appealing to women and their partners [85]. Women's desire to see their fetus is often so strong that it is difficult to decline this opportunity,[86] which is reflected in the high uptake rates of the fetal anomaly scan [87,88]. However, potentially unfavourable results may require repeated scans and hence induce uncertainty. If there is a serious anomaly with potentially severe clinical consequences, prospective parents may be confronted with the difficult decision to terminate the pregnancy. When there is an anomaly of uncertain severity, this decision becomes even more complicated. In addition, fetal anomaly scans may detect sonomarkers (also called 'soft markers'); subtle morphological changes that are often transient and have little or no pathological significance [89,90]. However, because of their association with fetal congenital anomalies, the detection of these soft markers might also cause distress in pregnant women [91]. Therefore, before deciding to undergo a fetal anomaly scan, women should be aware of the potential of these scans to detect serious anomalies or findings of unknown clinical relevance.

In the Netherlands, as in most other Western countries, second-trimester ultrasound screening for fetal anomalies has become a standard part of prenatal care [85,92,93]. Similar to prenatal screening for Down syndrome, the aim of ultrasound screening is defined as informing pregnant women and their partners in a timely manner about any possible disorder(s) their child may have and to allow them to choose the best course of action if the child is affected [94]. To achieve this goal, requirements are set concerning the offer of information.

## 3. Prenatal screening program for congenital anomalies in the Netherlands; policy

Up until 2004, pregnant women were screened on request by the so-called 'triple test', although there was no nationwide policy for prenatal screening for Down syndrome in the Netherlands. Women of 36 years of age or older were eligible for diagnostic testing by amniocentesis or chorionic villus sampling [92,95]. At that time, prenatal screening for Down syndrome using risk assessment tests followed by diagnostic tests, had been offered in several other Western countries for many years [96]. The Dutch Health Council published advisory reported in 2001 and 2004 on prenatal screening for Down syndrome and neural tube defects [69,72]. On the basis of this advice, the Dutch Minister of Health, Welfare and Sport decided in 2006 to offer information on prenatal screening for Down syndrome by the combined test to all pregnant women.

Neural tube defects may be detected by second-trimester ultrasound screening. In the Netherlands, ultrasound screening has been debated extensively [69]. Initially, ultrasound was only offered on genetic indication, i.e. targeted at women at increased risk of congenital anomalies in offspring [97]. The government's decision not to offer routine ultrasound screening resulted in large practice variations in antenatal care, e.g. some women had no ultrasound examination at all, other women had a two-scan regime and some women opted for having a 'pleasure scan' in a commercial setting, which may however create false reassurance as many of these ultrasound examinations were not apt for detecting fetal anomalies [66,69].
Up until 2003 there was no nationwide agreement concerning second-trimester ultrasound screening. In 2003, professionals involved in prenatal care agreed that all pregnant woman must be offered an ultrasound scan at around the twentieth week of pregnancy. This decision was endorsed by the minister of Health, Welfare and Sport and recorded in the National Ob-

stetric Directive (in Dutch; Verloskundig Vademecum). This document is the leading guideline for the Dutch Healthcare Inspectorate. The Health Council published advisory reports in 2001 and 2004 about prenatal screening for Down's Syndrome and neural tube defects [69,72]. On the basis of this advice, the Dutch Ministry of Health, Welfare and Sport decided to offer information on prenatal screening for Down syndrome to all pregnant women. Concerning neural tube defects, the screening itself (second- trimester ultrasound) should be offered to all pregnant women [92].

Current national screening programs for Down syndrome and neural tube defects in the Netherlands have been officially implemented in January 2007. In the national screening program for Down syndrome, information on the first-trimester combined test is offered to determine the individual need for information on screening. If a woman wants to receive information, counseling is provided and the pregnant woman is asked whether she is willing to participate in the screening program, in order to determine the individual probability of carrying a child with Down syndrome [72]. Invasive testing, i.e., chorionic villus sampling or amniocentesis, is offered if the screening indicates an increased risk (>1:200) of Down syndrome. Women aged 36 years or over have an age-based indication for prenatal diagnostic testing, and may choose for amniocentesis or chorionic villus sampling, without first having the combined test. Invasive testing is free of charge. Women younger than 36 years of age can only make use of risk assessment tests and must pay the costs of risk screening themselves, unless they have an additional insurance, or a listed genetic or medical indication for invasive testing. If the test result indicates an increased risk of Down syndrome, the costs of invasive testing are reimbursed [92].
Concerning the national screening program for neural tube defects, all women are offered second-trimester ultrasound screening. Ultrasound screening has been included in the basic insurance package since 1 January 2006, meaning that this screening test is covered by their insurance [92].

## 4. Prenatal screening for congenital anomalies in the Netherlands; organisation

In the Netherlands, the government has set out legal requirements concerning screening for Down syndrome and neural tube defects in the Population Screening Act (in Dutch; Wet op het BevolkingsOnderzoek) [68]. The Centre for Population Screening (in Dutch; Centrum voor Bevolkingsonderzoek [CvB]) of the RIVM developed national guidelines for the prenatal screening program and coordinates the organisation of prenatal screening at a national level. This organisation consists of three levels (Figure 3).
The first level is the Central Committee (Centraal Orgaan), with representatives of patient associations, the Dutch Healthcare Inspectorate, health insurance companies, professional groups and regional centres for prenatal screening. The Central Committee is responsible for setting national professional education requirements and quality standards. Furthermore, the Committee takes care of uniformity in the nationally distributed information material [98] and agreements on national evaluations, and reports on new developments in prenatal screening. The Centre for Population Screening is responsible for implementing decisions made by the Central Committee.

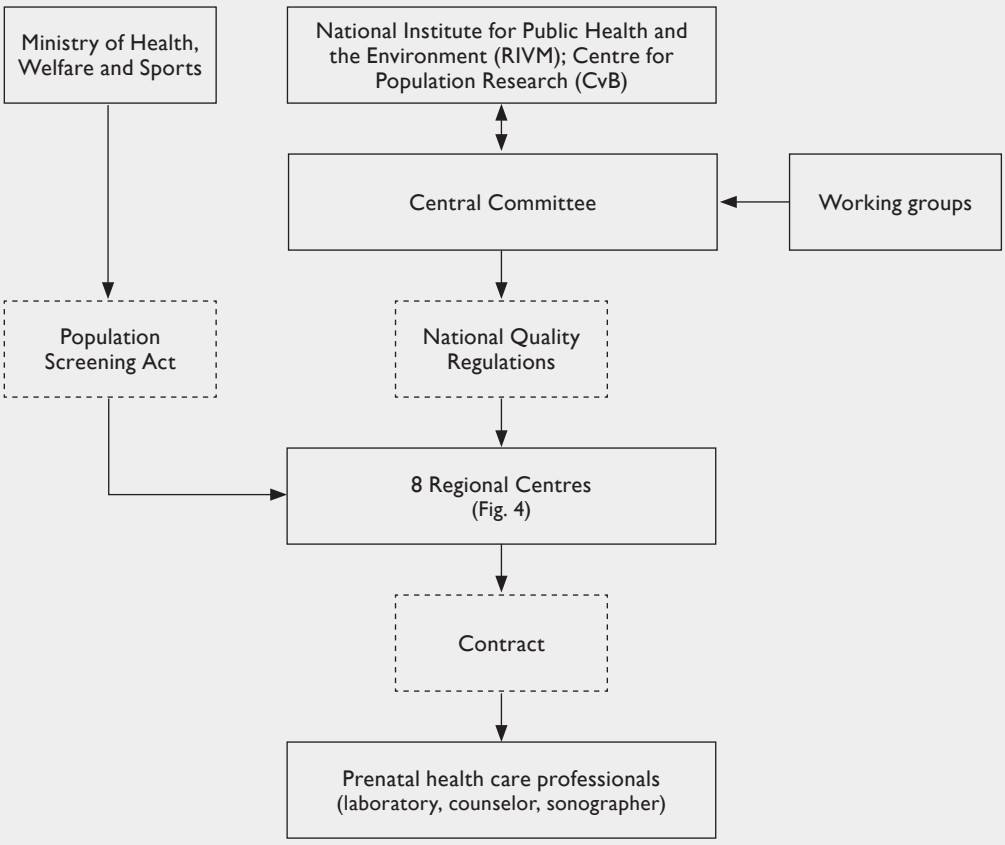


**Figure 3:** Organisation of prenatal screening in the Netherlands (with permission of J. Wieringa, RIVM)

The second levels consists of the regional centres for prenatal screening, which are the license holders. They conclude agreements with certified counselors, ultrasound specialists and laboratories and are responsible for quality assurance.

The third level includes the healthcare professionals, who are responsible for the quality of their care and for continuing training. They also provide details to inform on national and regional monitoring [99].

Counselors, ultrasound specialists and laboratories that wish to perform parts of the screening for Down Syndrome or second-trimester ultrasound screening, must conclude an agreement with a regional centre for prenatal screening in possession of the correct license. These regional centers can expand their agreements with regional arrangements to streamline operational processes among the different parties involved. The regional centers may only conclude agreements with counselors, ultrasound specialists and laboratories that meet all national training requirements for prenatal screening. These regional centers examine training courses to ensure they meet these educational requirements [100]. Currently, The Netherlands has eight regional centers for prenatal screening (Figure 4).

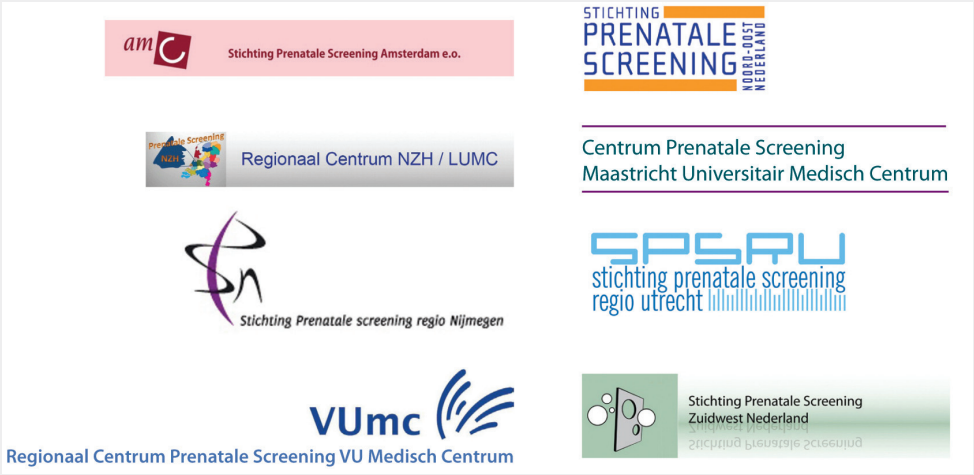


**Figure 4:** Regional Centres for Prenatal Screening in the Netherlands (Amsterdam -Amsterdam University Medical Centre; Leiden- Leiden University Medical Centre; Nijmegen, Amsterdam – VU University Medical Centre, Groningen, Maastricht, Utrecht, Rotterdam).

## 5. The information process

In the Netherlands, the information process on prenatal screening for Down syndrome is performed in practice in different stages [94]. In the first stage, the health care provider gives basic information about the screening program for Down syndrome and subsequently asks whether the pregnant woman is willing to receive detailed information about the prenatal screening (the 'information offer'). This first stage usually takes place during the initial visit for prenatal care. All women have the right not wanting to receive any information about prenatal screening; the 'right not to know'. In that case, the process of the information offer ends after the first stage.

Only if the information offer is accepted and the pregnant woman indicates she would like to be informed, the consultation is followed up by a counseling appointment (second stage). Provision of relevant, good quality information about prenatal screening, aims at informed decision-making by pregnant women about (non-) participation in the screening. This concept is explained in paragraph 7 of this chapter. To reach the goal of informed decision-making, the counseling should be provided in a non-directive manner.
If, after the counseling appointment, the woman indicates that she would like to participate in the screening program for Down syndrome, an appointment is made for the combined test (third stage). If the test result indicates an increased risk (≥1:200) of Down syndrome, invasive testing is offered (fourth stage).

A similar process of stages is followed for screening by second-trimester ultrasound screening; basic information is provided by the health care professional during the first appointment for antenatal care, the consultation is followed up with a counseling appointment if the pregnant woman wants to know more, and if the woman indicates she wants to participate, the counselor will refer her to a certified sonographer. If second-trimester ultrasound screening

yields an abnormal result, the pregnant woman is referred to a tertiary prenatal examination centre, if desired. A detailed ultrasound scan will be performed to confirm or disprove earlier findings and to discuss any necessary course of action [101].

To date, it has not been investigated whether counseling about prenatal screening for Down syndrome in the Netherlands is combined with counseling about second-trimester ultrasound screening in one session (during the first appointment for prenatal care), or whether counseling on these topics is done in two sessions, with counseling about prenatal screening for Down syndrome during the initial visit and counseling about second-trimester ultrasound screening in a separate session in the second-trimester, prior to the ultrasound examination. We expect variation between health care professionals concerning this practice. Health care professionals are only allowed to declare one counseling session of 20 minutes; therefore it is expected that most of them combine both topics in one session that takes place during the initial visit.

## 6. Information about prenatal screening

Internationally, the content of information material about prenatal screening varies. Most countries do not have a formal national prenatal screening program [102]; in these countries, information material may differ between regions and/or centers for prenatal care.
In the Netherlands, uniform information material exists to inform prospective parents about prenatal screening. The Central Committee takes care of uniformity in the nationally distributed information material. Health care professionals have a range of informational ma-


**Figure 5:** Dutch Information Leaflet; Information on Screening for Down Syndrome


**Figure 6:** Dutch Information Leaflet; Information on Ultrasound screening

terials from the Dutch National Institute for Public Health and the Environment to use during counseling: The "Information on Screening for Down Syndrome" (In Dutch: "Informatie over de screening op Downsyndroom"; Fig. 5) brochure [103] contains general information for pregnant women who are considering screening for Down syndrome. If the pregnant woman indicates she would like information about screening for Down Syndrome, practitioners should use this brochure. The "Information on second-trimester ultrasound screening" folder (In Dutch; "Informatie over het Structureel Echoscopisch Onderzoek"; Fig.6) [104] contains general information for pregnant women who consider the second-trimester ultrasound screening. If the pregnant woman indicates she would like information on second-trimester ultrasound screening, practitioners should use this leaflet. Both leaflets are available in different languages, e.g. Turkish, French, English. Despite the availability of information on prenatal screening in various languages, 58% of midwives participating in a recent Dutch study reported never using these translated information materials and 88% never used professional interpreters. Therefore, it was advised in this study to strive at interventions aiming at increasing healthcare professionals' competences to address language barriers in the provision of information about prenatal screening [105].
There is also online help available in making the decision for prenatal screening for Down syndrome. The information in this decision aid is adjusted to the mother's birth date and delivery date. This decision aid is available in the Dutch language only [106].

## 7. Informed decision-making

The goal of the active, routine offer of information about prenatal screening for Down syndrome and second-trimester ultrasound screening, is to enable pregnant women and their partners to make an autonomous informed decision about whether or not to participate in the prenatal screening program [72].
Different terms are used to encompass informed decision-making [107-111]. However, there is an emerging consensus that an informed decision has two core characteristics. First, it is based on relevant, good quality information, resulting in adequate decision-relevant knowledge. Secondly, an informed decision should reflect the decision-maker's values [112,113]. A third element, 'deliberation', is sometimes added to distinguish an informed decision from an informed choice. A choice refers to the product of a decision, whereas a decision refers to the process of choosing between alternatives and weighing up their pros and cons, which is called 'deliberation' [109,110,114].

To quantify whether an individual has made an informed-decision, the Multidimensional Measure of Informed Choice (MMIC) has been developed and validated [112,115]. This measure is based on three dimensions: knowledge, attitude and behaviour. Concerning participating or not in prenatal screening, women were classified as informed decision-makers when they have adequate knowledge about the screening program, and when their actual (non-) participation is consistent with their attitude. Both decisions to participate and decisions to not participate in the screening program can be informed; when a woman has adequate knowledge about the screening, a positive attitude about her own participation and she participates, she makes an informed decision; when she has adequate knowledge about the screening, a negative attitude towards her own participation and does not participate, she also makes an informed decision. The choices that occur when individuals do not have relevant knowledge or when their attitudes are not reflected in their behaviour are classified as uninformed [112].

As high quality information provision to those who want to be informed is an essential element in the Dutch program on prenatal screening, the level of informed decision-making can be used as an indicator of the quality of the information provision procedure.

Based on most international evaluations, the majority of pregnant women do not make informed choices about prenatal screening [108,112,116-118] and are unaware of the decisional implications of participation in screening [119,120]. In the Netherlands, experimental and small-scale observational studies reported informed decision-making about prenatal screening for Down syndrome in 51%-68% of women [121,122]. However, these studies were performed before the current national screening program, with the routine offer of information to all pregnant women, was implemented. In a recent Dutch study, performed after the implementation of the routine offer of prenatal screening in 2007, substantial ethnic differences in informed decision-making on prenatal screening for Down syndrome were reported [123].
To date, no evaluations have been performed of the quality of the information provision procedure on prenatal screening, in the real life setting of a national screening program for Down syndrome and fetal anomalies.

## 8. Databases on prenatal testing

Data collection on the practice of prenatal screening is essential for quality monitoring and assurance. At the start of the research underlying this thesis, no data were available on the information process, informed decision-making and participation in prenatal screening for Down syndrome and fetal anomalies. Available data were mainly on the outcomes of pregnancy, registered in The Netherlands Perinatal Registry (PRN-Foundation). All professional organizations have their own voluntary based medical registry: the LVR1-registry (midwives), the LVRh-registry (GP's), the LVR2-registry (obstetricians) and the LNR-registry (pediatricians / neonatologists). The LVR1, LVR2 and LNR registries are linked to one combined PRN-registry [124].
The RIVM has been developing a national digital database (Perinataal dossier - Peridos), in which information on prenatal screening can be registered. All healthcare professionals (midwives, sonographers, gynaecologists), associated with the eight regional centres for prenatal screening in the Netherlands, are expected to register data on the counseling procedure (for first- and second- trimester prenatal screening) and on the outcome of the pregnancy. In addition, data that are used for quality assurance should be registered by these health care professionals. To date, Peridos is being implemented and tested in all regions in the Netherlands.

## 9. Aim and research questions of this thesis

The objective of this thesis is to evaluate the information provision, informed decision-making and participation, in the context of the Dutch program for prenatal screening. The aims of the thesis are summarised in four central themes with the following specific research questions:

**Part 1- Knowledge**

1a. *What is the content of relevant knowledge needed to make an informed decision about (non-) participation in first- trimester prenatal screening for Down syndrome with the combined test?* **(Chapter 2)**.

1b. *What is the content of relevant knowledge needed to make an informed decision about (non-) participation in second- trimester ultrasound screening for fetal anomalies?* **(Chapter 3).**
1c. *What are differences between the content of decision-relevant knowledge for informed decision-making about second- trimester ultrasound screening (b) and decision-relevant knowledge for informed decision-making about first- trimester prenatal screening for Down syndrome with the combined test (a)?* **(Chapter 3).**

**Part 2 - Quality assurance of the information process**

***First- trimester prenatal screening for Down syndrome with the combined test***

2a. The process of providing information about first- trimester prenatal screening for Down syndrome with the combined test: *Are all pregnant women offered information about prenatal screening for Down syndrome? How many women accept the information offer and, of these women, how many do actually receive the information?* **(Chapter 4).**
2b. Informed decision-making as quality-indicator of the information provision procedure about first-trimester prenatal screening for Down syndrome with the combined test: *Is pregnant women's knowledge adequate? What is a pregnant woman her attitude towards undergoing prenatal screening for Down syndrome herself? To what extent is decision-making regarding (non-) participation in prenatal screening for Down syndrome based on an informed decision? What are the determinants of informed decision-making?* **(Chapter 4).**

***Second-trimester ultrasound screening for fetal anomalies***

2c. The process of providing information about second-trimester ultrasound screening for fetal anomalies: *Are all pregnant women offered information about second- trimester ultrasound screening? How many women accept the information offer and, of these women, how many do actually receive the information?* **(Chapter 5).**
2d. Informed decision-making (outcome of the information provision), as quality-indicator of the information provision procedure about second-trimester ultrasound screening for fetal anomalies: *Is pregnant women's knowledge adequate? What is a pregnant woman her attitude towards undergoing second-trimester ultrasound screening herself? To what extent is decision-making regarding (non-) participation in second- trimester ultrasound screening based on an informed decision? What are the determinants of informed decision-making?* **(Chapter 5).**

***Comparison between first-and second-trimester screening***

2e. *Do knowledge, attitude and uptake in second- trimester ultrasound screening for fetal anomalies, differ from knowledge, attitude and uptake in first-trimester screening for Down syndrome with the combined test? Does decision-making about participating in prenatal screening for Down syndrome differ from that for participating in the fetal anomaly scan?* **(Chapter 5).**

**Part 3- Ethnic differences in participation in prenatal screening for Down syndrome**

3a. *How many women from various ethnic backgrounds participate in prenatal screening in the south-west of the Netherlands?* **(Chapter 6).**
3b. *To what extent do women from various ethnic groups differ in participation in prenatal screening?*
3c. *Is participation in prenatal screening related to pregnant women's ethnic background, after adjustment for differences in socio-economic background and age?* **(Chapter 6).**

**Part 4 – Offering information on prenatal screening for Down syndrome prior to conception**

4a. *Do pregnant women wish to receive information on prenatal screening for Down syndrome prior to conception?* **(Chapter 7).**
4b. *What are the pros and cons of providing information on prenatal screening for Down syndrome preconceptionally, in addition to during the initial prenatal visit, from an ethical point of view?* **(Chapter 7).**

## 10. Overview of the thesis

Table 2 provides an overview of the studies represented in this thesis. In this overview, study method, sample and number of participants is provided.

**Table 2:** Overview of the studies presented in thesis

| Chapter | Focus of the study | Study method | Sample | N |
|---|---|---|---|---|
| 2 | Determination of decision-relevant knowledge needed for informed decision-making about (non-) participation in first-trimester prenatal screening for Down syndrome with the combined test | Literature search, expert consultation, qualitative testing in pregnant women | *Expert consultation:* 15 professionals from 12 relevant disciplines, and five pregnant women<br>*Qualitative testing:* 10 women attending prenatal outpatient clinic at Erasmus University Medical Centre (Rotterdam, The Netherlands) | *Expert consultation:* N=12 professionals, covering all 12 relevant disciplines, and three pregnant women<br>*Qualitative testing:* N=10 women |
| 3 | Determination of decision-relevant knowledge needed for informed decision-making about (non-) participation in second-trimester ultrasound screening for fetal anomalies, comparison with those for prenatal screening for Down syndrome | Literature search, expert consultation, qualitative testing in pregnant women | Same sample as in chapter 2 | *Expert consultation:* N=15 professionals, covering all 12 relevant disciplines, and two pregnant women<br>*Qualitative testing:* N=10 women |
| 4 | Informed decision-making on first-trimester prenatal screening for Down syndrome; evaluation of process and quality of information provision | Register-based survey, questionnaire survey | *Register-based survey:* Midwives practicing in one of the 65 midwifery practices registered by the regional centre for prenatal screening in the Southwest region of the Netherlands, registering data from pregnant women<br>*Questionnaire survey:* Unselective group of pregnant women visiting a subselection of 46 out of the 65 midwifery practices (based on an even distribution of urban and suburban areas) | *Register-based survey;* Data provided by N=59 midwifery practices for N=6435 pregnant women<br>*Questionnaire survey;* N=510 pregnant women in N=20 midwifery practices |
| 5 | Informed decision-making on second-trimester ultrasound screening; evaluation of process and quality of information provision, and comparison with Down syndrome screening | Register-based survey, questionnaire survey on informed decision-making in second-trimester ultrasound screening (1), comparison of (1) with questionnaire survey on informed decision-making about first-trimester prenatal screening for Down syndrome (2) | Same sample as in chapter 4 | *Register-based survey;* Data provided by N=59 midwifery practices for N=6435 pregnant women<br>*Questionnaire survey (1);* N=463 pregnant women in N=20 midwifery practices<br>*Comparison of (1) with (2);* N=210 pregnant women in N=20 midwifery practices |
| 6 | Assessment of ethnic differences in participation in the prenatal screening program for Down syndrome | Register-based study | Data on participation in prenatal screening in a defined postal code area in the Southwest region of the Netherlands | N=15,093 |
| 7 | Informing on prenatal screening for Down syndrome prior to conception | Questionnaire survey, ethical analysis | *Questionnaire survey:* Same sample as in chapter 3 | *Questionnaire survey;* N=510 pregnant women in N=20 midwifery practices |

# References


[1] Detrait ER, George TM, Etchevers HC, Gilbert JR, Vekemans M, Speer MC. Human neural tube defects: developmental biology, epidemiology, and genetics. Neurotoxicol.Teratol. 2005;27:515-524.

[2] Dolk H, Loane M, Garne E. The prevalence of congenital anomalies in Europe. Adv.Exp.Med.Biol. 2010;686:349-364.

[3] Stoll C, Tenconi R, Clementi M. Detection of Congenital Anomalies by Fetal Ultrasonographic Examination across Europe. Community Genet. 2001;4:225-232.

[4] Saari-Kemppainen A, Karjalainen O, Ylostalo P, Heinonen OP. Ultrasound screening and perinatal mortality: controlled trial of systematic one-stage screening in pregnancy. The Helsinki Ultrasound Trial. Lancet 1990;336:387-391.

[5] Grandjean H, Larroque D, Levi S. The performance of routine ultrasonographic screening of pregnancies in the Eurofetus Study. Am.J.Obstet.Gynecol. 1999;181:446-454.

[6] Down JL. Observations on an ethnic classification of idiots. Lond Hosp Clin Lect Rep 1866;3:259-262.

[7] Lejeune J, Gautier M, Turpin R. Etude des chromosomes somatiques de neuf enfants mongoliens. C R Hebd Seances Acad Sci 1959;248:1721-1722.

[8] Roizen NJ, Patterson D. Down's syndrome. Lancet 2003;361:1281-1289.

[9] Freeman SB, Taft LF, Dooley KJ, Allran K, Sherman SL, Hassold TJ, Khoury MJ, Saker DM. Population-based study of congenital heart defects in Down syndrome. Am.J.Med.Genet. 1998;80:213-217.

[10] Leonard S, Bower C, Petterson B, Leonard H. Survival of infants born with Down's syndrome: 1980-96. Paediatr.Perinat.Epidemiol. 2000;14:163-171.

[11] Bittles AH, Bower C, Hussain R, Glasson EJ. The four ages of Down syndrome. Eur.J.Public Health 2007;17:221-225.

[12] Glasson EJ, Sullivan SG, Hussain R, Petterson BA, Montgomery PD, Bittles AH. Comparative survival advantage of males with Down syndrome. Am.J.Hum.Biol. 2003;15:192-195.

[13] Yang Q, Rasmussen SA, Friedman JM. Mortality associated with Down's syndrome in the USA from 1983 to 1997: a population-based study. Lancet 2002;359:1019-1025.

[14] Shuttleworth GE. Mongolian imbecility. Brit Med J. 1909;2:661-665.

[15] Penrose LS. The relative effects of paternal and maternal age in mongolism. J. Genet 1933;27:219.

[16] Grijseels EWM, Laudy JAM, Galjaard RJ, Wildschut HIJ. Prenatal investigations for Down's syndrome: medical–technical considerations and dilemmas arising from current screening methods [Article in Dutch]. Ned.Tijdschr.Geneeskd. 2004:2166-2171.

[17] Morris, J.K., Mutton, D.E., Alberman, E. Revised estimates of the maternal age specific live birth prevalence of Down's syndrome. Journal of Medical Screening 2002;9:2-6.

[18] Shin M, Besser LM, Kucik JE, Lu C, Siffel C, Correa A, Congenital Anomaly Multistate Prevalence and Survival Collaborative. Prevalence of Down syndrome among children and adolescents in 10 regions of the United States. Pediatrics 2009;124:1565-1571.

[19] Cheffins T, Chan A, Haan EA, Ranieri E, Ryall RG, Keane RJ, Byron-Scott R, Scott H, Gjerde EM, Nguyen AM, Ford JH, Sykes S. The impact of maternal serum screening on the birth prevalence of Down's syndrome and the use of amniocentesis and chorionic villus sampling in South Australia. BJOG 2000;107:1453-1459.

[20] Bell R, Rankin J, Donaldson LJ, Northern Congenital Abnormality Survey Steering Group. Down's syndrome: occurrence and outcome in the north of England, 1985-99. Paediatr.Perinat.Epidemiol. 2003;17:33-39.

[21] Khoshnood B, Blondel B, de Vigan C, Breart G. Socioeconomic barriers to informed decision-making regarding maternal serum screening for down syndrome: results of the French National Perinatal Survey of 1998. Am.J.Public Health 2004;94:484-491.

[22] Siffel C, Correa A, Cragan J, Alverson CJ. Prenatal diagnosis, pregnancy terminations and prevalence of Down syndrome in Atlanta. Birth Defects Res.A.Clin.Mol.Teratol. 2004;70:565-571.

[23] Spencer K,. First trimester screening for aneuploidy. In: Wildschut HIJ, Weiner CP, Peters TJ eds.,. When to Screen in Obstetrics and Gynecology. Philadelphia: Saunders Elsevier Ltd., 2006;201-16.
[24] de Graaf G, Haveman M, Hochstenbach R, Engelen J, Gerssen-Schoorl K, Poddighe P, Smeets D, van Hove G. Changes in yearly birth prevalence rates of children with Down syndrome in the period 1986-2007 in the Netherlands. J.Intellect.Disabil.Res. 2011;55:462-473.
[25] de Walle HE, Cornel MC. Survival rates of children with Down syndrome in the Northern Netherlands, 1981-1991[in Dutch]. Tijdsch Kindergeneeskd 1995;63:40-44.
[26] Mohangoo AD, Buitendijk SE. TNO report on Congenital defects in the Netherlands 1997-2007 [in Dutch] 2009.
[27] De Graaf GW, Vis JC, Haveman M, van Hove G, de Graaf EAB, Tijssen JGP, Mulder BJM. Assessment of prevalence of persons with Down syndrome: a theory-based demographic model. Journal of Applied Research in Intellectual Disabilities 2010;DOI: 10.1111/j.1468-3148.2010.00593.x.
[28] Weijerman ME, van Furth AM, Vonk Noordegraaf A, van Wouwe JP, Broers CJ, Gemke RJ. Prevalence, neonatal characteristics, and first-year mortality of Down syndrome: a national study. J.Pediatr. 2008;152:15-19.
[29] Cornel MC, Breed AS, Beekhuis JR, te Meerman GJ, ten Kate LP. Down syndrome: effects of demographic factors and prenatal diagnosis on the future livebirth prevalence. Hum.Genet. 1993;92:163-168.
[30] Cocchi G, Gualdi S, Bower C, Halliday J, Jonsson B, Myrelid A, Mastroiacovo P, Amar E, Bakker MK, Correa A, Doray B, Melve KK, Koshnood B, Landau D, Mutchinick OM, Pierini A, Ritvanen A, Ruddock V, Scarano G, Sibbald B, Sipek A, Tenconi R, Tucker D, Anneren G. International trends of Down syndrome 1993-2004: Births in relation to maternal age and terminations of pregnancies. Birth Defects Res.A.Clin.Mol.Teratol. 2010;88:474-479.
[31] Stichting Downsyndroom; www.downsyndroom.nl Accessed on Sept. 15, 2011.
[32] European Down Syndrome Association; www.edsa.info Accessed on Sept. 15, 2011.
[33] Stichting Downsyndroom; wie zijn we en wat doen we; http://www.downsyndroom.nl/cms/publish/content/showpage.asp?pageid=372011 Accessed on Sept 15, 2011.
[34] Borstlap R, van Gameren-Oosterom HBM, Lincke C, Weijerman M, Wieringen H, van Wouwe JP. (2010) Een update van de multidisciplinaire richtlijn voor de medische begeleiding van kinderen met Downsyndroom.
[35] Padmanabhan R. Etiology, pathogenesis and prevention of neural tube defects. Congenit Anom (Kyoto) 2006;46:55-67.
[36] Copp AJ, Brook FA, Estibeiro JP, Shum AS, Cockroft DL. The embryonic development of mammalian neural tube defects. Prog.Neurobiol. 1990;35:363-403.
[37] Sadler TW. Mechanisms of neural tube closure and defects. Ment Retard Dev Disabil Res Rev 1998;4:247-253.
[38] Botto LD, Moore CA, Khoury MJ, Erickson JD. Neural-tube defects. N.Engl.J.Med. 1999;341:1509-1519.
[39] Campbell LR, Sohal GS. The pattern of neural tube defects created by secondary reopening of the neural tube. J.Child Neurol. 1990;5:336-340.
[40] Manning N, Archer N. Treatment and outcome of serious structural congenital heart disease. Semin.Neonatol. 2001;6:37-47.
[41] Health Council of the Netherlands. Towards an optimal use of folic acid 2008; Publication no. 2008/02.
[42] Au KS, Ashley-Koch A, Northrup H. Epidemiologic and genetic aspects of spina bifida and other neural tube defects. Dev.Disabil.Res.Rev. 2010;16:6-15.
[43] Melvin EC, George TM, Worley G, Franklin A, Mackey J, Viles K, Shah N, Drake CR, Enterline DS, McLone D, Nye J, Oakes WJ, McLaughlin C, Walker ML, Peterson P, Brei T, Buran C, Aben J, Ohm B, Bermans I, Qumsiyeh M, Vance J, Pericak-Vance MA, Speer MC. Genetic studies in neural tube defects. NTD Collaborative Group. Pediatr.Neurosurg. 2000;32:1-9.
[44] Lemire RJ. Neural tube defects. JAMA 1988;259:558-562.

[45] Joosten PHLJ, Toepoel M, Mariman ECM. Promotor haplotype combinations of the platelet-derived growth factor alpha-receptor gene predispose to human neural tube defects. Nat Genet 2001;27:215-217.
[46] van der Linden IJ, Afman LA, Heil SG, Blom HJ. Genetic variation in genes of folate metabolism and neural-tube defect risk. Proc.Nutr.Soc. 2006;65:204-215.
[47] den Ouden AL, Hirasing RA, Buitendijk SE, de Jong-van den Berg, L.T.W., de Walle HEK, Cornel MC. Prevalentie, klinisch beeld en prognose van neuralebuisdefecten in Nederland. Ned.Tijdschr. Geneeskd. 1996;140:2092-2095.
[48] Date I, Yagyu Y, Asari S, Ohmoto T. Long-term outcome in surgically treated spina bifida cystica. Surg.Neurol. 1993;40:471-475.
[49] Zurmohle UM, Homann T, Schroeter C, Rothgerber H, Hommel G, Ermert JA. Psychosocial adjustment of children with spina bifida. J.Child Neurol. 1998;13:64-70.
[50] Adzick NS, Thom EA, Spong CY, Brock JW,3rd, Burrows PK, Johnson MP, Howell LJ, Farrell JA, Dabrowiak ME, Sutton LN, Gupta N, Tulipan NB, D'Alton ME, Farmer DL, MOMS Investigators. A randomized trial of prenatal versus postnatal repair of myelomeningocele. N.Engl.J.Med. 2011;364:993-1004.
[51] MRC Vitamin Study Research Group. Prevention of neural tube defects: results of the Medical Research Council Vitamin Study. MRC Vitamin Study Research Group. Lancet 1991;338:131-137.
[52] De-Regil LM, Fernandez-Gaxiola AC, Dowswell T, Pena-Rosas JP. Effects and safety of periconceptional folate supplementation for preventing birth defects. Cochrane Database Syst.Rev. 2010;(10):CD007950.
[53] Czeizel AE, Dudas I. Prevention of the first occurence of neural-tube defects by periconceptional vitamin supplemention. N.Engl.J.Med. 1992;327:1832-1835.
[54] Health Council of the Netherlands. Dietary Reference Intakes: vitamin B6, folic acid, and vitamin B12 2003;Publication no. 2003/04.
[55] Garne E, Loane M, Dolk H, De Vigan C, Scarano G, Tucker D, Stoll C, Gener B, Pierini A, Nelen V, Rosch C, Gillerot Y, Feijoo M, Tincheva R, Queisser-Luft A, Addor MC, Mosquera C, Gatt M, Barisic I. Prenatal diagnosis of severe structural congenital malformations in Europe. Ultrasound Obstet.Gynecol. 2005;25:6-11.
[56] Dutch National Institute for Public Health and the Environment (RIVM). Screening for Down's Syndrome/20-week ultrasound http://www.rivm.nl/pns_en/down_ultrasound Accessed on Sept 15, 2011.
[57] Health Council of the Netherlands: Committee Genetic screening. Genetic Screening 1994;22.
[58] Nicolaides KH, Azar G, Byrne D, Mansur C, Marks K. Fetal nuchal translucency: ultrasound screening for chromosomal defects in first trimester of pregnancy. BMJ 1992;304:867-869.
[59] Fetal Medicine Foundation. The Fetal Medicine Foundation 2010;2011.
[60] Sheppard C, Platt LD. Nuchal translucency and first trimester risk assessment: a systematic review. Ultrasound Q. 2007;23:107-116.
[61] Cuckle HS, Arbuzova S,. Multimarker serum screening for chromosomal abnormalities. In: Milunksy A ed.,. Genetic Disorders and the Fetus; Diagnosis, Prevention and Treatment. MD, USA: John Hopkins University Press, 2004;795-835.
[62] Wald NJ, Hackshaw AK. Combining ultrasound and biochemistry in first-trimester screening for Down's syndrome. Prenat.Diagn. 1997;17:821-829.
[63] Malone FD, Canick JA, Ball RH, Nyberg DA, Comstock CH, Bukowski R, Berkowitz RL, Gross SJ, Dugoff L, Craigo SD, Timor-Tritsch IE, Carr SR, Wolfe HM, Dukes K, Bianchi DW, Rudnicka AR, Hackshaw AK, Lambert-Messerlian G, Wald NJ, D'Alton ME, First- and Second-Trimester Evaluation of Risk (FASTER) Research Consortium. First-trimester or second-trimester screening, or both, for Down's syndrome. N.Engl.J.Med. 2005;353:2001-2011.
[64] Wortelboer EJ, Koster MP, Stoutenbeek P, Elvers LH, Loeber JG, Visser GH, Schielen PC. First-trimester Down syndrome screening performance in the Dutch population; how to achieve further improvement?. Prenat.Diagn. 2009;29:588-592.
[65] Engels M, van Vugt J, Heijboer A, Blankenstein. M. Performance of first-trimester combined test for Down syndrome in different maternal age groups: reason for adjustments in screening policy?. Prenatal Diagnosis In Press.

[66] Wildschut HI, Peters TJ, Weiner CP. Screening in women's health, with emphasis on fetal Down's syndrome, breast cancer and osteoporosis. Hum.Reprod.Update 2006;12:499-512.
[67] Heckerling PS, Verp MS. Amniocentesis or chorionic villus sampling for prenatal genetic testing: a decision analysis. J.Clin.Epidemiol. 1991;44:657-670.
[68] Health Council of the Netherlands. Population Screening Act. Prenatal screening on Down's syndrome and neural tube defects. Health Council of the Netherlands 2007; Publication no. 2007/05.
[69] Health Council of the Netherlands. Prenatal Screening. Down's syndrome, neural tube defects, routine-ultrasonography. Health Council of the Netherlands 2001; Publication no. 2001/11.
[70] Simpson JL. Choosing the best prenatal screening protocol. N.Engl.J.Med. 2005;353:2068-2070.
[71] Grijseels EWM, Laudy JAM, Galjaard, R.J.H., Wildschut, H.I.J. [Prenatal testing for Down's syndrome: medico-technical considerations and dilemmas arising from current opportunities. In Dutch] Prenataal onderzoek naar Down syndroom: medisch-technische overwegingen en dilemma's voortkomend uit de huidige toepassingsmogelijkheden. Ned Tijdschr Geneeskd 2004;148:2166-2171.
[72] Health Council of the Netherlands. Prenatal Screening (2); Down's syndrome, neural tube defects. Health Council of the Netherlands 2004; Publication no. 2004/06.
[73] Kuc S, Koster MP, Visser GH, Schielen PC. Performance of first-trimester serum screening for trisomy 21 before and from 11 + 0 weeks of gestational age in The Netherlands. Prenat.Diagn. 2010;30:906-908.
[74] Koster MP, Heetkamp KM, Pennings JL, de Vries A, Visser GH, Schielen PC. Down syndrome screening: imagining the screening test of the future. Expert Rev.Mol.Diagn. 2010;10:445-457.
[75] Fan HC, Blumenfeld YJ, Chitkara U, Hudgins L, Quake SR. Noninvasive diagnosis of fetal aneuploidy by shotgun sequencing DNA from maternal blood. Proc.Natl.Acad.Sci.U.S.A. 2008;105:16266-16271.
[76] Go AT, Visser A, Mulders MA, Blankenstein MA, van Vugt JM, Oudejans CB. 44 single-nucleotide polymorphisms expressed by placental RNA: assessment for use in noninvasive prenatal diagnosis of trisomy 21. Clin.Chem. 2007;53:2223-2224.
[77] Lo YM. Fetal DNA in maternal plasma/serum: the first 5 years. Pediatr.Res. 2003;53:16-17.
[78] Chen EZ, Chiu RW, Sun H, Akolekar R, Chan KC, Leung TY, Jiang P, Zheng YW, Lun FM, Chan LY, Jin Y, Go AT, Lau ET, To WW, Leung WC, Tang RY, Au-Yeung SK, Lam H, Kung YY, Zhang X, van Vugt JM, Minekawa R, Tang MH, Wang J, Oudejans CB, Lau TK, Nicolaides KH, Lo YM. Noninvasive prenatal diagnosis of fetal trisomy 18 and trisomy 13 by maternal plasma DNA sequencing. PLoS One 2011;6:e21791.
[79] Chiu RW, Akolekar R, Zheng YW, Leung TY, Sun H, Chan KC, Lun FM, Go AT, Lau ET, To WW, Leung WC, Tang RY, Au-Yeung SK, Lam H, Kung YY, Zhang X, van Vugt JM, Minekawa R, Tang MH, Wang J, Oudejans CB, Lau TK, Nicolaides KH, Lo YM. Non-invasive prenatal assessment of trisomy 21 by multiplexed maternal plasma DNA sequencing: large scale validity study. BMJ 2011;342:c7401.
[80] Ehrich M, Deciu C, Zwiefelhofer T, Tynan JA, Cagasan L, Tim R, Lu V, McCullough R, McCarthy E, Nygren AO, Dean J, Tang L, Hutchison D, Lu T, Wang H, Angkachatchai V, Oeth P, Cantor CR, Bombard A, van den Boom D. Noninvasive detection of fetal trisomy 21 by sequencing of DNA in maternal blood: a study in a clinical setting. Am.J.Obstet.Gynecol. 2011;204:205.e1-205.11.
[81] Papageorgiou EA, Karagrigoriou A, Tsaliki E, Velissariou V, Carter NP, Patsalis PC. Fetal-specific DNA methylation ratio permits noninvasive prenatal diagnosis of trisomy 21. Nat.Med. 2011.
[82] Bricker L, Garcia J, Henderson J, Mugford M, Neilson J, Roberts T, Martin MA. Ultrasound screening in pregnancy: a systematic review of the clinical effectiveness, cost-effectiveness and women's views. Health Technol.Assess. 2000;4:i-vi, 1-193.
[83] Spencer K. Aneuploidy screening in the first trimester. Am.J.Med.Genet.C.Semin.Med.Genet. 2007;145C:18-32.
[84] Martinez-Zamora MA, Borrell A, Borobio V, Gonce A, Perez M, Botet F, Nadal A, Albert A, Puerto B, Fortuny A. False positives in the prenatal ultrasound screening of fetal structural anomalies. Prenat.Diagn. 2007;27:18-22.

[85] Garcia J, Bricker L, Henderson J, Martin MA, Mugford M, Nielson J, Roberts T. Women's views of pregnancy ultrasound: a systematic review. Birth 2002;29:225-250.
[86] Wertz DC, Fletcher JC. A critique of some feminist challenges to prenatal diagnosis. J.Womens Health 1993;2:173-188.
[87] Georgsson Ohman S, Waldenstrom U. Second-trimester routine ultrasound screening: expectations and experiences in a nationwide Swedish sample. Ultrasound Obstet.Gynecol. 2008;32:15-22.
[88] Healthcare Commission. Towards better births. A review of maternity services in England 2008.
[89] Borrell A. Promises and pitfalls of first trimester sonographic markers in the detection of fetal aneuploidy. Prenat.Diagn. 2009;29:62-68.
[90] Grijseels EW, Cohen-Overbeek TE, Adama van Scheltema PN, Groenenberg IA, Schoonderwaldt EM, Steegers EA, Wildschut HI. Sonomarkers: subtle ultrasound findings in the 20-week ultrasound examination, which have a low association with some chromosomal and non-chromosomal abnormalities in the fetus. Ned.Tijdschr.Geneeskd. 2008;152:2225-2231.
[91] Getz L, Kirkengen AL. Ultrasound screening in pregnancy: advancing technology, soft markers for fetal chromosomal aberrations, and unacknowledged ethical dilemmas. Soc.Sci.Med. 2003;56:2045-2057.
[92] Dutch National Institute for Public Health and the Environment (RIVM). A brief history of the 20-week ultrasound; http://www.rivm.nl/pns_en/down_ultrasound/history/ Accessed on Sept 15, 2011.
[93] Boyd PA, Devigan C, Khoshnood B, Loane M, Garne E, Dolk H, EUROCAT Working Group. Survey of prenatal screening policies in Europe for structural malformations and chromosome anomalies, and their impact on detection and termination rates for neural tube defects and Down's syndrome. BJOG 2008;115:689-696.
[94] Dutch National Institute for Public Health and the Environment (RIVM). Policy; timely information about possible disorders; http://www.rivm.nl/pns_en/down_ultrasound/policy/ Accessed on Sept 15, 2011.
[95] Wildschut HI, ten Hoope-Bender P, Borkent-Polet M, Traas H, van Agt HM, de Kroon ML, van der Maas PJ. Practice variation of test procedures reportedly used in routine antenatal care in The Netherlands. Acta Obstet.Gynecol.Scand. 1999;78:27-32.
[96] Boyd PA, Devigan C, Khoshnood B, Loane M, Garne E, Dolk H, EUROCAT Working Group. Survey of prenatal screening policies in Europe for structural malformations and chromosome anomalies, and their impact on detection and termination rates for neural tube defects and Down's syndrome. BJOG 2008;115:689-696.
[97] Health Council of the Netherlands. Prenatal screening: Down's syndrome, neural tube defects, routine-ultrasonography 2001;11.
[98] Dutch National Institute for Public Health and the Environment (RIVM). Information about screening for Down's Syndrome and the 20-week ultrasound; http://www.rivm.nl/pns_en/down_ultrasound/information/ Accessed om Sept 15, 2010
[99] Dutch National Institute for Public Health and the Environment (RIVM). The organisation of screening for Down's syndrome and the 20-week ultrasound; http://www.rivm.nl/pns_en/down_ultrasound/organisation/ Accessed on Sept 15, 2011
[100] Dutch National Institute for Public Health and the Environment. Execution of screening for Down's syndrome and the 20-week ultrasound; http://www.rivm.nl/pns_en/down_ultrasound/execution/ Accessed on Sept 15, 2011
[101] Dutch National Institute for Public Health and the Environment (RIVM). Description 20-week ultrasound; http://www.rivm.nl/pns_en/down_ultrasound/description/ Accessed on Sept 15, 2011
[102] EUROCAT. Special Report: Prenatal Screening Policies in Europe 2010.
[103] Rijksinstituut voor Volksgezondheid en Milieu, Ministerie van Volksgezondheid, Welzijn en Sport (2011). Informatie over de screening op Downsyndroom.
[104] Rijksinstituut voor Volksgezondheid en Milieu, Ministerie van Volksgezondheid, Welzijn en Sport (2011). Informatie over het Structureel Echoscopisch Onderzoek.

[105] Fransen M, Wildschut HIJ, Mackenbach JP, Steegers EAP, Essink-Bot ML. Differences and difficulties in providing information about prenatal screening for Down syndrome to women from diverse ethnic backgrounds. Submitted, 2011.
[106] Dutch National Institute for Public Health and the Environment (RIVM). Information about screening for Down's syndrome and the 20-week ultrasound http://www.rivm.nl/pns_en/down_ultrasound/information/ Accessed on Sept 15, 2011.
[107] Kohut RJ, Dewey D, Love EJ. Women's knowledge of prenatal ultrasound and informed choice. J Genet Couns 2002;11:265-76.
[108] Green JM, Hewison J, Bekker HL, Bryant LD, Cuckle HS. Psychosocial aspects of genetic screening of pregnant women and newborns: a systematic review. Health Technol Assess 2004;8:iii, ix-x, 1-109.
[109] Rimer BK, Briss PA, Zeller PK, Chan EC, Woolf SH. Informed decision making: what is its role in cancer screening?. Cancer 2004;101:1214-1228.
[110] Bekker HL, Hewison J, Thornton JG. Applying decision analysis to facilitate informed decision making about prenatal diagnosis for Down syndrome: a randomised controlled trial. Prenat Diagn 2004;24:265-75.
[111] Summers AM. Informed choice in prenatal screening. Can.Fam.Physician 1994;40:1688-91, 1694-7.
[112] Marteau TM, Dormandy E, Michie S. A measure of informed choice. Health Expect 2001;4:99-108.
[113] O'Connor A, O'Brien Pallas LL,. Decisional conflict. In: McFarlane GK, McFarlane EA eds.,. Nursing diagnosis and intervention. Toronto: Mosby, 1989;486-96.
[114] van den Berg M, Timmermans DR, ten Kate LP, van Vugt JM, van der Wal G. Informed decision making in the context of prenatal screening. Patient Educ.Couns. 2006;63:110-117.
[115] Michie S, Dormandy E, Marteau TM. The multi-dimensional measure of informed choice: a validation study. Patient Educ Couns 2002;48:87-91.
[116] Gourounti K, Sandall J. Do pregnant women in Greece make informed choices about antenatal screening for Down's syndrome? A questionnaire survey. Midwifery 2008;24:153-62.
[117] Gekas J, Gondry J, Mazur S, Cesbron P, Thepot F. Informed consent to serum screening for Down syndrome: are women given adequate information?. Prenat Diagn 1999;19:1-7.
[118] Al-Jader LN, Parry-Langdon N, Smith RJ. Survey of attitudes of pregnant women towards Down syndrome screening. Prenat.Diagn. 2000;20:23-29.
[119] Seror V, Ville Y. Prenatal screening for Down syndrome: women's involvement in decision-making and their attitudes to screening. Prenat Diagn 2009;29:120-8.
[120] Roelofsen EE, Kamerbeek LI, Tymstra TJ, Beekhuis JR, Mantingh A. Women's opinions on the offer and use of maternal serum screening. Prenat.Diagn. 1993;13:741-747.
[121] van den Berg M, Timmermans DR, Ten Kate LP, van Vugt JM, van der Wal G. Are pregnant women making informed choices about prenatal screening?. Genet Med 2005;7:332-8.
[122] van den Berg M, Timmermans DR, ten Kate LP, van Vugt JM, van der Wal G. Informed decision making in the context of prenatal screening. Patient Educ Couns 2006;63:110-7.
[123] Fransen M, Essink-Bot ML, Vogel I, Mackenbach JP, Steegers E, Wildschut H. Ethnic differences in informed decision-making about prenatal screening for Down syndrome. J Epidemiol Community Health 2009.
[124] The Netherlands Perinatal Registry. http://www.perinatreg.nl/home_english Accessed on Sept 15, 2011

# PART I
# KNOWLEDGE

# Chapter 2 Informed decision-making in prenatal screening for Down's syndrome: What knowledge is relevant?

Informed decision-making in prenatal screening for Down's syndrome: What knowledge is relevant? Schoonen, H.M.H.J.D., van Agt, H.M.E., Essink-Bot, M.L., Wildschut, H.I., Steegers, E.A.P., de Koning, H.J. Patient Education and Counseling. 2011; **84** (2): 265-70

**Abstract**

*Objective:* To determine the content of decision-relevant knowledge needed for informed decisionmaking about (non-) participation in prenatal screening for Down's syndrome (DS), in order to develop a knowledge questionnaire for routine application in large-scale programme evaluations.

*Methods:* A generic list of content domains for knowledge about screening was extracted from the literature. Items reflecting specific knowledge domains were constructed. An expert group of professionals and pregnant women expressed whether domains and items represented decisionrelevant information.

*Results:* All presented domains were scored as (very) important. Options when receiving an 'increased probability for DS' test result, the meaning of this result, the aim of the screening, and voluntary nature of the test were scored as most important. The condition being screened for, prevalence, and the screening procedure were scored as relatively less important, with a high amount of expert consensus.

*Conclusion:* A knowledge measure for prenatal screening for DS was developed, based on domains and items acquired by expert consensus.

*Practice implications:* This measure of decision-relevant knowledge can be used in routine, large-scale evaluations of the procedure for offering information about prenatal screening for DS.

# 1. Introduction

Prenatal screening for Down's syndrome (DS) aims at informing pregnant women about the chances of having a DS-affected child in a timely manner, in order to allow them the opportunity to act, that is prepare for the birth of a child with DS or termination of the pregnancy if DS is diagnosed [1].

The Dutch prenatal screening programme, organised in its present form (see Appendix A) since 2007, makes use of the combined test and is characterised by an active, standard information offer to every pregnant woman [2,3]. Before 2007, women aged 36 and over qualified for invasive tests (chorionic villus sampling or amniocentesis) to screen for DS [4]. Two major disadvantages of this approach include the exclusion of younger women (who have higher total numbers of pregnancies with DS) from screening, and the risk of iatrogenic miscarriage induced by testing. The combined test provides the opportunity for more accurate selection of candidates for invasive testing than maternal age [5]. This implies that, by offering the combined test to all pregnant women, the same number of fetuses with DS can be diagnosed with fewer invasive tests and hence a decrease of the number of induced miscarriages [2]. Furthermore, offering the combined test provides all women equal access to screening. However, an autonomous decision on participation is required, and therefore the purpose of the standard information offer is informed decision-making. An informed decision is based on sufficient knowledge, whereas the actual behaviour of (not-) participating in the screening is consistent with the decision-makers' values [6,7].

The proportion of women having sufficient relevant knowledge can be regarded as an indicator of the quality of the information offer. However, no gold standard exists for the content of knowledge relevant to making an informed decision on participation in prenatal screening for DS, and the tools that have been used to measure this knowledge are inadequate [8,9]. A knowledge measure to evaluate the effectiveness of the information procedure in reaching adequate knowledge, is needed. To be suitable for routine application in large-scale programme evaluations, the questionnaire needs to be short, suitable for self-completion and easy to complete.

The objective of this study was to determine the content of relevant knowledge needed to make an informed decision about (non-) participation in prenatal screening for DS, in order to develop a knowledge questionnaire to be used in large-scale evaluations of IDM.

# 2. Methods

### 2.1. Evaluation of the content of decision-relevant knowledge

A generic list of content domains representing the knowledge areas considered essential for making an informed choice on participation in screening, was extracted from the literature [10–14]. These domains were adapted for prenatal screening with the combined test, using the scientific literature and national information material (public information targeted at pregnant women and their partners, regarding prenatal screening for DS [15]). Because in the literature only information concerning the content, not concerning the level of knowledge relevant to prenatal screening for DS was found, the national information material was also used to estimate the level of knowledge considered relevant to making an informed choice. Knowledge items (statements with response options "true", "false", or "do not know") were drafted for each knowledge domain.

A group of experts consisting of professionals (n = 15 – from 12 relevant disciplines – representing the broad field of professions involved in prenatal screening) and pregnant women (n = 5; potential participants in the screening) was requested to evaluate the draft content of the knowledge questionnaire. Pregnant women of a high educational level were purposively selected for evaluating the content of domains and items of the questionnaire at a meta-level.

All participating experts responded to the following questions:

A. Regarding each knowledge domain:
   1. How important is this domain for making an informed decision about participating in prenatal screening for DS?

B. Regarding the specification of knowledge in draft items:
   2. How important is the content of the item associated with the knowledge domain?
   3. For each knowledge domain, are there redundant/unnecessary or missing items? If yes, which ones?
   4. For each item, are there any suggestions for a better expression for or wording of the item?
   5. For the entire questionnaire, are there knowledge domains missing? If yes, which ones?

Responses to questions 1 and 2 were scaled from 1 (very important) to 4 (not important at all). Assuming measurement at interval levels, mean values of these scores can be regarded as an indicator of the importance of a domain or item, respectively, in that the lower the value of the mean, the higher the importance.
Standard deviations can be considered to be an indicator of the level of consensus on the reported importance among the experts, in that the lower the standard deviation of the scores, the higher the level of consensus. Experts consultations were analysed to rank the domains in order of importance (from lowest to highest mean scores) and to determine the level of consensus among experts regarding this ranking (standard deviations). If domains had equal means, a lower standard deviation resulted in a higher ranking. We applied the same method for ranking items. Questionnaire items were selected based on the results of this expert consultation.

### 2.2. Qualitative testing of the knowledge measure

10 women attending the prenatal outpatient clinic of Erasmus University Medical Center (Rotterdam, the Netherlands) being less than 3 months pregnant (i.e., target population) were asked by their obstetrician to participate in an interview. Women who could not speak or write Dutch were excluded. The Three-Step Test-Interview Method (TSTI) was used, consisting of concurrent thinking aloud and a focused and semi-structured interview [16]. Women were asked to give their opinion about the relevance of the items, level of understanding, expression and wording, and level of difficulty. Time needed to complete the questionnaire and education level of the pregnant women were registered. We used women's feedback to establish the final questionnaire
This study was approved by the Ethical Committee of the Erasmus University.

**Table I:**
Knowledge domains and items associated with these domains (items selected to be included in final knowledge questionnaire in **bold**)

| Knowledge domain | Mean importance domain | SD importance domain | Item(s) | Mean importance item | SD importance item |
|---|---|---|---|---|---|
| 8. What to do in the event of an 'increased probability for DS' test result | **1.1** | **0.3** | **8.2 Amniocentesis and chorionic villus sampling may induce a spontaneous miscarriage.** | **1.3** | **0.5** |
| | | | 8.3 The risk of having a miscarriage when undergoing amniocentesis or chorionic villus sampling is slight. | 1.4 | 0.5 |
| | | | 8.1 Should the result of the combined test be positive, it is compulsory to have a further examination carried out (in the form of amniocentesis and chorionic villus sampling). | 1.7 | 0.7 |
| | | | 8.4 Amniocentesis involves taking a sample amniotic fluid with a fine needle through the abdominal wall of the mother. | 2.1 | 0.7 |
| | | | 8.6 Chorionic villus sampling involves removing tissue from the placenta. | 2.4 | 0.8 |
| | | | 8.5 The risk of having a spontaneous miscarriage is larger in a pregnant woman carrying a child with Down's syndrome than in a normal pregnancy. | 2.6 | 0.9 |
| | | | 8.7 Chorionic villus sampling can be carried out through the vagina or the abdominal wall. | 2.6 | 1 |
| 5. The meaning of an 'increased probability for DS' test result. (including the possibility of false positives) | **1.1** | **0.4** | **5.1 Should the result of the combined test be positive, this means that the child has Down's syndrome with certainty.** | **1.2** | **0.4** |
| | | | 5.2 Should the result of the combined test be positive, the pregnant woman will be offered a further examination (amniocentesis or chorionic villus sampling). | 1.3 | 0.4 |
| | | | 5.3 Should the result of the combined test be positive, a further examination will be necessary before being able to confirm whether or not the child has Down's syndrome. | 1.3 | 0.6 |
| 1. Purpose of screening | **1.2** | **0.4** | 1.1 Prenatal screening for Down's syndrome provides certainty on the health of the unborn child. | 1.3 | 0.6 |
| | | | 1.3 Prenatal screening for Down's syndrome only provides information on the possible presence of Down's syndrome in an unborn child. | 1.4 | 0.6 |

**Table 1 (continued):**
Knowledge domains and items associated with these domains (items selected to be included in final knowledge questionnaire in **bold**)

| Knowledge domain | Mean importance domain | SD importance domain | Item(s) | Mean importance item | SD importance item |
|---|---|---|---|---|---|
| | | | **1.2 The individual risk that a child has Down's syndrome can be determined through prenatal screening.** | **1.4** | **0.7** |
| 12. Voluntary nature of the test | **1.2** | **0.4** | **12.1 Prenatal screening for Down's syndrome is compulsory for every pregnant woman in the Netherlands.** | **1.4** | **0.8** |
| 6. The meaning of a 'decreased probability for DS' test-result. (including the possibility of false negatives) | **1.3** | **0.5** | **6.1 Should the result of the combined test be negative, the child may still prove to have Down's syndrome when born.** | **1.3** | **0.4** |
| | | | 6.2 A negative result of the combined test does not guarantee that a child will be healthy. | 1.6 | 0.7 |
| 10. What to do after a further examination | **1.4** | **0.5** | **10.1 Should Down's syndrome be diagnosed during the first half of the pregnancy, it is an option for a pregnant woman to terminate the pregnancy.** | **1.2** | **0.4** |
| | | | 10.2 Should the unborn child prove to have Down's syndrome, I may decide to continue the pregnancy. | 1.3 | 0.4 |
| 9. Possible findings resulting from a further examination | **1.5** | **0.5** | **9.2 Both amniocentesis and chorionic villus sampling provide certainty about the presence of Down's syndrome in an unborn child.** | **1.1** | **0.3** |
| | | | 9.3 A further examination carried out following a positive result of the combined test may show that the unborn child does not have Down's syndrome. | 1.1 | 0.4 |
| | | | 9.1 Amniocentesis or chorionic villus sampling may unintentionally induce the spontaneous miscarriage of a healthy child. | 1.4 | 0.6 |
| 11. Possible side effects of the test procedure | **1.5** | **0.5** | 11.4 Carrying out a further examination (amniocentesis or chorionic villus sampling) provides certainty about the presence or absence of Down's syndrome in an unborn child. | 1.4 | 0.8 |
| | | | **11.3 The result of prenatal screening for Down's syndrome may lead to difficult choices and decisions.** | **1.5** | **0.5** |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | 11.2 The result of prenatal screening for Down's syndrome may cause anxiety. | 1.7 | 0.6 |
| | | | | 11.5 Participating in prenatal screening for Down's syndrome may result in having to consider terminating the pregnancy. | 1.8 | 0.9 |
| | | | | 11.1 The result of prenatal screening for Down's syndrome provides certainty. | 2.1 | 1.1 |
| 2. | The condition being screened for | **1.6** | **0.5** | **2.1 All children with Down's syndrome are mentally handicapped.** | **1.4** | **0.6** |
| | | | | 2.3 There is a lot of variation in the development and health problems of children with Down's syndrome. | 1.8 | 0.7 |
| | | | | **2.2 Heart defects in children with Down's syndrome can generally be treated effectively.** | **1.9** | **0.7** |
| 3. | Prevalence in the population (The theoretical risk that the disorder that is tested is present) | **1.6** | **0.5** | **3.1 The risk that an unborn child has Down's syndrome is generally very slight.** | **1.8** | **0.8** |
| | | | | 3.2 An older pregnant woman has a greater risk of having a child with Down's syndrome than a younger woman. | 1.8 | 0.8 |
| | | | | 3.3 Down's syndrome only occurs in families which already have children that have been born with Down's syndrome. | 2.3 | 0.8 |
| | | | | 3.4 If a pregnant woman leads a healthy life, the risk of having a child with Down's syndrome is slighter than that of a pregnant woman leading an unhealthy life. | 2.4 | 1 |
| 4. | Test procedure | **1.6** | **0.7** | **4.1 The combined test consists of a measurement of the thickness of the nuchal fold and carrying out a blood test.** | **1.3** | **0.6** |
| | | | | 4.2 Repeatedly carrying out an ultrasound is dangerous to the unborn child. | 2.4 | 0.9 |
| 7. | The expected percentage of detection | **1.8** | **0.8** | 7.1 If the child has Down's syndrome, this will always be detected through screening. | 1.7 | 0.8 |

a Items were selected to be included in the draft knowledge measure, if they were scored as the most important (lowest mean) by the majority of experts (lowest standard deviation). Exceptions were made for this selection method if the answers to questions 3 and/or 4 indicated that the item with the highest level of importance and consensus was not useful in its presented form, which was the case for items from domains 1, 3, and 11. A more suitable item in terms of wording or formulation was chosen from the same domain then.

b Practical reasons were sometimes decisive in changing or excluding an item. All of these reasons were analysed and discussed extensively in our research group until consensus was reached. For example, item 7.1 was excluded because of the overlap with item 6.1. In addition, we included two items concerning the domain 'the condition being screened for (items 2.1 and 2.2).

# 3. Results

### 3.1. Evaluation of the content of decision-relevant knowledge

Of the experts, 12 professionals (80%), covering all 12 relevant disciplines,[1] and three pregnant women (60%) filled in the questionnaire about draft content. They scored all domains as (very) important (mean score ranging from 1.1 to 1.8) (Table 1).
Based on these results, we included all domains in the draft knowledge measure.
Feedback on the wording and/or expression of the items is presented in Table 2. We supplemented or rephrased items if necessary from the responses to questions 3 and 4.
We selected12 items to be included in the final knowledge measure (Table 1, bolded items).

### 3.2. Qualitative testing of the knowledge measure

All 10 women asked to participate, agreed to fill in the questionnaire and were interviewed. Of these women, 80% had a high education level (higher vocational education or university degree). None of the women needed more than 5 min to fill in the questionnaire. They made relevant critical comments on 5 of the 12 items (Table 2). Based on this feedback, we replaced some words and rephrased sentences, after being discussed in our research group. We reordered items, based on content and logic. Fig. 1 shows the final knowledge measure.

# 4. Discussion and conclusions

### 4.1. Discussion

We developed an instrument to measure knowledge about prenatal screening for DS with the combined test, using input from a broad range of professionals, and of potential participants. Using this approach we took into account the differences that might exist between clinicians and patients regarding goals, purposes, and values on testing [9,17]. The questionnaire is short and suitable for self-completion. Its psychometric properties and feasibility for programme evaluation now need to be investigated by application in a large unselected group of women potentially eligible for screening. We expect acceptance by professionals to be high, because they were involved in the development process.

Contrary to other knowledge measures [9,18–20], this measure represents all eight knowledge domains proposed by the Royal College of Obstetricians and Gynaecologists (RCOG) [14]. The importance of knowledge concerning DS is considered essential [21], therefore, two items of the knowledge measure relate to the RCOG knowledge area "the condition being screened for". Our expert consultation led to the inclusion of several very important domains that were lacking in earlier research.

[1] Experts from the following institutes provided feedback on the knowledge questionnaire: Royal Dutch Midwives Organization (KNOV); Dutch Association of Obstetrics and Gynaecology (NVOG); Dutch Organization of Pediatrics (NVK); Dutch Genetic Alliance (VSOP; representing the consumers' perspective); Dutch Association of Clinical Genetics (VKGN); Dutch Association of Community Genetics (NACG); Department of Medical Ethics, Erasmus Medical Centre / Maastricht University; Dutch Association of Pediatric Neurology (NVKN); Department of Clinical Epidemiology, Erasmus Medical Centre; Dutch Organization of General Practitioners (NHG); Dutch Organization for Ultrasound (BEN); and the Health Council (GR).

Statements on prenatal screening for Down's syndrome. What do you know?

The statements in this list relate to prenatal screening for Down's syndrome. Throughout this document, this refers to prenatal screening using the combined test.

You will firstly be given a number of statements on prenatal screening for Down's syndrome (with the combined test) and possible follow-up diagnostics (involving amniocentesis or chorionic villus sampling). The purpose of providing these statements is to determine how much you know about these tests. For each statement, please indicate whether you believe that it is true, not true or whether you do not know whether the statement is true or not ('do not know').

1. The probability that your child has Down's syndrome can be determined through prenatal screening in the early stages of pregnancy (true).
2. The probability that an unborn child has Down's syndrome is generally very slight (less than 1%) (true)
3. All children with Down's syndrome are mentally handicapped (true)
4. Heart defects in children with Down's syndrome can generally be treated effectively (true)
5. The combined test consists of a measurement of the thickness of the nuchal fold of the unborn child (a nuchal ultrasound) and a blood test on the mother (true)
6. Should the result of the combined test be unfavourable, this means that the child has Down's syndrome (not true)
7. Should the result of the combined test be favourable, the child may still prove to have Down's syndrome when born (true)
8. Amniocentesis or chorionic villus sampling may induce a miscarriage (true)
9. Both amniocentesis and chorionic villus sampling provide certainty about the presence of Down's syndrome in an unborn child (true)
10. Should Down's syndrome be diagnosed during the first four months of pregnancy, it is possible for a pregnant woman to terminate the pregnancy (true)
11. The result of prenatal screening for Down's syndrome may lead to difficult choices (true)
12. Prenatal screening for Down's syndrome is compulsory for every pregnant woman in the Netherlands (not true)

**Figure 1.** Final knowledge measure, with instruction (correct answers between brackets).

This knowledge measure was tested mostly among highly educated women. We recommend re-testing the measure among a group of women that is more representative of the general population of pregnant women.

### 4.2. Conclusions

We developed a knowledge measure for prenatal screening for DS with the combined test, based on a extensive determination of the content of knowledge relevant to IDM in this screening.

### 4.3. Practice implications

After proper validation of this knowledge measure, it can be included in a measurement of informed choice for large-scale evaluations of the quality of offering prenatal screening for DS.

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**Table 2:**
Original items, feedback professionals (experts and pregnant women), feedback pregnant women (TSTI), items to be included in the final knowledge measure

| | |
|---|---|
| Original item (1.2) | The individual risk that a child has Down's syndrome can be determined through prenatal screening. |
| Feedback professionals | Item is too general; make it more personal.<br>Replace the word 'risk' by the word 'probability' |
| Feedback pregnant women (TSTI) | Item is too general; make it more personal.<br>Individual might be a difficult word.<br>It might be difficult to understand which kind of screening, add that it is about screening early in pregnancy. |
| **New item (1)** | **The probability that your child has Down's syndrome can be determined through prenatal screening in the early stages of pregnancy.** |
| Original item (3.1) | The risk that an unborn child has Down's syndrome is generally very slight. |
| Feedback professionals | "Very slight" is a subjective expression; make it more quantitative.<br>Replace the word 'risk' by the word 'probability' |
| Feedback pregnant women (TSTI) | None. |
| **New item (2)** | **The probability that an unborn child has Down's syndrome is generally very slight (<1%).** |
| Original item (2.1) | All children with Down's syndrome are mentally handicapped. |
| Feedback professionals | None. |
| Feedback pregnant women (TSTI) | None. |
| **New item (3)** | **All children with Down's syndrome are mentally handicapped.** |
| Original item (2.2) | Heart defects in children with Down's syndrome can generally be treated effectively. |
| Feedback professionals | None. |
| Feedback pregnant women (TSTI) | None. |
| **New item (4)** | **Heart defects in children with Down's syndrome can generally be treated effectively.** |
| Original item (4.1) | The combined test consists of a measurementof the thickness of the nuchal fold and carrying out a blood test. |
| Feedback professionals | For the blood test, the serum of the mother is used. |
| Feedback pregnant women (TSTI) | Add that an ultrasound is used for nuchal translucency measurement, add that the nuchal translucency measurement is done in the unborn child. |

| | |
|---|---|
| **New item (5)** | **The combined test consists of a measurement of the thickness of the nuchal fold of the unborn child (a nuchal ultrasound) and a blood test on the mother** |
| Original item (5.1) | Should the result of the combined test be positive, this means that the child has Down's syndrome with certainty. |
| Feedback professionals | Term ' positive' might be confusing. |
| Feedback pregnant women (TSTI) | Delete ' with certainty'; with the combined test, you do not have certainty. |
| **New item (6)** | **Should the result of the combined test be unfavourable, this means that the child has Down's syndrome.** |
| Original item (6.1) | Should the result of the combined test be negative, the child may still prove to have Down's syndrome when born |
| Feedback professionals | Term 'negative' might be confusing. |
| Feedback pregnant women (TSTI) | None. |
| **New item (7)** | **Should the result of the combined test be favourable, the child may still prove to have Down's syndrome when born.** |
| Original item (8.2) | Amniocentesis and chorionic villus sampling may induce a spontaneous miscarriage. |
| Feedback professionals | 'Spontaneous miscarriage' is jargon. |
| Feedback pregnant women (TSTI) | Some pregnant women only know the risk of a spontaneous miscarriage for one of the procedures (amniocentesis or chorionic villus sampling), therefore advice to change ' and' in 'or' . |
| **New item (8)** | **Amniocentesis or chorionic villus sampling may induce a miscarriage.** |
| Original item (9.2) | Both amniocentesis and chorionic villus sampling give certainty about the presence of Down's syndrome in an unborn child. |
| Feedback professionals | None. |
| Feedback pregnant women (TSTI) | None. |
| **New item (9)** | **Both amniocentesis and chorionic villus sampling give certainty about the presence of Down's syndrome in an unborn child.** |
| Original item (10.1) | Should Down's syndrome be diagnosed during the first half of the pregnancy, it is an option for a pregnant woman to terminate the pregnancy. |
| Feedback professionals | Specify ' first half' ; terminate pregnancy can only be done in the first 4 months. |
| Feedback pregnant women (TSTI) | Some pregnant women do not know the meaning of the word ' option' ; advice to change this word. |

**Table 2 (continued):**
Original items, feedback professionals (experts and pregnant women), feedback pregnant women (TSTI), items to be included in the final knowledge measure

| | |
|---|---|
| **New item (10)** | **Should Down's syndrome be diagnosed during the first four months of pregnancy, it is possible for a pregnant woman to terminate the pregnancy.** |
| Original item (11.3) | The result of prenatal screening for Down's syndrome may lead to difficult choices and decisions. |
| Feedback professionals | What is the difference between ' choices' and ' decisions' . |
| Feedback pregnant women (TSTI) | None. |
| **New item (11)** | **The result of prenatal screening for Down's syndrome may lead to difficult choices.** |
| Original item (12.1) | Prenatal screening for Down's syndrome is compulsory for every pregnant woman in the Netherlands. |
| Feedback professionals | None. |
| Feedback pregnant women (TSTI) | None. |
| **New item (12)** | **Prenatal screening for Down's syndrome is compulsory for every pregnant woman in the Netherlands.** |

# Appendix A

**Description of the Dutch programme for prenatal Down's syndrome screening**

In the Netherlands, all pregnant women must be asked if they would like to receive information about first trimester screening for DS with the combined test. The combined test consists of two examinations: a maternal serum test between 9 and 14 weeks of pregnancy and a nuchal translucency measurement between 11 and 14 weeks of pregnancy. Together with information on the duration of pregnancy and the age of the pregnant woman, an individualized risk estimation of having a child with DS can be obtained. Only women 36 years of age or older are compensated for the expense. Women younger than 36 years can still be screened but must pay the costs themselves unless they have a listed indication for invasive testing. Women found to have an increased probability of having a child with DS (1:200 or greater) can opt for invasive testing (i.e. chorionic villus sampling or amniocentesis) to determine the fetal karyotype. If DS is detected, the parents-to-be can choose to either continue the pregnancy and prepare for the birth of a child with DS, or to terminate the pregnancy. If the test result indicates an increased probability of DS, the costs of invasive testing and selective termination are reimbursed.

# References


[1] Health council of The Netherlands: committee genetic screening. Genet Screen 1994;22.
[2] Health Council of the Netherlands. Prenatal screening (2); Down's syndrome, neural tube defects, Health Council of the Netherlands; 2004, 2004/06.
[3] Health Council of the Netherlands, Population screening act: inition of a national programme for prenatal screening: Down's syndrome and neural tube defects [Wet Bevolkingsonderzoek: aanzet voor een landelijk programma voor prenatale screening]; 2006, 2006/03.
[4] Health Council of the Netherlands: Committee on the Population Screening Act, Population screening act: the assessment of permit applications; 1996, P 09WBO.
[5] Grijseels EWM, Laudy JAM, Galjaard RJH, Wildschut HIJ. [Prenatal testing for Down's syndrome: medico-technical considerations and dilemmas arising from current opportunities. In Dutch]. Prenataal onderzoek naar Down syndroom: medisch-technische overwegingen en dilemma's voortkomend uit de huidige toepassingsmogelijkheden. Ned Tijdschr Geneeskd 2004;148: 2166–71.
[6] Marteau TM, Dormandy E, Michie S. A measure of informed choice. Health Expect 2001;4:99–108.
[7] Michie S, Dormandy E, Marteau TM. The multi-dimensional measure of informed choice: a validation study. Patient Educ Couns 2002;48:87–91.
[8] Michie S, Dormandy E, Marteau TM. Informed choice: understanding knowledge in the context of screening uptake. Patient Educ Couns 2003;50:247–53.
[9] Green JM, Hewison J, Bekker HL, Bryant LD, Cuckle HS. Psychosocial aspects of genetic screening of pregnant women and newborns: a systematic review. Health Technol Assess 2004;8:1–109.
[10] Wald N. Information leaflets in medical screening. J Med Screen 2006;13:109.
[11] Kohut RJ, Dewey D, Love EJ. Women's knowledge of prenatal ultrasound and informed choice. J Genet Couns 2002;11:265–76.
[12] Smith RP, Titmarsh S, Overton TG. Improving patients' knowledge of the fetal anomaly scan. Ultrasound Obstet Gynecol 2004;24:740–4.
[13] Zapka JG, Geller BM, Bulliard JL, Fracheboud J, Sancho-Garnier H, Ballard-Barbash R, Group ICW. Print information to inform decisions about mammography screening participation in 16 countries with population-based programs. Patient Educ Couns 2006;63:126–37.
[14] Royal College of Obstetricians and Gynaecologists. Report of the working party on biochemical markers and the detection of Down's syndrome. RCOG Press; 1993.
[15] Dutch National Institute for Public Health and the Environment (RIVM). Information about screening for Down's Syndrome and the 20-week ultrasound, http://www.rivm.nl/pns_en/down_ultrasound/information/; 2010.
[16] Hak T, van der Veer K, Jansen H. The Three-Step Test-Interview (TSTI): an observational instrument for pretesting self-completion questionnaires. Report Series Research in Management; 2004.
[17] Hunt LM, de Voogd KB, Castaneda H. The routine and the traumatic in prenatal genetic diagnosis: does clinical information inform patient decision-making? Patient Educ Couns 2005;56:302–12.
[18] Goel V, Glazier R, Holzapfel S, Pugh P, Summers A. Evaluating patient's knowledge of maternal serum screening. Prenat Diagn 1996;16:425–30.
[19] van den Berg M, Timmermans DR, Ten Kate LP, van Vugt JM, van der Wal G. Are pregnant women making informed choices about prenatal screening? Genet Med 2005;7:332–8.
[20] van den Berg M, Timmermans DR, ten Kate LP, van Vugt JM, van der Wal G. Informed decision making in the context of prenatal screening. Patient Educ Couns 2006;63:110–7.
[21] Chilaka VN, Konje JC, Stewart CR, Narayan H, Taylor DJ. Knowledge of Down syndrome in pregnant women from different ethnic groups. Prenat Diagn 2001;21:159–64.

# Chapter 3 Informed decision-making about the fetal anomaly scan: What knowledge is relevant?

Informed decision-making about the fetal anomaly scan: what knowledge is relevant? Schoonen, H.M.H.J.D., Essink-Bot, M.L., van Agt, H.M., Wildschut, H.I., Steegers, E.A., de Koning, H.J.
Ultrasound in Obstetrics and Gynecology. 2011; **37** (6): 649-57

**Abstract**

*Objectives:* This study had two objectives. The first was to determine the contents of relevant knowledge needed for informed decision-making (IDM) in secondtrimester ultrasound screening for fetal anomalies, with the goal of developing a knowledge measure for use in large-scale program evaluations. The second was to compare the contents of decision-relevant knowledge for second-trimester ultrasound screening with those for first-trimester screening for Down syndrome using the combined test.

*Methods:* A generic list of content domains for knowledge about screening was extracted from the literature. Items reflecting specific knowledge domains for secondtrimester ultrasound screening were constructed. An expert group of professionals and pregnant women expressed whether domains and items represented decision-relevant knowledge.

*Results:* Regarding second-trimester ultrasound screening, the experts scored all knowledge domains as (very) important. The meaning of an abnormal test result, the disorders being screened for, and the purpose of the screening were rated as very important for IDM, along with the voluntary nature of the test. All knowledge domains were included in the final measure. Importance ratings of knowledge domains for first-trimester Down syndrome screening and for second-trimester ultrasound screening were highly correlated (Pearson's $r$ = 0.71). The domain 'consequences of a positive test result' was considered more important in first-trimester Down syndrome screening than in second-trimester ultrasound screening.

*Conclusions:* We have developed a knowledge measure for second-trimester ultrasound screening for fetal anomalies for use in routine, large-scale program evaluations.

# Introduction

Second-trimester ultrasound screening for fetal anomalies (or fetal anomaly scan), primarily aims to detect structural malformations when termination of pregnancy is still legal[1]. In The Netherlands, as in most other Western European countries, second-trimester ultrasound screening for fetal anomalies has become a standard part of prenatal care[2–4] (Appendix 1). To enable informed decision-making (IDM) about whether to undergo this screening, Dutch healthcare professionals are required to ask every pregnant woman if she wants information about the fetal anomaly scan[5].
In contrast to first-trimester screening for Down syndrome, second-trimester screening is attractive to women and to their partners[4], and uptake rates are high (up to 100%)[6,7]. Ultrasound scans provide visual confirmation of pregnancy and possible reassurance about fetal wellbeing. However, potentially unfavorable results may require repeat scans and induce uncertainty. If there is a severe anomaly, prospective parents may be confronted with the difficult decision of whether to terminate the pregnancy. The detection of soft markers (subtle morphological changes that are often transient and have little or no pathological significance[8,9]) or the observation that there is an anomaly of uncertain severity, can cause substantial additional uncertainty and distress[10]. These features highlight the relevance of IDM, emphasized by international guidelines on ultrasound screening[11,12].

An informed decision is based on adequate knowledge, whereas actual behavior is consistent with the decisionmakers' values[13,14]. The proportion of women eligible for screening who have adequate relevant knowledge may be regarded as an indicator of the quality of the information offer. There is currently no knowledge measure designed for use in large-scale evaluations of IDM about the fetal anomaly scan. Recently, we determined the contents of decision-relevant knowledge needed for IDM in firsttrimester screening for Down syndrome[15].
The first objective of this study was to determine the contents of relevant knowledge needed for IDM in secondtrimester ultrasound screening for fetal anomalies, with the ultimate goal of developing a knowledge measure for use in large-scale evaluations of IDM. The second objective was to compare the contents of decision-relevant knowledge for IDM in second-trimester ultrasound screening with those for first-trimester screening for Down syndrome using the combined test, as determined previously[15].

# Methods

### Determining the contents and the level of decision-relevant knowledge

An overview of the method we used to develop a knowledge measure for second-trimester ultrasound screening for fetal anomalies (subsequent actions we performed, specification of these actions and the results), is presented in Figure 1.

First, we established a list of content domains representing knowledge areas considered essential for making an informed choice regarding participation in screening *in general* (not specific for secondtrimester ultrasound screening). The content domains in this list were extracted from the literature[16–18] and from international guidelines[19,20]. Second, we specified these generic content domains into content domains representing knowledge areas *specific* for second-trimester ultrasound screening. In doing this, we used scientific literature and national information material on this screening (i.e. public outreach information targeting

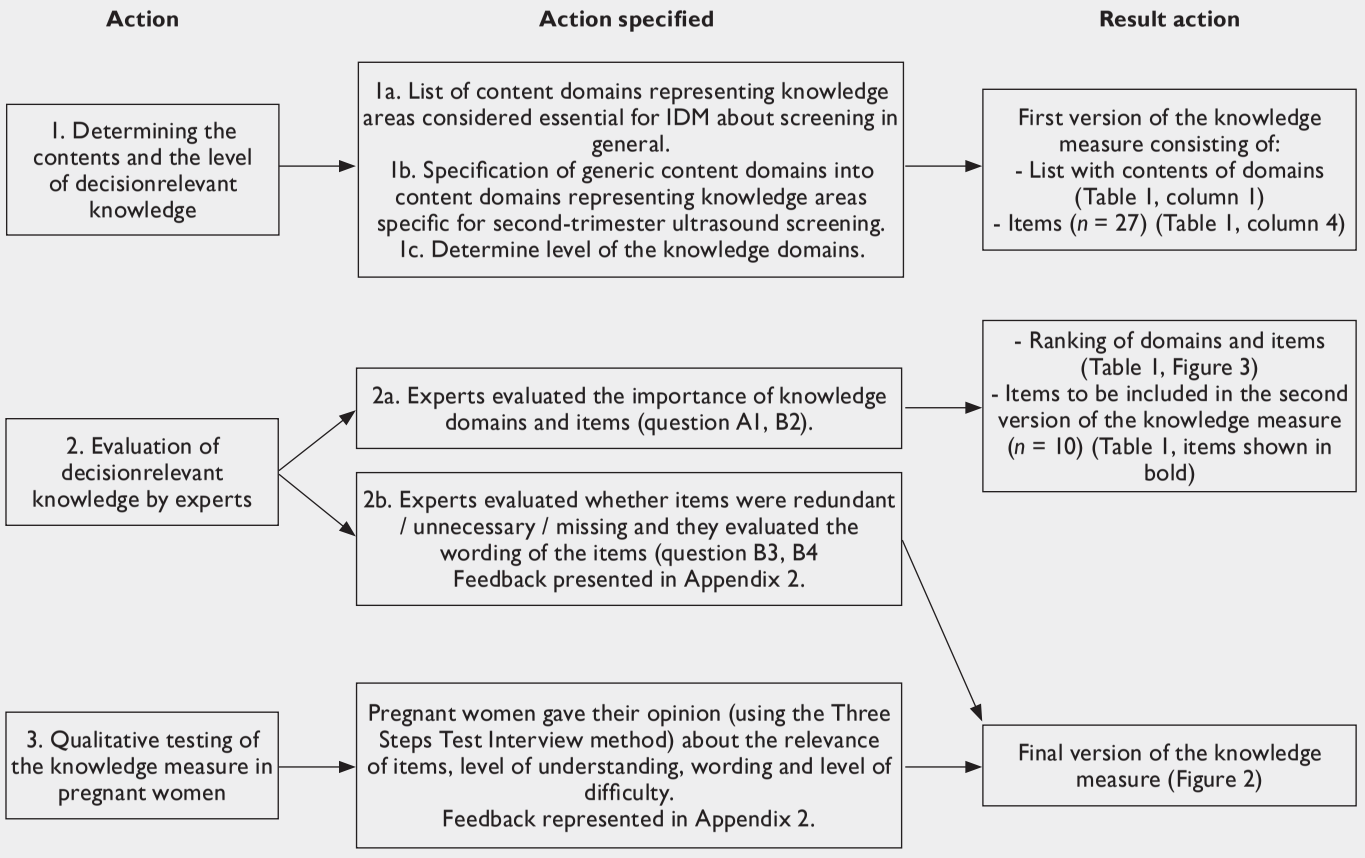


**Figure 1** Overview of the method used to develop a knowledge measure for second-trimester ultrasound screening for fetal anomalies.

pregnant women and their partners[21]). In addition, we used the national quality standard, 'Prenatal Screening for Fetal Disorders', of the Dutch Association of Obstetrics and Gynaecology (NVOG)[22]. The NVOG based the content domains mentioned in this standard on the domains of the Royal College of Obstetricians and Gynaecologists (RCOG)[23].

Our literature search revealed information regarding the *contents* of domains constituting relevant knowledge for second-trimester ultrasound screening for fetal anomalies, but there was no information on the *level* of the knowledge required. So, as a third step, we used the Dutch national information material to estimate the level of knowledge considered necessary for IDM. These three steps resulted in a list of contents of knowledge domains that are specific for IDM regarding secondtrimester ultrasound screening.

Finally, we drafted items (statements with response options of 'true', 'false' or 'do not know') for each of the knowledge domains. Each item reflected the contents and the level of one of the knowledge domains for second-trimester ultrasound screening that we listed. We included these items in a first version of the knowledge measure.

**Evaluation of decision-relevant knowledge by experts**

A group of experts consisting of 15 professionals from 12 relevant disciplines (representing the broad field of professions involved in prenatal screening) and five pregnant women (representing the potential participants in the screening) were asked to evaluate the importance of the knowledge domains, and the importance of the items reflecting these domains, included in the first version of the knowledge measure. We selected highly educated pregnant women who were able to evaluate the content domains and items of the knowledge measure at a meta level.

The experts responded to the following questions.

A. Regarding each knowledge domain:
   1. How important is this domain for making an informed decision about participating or not participating in second-trimester ultrasound screening for fetal anomalies?

B. Regarding the specification of knowledge in the draft knowledge measure:
   2. How important are the contents of the items associated with the knowledge domain?
   3. For each knowledge domain, are there redundant/unnecessary or missing items? If yes, which ones?
   4. For each item, do you have suggestions for better ways to express or word the item? For the entire measure, do you miss knowledge domains? If yes, which ones?

Responses to questions 1 and 2 were scaled from 1 (very important) to 4 (not important at all). Assuming measurement at interval levels, the mean values of these scores can be regarded as indicators of the importance of a domain or item: the lower the mean value, the greater the importance. Standard deviations can be considered as indicators of the experts' level of consensus on the reported importance of the domain or item: the smaller the standard deviation, the greater the level of consensus. The experts' responses were analyzed to rank the domains in order of importance (from the lowest to the highest mean scores) and to determine the level of consensus among experts regarding this ranking (standard deviations). If domains had the same mean scores, the domain with the smaller standard deviation was ranked higher. We applied the same methods to ranking items.

We selected items to be included in the second version of the knowledge measure, based on the results of this expert consultation.

### Qualitative testing of the knowledge measure in pregnant women

Ten women attending the prenatal outpatient clinic at Erasmus University Medical Center (Rotterdam, The Netherlands) were asked by their obstetrician to participate in an interview. Women who could not speak or write in Dutch were excluded. The Three-Step Test-Interview (TSTI) method was used, which consists of 'thinking aloud' plus a focused and semistructured interview[24]. We asked these women to give their opinion about the relevance of the items, their level of understanding, the wording, and the level of difficulty of the second version of the knowledge measure. We registered the time required to complete this version of the knowledge measure, the woman's education level, and gestational age at the time of the interview. We used the women's feedback to finalize the knowledge measure.

### Comparison of decision-relevant knowledge in first-trimester screening for Down syndrome with that in second-trimester ultrasound screening for fetal anomalies

In a previous study[15], we determined the contents of the decision-relevant knowledge required for IDM about participating in first-trimester screening for Down syndrome using the combined test. We used the same methods in that study as in the current study, providing us with a unique opportunity to compare the decisionrelevant knowledge in first-trimester screening for Down syndrome with that in second-trimester ultrasound screening for fetal anomalies.
The same domains were applied in both studies with one exception: the domains 'The condition being screened for' and 'Purpose of the screening' were combined into one item in the knowledge measure for the fetal anomaly scan ('Disorders being screened for and purpose of the screening'). Domains were ranked based on the importance ratings of the experts (from the lowest mean scores to the highest mean scores) in both studies. The relationship between the importance rankings of the domains for second-trimester ultrasound screening for fetal anomalies and for first-trimester screening for Down syndrome was investigated using the Pearson productmoment correlation coefficient. Data were analyzed using SPSS version 15.0 (SPSS, Chicago, IL, USA).

This study was approved by the Ethical Committee of the Erasmus University Medical Center (Rotterdam, The Netherlands) (MEC-2007-166).

## Results

### Determining the contents and the level of decision-relevant knowledge

Table 1 presents the list of knowledge domains (column 1) and the list of items (column 4) that we determined to be relevant for IDM in second-trimester ultrasound screening. All items presented in Table 1 were included in a first version of the knowledge measure.

**Table 1:**
Knowledge domains, in descending order of assigned importance, and items associated with these domains

| Knowledge domain | Importance score of domain | Item(s) | Importance score of item |
|---|---|---|---|
| 11. Voluntary nature of the test | 1.1 (0.4) | **11.1 Every pregnant woman in the Netherlands is obliged to have a fetal anomaly scan** | 1.6 (0.8) |
| 4. The meaning of an 'abnormal' test-result (including the possibility of false positives) | 1.3 (0.5) | **4.2 If the results of the fetal anomaly scan are 'unfavorable', further examinations must be performed to confirm this result** | 1.3 (0.5) |
| | | 4.3 If the result of the fetal anomaly scan is 'unfavorable', there is a high risk that the child will have a defect | 1.5 (0.5) |
| | | 4.1 If the result of the fetal anomaly scan is 'unfavorable', it is certain that the child will have a defect | 1.5 (0.6) |
| 1. Disorders being screened for and purpose of the screening | 1.4 (0.5) | **1.1 The fetal anomaly scan is used to determine whether your child has severe physical birth defects.** | 1.3 (0.5) |
| | | 1.4 Children who are born with spina bifida often have physical handicaps | 1.5 (0.6) |
| | | 1.3 The fetal anomaly scan is aimed at preparing pregnant women for a child who possibly has a severe physical defect | 1.8 (0.9) |
| | | 1.5 Children who are born with spina bifida often require assistance with their daily care for the rest of their lives | 1.9 (0.9) |
| | | 1.2 The fetal anomaly scan is used to determine whether the child is growing as expected | 2.7 (0.8) |
| 9. What to do after a further examination | 1.4 (0.5) | **9.1 If the unborn child is found to have a severe physical defect, termination of the pregnancy is one of the options** | 1.3 (0.5) |
| | | 9.2 If the unborn child is found to have a severe physical defect, this can be cured after birth | 2.1 (0.9) |
| 5. The meaning of a 'normal' test-result (including the possibility of false negatives) | 1.4 (0.5) | **5.2 If the result of the fetal anomaly scan is 'favorable', there is still the possibility of the child having a defect when it is born** | 1.2 (0.4) |
| | | 5.1 A 'favorable' result on the fetal anomaly scan is a guarantee that the baby is healthy | 1.4 (0.5) |
| | | 5.3 If the result of the fetal anomaly scan is 'favorable', there is a small risk that the child will have a defect | 1.7 (0.8) |

**Table 1 (continued):**
Knowledge domains, in descending order of assigned importance, and items associated with these domains

| Knowledge domain | Importance score of domain | Item(s) | Importance score of item |
|---|---|---|---|
| 7. What to do in the event of an 'abnormal' test-result | 1.5 (0.5) | 7.2 Further examination is required after an abnormal result of the fetal anomaly scan | 1.5 (0.5) |
| | | 7.1 If the result of the fetal anomaly scan is 'unfavorable', an amniocentesis may be offered | 2.1 (0.8) |
| 8. Possible findings resulting from a further examination | 1.5 (0.5) | **8.1 Further examination after an 'unfavorable' result of the fetal anomaly scan may reveal that the child does not have any severe physical defects** | 1.7 (0.5) |
| | | 8.2 Further examination after an 'unfavorable' result of the fetal anomaly scan may confirm that the child does have a severe physical defect | 1.7 (0.5) |
| 10. Possible side effects of the test procedure | 1.5 (0.5) | **10.3 Participation in the fetal anomaly scan may lead to having to decide whether or not to have an abortion** | 1.3 (0.6) |
| | | 10.2 An amniocentesis may result in an unintentional miscarriage | 1.7 (0.9) |
| | | 10.1 The results of the fetal anomaly scan may cause distress | 1.9 (0.8) |
| 6. The expected percentage of detection | 1.7 (0.5) | **6.1 Spina bifida is easy to recognise on the fetal anomaly scan** | 1.7 (0.6) |
| | | 6.2 Spina bifida is easier to recognise on the fetal anomaly scan than a heart defect | 2.5 (0.8) |
| 3. Test procedure | 1.9 (0.6) | **3.1 Repeatedly performing a scan is dangerous for the unborn child** | 2.1 (0.8) |
| 2. Prevalence in the population (The theoretical risk that the disorder that is tested is present) | 1.9 (0.8) | **2.1 The chances that a child will be born with a severe physical defect are relatively low** | 1.7 (0.6) |
| | | 2.2 The chances that a child will be born with a severe physical defect increase as the mother's age increases | 2.1 (0.9) |
| | | 2.3 The chances that a child will be born with a severe defect of the brain or spinal cord increase if these defects occur within the family | 2.2 (0.9) |

Items selected for the final knowledge questionnaire are shown in **bold.** Values represent mean (SD)

### Evaluation of decision-relevant knowledge by experts

Experts were asked to evaluate the importance of all items presented in Table 1. In addition, they were asked to evaluate the importance of the knowledge domains.

Of the expert group, 15 professionals from all 12 relevant disciplines and two pregnant women completed the questionnaire about the first version of the knowledge measure. Experts from the following organizations provided feedback on the knowledge measure: the Royal Dutch Midwives Organization (KNOV); the NVOG; the Dutch Organization of Pediatrics (NVK); the Dutch Genetic Alliance (VSOP; representing the consumers' perspective); the Dutch Association of Community Genetics (NACG); the Department of Medical Ethics, Erasmus Medical Center/Maastricht University; the Dutch Association of Pediatric Neurology (NVKN); the Department of Clinical Epidemiology, Erasmus Medical Center; the Dutch Organization of General Practitioners (NHG); the Dutch Organization for Ultrasound (BEN); the Dutch Health Council (GR); and the Dutch Association for Neurosurgery (NVVN). Additionally, a child neurologist and an expert in the field of screening provided feedback.

In Table 1, we provide, for each of the domains and the accompanying item, mean scores (reflecting the importance ratings as provided by the experts) and standard deviations (expressing the experts' level of consensus on the reported importance of the domain or the item). We ranked the domains and the items shown in Table 1 according to the mean importance ratings (starting with the most important domains). From Table 1, it can be seen that all domains were scored as (very) important, with mean scores ranging from 1.1 to 1.9. Therefore, we decided to include items for all domains in the second version of the knowledge measure.

To create a short knowledge measure, we had to determine which of the items we should include in the second version of the knowledge measure. Therefore, we selected the items scored as most important (i.e. those with the lowest mean scores) by the majority of the experts (i.e. those with the lowest standard deviation). In Table 1, these items are presented in bold type.
Practical reasons were sometimes decisive in changing or excluding an item. All of these reasons were analyzed and discussed extensively in our research group until a consensus was reached. For example, items from domain 7 ('What to do in the event of an abnormal test result') were excluded because they overlapped too much with items from domain 4 ('The meaning of an 'abnormal' testresult'). This change resulted in a second version of the knowledge measure with 10 items that was subsequently tested in pregnant women.

### Qualitative testing of the knowledge measure in pregnant women

All 10 women who were asked to participate agreed to fill in the draft knowledge measure and to be interviewed. Of these women, 80% had a high educational level (higher vocational education or a university degree). The median gestational age of these women was 27 (range, 18–37) weeks. None of the women needed more than 5 min to complete the knowledge measure, and there were relevant critical comments on five of the 12 items. The feedback on the wording of the items, from both the experts (their answers to questions B3 and B4; see the Methods) and the pregnant women (in the qualitative testing panel), is presented in Appendix 2. We reworded or expanded the items if this feedback indicated that this was appropriate. In addition, we replaced some words and rephrased some items after discussion

Statements on prenatal screening using the fetal anomaly scan.
What do you know?

There are 10 statements listed below. The statements in this list relate to second-trimester ultrasound screening for fetal anomalies. The purpose of providing these statements is to determine how much you know about this screening. For each statement, please indicate whether you believe that it is true, not true, or whether you do not know whether the statement is true or not ('do not know').

1. The fetal anomaly scan is aimed at examining the unborn child for certain physical abnormalities (true).
2. The result of prenatal screening with the fetal anomaly scan may lead to difficult choices, for example termination of the pregnancy (true).
3. Spina bifida is usually clearly recognized using the fetal anomaly scan (true).
4. The chance that a child has a congenital abnormality is generally relatively small (less than 5%) (true).
5. Repeatedly performing a scan is dangerous for the unborn child (not true).
6. If the result of the fetal anomaly scan is 'abnormal', further examination is usually required to obtain more certainty (true).
7. If the result of the fetal anomaly scan is 'no abnormality', there is still the possibility of the child having an abnormality when it is born (true).
8. Further examination after an abnormal result on the fetal anomaly scan may reveal that the child does not have any major physical abnormalities (true).
9. Should a major physical abnormality be found in the fetal anomaly scan, termination of the pregnancy would be a possibility (true).
10. Every pregnant woman in the Netherlands is obliged to have a fetal anomaly scan (not true).

**Figure 2:**
Final knowledge measure, with instruction (the correct answers are shown in parentheses).

within our research group. We also re-ordered items, based on their contents and on simple logic. Figure 2 shows the final knowledge measure.

### Comparison of decision-relevant knowledge in first-trimester screening for Down syndrome with that in second-trimester ultrasound screening for fetal anomalies

In the expert consultation, all domains were scored as (very) important (mean scores ranged from 1.1 to 1.8 for first-trimester screening for Down syndrome15 and from 1.1 to 1.9 for second-trimester ultrasound screening for fetal anomalies).

For both screenings, the domains ranked as most important were 'The meaning of an abnormal test result' (termed 'The meaning of an increased probability for DS test result' in the Down syndrome screening), 'Disorders being screened for and purpose of the screening' ('Purpose of the screening' in the Down syndrome screening), and the voluntary nature of the test.
The domains ranked as least important in both screening programs were 'Test procedure', 'Prevalence in the population' (the theoretical risk that the disorder that is tested is present), and 'Expected percentage of detection'.
The domain 'what to do in the event of a positive test result' received a higher expert ranking in first-trimester screening than in second-trimester screening.

Figure 3 shows the experts' ranking of the domains for second-trimester ultrasound screening for fetal anomalies (left column), and the experts' ranking of the domains for first-trimester

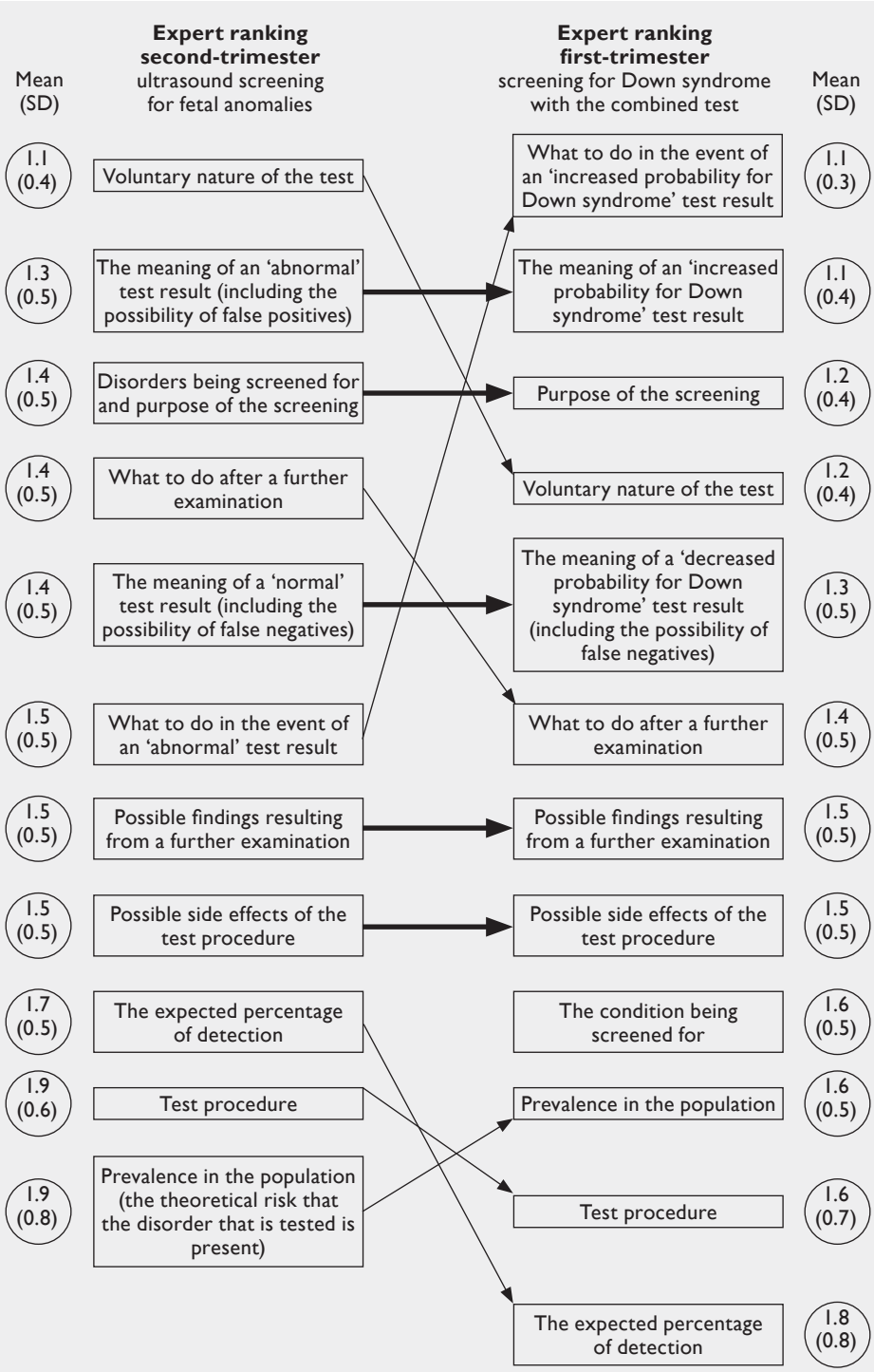


**Figure 3:** Expert rankings of knowledge domains relevant for informed decision-making on second-trimester ultrasound screening and on first-trimester screening for Down syndrome, showing domains which differed (——) and those which were similar (▬▬) in rank between the two examinations.

screening for Down syndrome using the combined test (right column). Five domains (thick lines) were considered as equally important for both screening programs. The meaning of a positive test result was considered as less important knowledge (to make an informed decision) in second-trimester ultrasound screening for fetal anomalies than the meaning of a positive test result in first-trimester screening for Down syndrome.

In Figure 4, the relationship between the importance of the domains for both screening programs is visualized using a scatter plot, with each plot representing a knowledge domain. There was a positive correlation between the importance rankings of the domains for the two screening programs ($r = 0.71$, $n = 11$, $P = 0.015$).

## Discussion

We developed a measure to determine decision-relevant knowledge about second-trimester ultrasound screening for fetal anomalies. The measure is short and suitable for self-completion and can therefore be used routinely in large-scale program evaluations.

Knowledge measures specific to second-trimester ultrasound screening for fetal anomalies are scarce and, in contrast to our measure, are not based on all eight of the knowledge domains proposed by the Royal College of Obstetricians and Gynaecologists[23]. Furthermore, some of these knowledge measures assess perceived knowledge (e.g. 'I know how an ultrasound scan is performed' and 'I feel I was given enough information about the scan') rather than objective knowledge[17]. Perceived knowledge ('subjective knowledge'), although a relevant variable, can only be used to evaluate the quality of the information process in direct connection with measures of objective knowledge. For evaluation of IDM, objective knowledge is the relevant variable. It seems unreasonable to expect women to subjectively judge the adequacy of their knowledge if their objective knowledge is, in fact, inadequate. That is, how can they judge whether they have adequate knowledge if they do not know what exactly constitutes adequate knowledge? The difference between objective and subjective knowledge can be compared with the difference between two key variables in social metacognition: perceived intelligence and perceived levels of knowledge about a specific content domain. Similarly to subjective knowledge, perceived intelligence represents a judgment of one's knowledge at an abstract level ('How much do I know'). Hence, objective knowledge is similar to a judgment of one's knowledge in a specific content domain (what does one really know about a concrete topic)[25,26].

In determining the contents of decision-relevant knowledge required for IDM in second-trimester ultrasound screening for fetal anomalies, we used input from potential participants and from a broad range of professionals. Using this approach helped us to take into account the different viewpoints of clinicians and patients[27,28]. The psychometric properties of the knowledge measure, and its feasibility for program evaluation, now need to be investigated in a large unselected group of women eligible for prenatal screening. We expect good acceptance by professionals because of their active participation in the development process.

Second-trimester screening for fetal abnormalities and first-trimester screening for Down syndrome have one goal in common, namely the detection of fetal malformations. However, these screening programs are quite different entities and have different characteristics: Down screening – with its (seemingly) straightforward purpose; and 20-week screening with its

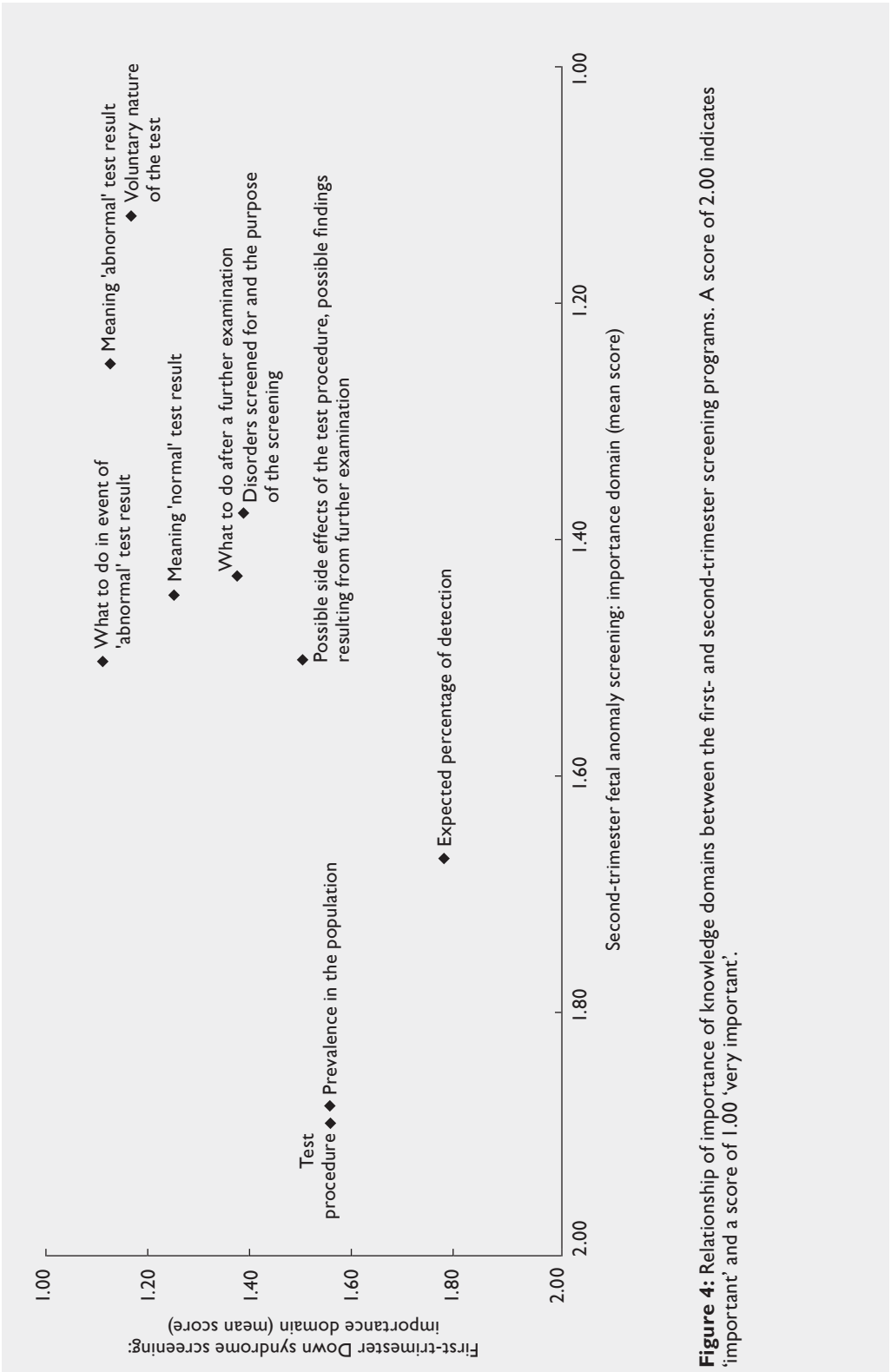


**Figure 4:** Relationship of importance of knowledge domains between the first- and second-trimester screening programs. A score of 2.00 indicates 'important' and a score of 1.00 'very important'.

myriad of possible syndromes, its soft markers and its assessment of structures outside the baby, such as the placenta and the umbilical cord. In addition to these different technical aspects and test characteristics of secondtrimester screening for fetal abnormalities, compared with first-trimester screening for Down syndrome, women attribute different goals to these screening programs and also perceive them as substantially different[29]. Pregnant women often wish to undergo an ultrasound scan for nonmedical reasons, such as to see the baby, to make the pregnancy seem more real, and to discover the sex of the baby[29–31]. Hence, women expect ultrasound to be a positive and pleasant event[1,4,29,31]. In contrast, pregnant women show ambivalence towards screening for Down syndrome[32]. They associate participating in prenatal screening for Down syndrome with abortion and often cite unwillingness to have an abortion as a reason for not participating in the screening program[27]. To summarize, it seems that first-trimester screening for Down syndrome is perceived by pregnant women as being primarily focused on the detection of 'abnormalities', whereas the second-trimester ultrasound is perceived as aiming to confirm 'normality'[29,31]. We recognize these different perceptions in clinical practice, and community midwives, who we contacted during this study, confirmed that pregnant women held these views. Because of these differences in both test characteristics and perceptions of pregnant women of these screening programs, we did not expect to find such a high correlation between experts' rankings for importance of the knowledge domains between firsttrimester and second-trimester screening. On the other hand, one might argue that both screening programs share the goal of early detection of fetal abnormalities. The high correlation that we observed in this study reflects the fact that experts were aware of this common goal and of the equal relevance of domains in this context.

After proper validation of the knowledge measure developed in this study, it may be included in a measurement of informed choice for large-scale evaluations of the quality of the offer of information regarding second-trimester ultrasound screening for fetal anomalies. Each item of the knowledge measure needs to be regarded as an indicator, drawn from a larger sample of other potential indicators, for the contents of its domain. A determination of IDM should, in addition to determining levels of knowledge, include measurement of attitude and consistency between attitude and actual participation in the screening program[13].

The procedure for providing information about prenatal screening for Down syndrome should be monitored and evaluated nationwide on a regular basis. Such monitoring is a way to assess whether the objective of IDM is fulfilled. Assessment of IDM can generate further investigations into the underlying causes of differences in IDM between groups or regions and provide a starting point for improvements in the (procedure of the offer of) information.

The assessment of gaps in knowledge using this measure should contribute to the development of improved information provided through oral and/or written communication to pregnant women and their partners about second-trimester ultrasound screening for fetal anomalies.

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# Appendix 1

**Description of the Dutch program for second trimester ultrasound screening for fetal anomalies**

Each pregnant woman receives basic information about prenatal screening with the fetal anomaly scan during her first appointment with her midwife. The appointment is followed up with a counseling consultation only if the woman indicates that she would like to know more. The fetal anomaly scan is usually performed at around the twentieth week of pregnancy.
If the fetal anomaly scan yields an unfavorable result, the pregnant woman is referred to a prenatal examination center, if desired. An advanced ultrasound scan can be performed to confirm or disprove earlier findings and to discuss any necessary course of action[32].

# Appendix 2

**Original items, feedback experts (professionals and pregnant women), feedback pregnant women (TSTI), items to be included in the final version of the knowledge measure**

| | |
|---|---|
| Original item (1.1) | The fetal anomaly scan is used to determine whether your child has severe physical birth defects. |
| Feedback professionals | Replace 'birth defects' by 'abnormalities'<br>Explain the aim of the screening<br>Replace 'determine' by 'examine' |
| Feedback pregnant women (TSTI) | Not only severe, but also less severe physical birth defects can be recognised; remove the word 'severe'<br>It is about the unborn child |
| **New item (1)** | **The fetal anomaly scan is aimed at examining the unborn child for certain physical abnormalities** |
| Original item (10.3) | Participation in the fetal anomaly scan may lead to having to decide whether or not to have an abortion |
| Feedback professionals | Replace 'abortion' by 'termination of the pregnancy'<br>It is about the result of prenatal screening with the fetal anomaly scan, not about participation<br>Make it broader; explain that the result of the fetal anomaly scan may lead to difficult choices |
| Feedback pregnant women (TSTI) | Remove part 'whether or not' |
| **New item (2)** | **The result of prenatal screening with the fetal anomaly scan may lead to difficult choices, for example termination of the pregnancy** |
| Original item (6.1) | Spina bifida is easy to recognise on the fetal anomaly scan |
| Feedback professionals | Replace 'easy to recognise by 'clearly recognised'. |
| Feedback pregnant women (TSTI) | Whether it is easy to recognise depends also on how the fetus is positioned; add 'usually' |
| **New item (3)** | **Spina bifida is usually clearly recognised using the fetal anomaly scan** |

| | |
|---|---|
| Original item (2.1) | The chances that a child will be born with a severe physical defect are relatively low |
| Feedback professionals | Specify 'relatively low'<br>Replace 'defect' by 'abnormality' |
| Feedback pregnant women (TSTI) | None |
| **New item (4)** | **The chance that a child has a congenital abnormality is generally relatively small (less than 5 %)** |
| Original item (3.1) | Repeatedly performing a scan is dangerous for the unborn child |
| Feedback professionals | None |
| Feedback pregnant women (TSTI) | None |
| **New item (5)** | **Repeatedly performing a scan is dangerous for the unborn child** |
| Original item (4.2) | If the results of the fetal anomaly scan are 'unfavourable', further examinations must be performed to confirm this result |
| Feedback professionals | Replace 'unfavourable' by 'abnormal'<br>It is not that further examinations must be performed, they are usually required to obtain more certainty |
| Feedback pregnant women (TSTI) | None |
| **New item (6)** | **If the result of the fetal anomaly scan is 'abnormal', further examination is usually required to obtain more certainty** |
| Original item (5.2) | If the result of the fetal anomaly scan is 'favourable', there is still the possibility of the child having a defect when it is born |
| Feedback professionals | Replace 'favourable' by 'no abnormality'<br>Replace 'defect' by 'abnormality' |
| Feedback pregnant women (TSTI) | None |
| **New item (7)** | **If the result of the fetal anomaly scan is 'no abnormality', there is still the possibility of the child having an abnormality when it is born** |
| Original item (8.1) | Further examination after an 'unfavourable' result on the fetal anomaly scan may reveal that the child does not have any severe physical defects |
| Feedback professionals | Replace 'unfavourable' by 'abnormal'<br>Replace 'defects' by 'abnormalities'<br>Replace 'severe' by 'major' |
| Feedback pregnant women (TSTI) | Replace 'unfavourable' by 'abnormal' |
| **New item (8)** | **Further examination after an abnormal result on the fetal anomaly scan may reveal that the child does not have any major physical abnormalities** |
| Original item (9.1) | If the unborn child is found to have a severe physical defect, termination of the pregnancy is one of the options |
| Feedback professionals | Replace 'defect' by 'abnormality'<br>Replace 'severe' by 'major'<br>Focus on result of fetal anomaly scan, not on unborn child |
| Feedback pregnant women (TSTI) | Replace 'option' by possibility |
| **New item (9)** | **Should a major physical abnormality be found in the fetal anomaly scan, termination of the pregnancy would be a possibility** |

| | |
|---|---|
| Original item (11.1) | Every pregnant woman in the Netherlands is obliged to have a fetal anomaly scan |
| Feedback professionals | None |
| Feedback pregnant women (TSTI) | None |
| **New item (10)** | **Every pregnant woman in the Netherlands is obliged to have a fetal anomaly scan** |

# References


1. Bricker L, Garcia J, Henderson J, Mugford M, Neilson J, Roberts T, Martin MA. Ultrasound screening in pregnancy: a systematic review of the clinical effectiveness, cost-effectiveness and women's views. Health Technol Assess 2000; 4: i,vi, 1–193.
2. RIVM (Dutch National Institute for Public Health and the Environment). A brief history of the 20-week ultrasound; 2009. http://www.rivm.nl/pns en/down ultrasound/history [Accessed 3 May 2010].
3. Boyd PA, Devigan C, Khoshnood B, Loane M, Garne E, Dolk H, EUROCAT Working Group. Survey of prenatal screening policies in Europe for structural malformations and chromosome anomalies, and their impact on detection and termination rates for neural tube defects and Down's syndrome. BJOG 2008; 115: 689–696.
4. Garcia J, Bricker L, Henderson J, Martin MA, Mugford M, Nielson J, Roberts T. Women's views of pregnancy ultrasound: a systematic review. Birth 2002; 29: 225–250.
5. RIVM (Dutch National Institute for Public Health and the Environment). Policy; timely information about possible disorders; 2009. http://www.rivm.nl/pns en/down ultrasound/policy [Accessed 3 May 2010].
6. Georgsson Ohman S, Waldenstrom U. Second-trimester routine ultrasound screening: expectations and experiences in a nationwide Swedish sample. Ultrasound Obstet Gynecol 2008; 32: 15–22.
7. Healthcare Commission. Towards better births. A review of maternity services in England.2008.
8. Borrell A. Promises and pitfalls of first trimester sonographic markers in the detection of fetal aneuploidy. Prenat Diagn 2009; 29: 62–68.
9. Grijseels EW, Cohen-Overbeek TE, Adama van Scheltema PN, Groenenberg IA, Schoonderwaldt EM, Steegers EA, Wildschut HI. Sonomarkers: subtle ultrasound findings in the 20-week ultrasound examination, which have a low association with some chromosomal and non-chromosomal abnormalities in the fetus. Ned Tijdschr Geneeskd 2008; 152: 2225–2231.
10. Sommerseth E, Sundby J. Women's experiences when ultrasound examinations give unexpected findings in the second trimester. Women Birth 2010; 23: 111–116.
11. Kirwan D. NHS fetal anomaly screening programme (NHS FASP). 2010.
12. RCOG. Report of the RCOG Working Party on Ultrasound Screening for Fetal Abnormalities. RCOG Press: London, 1997.
13. Marteau TM, Dormandy E, Michie S. A measure of informed choice. Health Expect 2001; 4: 99–108.
14. Michie S, Dormandy E, Marteau TM. The multi-dimensional measure of informed choice: a validation study. Patient Educ Couns 2002; 48: 87–91.
15. Schoonen HM, van Agt HM, Essink-Bot ML, Wildschut HI, Steegers EA, de Koning HJ. Informed decision-making in prenatal screening for Down's syndrome: what knowledge is relevant? Patient Educ Couns 2010 [Epub ahead of print].
16. Kohut RJ, Dewey D, Love EJ. Women's knowledge of prenatal ultrasound and informed choice. J Genet Couns 2002; 11: 265–276.
17. Smith RP, Titmarsh S, Overton TG. Improving patients' knowledge of the fetal anomaly scan. Ultrasound Obstet Gynecol 2004; 24: 740–744.
18. Zapka JG, Geller BM, Bulliard JL, Fracheboud J, Sancho- Garnier H, Ballard-Barbash R, IBSN Communications Working Group. Print information to inform decisions about mammography screening participation in 16 countries with populationbased programs. Patient Educ Couns 2006; 63: 126–137.
19. Council of Europe, Committee of Ministers. Recommendation No. R (90) 13 of prenatal genetic screening, prenatal genetic diagnosis and associated genetic counselling; 1990. http://www1.umn.edu/humanrts/instree/coerecr90-13. html [Accessed 3 July 2010].
20. UK National Screening Committee (NHS). Antenatal screeningworking standards incorporating those for the national down syndrome screening programme for England; 2003. http://cpd.screening.nhs.uk/choicestoolbox/docs/working-standards.pdf [Accessed 3 July 2010].

21. RIVM (Dutch National Institute for Public Health and the Environment). Information about screening for Down's Syndrome and the 20-week ultrasound; 2009. http://www.rivm.nl/pns en/ down ultrasound/information [Accessed 3 May 2010].
22. NVOG (Dutch Association of Obstetrics and Gynaecology). Kwaliteitsnorm 6-Prenatale screening op foetale afwijkingen; 2005. http://www.knov.nl/docs/uploads/pns-kwn 06 pren screening op foetale afwijkingen 1.pdf [Accessed 3 June 2010].
23. Royal College of Obstetricians and Gynaecologists. Report of the Working Party on Biochemical Markers and the Detection of Down's Syndrome. RCOG Press: London, 1993.
24. Hak T, van der Veer K, Jansen H. The Three-Step Test- Interview (TSTI): an observational instrument for pretesting self-completion questionnaires. ERIM Report ERS-2004-029-ORG. Erasmus Research Institute of Management: Rotterdam, 2004. http://hdl.handle.net/1765/1265.
25. Jaccard J, Dodge T, Guilamo-Ramos V. Metacognition, risk behavior, and risk outcomes: the role of perceived intelligence and perceived knowledge. Health Psychol 2005; 24: 161–170.
26. Raju PS, Lonial SC, Mangold WG. Differential effects of subjective knowledge, objective knowledge, and usage experience on decision making: an exploratory investigation. J Consum Psychol 1995; 4: 153–180.
27. Green JM, Hewison J, Bekker HL, Bryant LD, Cuckle HS. Psychosocial aspects of genetic screening of pregnant women and newborns: a systematic review. Health Technol Assess 2004; 8: iii, ix,x, 1–109.
28. Hunt LM, de Voogd KB, Castaneda H. The routine and the traumatic in prenatal genetic diagnosis: does clinical information inform patient decision-making? Patient Educ Couns 2005; 56: 302–312.
29. Santalahti P, Aro AR, Hemminki E, Helenius H, Ryynanen M. On what grounds do women participate in prenatal screening? Prenat Diagn 1998; 18: 153–165.
30. Stephens MB, Montefalcon R, Lane DA. The maternal perspective on prenatal ultrasound. J Fam Pract 2000; 49: 601–604.
31. Ahman A, Runestam K, Sarkadi A. Did I really want to know this? Pregnant women's reaction to detection of a soft marker during ultrasound screening. Patient Educ Couns 2010; 81: 87–93.
32. Vassy C. How prenatal diagnosis became acceptable in France. Trends Biotechnol 2005; 23: 246–249.

# PART 2
# QUALITY ASSURANCE OF THE INFORMATION PROCESS

# Chapter 4 Evaluating the provision of information and informed decision-making on prenatal screening for Down syndrome: a questionnaire- and register-based survey in a non-selected population

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**Abstract**

*Objective:* Evaluating the information provision procedure about prenatal screening for Down syndrome, using informed decision-making as a quality-indicator.

*Methods:* Questionnaire- and register-based surveys. Midwives associated with 59 midwifery practices completed process data for 6435 pregnancies. Pregnant women (n=510) completed questionnaires on informed decision-making.

*Results:* Midwives offered information to 98.5% of women; 62.6% of them wished to receive information, of these, 81.9% actually received information. Decision-relevant knowledge was adequate in 89.0% of responding women. Knowledge about Down syndrome was less adequate than knowledge about the screening program. Participants in the screening program had higher knowledge scores on Down syndrome and on the screening program than non-participants. Of the women who intended to participate (35.8%), 3.1% had inadequate knowledge. A total of 75.5% of women made an informed decision; 94.3% of women participating in the screening program, and 64.9% of women not participating.

*Conclusion:* This quality assurance study showed high levels of informed decision-making and a relatively low participation rate in the national screening program for Down syndrome in the Netherlands. Knowledge of the Down syndrome condition needs to be improved.

*Practice implications:* This evaluation may serve as a pilot study for quality monitoring studies at a national level.

# 1. Introduction

Prenatal screening for Down syndrome aims to inform pregnant women and their partners about the likelihood of having a child affected by this condition. If the fetus is diagnosed with Down syndrome, prospective parents have the opportunity either to prepare for the birth of a child with Down syndrome or to consider termination of the pregnancy. In many Western countries, prenatal screening for Down syndrome is offered to pregnant women [1].
In the Netherlands, a national screening program for Down syndrome, open to all pregnant women, has been in existence since 2007 [2]. In the current program, all pregnant women are actively offered information on the possibility of having a screening test for Down syndrome. This is performed in practice by asking pregnant women whether they wish to receive information. The actual provision of information (counseling), only occurs if the pregnant woman indicates she is interested in receiving this information. By rejecting the initial information offer, counseling is refused and the women receives no further information. By offering the information (instead of providing information) prospective parents are enabled to either accept or decline the information, which respects both their right to know and their right not-to-know.

Before implementation of the current program, offering pregnant women information about a risk estimation test for Down syndrome was only allowed upon request. Only invasive diagnostic testing was actively offered, to women aged 36 years or over, in high-risk categories, or with medical indications [3]. All other women were not routinely offered information on the possibility of screening.
The goal of the current active, standardised offer of information is to enable all pregnant women to make an autonomous, informed decision about whether to participate in the prenatal screening program for Down syndrome [4]. According to the definition by Marteau, an informed decision is made when a woman has adequate decision-relevant knowledge and when her participation or non-participation is consistent with her attitude towards undergoing the screening herself [5].

Although adequate knowledge is a prerequisite for making an informed decision, previous studies on prenatal screening for Down syndrome have shown that this knowledge is often limited [6]. The level of informed choice about prenatal screening for Down syndrome can be regarded as an indicator of the quality of the information provision procedure.
The process and quality of providing information about prenatal screening for Down syndrome have not yet been evaluated in a nation-wide screening program. To date, this topic has only been investigated on a small scale and/or in a selected group of pregnant women (e.g. single centre studies, trials) [7-13]. Previous studies found that levels of informed decision making were associated with age, educational attainment level, and ethnicity [12,13].
We performed a quality assurance study in the Southwest region of the Netherlands to examine the process by which information is provided about prenatal screening for Down syndrome using informed decision making as a quality indicator. This study served as a pilot study for quality monitoring studies at a national level. We addressed the following questions on two main topics:

1. *The process of providing information about prenatal screening for Down syndrome:* are pregnant women offered information about the screening program? How many women accept the information offer and, of these women, how many actually receive the information?

2. *Informed decision-making as a quality indicator of the information provision procedure:* is the knowledge of pregnant women adequate? What is a pregnant woman's attitude towards undergoing prenatal screening for Down syndrome herself? To what extent is decision-making regarding (non-) participation in prenatal screening for Down syndrome based on an informed decision? What are the determinants of informed decision-making?

# 2. Methods

## 2.1. Participants and data collection

*Data on the process of providing information about prenatal screening for Down syndrome* were obtained from midwives through a web-based registration form. Eligible midwives worked in one of the 65 midwifery practices registered by the regional centre for prenatal screening in the Southwest region of the Netherlands (80% situated in suburban areas).
*Data on informed decision-making* were obtained from pregnant women by self-completion questionnaires. A sub-selection of 46 out of the 65 midwifery practices, based on an even distribution of urban and suburban areas [14], was informed about this part of the study. Midwives distributed the questionnaires to pregnant women after counselling about prenatal screening for Down syndrome, but before possible participation in the screening. Questionnaires were also given to women who were not interested in receiving information about prenatal screening for Down syndrome and thus receiving no counselling. The study covered a one-year period (May 2008 to May 2009).

In these studies, midwives were the data providers (data on process of information provision), or provided access to the study population (study on informed decision-making). Not all pregnant women in the Netherlands start their prenatal care carrier at the midwifery practice. The most recent data on prenatal care show that in 2006 [15] 77.3% of all pregnant women started prenatal care in the primary care system (midwives). The remaining 22.7% started prenatal care at the secondary care level. Since we only asked midwives to register data and / or hand out questionnaires to pregnant women, all women starting prenatal care at the secondary care level (22.7% of all pregnant women) were excluded from our research sample.

## 2.2. The process of providing information about prenatal screening for Down syndrome; web- based registration form

In the web-based registration form, we asked prenatal health care professionals to report whether they had offered information about the prenatal screening program and whether the pregnant woman who accepted the offer actually received the information.

## 2.3.The quality of providing information about prenatal screening for Down syndrome; informed decision-making questionnaire

*Knowledge* was measured by 12 statements, with the response options of 'true', 'not true', or 'do not know'. The development of this knowledge questionnaire is described in a previous study [16]. In brief, the content was based on a generic list of domains of screening considered to be essential for an informed choice [17,18], including the condition being screened for (in this case, Down syndrome) and characteristics of the screening program. The items were acquired through expert consensus.

The total knowledge score ranged from 0 to 10, and was obtained by summing scores on the individual items ('correct' =1 point; 'not correct' and 'do not know'=0 points) and dividing the total by 1.2. We defined inadequate knowledge as a score lower than 6.0 and adequate knowledge as a score equal to or greater than 6.0. Cronbach's alpha for the knowledge measure was 0.69 in this study.
Domain-specific knowledge scores regarding the condition being screened for (items 2, 3, 4) and the screening program (remaining items) were obtained by summing correct responses and transforming them to scores ranging from 0 to 10 by dividing by 0.3 and 0.9, respectively.

*Attitude* of pregnant women towards undergoing prenatal screening for Down syndrome themselves was measured using a scale based on the multi-dimensional measure of informed choice (MMIC) [5]. The scale contained four items (see Appendix 1) that were scored on a seven-point scale, giving a minimum attitude score of 4 (negative) and a maximum score of 28 (positive). Total scores were transformed to a 1 (rounded) to 10 scale by summing the item scores and dividing by 2.8. We defined a negative attitude of a pregnant woman towards undergoing prenatal screening for Down syndrome herself as an attitude score lower than 6.0, and a positive attitude towards undergoing prenatal screening for Down syndrome herself as an attitude score equal to or greater than 6.0. Cronbach's alpha was 0.85 for the attitude measure in this study.

*Intention to participate* Women were asked whether they intended to participate in prenatal screening for Down syndrome. The response options were 'Yes', 'No', and 'Do not know'. Because all women received the instruction to fill out the questionnaire before actual participation in the screening program, actual participation was not assessed. To determine informed decision-making, only data from women answering 'Yes' or 'No' on the previous question were considered and classified into the categories 'intention to participate' and ' intention not to participate'.

*Informed decision-making* Following Marteau et al. [5], an informed choice (decision) is based on adequate knowledge and a behaviour that is consistent with attitude. Hence, an informed decision to participate was defined as having adequate knowledge (total knowledge score ≥ 6.0), a positive attitude towards undergoing screening for Down syndrome yourself (attitude score ≥ 6), and an intention consistent with this attitude; the intention to participate. An informed choice not to participate was defined as having adequate knowledge, a negative attitude towards undergoing screening for Down syndrome yourself, and the intention not to participate. All other combinations were defined as uninformed. Hence, a non-informed decision can be due to inadequate knowledge and/or value inconsistency (e.g., an attitude towards undergoing first-trimester prenatal screening for Down syndrome yourself, which is not consistent with actual participation). We used the midpoints of the scales as objective thresholds to make a distinction between adequate and inadequate knowledge and between a positive and a negative attitude [8,19,20].

### 2.4. Demographics and other data in the web-based registration form

*Age* was measured by the women's date of birth and classified into 'low' (younger than 36 years of age) and 'high' (36 years of age or above).
*Gravidity* was dichotomised into 'none' (no previous pregnancies) and '1 or more' (1 or more previous pregnancies).

*Parity* was dichotomised into 'nulliparous' (not having delivered before) and 'multiparous' (one or more deliveries).
*Pregnancy duration at the time of the booking visit* was defined as the prenatal health care professional's estimate of gestational age (in days) at the moment of the booking visit for prenatal care and was dichotomised into 'shorter than or equal to 13 weeks' (91 days) and 'longer than 13 weeks'.
*Dutch language proficiency* was classified according to the registration system used by the Netherlands Perinatal Registry (PRN-foundation); prenatal midwives classified Dutch language proficiency of pregnant women into four levels: 'good', 'moderate', 'serious difficulties' and 'not speaking Dutch at all' [21].

### 2.5. Demographics and other data in the informed decision-making questionnaire

*Educational attainment level* was classified as 'low' (no education, primary and secondary education, or middle vocational education) or 'high' (tertiary education or higher; university, higher vocational education).
*Ethnic origin* was classified as 'non-Dutch' or 'Dutch' (based on country of birth of the pregnant woman [22]).
*Residence* was defined as 'suburban' when the residence population density was less than 1000 (i.e., less than 1000 addresses per km$^2$) and as 'urban' when the area had a population density of 1000 or higher [14].
*Self-reported religious affiliation* was dichotomised into 'religious' and 'not religious', and *religious activity* as 'often' (attending a religious meeting at least monthly) or 'seldom/never' (attending a religious meeting less than twice a year/only for religious festivities or never).

### 2.6. Analyses

We used one-way analysis of variance (ANOVA) to compare the continuous variable gestational age at the booking visit for prenatal care among the four levels of Dutch language proficiency. The relationship between the categorical variables of parity, information offered by the midwife and acceptance of the offer of information by the pregnant woman was explored using the $\chi^2$ analysis. Independent-samples T-tests were used to compare mean knowledge and attitude scores between different groups (participants/non participants, women aged 36 year or above/women aged below 36 years). Stepwise backward linear regression analysis (probability of F for entry <0.05, for removal >0.10) was used to investigate the association of the determinants (age, education, residence, religious affiliation, religious activity, ethnic origin) with continuous outcome variables (knowledge, attitude). For dichotomous outcome variables (intention to participate, informed decision-making), conditional logistic regression with backward selection (based on Likelihood Ratio's and probability of F for entry <0.05, for removal >0.10) was used to calculate odds ratios (ORs) and 95% confidence intervals (95% CIs). Both analyses were performed with age in the first block, thus controlling for age as a confounder. For missing values, the option 'exclude cases pairwise' was used. Data were analysed using SPSS version 15.0.

# 3. Results

## 3.1. Response and representativeness

*Concerning the process of providing information about prenatal screening for Down syndrome,* we obtained data for 6435 pregnancies, registered by 59 out of the 65 practices in the region (86.8%). Of these data, 23.4% (n=1509) came from midwifery practices in urban areas and 76.6% (n=4926) came from practices in suburban areas.
*Concerning informed decision-making,* 20 midwifery practices (out of 46 midwifery practices contacted for this part of the study; 43.5%) participated in distributing questionnaires regarding informed decision-making among pregnant women. Of these participating practices, 75% (n=15) were situated in urban areas. The response rate from pregnant women on the questionnaires that were distributed was estimated to be 30-35%, and it was almost evenly distributed between urban (53.7%) and suburban (46.3%) areas. We had to rely on estimates regarding the response rate because of the anonymous nature of the questionnaires. Since this study serves as a pilot study for quality monitoring at a national level, the relatively low response rate is considered as an important result. In the Discussion section of this manuscript, we elaborate on possible reasons this low response rate, as a higher response rate is essential in future quality monitoring studies.

Table 1 shows the background characteristics of women for both parts of the study. As reference data, percentages for educational level [23] and ethnic origin [24] in the population of Dutch women in the age group 15–45 years are provided. The mean age in both groups is representative of the mean age of Dutch mothers at the birth of their first child in 2008 (29.4 years) [25]. Among those who completed the informed decision-making questionnaire, lower educated women and women of non-Dutch ethnic origin were underrepresented.

## 3.2. The process of providing information about prenatal screening for Down syndrome

The process of providing information was evaluated for the women who booked their prenatal care visit at the midwifery practice at 13 weeks of gestation or earlier (N=5181; 92.0% of women for whom data were provided concerning the duration of gestation) (Figure 1). Prenatal health care professionals offered information to almost all pregnant women (98.5%; n=4988), and 62.6% of these women (n=3123/4988) wished to receive information. Of the women that wished to receive information, 81.9% (n=2558/3123) actually received the information.

The median duration of gestation at the time of booking a visit for prenatal care at the midwifery practice was 9 weeks (range: 4 weeks–36 2/7 weeks). Gestational age at the time of booking differed among the four levels of Dutch language proficiency ($F(1,3)=81.82$, $p<0.001$). Women with good Dutch language proficiency booked the visit for prenatal care 22.7 days earlier in pregnancy than those who did not have good proficiency in Dutch.
Parity was not associated with whether the health care professional asked if the pregnant woman wished to receive information ($\chi^2$ (1, N=5064)=1.44, p=0.23) or whether the offer was accepted ($\chi^2$ (1, N=4137)=0.23, p=0.64).

**Table 1:** Background characteristics of pregnant women

*Pregnant women of which data on the information process were provided by prenatal health care professionals*

| Variable | Mean (SD) | N | % |
|---|---|---|---|
| Age (years) | 29.8 (5.1) | | |
| Low (<36) | | 5259 | 88.3 |
| High (≥36) | | 698 | 11.7 |
| Gravidity | 1.0 (1.4) | | |
| None | | 2723 | 42.3 |
| 1 or more | | 3712 | 57.7 |
| Parity | 0.8 (1.0) | | |
| Nulliparous | | 3253 | 50.6 |
| Multiparous | | 3182 | 49.4 |
| Pregnancy duration (days) | 69.2 (20.3) | | |
| ≤13 weeks | | 5181 | 92.0 |
| >13 weeks | | 449 | 8.0 |
| Dutch language proficiency | | | |
| Good | | 5549 | 91.8 |
| Moderate | | 248 | 4.1 |
| Serious difficulties | | 113 | 1.9 |
| Not speaking Dutch | | 134 | 2.2 |

*Pregnant women who provided data themselves, on the quality of information provision procedure*

| Variable | Mean (SD) | N | % | % of Dutch population |
|---|---|---|---|---|
| Age (years) | 30.8 (4.2) | | | |
| Low (<36) | | 433 | 87.7 | |
| High (≥36) | | 61 | 12.3 | |
| Educational attainment level | | | | |
| Low | | 223 | 44.1 | 72.2 |
| High | | 283 | 55.9 | 27.8 |
| Ethnic origin | | | | |
| Non-Dutch | | 40 | 7.8 | 26.3 |
| Dutch | | 470 | 92.2 | 73.7 |
| Residence | | | | |
| Suburban | | 230 | 46.3 | |
| Urban | | 267 | 53.7 | |
| Religious affiliation | | | | |
| Religious | | 205 | 40.8 | |
| Not religious | | 297 | 59.2 | |
| Religious activity | | | | |
| Often | | 65 | 13.3 | |
| Seldom/never | | 423 | 86.7 | |

### 3.3. Informed decision-making: knowledge, attitude, and intention to participate

Table 2 shows the items of the knowledge questionnaire, the knowledge domains, and percentages and numbers of correct, not correct, and 'do not know' responses.

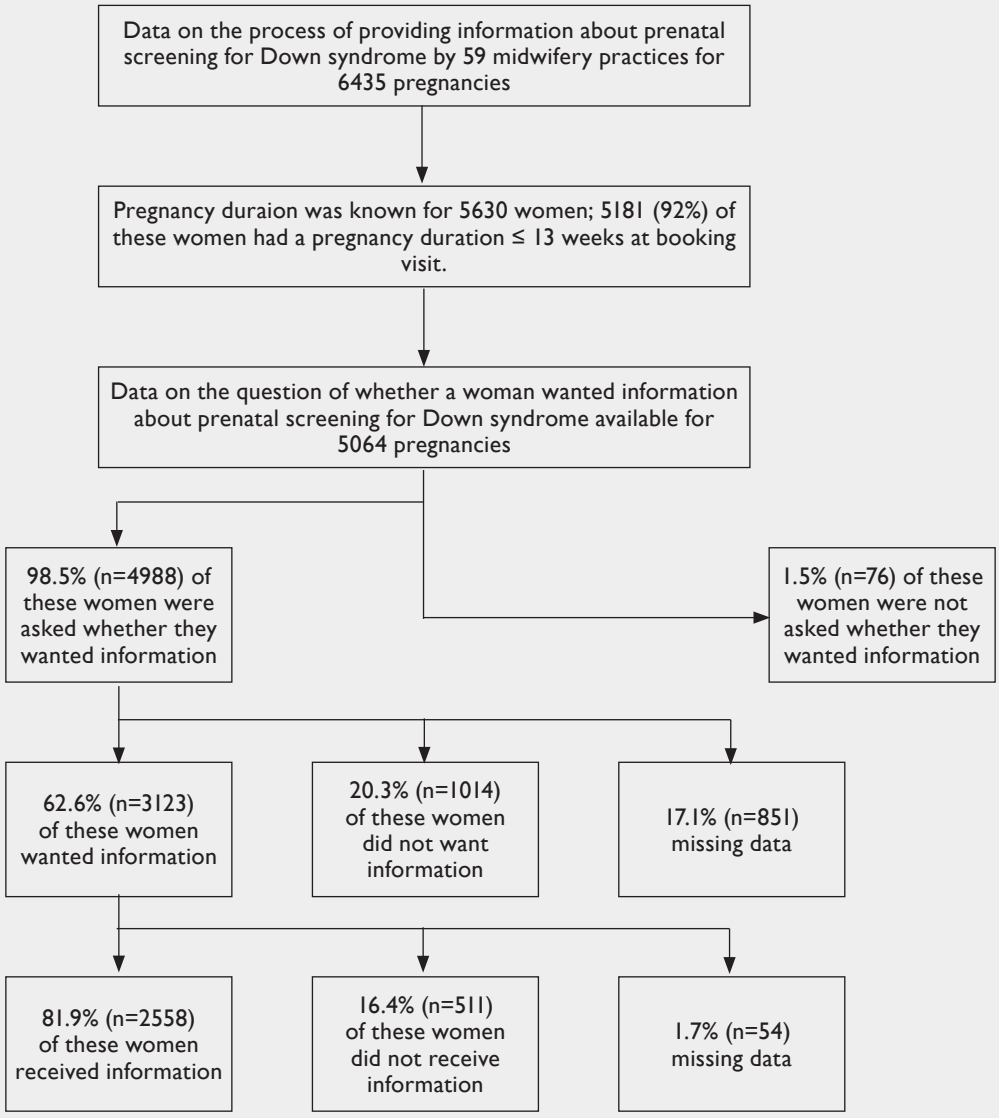


**Figure 1:** The information process.

Table 3 presents the knowledge scores, attitude scores, intention to participate and differences on knowledge and attitude between participants and non-participants. Knowledge scores were obtained for 501 pregnant women, provided by 20 participating practices. For 24.5% of the pregnant women, we were able to compare their statement about their intention to screen with health care professional data on actual participation. Agreement was found in 96.5% of the cases.

**Table 2:** Items of the knowledge questionnaire, the knowledge domains, and percentages and numbers of correct, not correct and 'do not know' responses (data from pregnant women, on the quality of the information provision procedure)

| Item (correct answer) | Knowledge domain | % Correct (N) | % Not correct (N) | % Do not know (N) |
|---|---|---|---|---|
| 1. The probability that your child has Down's syndrome can be determined through prenatal screening in the early stages of pregnancy (true). | Purpose of the screening | 96.3 (490) | 2 (10) | 1.8 (9) |
| 2. The probability that an unborn child has Down's syndrome is generally very small (less than 1%) (true). | Prevalence in the population (the theoretical risk that the disorder that is tested is present) | 59.9 (305) | 16.3 (83) | 23.8 (121) |
| 3. All children with Down's syndrome are mentally handicapped (true). | The condition being screened for | 69.4 (353) | 18.1 (92) | 12.6 (64) |
| 4. Heart defects in children with Down's syndrome can generally be treated effectively (true). | The condition being screened for | 54.1 (276) | 4.9 (25) | 41.0 (209) |
| 5. The combined test consists of a measurement of the thickness of the nuchal fold of the unborn child (a nuchal ultrasound) and a blood test on the mother (true). | Test procedure | 89.4 (454) | 2.2 (11) | 8.5 (43) |
| 6. Should the result of the combined test be unfavourable, this means that the child has Down's syndrome (not true). | The meaning of an increased probability for Down's syndrome test result (including the possibility of false positives) | 84.3 (430) | 7.6 (39) | 8.0 (41) |
| 7. Should the result of the combined test be favourable, the child may still prove to have Down's syndrome when born (true). | The meaning of a decreased probability for Down's syndrome test result (including the possibility of false negatives) | 89.2 (455) | 2.0 (10) | 8.8 (45) |
| 8. Amniocentesis or chorionic villus sampling may induce a miscarriage (true). | What to do in the event of an increased probability for DS test result | 87.6 (447) | 5.9 (30) | 6.5 (33) |
| 9. Both amniocentesis and chorionic villus sampling provide certainty about the presence of Down's syndrome in an unborn child (true). | Possible findings resulting from a further examination | 57.3 (290) | 32.0 (162) | 10.7 (54) |
| 10. Should Down's syndrome be diagnosed during the first four months of pregnancy, it is possible for a pregnant woman to terminate the pregnancy (true). | What to do after a further examination | 86.0 (436) | 2.4 (12) | 11.6 (59) |
| 11. The result of prenatal screening for Down's syndrome may lead to difficult choices (true). | Possible side effects of the test procedure | 96.9 (492) | 0.6 (3) | 2.6 (13) |
| 12. Prenatal screening for Down's syndrome is compulsory for every pregnant woman in the Netherlands (not true). | Voluntary nature of the test | 98.6 (501) | 0.4 (2) | 1.0 (5) |

**Table 3:** Descriptives for knowledge, attitude and intention to participate in prenatal screening for Down syndrome (data from pregnant women, on the quality of the information provision procedure)

| Variable | N | % | All respondents | Participants in the screening | | | Non-participants in the screening | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | Mean (SD) | N | % | Mean (SD) | N | % | Mean (SD) |
| Knowledge: all domains | 501 | | 8.1 (1.6) | 163 | | 8.7 (1.2) | 294 | | 7.8 (1.7) |
| Inadequate (knowledge score<6.0) | 55 | 11.0 | | 6 | 3.7 | | 44 | 15.0 | |
| Adequate (knowledge score≥6.0) | 446 | 89.0 | | 157 | 96.3 | | 250 | 85.0 | |
| Knowledge on Down syndrome | 508 | | 6.1 (3.1) | 165 | | 6.5 (3.1) | 298 | | 5.9 (3.0) |
| *Cut off 6.0* | | | | | | | | | |
| Inadequate (knowledge score<6.0) | 170 | 33.5 | | 49 | 29.7 | | 106 | 35.6 | |
| Adequate (knowledge score≥6.0) | 338 | 66.3 | | 116 | 70.3 | | 192 | 64.4 | |
| Knowledge on the screening programme | 503 | | 8.7 (1.6) | 163 | | 9.4 (1.0) | 295 | | 8.4 (1.7) |
| *Cut off 6.0* | | | | | | | | | |
| Inadequate (knowledge score<6.0) | 39 | 7.8 | | 3 | 1.8 | | 32 | 10.8 | |
| Adequate (knowledge score≥6.0) | 464 | 92.2 | | 160 | 98.2 | | 263 | 88.0 | |
| Attitude | 491 | | 6.3 (2.6) | 165 | | 8.9 (1.3) | 289 | | 4.8 (2.0) |
| Negative (attitude score<6.0) | 239 | 48.7 | | 5 | 3.1 | | 216 | 74.7 | |
| Positive (attitude score≥6.0 | 252 | 51.3 | | 155 | 96.9 | | 73 | 25.3 | |
| Intention to participate | 503 | | | | | | | | |
| Yes | 165 | 32.8 | | | | | | | |
| No | 299 | 59.4 | | | | | | | |
| Not (yet) made a decision | 39 | 7.8 | | | | | | | |

Participants in the screening program had higher knowledge scores for items on Down syndrome (mean score=6.5±3.1) and on the screening program (mean score=9.4±1.0) than non-participants (mean score=5.9±3.0 and 8.4±1.7, respectively). The differences between participants and non-participants were statistically significant for both domains of screening (t=-2.02, p=0.04 for Down syndrome and t=6.9, p=0.00 for the screening program). Women aged 36 years or above had significantly higher knowledge scores (mean score=8.7±1.1) than younger women (mean score=7.9±1.6, t=-4.4, p=0.00). They were also more positive about participating (mean attitude score=7.5±2.8) compared with younger women (mean attitude score 6.1±2.5, t=-3.86, p=0.00). Attitude towards undergoing prenatal screening for Down syndrome yourself was more positive for participants (mean score=8.9±1.3) than for non-participants (mean score=4.8±2.0, t=-23.7, p=0.00). A total of 444 women provided complete data on attitude, knowledge, and intention to participate. Of these, 75.5% (n=335) made an informed choice, according to the definition of Marteau [5] (Table 4).

Religious activity was associated with lower levels of knowledge, attitude, and intention to participate. In multivariate analysis, educational level was the only significant determinant of informed decision-making. Adequate knowledge about prenatal screening for Down syndrome (OR 1.61, 95% CI 1.36 to 1.90) and a positive attitude towards undergoing prenatal screening for Down syndrome yourself (OR 3.22, 95% CI 2.63 to 3.95) were associated with a positive intention to participate in the screening program (Table 5).

# 4. Discussion and Conclusion

## 4.1. Discussion

This is the first evaluation of the process and quality of information provision in the real life setting of a national prenatal screening program for Down syndrome. Pregnant women had fairly good decision-relevant knowledge of the screening program, but only moderate knowledge of Down syndrome as the condition being screened for. The majority of women made an informed decision to participate or not to participate in the screening. From the viewpoint of future routine monitoring of the quality of the information process, the low participation to the questionnaire study is worrisome.
Our results were gathered from a real-life setting including all pregnant women in a defined geographical area. Data on informed decision-making were obtained both from women participating in prenatal screening, and women who were not participating. This is a major strength of this study because other studies on informed decision-making have often failed to obtain reliable data due to low response rates among non-participants [26-28].

Because the questionnaires on informed decision-making were handed out before any actual participation in prenatal screening for Down syndrome, only the intention to participate in the screening program was identified. In a recent study on prenatal testing choices, screening intention was highly predictive of actual screening behaviour [29]. A comparison between intention to participate, as expressed by pregnant women themselves, and uptake information from midwives for a subset of the women in our sample showed broad agreement between these two data sources.
Based on most international evaluations, the majority of pregnant women do not make informed choices about prenatal screening [5,6,9,30,31] and are unaware of the decisional implications of participation in screening [32,33]. In the Netherlands, the evaluation of informed

**Table 4:** Numbers and percentages of (un-) informed decision-making about participating in prenatal screening for Down syndrome (data from pregnant women, on the quality of the information provision procedure)

| Choice | Knowledge | Attitude | Intention to participate | N | % of total informed and uninformed |
|---|---|---|---|---|---|
| Informed choice | | | | 335 | 75.5 |
| *Specification informed choice* | | | | N | % of total informed choice |
| Informed choice to participate | Adequate | Positive | Yes | 150 | 44.8 |
| Informed choice to not participate | Adequate | Negative | No | 185 | 55.2 |
| | | | | N | % of total informed and uninformed |
| Non- informed choice | | | | 109 | 24.5 |
| *Specification uninformed choice; Inadequate knowledge* | | | | N | % of total uninformed choice |
| | Inadequate | Positive | Yes | 4 | 3.7 |
| | Inadequate | Positive | No | 12 | 11 |
| | Inadequate | Negative | Yes | 1 | 0.9 |
| | Inadequate | Negative | No | 27 | 24.8 |
| *Specification uninformed choice; Value- inconsistency* | | | | | |
| | Adequate | Positive | No | 61 | 55.9 |
| | Adequate | Negative | Yes | 4 | 3.7 |

**Table 5:** Association of background characteristics with knowledge, attitude, intention to participate and informed decision-making (data from pregnant women, on the quality of the information provision procedure)

| | Knowledge | | | | Attitude | | | | Intention to participate | | | | | | Informed decision-making | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Univariate | | Multivariate | | Univariate | | Multivariate | | Univariate | | | | Multivariate | | Univariate | | | | Multivariate | |
| | Mean (SD) | p value | B | p value | Mean (SD) | p value | B | p value | No (%) | Yes (%) | OR | p value | OR | p value | No (%) | Yes (%) | OR | p value | OR | p value |
| Age (continuous) | | 0.00 | 0.07 | 0.00 | | 0.00 | 0.11 | 0.00 | | | 1.19 | 0.00 | 1.15 | 0.01 | | | 1.08 | 0.01 | 1.05 | 0.11 |
| <36 | 7.99 (1.64) | | | | 6.12 (2.46) | | | | 270 (69.1) | 121 (30.9) | | | | | 98 (26.3) | 275 (73.7) | | | | |
| ≥36 | 8.71 (1.10) | | | | 7.46 (2.76) | | | | 18 (31.6) | 39 (68.4) | | | | | 7 (12.7) | 48 (87.3) | | | | |
| Education | | | | | | | | | | | | | | | | | | | | |
| High | 8.49 (1.33) | 0.00 | 0.77 | 0.00 | 6.39 (2.60) | 0.24 | | | 148 (57.1) | 111 (42.9) | 2.08 | 0.00 | 2.62 | 0.02 | 39 (15.4) | 214 (84.6) | 3.17 | 0.00 | 3.18 | 0.00 |
| Low | 7.60 (1.75) | | | | 6.11 (2.52) | | | | 150 (73.5) | 54 (26.5) | | | | | 70 (36.6) | 121 (63.4) | | | | |
| Residence | | | | | | | | | | | | | | | | | | | | |
| Urban | 8.14 (1.60) | 0.42 | | | 6.32 (2.51) | 0.72 | | | 150 (61.0) | 96 (39.0) | 1.41 | 0.09 | | | 50 (21.3) | 185 (78.7) | 1.49 | 0.07 | | |
| Suburban | 8.02 (1.62) | | | | 6.23 (2.64) | | | | 143 (68.8) | 65 (31.2) | | | | | 58 (28.7) | 144 (71.3) | | | | |
| Religious affiliation | | | | | | | | | | | | | | | | | | | | |
| Religious | 7.88 (1.78) | 0.01 | | | 5.59 (2.55) | 0.00 | | | 147 (75.8) | 47 (24.2) | 0.41 | 0.00 | 0.43 | 0.04 | 51 (27.6) | 134 (72.4) | 0.76 | 0.21 | | |
| Not religious | 8.25 (1.39) | | | | 6.72 (2.49) | | | | 148 (56.1) | 116 (43.9) | | | | | 57 (22.4) | 198 (77.6) | | | | |
| Religious activity | | | | | | | | | | | | | | | | | | | | |
| Often | 7.55 (1.99) | 0.00 | -0.54 | 0.01 | 4.00 (2.13) | 0.00 | -2.23 | 0.00 | 58 (92.1) | 5 (7.9) | 0.13 | 0.00 | | | 16 (26.2) | 45 (73.8) | 0.91 | 0.78 | | |
| Seldom/never | 8.20 (1.46) | | | | 6.57 (2.48) | | | | 232 (60.6) | 151 (39.4) | | | | | 90 (24.5) | 277 (75.5) | | | | |
| Ethnic origin | | | | | | | | | | | | | | | | | | | | |
| Dutch | 8.14 (1.53) | 0.00 | 0.68 | 0.01 | 6.21 (2.56) | 0.04 | -1.20 | 0.00 | 283 (66.3) | 144 (33.7) | 0.39 | 0.01 | 0.09 | 0.00 | 104 (25.2) | 309 (74.8) | 0.57 | 0.26 | | |
| Non-Dutch | 7.40 (2.15) | | | | 7.19 (2.45) | | | | 16 (43.2) | 21 (56.8) | | | | | 5 (16.1) | 26 (83.9) | | | | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Knowledge (continuous) | | | | | | | | | | |
| Adequate | 6.36 (2.57) | 0.00 | 0.18 | 0.01 | 250 (61.4) | 157 (38.6) | 1.61 | 0.00 | 1.47 | 0.01 |
| Inadequate | 5.54 (2.40) | | | | 44 (88.0) | 6 (12.0) | | | | |
| Attitude (continuous) | | | | | | | | | | |
| Positive | | | | | 73 (32.0) | 155 (68.0) | 3.22 | 0.00 | 3.25 | 0.00 |
| Negative | | | | | 216 (97.7) | 5 (2.3) | | | | |

decision-making about prenatal screening has been investigated previously in a randomised controlled trial. In this trial, two information strategies were compared among trial participants who all had expressed interest in prenatal screening for Down syndrome, had received information material, and had a consultation with the health care professional. This study showed informed decisions in 51-68% of the sample [12,34]. Our study also included women who were not interested in the prenatal screening program. A recent Dutch study performed after 2007, that focused on ethnic variations in decision-making, reported levels of informed decision-making for the ethnic Dutch group (71%) that were comparable to our study [13].

The results of the present study confirm the findings of previous screening studies that showed a better knowledge among participants [28,35,36]. The finding that women often do not have adequate knowledge about the condition Down syndrome is in agreement with previous studies, and it underscores the relevance of improving the process of providing information about Down syndrome [37,38]. Midwives should pay particular attention to providing information about Down syndrome (e.g., on the fact that all children with Down syndrome are mentally handicapped). The finding that knowledge about the condition being screened for is lower than knowledge about the screening program may be context-specific. Participants in a screening program for lung cancer were recently shown to have better knowledge of lung cancer and worse knowledge of that screening program [28].
The participation rates in prenatal screening for Down syndrome observed in this study are low compared with those reported in international studies [39,40]. However, a significant reduction in the high uptake rates of these international studies has been recently reported [41]. The uptake rates in the current study are comparable with uptake rates previously observed in the Netherlands [42].

A minority of midwifery practices were willing to distribute the informed decision-making questionnaires. In addition, for pregnant women receiving these questionnaires, a low response was observed. We contacted midwifery practices about this after the study period, and several possible reasons for the low response of pregnant women were mentioned. First, midwives expressed the impression that women not participating in the screening program would also be less interested in completing the questionnaire. We perceived this comment as speculation on their part, after the study had ended; they also mentioned distributing the questionnaires to women participating as well as women not participating in prenatal screening for Down syndrome. However, we cannot exclude the possibility that midwives were more inclined to offer the informed decision-making questionnaire to those participating in prenatal screening for Down syndrome. If this occurred, it would imply an overestimation of the uptake rate in prenatal screening for Down syndrome in this study. Second, an 'information overload' can occur in the first trimester of pregnancy, the period in which pregnant women were expected to complete the questionnaire. Third, some midwifery practices also participated in additional evaluation studies (unrelated to our study) in which questionnaires had to be provided to pregnant women. Finally, in the midwifery practice with the highest response (77/170=45.3%) midwives reminded pregnant women of filling out the questionnaire during later visits for prenatal care. This reminder could have resulted in a higher response.

## 4.2. Conclusion

This quality assurance study showed high levels of informed decision-making in the relatively low number of participants, as well as in non-participants, in the national screening program

for Down syndrome in the Netherlands. Knowledge on the condition itself needs to be improved.

### 4.3. Practice implications

The goal of offering information about prenatal screening for Down syndrome is to enable all pregnant women to make an autonomous, informed decision about whether or not to participate in this screening program. This study showed how to perform an evaluation of the process of providing information with informed decision-making as a quality indicator.
The participation rate in prenatal screening for Down syndrome we report, is relatively low as compared with other European countries (in Denmark, uptake rates of 99% have been observed [43], in the United Kingdom, uptake rates of 66% [29]). The Dutch programme for prenatal screening for Down syndrome is not directed at achieving high uptake rates. Therefore, this relatively low number of women participating in the screening program is not a matter of concern, at least, as long as these uptake rates are based on informed decision-making. Most women in this study made informed decisions on participating in prenatal screening for Down syndrome.

Future quality assurance studies on information provision are essential in nation wide programs on prenatal screening for Down syndrome. If future, national, routine evaluations of informed choices are implemented, a high response rate in these studies among participants and non-participants is required. Furthermore, a higher participation of health care professionals in these studies is needed. The current study may function as a starting point for performing these evaluations.

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# Appendix; Attitude measure used in the present study.

**Participating in prenatal screening for Down syndrome: What is your opinion?**

What is your opinion of participating in prenatal screening for Down syndrome? Please indicate this in the following four questions by marking for each line one of the boxes under the numbers one through seven.

**Example**

If you are of the opinion that participating in prenatal screening for Down syndrome would be 'a bad idea' for you, mark box 1 in the first line. If your opinion is that it is not such a bad idea, then you should choose one of the numbers more towards the right when making the assessment. If your opinion is that participating in prenatal screening for Down syndrome is 'not a bad idea' for you, you should then mark box 7. The other three questions should be answered in the same way.

Participating in first trimester prenatal screening for Down syndrome is, in my opinion:

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| A bad idea | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 | ☐ 6 | ☐ 7 | Not a bad idea |
| Useful | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 | ☐ 6 | ☐ 7 | Not useful |
| Harmful | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 | ☐ 6 | ☐ 7 | Not harmful |
| A good idea | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 | ☐ 6 | ☐ 7 | Not a good idea |

Source: [5]

# References


[1] Boyd PA, Devigan C, Khoshnood B, Loane M, Garne E, Dolk H, EUROCAT Working Group. Survey of prenatal screening policies in Europe for structural malformations and chromosome anomalies, and their impact on detection and termination rates for neural tube defects and Down's syndrome. BJOG 2008;115:689-696.

[2] Health Council of the Netherlands (2007). Population Screening Act. Prenatal screening on Down's syndrome and neural tube defects. Health Council of the Netherlands 2007/05.

[3] Health Council of the Netherlands (2001). Prenatal screening: Down's syndrome, neural tube defects, routine-ultrasonography 2001/11.

[4] Health Council of the Netherlands (2004). Prenatal Screening (2); Down's syndrome, neural tube defects. Health Council of the Netherlands 2004/06.

[5] Marteau TM, Dormandy E, Michie S. A measure of informed choice. Health Expect 2001;4:99-108.

[6] Green JM, Hewison J, Bekker HL, Bryant LD, Cuckle HS. Psychosocial aspects of genetic screening of pregnant women and newborns: a systematic review. Health Technol Assess 2004;8:iii, ix-x, 1-109.

[7] Dormandy E, Hooper R, Michie S, Marteau TM. Informed choice to undergo prenatal screening: a comparison of two hospitals conducting testing either as part of a routine visit or requiring a separate visit. J Med Screen 2002;9:109-14.

[8] Dormandy E, Michie S, Hooper R, Marteau TM. Informed choice in antenatal Down syndrome screening: a cluster-randomised trial of combined versus separate visit testing. Patient Educ Couns 2006;61:56-64.

[9] Gourounti K, Sandall J. Do pregnant women in Greece make informed choices about antenatal screening for Down's syndrome? A questionnaire survey. Midwifery 2008;24:153-62.

[10] Jaques A, Sheffield L, Halliday J. Informed choice in women attending private clinics to undergo first trimester screening for Down syndrome. Prenatal diagnosis 2005;25:656-664.

[11] van den Berg M, Timmermans DR, ten Kate LP, van Vugt JM, van der Wal G. Informed decision making in the context of prenatal screening. Patient Educ Couns 2006;63:110-7.

[12] van den Berg M, Timmermans DR, Ten Kate LP, van Vugt JM, van der Wal G. Are pregnant women making informed choices about prenatal screening?. Genet Med 2005;7:332-8.

[13] Fransen MP, Essink-Bot ML, Vogel I, Mackenbach JP, Steegers EA, Wildschut HI. Ethnic differences in informed decision-making about prenatal screening for Down's syndrome. J.Epidemiol.Community Health 2010;64:262-268.

[14] Statistics Netherlands. Gebieden in Nederland 2007 http://statline.cbs.nl/StatWeb/publication/?DM=SLNL&PA=71377NED&D1=2,48&D2=a&HDR=T&STB=G1&VW=T Accessed on 14/05/2010

[15] The Netherlands Perinatal Registry (PRN-foundation). Perinatal Care in the Netherlands, 2006, p. 94, table 9.1.1 http://www.perinatreg.nl/uploads/150/114/Jaarboek_Perinatale_Zorg_2006.pdf Accessed on 26/09/2011

[16] Schoonen HMHJD, van Agt HME, Essink-Bot ML, Wildschut HI, Steegers EAP, de Koning HJ. Informed decision-making in prenatal screening for Down's syndrome: What knowledge is relevant. Patient Educ Couns 2011:265-270.

[17] Royal College of Obstetricians and Gynaecologists. Report of the working party on biochemical markers and the detection of Down's syndrome. RCOG Press 1993.

[18] Wald N. Information leaflets in medical screening. J Med Screen 2006;13:109.

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

[20] Dormandy E, Tsui EY, Marteau TM. Development of a measure of informed choice suitable for use in low literacy populations. Patient Educ Couns 2007;66:278-95.

[21] The Netherlands Perinatal Registry (PRN Foundation) In Dutch: Stichting Perinatale Registratie. The Netherlands Perinatal Registry http://www.perinatreg.nl/home_english;2011 Accessed on 26/09/2011

[22] Stronks K, Kulu-Glasgow I, Agyemang C. The utility of 'country of birth' for the classification of ethnic groups in health research: the Dutch experience. Ethn.Health 2009;14:1-14.

[23] Statistics Netherlands. Beroepsbevolking; behaalde onderwijs naar herkomst geslacht en leeftijd 2009 http://statline.cbs.nl/StatWeb/publication/?DM=SLNL&PA=71822NED&D1=0&D2=l&D3=1-3&D4=0&D5=a&D6=0&D7=l&VW=T Accessed on 29/04/2010
[24] Statistics Netherlands. Geboorte; herkomstgroepering en leeftijd moeder (op 31 december) 2009 http://statline.cbs.nl/StatWeb/publication/?VW=T&DM=SLNL&PA=37884&D1=0-2,8-9-&D2=0&D3=0-2&D4=l&HD=100429-1135&HDR=T&STB=G2,G1,G3 Accessed on 29/04/2010
[25] Statistics Netherlands. Geboorte naar diverse kenmerken 2009 http://statline.cbs.nl/StatWeb/publication/?DM=SLNL&PA=37422NED&D1=40-44&D2=l&HDR=T&STB=G1&VW=T Accessed on 29/04/2010
[26] Eborall HC, Griffin SJ, Prevost AT, Kinmonth AL, French DP, Sutton S. Psychological impact of screening for type 2 diabetes: controlled trial and comparative study embedded in the ADDITION (Cambridge) randomised controlled trial. BMJ 2007;335:486.
[27] Nijs HG, Essink-Bot ML, DeKoning HJ, Kirkels WJ, Schroder FH. Why do men refuse or attend population-based screening for prostate cancer?. J.Public Health Med. 2000;22:312-316.
[28] van den Bergh KA, Essink-Bot ML, van Klaveren RJ, de Koning HJ. Informed participation in a randomised controlled trial of computed tomography screening for lung cancer. Eur.Respir.J. 2009;34:711-720.
[29] Bryant LD, Green JM, Hewison J. The role of attitudes towards the targets of behaviour in predicting and informing prenatal testing choices. Psychol.Health 2009:1-20.
[30] Gekas J, Gondry J, Mazur S, Cesbron P, Thepot F. Informed consent to serum screening for Down syndrome: are women given adequate information?. Prenat Diagn 1999;19:1-7.
[31] Al-Jader LN, Parry-Langdon N, Smith RJ. Survey of attitudes of pregnant women towards Down syndrome screening. Prenat.Diagn. 2000;20:23-29.
[32] Seror V, Ville Y. Prenatal screening for Down syndrome: women's involvement in decision-making and their attitudes to screening. Prenat Diagn 2009;29:120-8.
[33] Roelofsen EE, Kamerbeek LI, Tymstra TJ, Beekhuis JR, Mantingh A. Women's opinions on the offer and use of maternal serum screening. Prenat.Diagn. 1993;13:741-747.
[34] van den Berg M, Timmermans, D.R.M., ten Kate, L.P., van Vugt, J.M.G., van der Wal, G. Informed decision making concerning prenatal screening. Patient Education and Counseling 2006:110-117.
[35] Briss P, Rimer B, Reilley B, Coates RC, Lee NC, Mullen P, Corso P, Hutchinson AB, Hiatt R, Kerner J, George P, White C, Gandhi N, Saraiya M, Breslow R, Isham G, Teutsch SM, Hinman AR, Lawrence R, Task Force on Community Preventive Services. Promoting informed decisions about cancer screening in communities and healthcare systems. Am.J.Prev.Med. 2004;26:67-80.
[36] Hewitson P, Austoker J. Part 2: Patient information, informed decision-making and the psychosocial impact of prostate-specific antigen testing. BJU Int. 2005;95 Suppl 3:16-32.
[37] Chilaka VN, Konje JC, Stewart CR, Narayan H, Taylor DJ. Knowledge of Down syndrome in pregnant women from different ethnic groups. Prenat Diagn 2001;21:159-64.
[38] Gottfredsdottir H, Bjornsdottir K, Sandall J. How do prospective parents who decline prenatal screening account for their decision? A qualitative study. Soc.Sci.Med. 2009;69:274-277.
[39] Spencer K, Spencer CE, Power M, Moakes A, Nicolaides KH. One stop clinic for assessment of risk for fetal anomalies: a report of the first year of prospective screening for chromosomal anomalies in the first trimester. BJOG 2000;107:1271-1275.
[40] Salonen R, Turpeinen U, Kurki L, Lappalainen M, Ammala P, Hiilesmaa V, Teramo K, von Koskull H, Gahmberg N, Stenman UH. Maternal serum screening for Down's syndrome on population basis. Acta Obstet.Gynecol.Scand. 1997;76:817-821.
[41] Gidiri M, McFarlane J, Holding S, Lindow S. Maternal serum screening for Down syndrome: are women's perceptions changing?. BJOG 2007;114:458-461.
[42] Fracheboud J, van Agt HME, de Koning HJ. Landelijke inventarisatie van verrichtingen in het kader van de prenatale screening op Downsyndroom en het Structureel Echoscopisch Onderzoek-o.b.v. beschikbare data 2008- 2010.
[43] Ekelund CK, Jorgensen FS, Petersen OB, Sundberg K, Tabor A, Danish Fetal Medicine Research Group. Impact of a new national screening policy for Down's syndrome in Denmark: population based cohort study. BMJ 2008;337:a2547.

# Chapter 5 Informed decision-making on the fetal anomaly scan; evaluation of the process and quality of information provision, and comparison with Down syndrome screening

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*Submitted*

**Abstract**

*Objectives:* To evaluate the process of information provision about second-trimester ultrasound screening for fetal anomalies, using informed decision-making as a quality-indicator, and to compare informed decision-making on second-trimester ultrasound screening with first-trimester screening for Down syndrome with the combined test.

*Methods:* Questionnaire-and register-based survey. Midwives, associated with 59 midwifery practices, registered data on the information process for 6,435 pregnancies. An unselected group of pregnant women (n=472) completed informed decision-making questionnaires. A comparison between informed decision-making on ultrasound screening and screening for Down syndrome could be made for 45.3% of women.

*Results:* Midwives offered information on second-trimester ultrasound screening to 97.7% of pregnant women; 92.3% of them wished to receive information, of these, 94.3% actually received information. Mean knowledge score was 8.3, mean attitude score 8.8 (1–10 scales). A total of 88.0% of women made an informed decision. The majority of the informed decisions (95.7%) was a decision to participate. Of all women who intended to participate, 5.1% had inadequate knowledge. Compared to screening for Down syndrome, women had less knowledge about the possible (negative) side effects of the test procedure in ultrasound screening, the test procedure itself, options after a further diagnostic work-up, and the voluntariness of the test. Women showed a more positive attitude, higher uptake rates, and higher rates of informed decision-making in ultrasound screening.

*Conclusions:* Second-trimester ultrasound screening is perceived more positively than first-trimester Down syndrome screening. This is reflected in higher uptake levels, that are based on high levels of informed decision-making.

# Introduction

Congenital abnormalities are the main cause of fetal death in industrialised countries [1,2]. Second-trimester ultrasound screening (or fetal anomaly scanning) is considered the most important tool for prenatal diagnosis of structural fetal congenital abnormalities, and has become an almost universal feature of pregnancy care in countries with developed health care services.
Fetal anomaly scans are very attractive to women and their partners [3-6]. Often, women's desire to see their fetus is so strong that it is difficult to decline the opportunity [7], which is reflected in high uptake rates [8,9]. However, literature reports show that women often lack information about the purpose of ultrasound examinations and its technical limitations, which makes them unprepared for adverse findings [6,10]. These adverse findings might ultimately result in prospective parents having to decide whether or not to continue pregnancy [11]. These features augment the relevance of informed decision-making, emphasised by international guidelines on routine ultrasound screening [12,13]. To enable informed decision-making about whether or not to undergo this screening, Dutch healthcare professionals are required to ask every pregnant woman if she wants information about the fetal anomaly scan [14].

Following Marteau, an informed decision is made when a woman has adequate decision-relevant knowledge on the screening program, and when her actual participation or non-participation in the screening is consistent with her attitude towards undergoing the screening herself [15]. At group level, the level of informed choice about second-trimester ultrasound screening can be regarded as an indicator of the quality of the information provision procedure. Until now, informed decision-making in the context of prenatal screening has only been investigated for first-trimester prenatal screening for Down syndrome [16-22].
In this study we evaluated the process of information provision, and the quality of this information provision procedure using informed decision-making as a quality indicator, in the Dutch national program for second-trimester ultrasound screening for fetal anomalies. In addition, we compared results on informed decision-making in second-trimester ultrasound screening with those obtained for first-trimester prenatal screening for Down syndrome with the combined test [23].

# Methods

Previously, we investigated the provision of information and informed decision-making on prenatal screening for Down syndrome [23]. In the current study, the same methods will be applied to evaluate information provision and informed decision-making on second-trimester ultrasound screening for fetal anomalies. Therefore, considerable overlap exists between the Methods sections of these two papers. In addition, the results of that study on first-trimester prenatal screening for Down syndrome will be used for a comparison with the results from the current study on second-trimester ultrasound screening. Therefore, in the Results section of our current paper, we will often refer to the paper on prenatal screening for Down syndrome.

## Participants and data collection

*Data on the process of providing information about the fetal anomaly scan* were obtained from midiwives through a web-based registration form. Eligible midwives worked in one of the 65 midwifery practices registered by the regional centre for prenatal screening in the Southwest region of the Netherlands (80% situated in suburban areas).

*Data on informed decision-making (outcome of the information provision), as quality-indicator of the information provision procedure* were obtained from pregnant women by self-completion questionnaires. A subselection of 46 out of the 65 midwifery practices, based on an even distribution of urban and suburban areas [24], was informed about this part of the study. Prenatal healthcare professionals distributed the questionnaires to pregnant women after counseling about second-trimester ultrasound screening for fetal anomalies, but before possible participation in the screening, and to all women not interested in receiving information on second-trimester ultrasound screening and thus receiving no counseling. The study covered a one-year period (May 2008 to May 2009).

*Data used for the comparison with informed decision-making on first-trimester prenatal screening for Down syndrome with the combined test*

In a previous study, we measured informed decision-making on first-trimester prenatal screening for Down syndrome with the combined test [23]. That study was performed at the same time as the current study, with the same midwifery practices concerned. Therefore, some women who filled out a questionnaire on informed decision-making about second-trimester ultrasound screening, also completed a questionnaire on informed decision-making about first-trimester screening with the combined test. This provided us with the opportunity of within-group comparison of knowledge on second-trimester ultrasound screening for fetal anomalies with knowledge on first-trimester prenatal screening for Down syndrome with the combined test.

In these studies, midwives were the data providers (data on process of information provision), or provided access to the study population (study on informed decision-making). Not all pregnant women in the Netherlands start their prenatal care carrier at the midwifery practice. The most recent data on prenatal care [15] show that in 2006, 77.3% of all pregnant women started prenatal care in the primary care system (midwives). The remaining 22.7% started prenatal care at the secondary care level. Since we only asked midwives to register data and / or hand out questionnaires to pregnant women, all women starting prenatal care at the secondary care level (22.7% of all pregnant women) were excluded from our research sample.

*The process of providing information about the fetal anomaly scan; web- based registration form*

In the web-based registration form, we asked midwives to report whether they had offered information about the prenatal screening program and whether the pregnant woman who accepted the offer actually received the information.

*The quality of the information provision procedure about the fetal anomaly scan: informed decision-making questionnaire*

*Knowledge* was measured by 10 statements, with the response options of 'true', 'not true', or 'do not know'. The development of this knowledge questionnaire is described in a previous study [25]. In brief, the content was based on a generic list of domains of screening considered to be essential for an informed choice [26-29]. These generic content domains were made specific for second-trimester ultrasound screening using scientific literature, national

information material and a national quality standard on prenatal screening for fetal disorders [30,31]. The items to be included in the knowledge questionnaire, were acquired by expert consensus.

The total knowledge score ranged from 0 to 10, and was obtained by summing scores on the individual items ('correct' =1 point; 'not correct' and 'do not know'=0 points). We defined inadequate knowledge as a score lower than 6.0, and adequate knowledge as a score equal to or greater than 6.0. Cronbach's alpha for the knowledge measure was 0.59 in this study.

*Attitude of pregnant women towards undergoing second-trimester ultrasound screening themselves* was measured using a scale based on the multi-dimensional measure of informed choice (MMIC) [15]. The scale contained four items (see Appendix 1), that were scored on a seven-point scale, giving a minimum attitude score of 4 (negative) and a maximum score of 28 (positive). By summing up the item scores and dividing by 2.8, total scores were transformed to a 1 (rounded) to 10 scale. Total scores were transformed to a 1 (rounded) to 10 scale by summing the item scores and dividing by 2.8. We defined a negative attitude of a pregnant woman towards undergoing second-trimester ultrasound screening herself, as an attitude score lower than 6.0, and a positive attitude towards undergoing second-trimester ultrasound screening herself, as an attitude score equal to or greater than 6.0. Cronbach's alpha was 0.74 for the attitude measure in this study.

*Intention to participate*

Women were asked whether they intended to participate in second-trimester ultrasound screening. Response options were 'Yes', 'No', and 'Do not know'. Because all women received the instruction to fill out the questionnaire before actual participation in the screening program, only the intention to participate in the screening (and not the actual participation) was provided. To determine informed decision-making, only data from women answering 'Yes' or 'No' on the previous question were considered, and classified into the categories 'intention to participate' and 'intention not to participate'.

*Informed decision-making*

Following Marteau et al. [15], an informed choice (decision) is based on adequate knowledge and a behaviour that is consistent with attitude. Hence, an informed decision to participate was defined as having adequate knowledge (total knowledge score ≥ 6.0), a positive attitude towards undergoing second-trimester ultrasound screening yourself (attitude score ≥ 6), and an intention consistent with this attitude; the intention to participate. An informed choice not to participate was defined as having adequate knowledge, a negative attitude towards undergoing second-trimester ultrasound screening yourself, and the intention not to participate. All other combinations were defined as uninformed. Hence, a non-informed decision can be due to inadequate knowledge and/or value inconsistency (e.g., an attitude towards undergoing second-trimester ultrasound screening yourself, which is not consistent with actual participation). We used the midpoints of the scales as objective thresholds to make a distinction between adequate and inadequate knowledge and between a positive and a negative attitude [17,32,33].

*Comparing informed decision-making with first-trimester prenatal screening for Down syndrome with the combined test*

We could compare knowledge scores on second-trimester ultrasound screening for fetal anomalies with knowledge scores for first-trimester screening for Down syndrome with the combined test [23] for all knowledge domains, except for the domains 'Purpose of the screening', 'Condition being screened for' (measured with 1 item in second-trimester screening and

with two separate items in first-trimester screening for Down syndrome), 'Expected % of detection' (was not measured in first-trimester screening for Down syndrome) and 'What to do in the event of an increased probability / abnormal test result' (was not measured in second-trimester ultrasound screening) [25,34].

*Demographic and other data in the web-based registration form*
*Age* was measured by women's date of birth and classified into 'young' (younger than 36 years of age) and 'old' (36 years of age or above).
*Gravidity* was dichotomised into 'none' (no previous pregnancies) and 'I or more' (I or more previous pregnancies).
*Parity* was dichotomised into 'nulliparous' (not having delivered before) and 'multiparous' (one ore more deliveries).

*Demographic and other data in the informed decision-making questionnaire*
*Educational attainment level* was classified as 'low' (no education, primary and secondary education, or middle vocational education) or 'high' (tertiary education or higher; university, higher vocational education).
*Ethnic origin* was classified as 'non-Dutch' or 'Dutch' (based on country of birth of the pregnant woman [35]).
*Residence* was defined as 'suburban' when the residence population density was less than 1000 (i.e., less than 1000 addresses per $km^2$) and as 'urban' when the area had a population density of 1000 or higher [24].
*Self-reported religious affiliation* was dichotomised into 'religious' and 'not religious', and *religious activity* as 'often' (attending a religious meeting at least monthly) or 'seldom/never' (attending a religious meeting less than twice a year/only for religious festivities or never).

**Analyses**

To explore the relationship between the categorical variables parity, information offered by the health care professional and acceptance of the information offer by the pregnant woman, $\chi^2$ was used. Independent-samples T-tests were used to to compare mean knowledge- and attitude scores between different groups (participants/non participants, old and young pregnant women). Stepwise backward linear regression analysis (probability of F for entry <0.05, for removal >0.10) was used to investigate the association of the determinants (age, education, residence, religious affiliation, religious activity, ethnic origin) with continuous outcome variables (knowledge, attitude). For dichotomous outcome variables (intention to participate, informed decision-making), conditional logistic regression with backward selection (based on Likelihood Ratio's and probability of F for entry <0.05, for removal >0.10) was used to calculate odds ratios (ORs) and 95% confidence intervals (95% CIs). Both analyses were performed with age in the first block, thus controlling for age as a confounder. Mc Nemar was used to compare nominal knowledge data (% correct) between matcher pairs of subjects (pregnant women filling out knowledge items on second-trimester ultrasound screening as well as items on first-trimester prenatal screening for Down syndrome). For missing values, the option 'exclude cases pairwise' was used. Data were analysed using SPSS version 15.0.

# Results

## Response and representativeness

*Concerning the process of providing information about the fetal anomaly scan,* we obtained data for 6435 pregnancies, registered by 59 out of the 65 practices in the region (86.8%). Of these data, 23.4% (n=1509) came from midwifery practices in urban areas and 76.6% (n=4926) from practices in suburban areas.

*Concerning the quality of the information provision procedure about the fetal anomaly scan (informed decision-making)* 20 midwifery practices (out of 46 midwifery practices contacted for this part of the study; 43.5%) participated in distributing questionnaires regarding informed decision-making among pregnant women. Of these participating practices,75% (n=15) were situated in urban areas. The response rate from pregnant women on the questionnaires that were distributed was estimated to be 30-35%, and it was almost evenly distributed between urban (46.7%) and suburban (53.3%) areas. We had to rely on estimates regarding the response rate because of the anonymous nature of the questionnaires.

*Concerning the comparison of results on informed decision-making*
Of all women that filled out a questionnaire on informed decision-making about second-trimester ultrasound screening, 45.3% (N=214/472 also completed a questionnaire on informed decision-making about first-trimester prenatal screening for Down syndrome with the combined test [23].

Table 1 shows the background characteristics of women of which data on the process of providing information about second-trimester ultrasound screening were provided by midwives, of women who filled out the questionnaire on informed decision-making about second-trimester ultrasound screening, and of women who filled out both questionnaires (on informed decision-making about second-trimester ultrasound screening and on informed decison-making about first-trimester screening for Down syndrome). As reference data, percentages (for educational level [36] and ethnic origin [37]) in the population of Dutch women in the age group 15–45 years are provided. Mean age in both groups was representative of mean age of Dutch mothers at the birth of their first child in 2008 (29.4 years) [38]. In the group who completed the informed decision-making questionnaire, lower educated women and women of non-Dutch ethnic origin were underrepresented.

## The process of providing information about the fetal anomaly scan

The process of providing information was evaluated for the women who booked their prenatal care visit at the midwifery practice at 13 weeks of gestation or earlier (N=5181; 92.0% of women for whom data were provided concerning the duration of gestation). Almost all pregnant women (97.7%; n=4668) were asked by their prenatal health care professional whether they wanted information; 92.3% (n=4310/4668) of these pregnant women wished to receive information and 94.3% (n=4065/4310) of them actually received the information.
Parity (nulliparous/multiparous) was not associated with whether the health care professional asked if the pregnant woman wished to receive information ($\chi^2$ (1, N=4780)=0.53, P=0.47). Women being multiparous more often rejected receiving information (3.6%) than women being nulliparous (1.3%) ($\chi^2$ (1, N=4452)=23.48, P<0.0001.

**Table 1:** Background characteristics of pregnant women

*Pregnant women of which data on process of providing information on second-trimester ultrasound screening were provided by health care professionals*

| Characteristic | Mean (SD) | N | % |
|---|---|---|---|
| Age (years) | 29.8 (5.1) | | |
| Young (<36) | | 5259 | 88.3 |
| Old (≥36) | | 698 | 11.7 |
| Gravidity | 1.0 (1.4) | | |
| None | | 2723 | 42.3 |
| 1 or more | | 3712 | 57.7 |
| Parity | 0.8 (1.0) | | |
| Nulliparous | | 3253 | 50.6 |
| Multiparous | | 3182 | 49.4 |
| Pregnancy duration (days) | 69.2 (20.3) | | |
| ≤13 weeks | | 5181 | 92.0 |
| >13 weeks | | 449 | 8.0 |
| Dutch language proficiency | | | |
| Good | | 5549 | 91.8 |
| Moderate | | 248 | 4.1 |
| Serious difficulties | | 113 | 1.9 |
| Not speaking Dutch | | 134 | 2.2 |

*Pregnant women who provided data themselves, on informed decision-making*

| Second-trimester ultrasound screening, all women (N=472) | | | | | Women who filled out both questionnaires (N=214) | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Characteristic | Mean (SD) | N | % | % in Dutch population | Characteristic | Mean (SD) | N | % | % in Dutch population |
| Age (years) | 30.3 (4.4) | | | | Age (years) | 30.3 (3.9) | | | |
| Young (<36) | | 400 | 87.3 | | Young (<36) | | 191 | 91.4 | |
| Old (≥36) | | 58 | 12.7 | | Old (≥36) | | 18 | 8.6 | |
| Educational attainment level | | | | | Educational attainment level | | | | |
| Low | | 228 | 49.0 | 72.2 | Low | | 109 | 50.9 | 72.2 |
| High | | 237 | 51.0 | 27.8 | High | | 104 | 48.6 | 27.8 |
| Ethnic origin | | | | | Ethnic origin | | | | |
| Non-Dutch | | 32 | 6.8 | 26.3 | Non-Dutch | | 6 | 2.8 | 26.3 |
| Dutch | | 437 | 93.2 | 73.7 | Dutch | | 207 | 97.2 | 73.7 |
| Residence | | | | | Residence | | | | |
| Suburban | | 247 | 53.3 | | Suburban | | 170 | 79.4 | |
| Urban | | 216 | 46.7 | | Urban | | 42 | 19.6 | |
| Religious affiliation | | | | | Religious affiliation | | | | |
| Not religious | | 248 | 53.1 | | Not religious | | 113 | 53.1 | |
| Religious | | 219 | 46.9 | | Religious | | 100 | 46.9 | |
| Religious activity | | | | | Religious activity | | | | |
| Seldom/never | | 375 | 84.1 | | Seldom/never | | 171 | 83.4 | |
| Often | | 71 | 15.9 | | Often | | 34 | 16.6 | |

**Informed decision-making: knowledge, attitude, and intention to participate**

Table 2 shows the items of the knowledge questionnaire, the knowledge domains, and percentages and numbers of correct, not correct, and 'do not know' responses. Knowledge scores were obtained from 463 pregnant women, provided by 20 participating practices. Pregnant women had relatively little knowledge on the fact that the result of the fetal anomaly scan may lead to difficult choices, for example termination of the pregnancy (11.9 % thinks that this is not the case) and on the probability that a child has a congenital abnormality (35.5 % does not know that this probability is generally relatively small, 7.9% of the women thinks that this probability is 5% or more).

Table 3 provides descriptives for knowledge, attitude, and intention to participate in second-trimester ultrasound screening. Mean knowledge score (on a scale from 0 to 10) was 8.3. Of the pregnant women, 6.5 % (N=30) did not have adequate levels of relevant knowledge on the fetal anomaly scan (knowledge score <6.0), the remaining 93.5 % (N=433) had adequate levels of relevant knowledge (knowledge score ≥ 6.0). Mean knowledge scores did not differ significantly between participants (mean score=8.4±1.6) and non-participants (mean score =8.0±1.7) (t=-1.4, p=0.17), neither between old (mean score=8.7±1.5) and young (mean score=8.3±1.7) (t=-1.9, p=0.06) pregnant women. Women with a high educational level had significantly higher knowledge scores (mean score=8.7±1.5) than women with a low educational level (mean score=8.0±1.7) (t=-5.09, p<0.0001).
Attitude scores were obtained for 456 pregnant women. Mean attitude score (on a scale from 1 to 10) was 8.8. Of the pregnant women, 90.4 % (N=412) had a positive attitude towards her own participation in second-trimester ultrasound screening (attitude score ≥ 6.0), the remaining 9.6 % (N=44) had a negative attitude towards her own participation (attitude score < 6.0). Mean attitude scores were significantly higher in participants (mean score=9.1±1.4) as compared with non-participants (mean score=5.9±1.8) (t=-9.5, p<0.001). Mean attitude scores did not differ significantly between old (8.9±1.6) and young (8.8±1.7) pregnant women(t=-0.37, p=0.71).
Information about the intention to participate in the screening test was obtained for 470 pregnant women. 87.7% (N=412) of these women had the intention to participate in second-trimester ultrasound screening, 7.0% (N=33) had the intention not to participate and the remaining 5.3 % (N=25) had not yet made a decision on participation when filling in the questionnaire. With data obtained from the web-based questionnaire, filled out by midwives, we were able to compare uptake information as provided by pregnant women themselves and according to midwives. For 39.6% of the pregnant women from which uptake information was known from the questionnaires, uptake information was also available from the web-based questionnaires. There was consensus between these two sources of information in 80.7% of the cases.

A total of 426 women provided complete data on attitude, knowledge, and intention to participate in second-trimester ultrasound screening. Of these women, 88.0% (n=375) made an informed choice, and 95.7% (n=359) of these were informed choices to participate. Out of 12.0% (n=51) uninformed choices, 72.5% (n=37) were choices to participate (Table 4).

In multivariate analysis, age and educational level were the only significant determinants of informed decision-making (Table 5).

**Table 2:** Items of the knowledge questionnaire, knowledge domains and percentages and numbers correct, not correct and 'do not know' (data on informed decision-making, from pregnant women)

| Item (correct answer) | Domain | % Correct (N) | % Not correct (N) | % Do not know (N) |
|---|---|---|---|---|
| 1. The fetal anomaly scan is aimed at examining the unborn child for certain physical abnormalities (true). | Disorders being screened for and purpose of the screening | 98.7 (466) | 0.6 (3) | 0.6 (3) |
| 2. The result of the fetal anomaly scan may lead to difficult choices, for example termination of the pregnancy (true). | Possible side effects of the test procedure | 79.4 (374) | 11.9 (56) | 8.7 (41) |
| 3. Spina bifida is usually clearly recognised using the fetal anomaly scan (true). | The expected percentage of detection | 91.3 (430) | 0.8 (4) | 7.9 (37) |
| 4. The chance that a child has a congenital abnormality is generally relatively small (less than 5%) (true). | Prevalence in the population (the theoretical risk that the disorder that is tested, is present) | 56.7 (267) | 7.9 (37) | 35.5 (167) |
| 5. Repeatedly performing a scan is dangerous for the unborn child (not true). | Test procedure | 81.7 (384) | 5.1 (24) | 13.2 (62) |
| 6. If the result of the fetal anomaly scan is 'abnormal', further examination is usually required to obtain more certainty (true). | The meaning of an 'abnormal' test result (including the possibility of false positives) | 88.3 (416) | 1.7 (8) | 10.0 (47) |
| 7. If the result of the fetal anomaly scan is 'no abnormality', there is still the possibility of the child having an abnormality when it is born (true). | The meaning of a 'normal' test result (including the possibility of false negatives) | 96.8 (457) | 0.6 (3) | 2.5 (12) |
| 8. Further examination after an abnormal result on the fetal anomaly scan may reveal that the child does not have any major physical abnormalities (true). | Possible findings resulting from a further examination | 79.1 (372) | 3.8 (18) | 17.0 (80) |
| 9. Should a major physical abnormality be found in the fetal anomaly scan, termination of the pregnancy would be a possibility (true). | What to do after a further examination | 73.3 (344) | 8.5 (40) | 18.1 (85) |
| 10. Every pregnant woman in the Netherlands is obliged to have a fetal anomaly scan (not true). | Voluntary nature of the test | 86.6 (407) | 6.2 (29) | 7.2 (34) |

**Table 3:** Descriptives for knowledge, attitude, and intention to participate in second trimester ultrasound screening (data on informed decision-making, from pregnant women)

| Variable | N | % | All respondents | Participants in the screening | | | Non-participants in the screening | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | Mean (SD) | N | % | Mean (SD) | N | % | Mean (SD) |
| Knowledge | 463 | | 8.3 (1.6) | | | 8.4 (1.6) | | | 8.0 (1.7) |
| Inadequate (knowledge score<6.0) | 30 | 6.5 | | 22 | 5.4 | | 5 | 15.6 | |
| Adequate (knowledge score≥6.0) | 433 | 93.5 | | 384 | 94.6 | | 27 | 84.4 | |
| Attitude | 456 | | 8.8 (1.7) | | | 9.1 (1.4) | | | 5.9 (1.8) |
| Negative (attitude score<6.0) | 44 | 9.6 | | 21 | 5.2 | | 18 | 60.0 | |
| Positive (attitude score≥6.0 | 412 | 90.4 | | 379 | 94.8 | | 12 | 40.0 | |
| Intention to participate | 470 | | | | | | | | |
| Yes | 412 | 87.7 | | | | | | | |
| No | 33 | 7.0 | | | | | | | |
| Not (yet) made a decision | 25 | 5.3 | | | | | | | |

**Table 4:** Numbers and percentages of (un-) informed decision-making in second-trimester ultrasound screening and Down syndrome (data on informed decision-making, from pregnant women)

| Choice | Knowledge | Attitude | Uptake | Second-trimester ultrasound screening | | First-trimester screening for Down's syndrome | |
|---|---|---|---|---|---|---|---|
| | | | | N | % of total informed and uninformed | N | % of total informed and uninformed |
| Informed choice | | | | 375 | 88.0 | 335 | 75.5 |
| *Specification informed choice* | | | | N | % of total informed choice | N | % of total informed choice |
| Informed choice to participate | Adequate | Positive | Yes | 359 | 95.7 | 150 | 44.8 |
| Informed choice to not participate | Adequate | Negative | No | 16 | 4.3 | 185 | 55.2 |
| | | | | N | % of total informed and uninformed | N | % of total informed and uninformed |
| Non- informed choice | | | | 51 | 12.0 | 109 | 24.5 |
| *Specification uninformed choice; inadequate knowledge* | | | | N | % of total uninformed choice | N | % of total uninformed choice |
| | Inadequate | Positive | Yes | 16 | 31.4 | 4 | 3.7 |
| | Inadequate | Positive | No | 2 | 3.9 | 12 | 11 |
| | Inadequate | Negative | Yes | 4 | 7.8 | 1 | 0.9 |
| | Inadequate | Negative | No | 2 | 3.9 | 27 | 24.8 |
| *Specification uninformed choice; value-inconsistency* | | | | | | | |
| | Adequate | Positive | No | 10 | 19.6 | 61 | 55.9 |
| | Adequate | Negative | Yes | 17 | 33.3 | 4 | 3.7 |

**Table 5:** Association of background characteristics with knowledge, attitude, intention to participate and informed decision-making (data on informed decision-making, from pregnant women)

| | Knowledge | | | | Attitude | | | | Intention to participate | | | | | | Informed decision-making | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Univariate | | Multivariate | | Univariate | | Multivariate | | Univariate | | | | Multivariate | | Univariate | | | | Multivariate | |
| | Mean (SD) | p value | B | p value | Mean (SD) | p value | B | p value | No (%) | Yes (%) | OR | p value | OR | p value | No (%) | Yes (%) | OR | p value | OR | p value |
| Age (continuous) | | 0.06 | 0.05 | <0.01 | | 0.71 | 0.04 | 0.05 | | | 1.19 | 0.00 | 1.07 | 0.24 | | | 1.08 | 0.01 | 1.11 | <0.01 |
| Young (<36 years) | 8.25 (1.68) | | | | 8.83 (1.66) | | | | 31 (8.2) | 347 (91.8) | | | | | 46 (12.6) | 319 (87.4) | | | | |
| Old (≥36 years) | 8.70 (1.48) | | | | 8.92 (1.55) | | | | 1 (1.8) | 54 (98.2) | | | | | 5 (10.0) | 45 (90.0) | | | | |
| Education | | | | | | | | | | | | | | | | | | | | |
| High | 8.71 (1.50) | 0.00 | 0.66 | 0.00 | 8.96 (1.50) | 0.14 | | | 9 (3.9) | 219 (96.1) | 2.08 | 0.00 | 2.49 | 0.08 | 16 (7.2) | 205 (92.8) | 3.17 | 0.00 | 1.98 | 0.05 |
| Low | 7.96 (1.66) | | | | 8.72 (1.79) | | | | 23 (10.8) | 189 (89.2) | | | | | 33 (16.4) | 168 (83.6) | | | | |
| Residence | | | | | | | | | | | | | | | | | | | | |
| Urban | 8.42 (1.68) | 0.25 | | | 8.94 (1.53) | 0.23 | | | 8 (3.8) | 200 (96.2) | 1.41 | 0.09 | 2.30 | 0.11 | 22 (10.9) | 180 (89.1) | 1.49 | 0.07 | | |
| Suburban | 8.24 (1.58) | | | | 8.75 (1.76) | | | | 25 (10.8) | 207 (89.2) | | | | | 27 (12.2) | 194 (87.8) | | | | |
| Religious affiliation | | | | | | | | | | | | | | | | | | | | |
| Religious | 8.26 (1.67) | 0.27 | | | 8.60 (1.80) | <0.01 | | | 18 (8.9) | 184 (91.1) | 0.41 | 0.00 | | | 24 (12.5) | 168 (87.5) | 0.76 | 0.21 | | |
| Not religious | 8.42 (1.51) | | | | 9.05 (1.48) | | | | 15 (6.3) | 225 (93.7) | | | | | 26 (11.2) | 206 (88.8) | | | | |
| Religious activity | | | | | | | | | | | | | | | | | | | | |
| Often | 8.17 (1.66) | 0.28 | | | 7.93 (2.00) | 0.00 | -0.96 | 0.00 | 9 (14.8) | 52 (85.2) | 0.13 | 0.00 | | | 7 (12.5) | 49 (87.5) | 0.91 | 0.78 | | |
| Seldom/ never | 8.40 (1.56) | | | | 9.00 (1.54) | | | | 23 (6.4) | 337 (93.6) | | | | | 40 (11.5) | 307 (88.5) | | | | |
| Ethnic origin | | | | | | | | | | | | | | | | | | | | |
| Dutch | 8.39 (1.52) | <0.01 | 0.89 | <0.01 | 8.87 (1.62) | 0.24 | | | 31 (7.5) | 383 (92.5) | 0.39 | 0.01 | | | 44 (11.0) | 356 (89.0) | 0.57 | 0.26 | | |
| Non-Dutch | 7.45 (2.31) | | | | 8.39 (2.05) | | | | 2 (6.9) | 27 (93.1) | | | | | 7 (26.9) | 19 (73.1) | | | | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Knowledge (continuous) | | | 0.09 | 0.07 | | | | | | |
| Adequate | 8.90 (1.61) | <0.01 | | | 27 (6.6) | 384 (93.4) | 1.61 | 0.00 | | |
| Inadequate | 7.82 (2.02) | | | | 5 (18.5) | 22 (81.5) | | | | |
| Attitude (continuous) | | | | | | | | | | |
| Positive | | | | | 12 (3.1) | 379 (96.9) | 3.22 | 0.00 | 2.34 | 0.00 |
| Negative | | | | | 18 (46.2) | 21 (53.8) | | | | |

### Comparing informed decision-making with first-trimester prenatal screening for Down syndrome with the combined test

Comparing second-trimester ultrasound screening with first-trimester screening for Down syndrome with the combined test [23], women had better knowledge of the meaning of a normal test result (as compared to the meaning of a low probability test result) and of possible findings resulting from a further diagnostic work-up in second-trimester ultrasound screening for fetal anomalies. However, they had less knowledge about the possible (negative) side effects of the test procedure, the test procedure itself, the options after a further diagnostic work-up, and the voluntariness of the test in second-trimester ultrasound screening for fetal anomalies as compared with first-trimester screening for Down syndrome with the combined test [23]. Results of this comparison are presented in Table 6. In this Table, knowledge scores are presented for both screening programs, organised per knowledge domain.

Concerning attitude towards own participation in the screening program, women had a more positive attitude towards participating in second-trimester ultrasound screening for fetal anomalies (attitude score=8.8 ± 1.7) as compared to participating in first-trimester screening for Down syndrome (attitude score=6.2 ± 2.5) ($p < 0.01$).
All women having the intention not to participate in second-trimester ultrasound screening (13/186), also did not want to participate in first-trimester prenatal screening for Down syndrome. Of all women having the intention to participate in second-trimester ultrasound screening (173/186), 34.0% also wanted to participate in first-trimester prenatal screening for Down syndrome.

## Discussion

### Principal findings

Almost all pregnant women in an unselected population in the Southwest region of the Netherlands were offered and provided information about second-trimester ultrasound screening for fetal anomalies. High levels of informed decision-making were found, most of these were decisions to participate in the screening program. The majority of the uninformed decisions were due to inconsistencies between attitudes and screening behavior. In most of these cases (63.0%; 17/27) women decided to participate in second-trimester ultrasound screening for fetal anomalies, in spite of a negative attitude about participating in this screening program. Compared to first-trimester prenatal screening for Down syndrome [23], pregnant women had less knowledge on the possible (negative) side effects of the test procedure, the test procedure itself, the options after a further diagnostic work-up, and the voluntariness of the test in second-trimester ultrasound screening. Women had a more positive attitude and higher uptake rates in second-trimester ultrasound screening as compared to first-trimester prenatal screening for Down syndrome [23].

### Strengths and weaknesses

No gold standard exists for the precise content of decision-relevant knowledge for informed decision making on second-trimester ultrasound screening. As a consequence, to date a diversity in measures of knowledge is used in studies evaluating informed decision making [39]. In this study, we used a knowledge questionnaire which covers domains and items recom-

**Table 6:** Comparison of knowledge, organized per knowledge domain, between second-trimester ultrasound screening and first-trimester screening for Down syndrome with the combined test, for women who filled out both questionnaires (N=214)

| Knowledge domain | Item<br>Second-trimester ultrasound screening (correct answer) | Item<br>First-trimester screening for Down syndrome (correct answer) | % correct<br>Second-trimester ultrasound screening | % correct<br>First-trimester prenatal screening for Down syndrome | P<br>(McNemar) |
|---|---|---|---|---|---|
| Possible side effects test procedure | *The result of the fetal anomaly scan may lead to difficult choices, for example termination of the pregnancy (true)* | *The result of prenatal screening for Down syndrome may lead to difficult choices (true)* | 74.8 | 96.2 | < 0.01 |
| Prevalence in population | *The chance that a child has a congenital abnormality is generally relatively small (less than 5%) (true)* | *The probability that an unborn child has Down syndrome is generally very small (less than 1%) (true)* | 54.7 | 56.3 | 0.78 |
| Test procedure | *Repeatedly performing a scan is dangerous for the unborn child (not true)* | *The combined test consists of a measurement of the thickness of the nuchal fold of the unborn child (a nuchal ultrasound) and a blood test on the mother (true)* | 80.8 | 88.7 | 0.01 |
| Meaning abnormal / increased probability test result | *If the result of the fetal anomaly scan is 'abnormal' further examination is usually required to obtain more certainty (true)* | *Should the result of the combined test be unfavourable, this means that the child has Down syndrome (not true)* | 87.4 | 81.8 | 0.15 |
| Meaning normal / decreased probability test result | *If the result of the fetal anomaly scan is 'no abnormality' there is still the possibility of the child having an abnormality when it is born (true)* | *Should the result of the combined test be favourable, the child may still prove to have Down syndrome when born (true)* | 96.3 | 87.4 | < 0.01 |
| Possible findings further examination | *Further examination after an abnormal result on the fetal anomaly scan may reveal that the child does not have any major physical abnormalities (true)* | *Both amniocentesis and chorionic villus sampling provide certainty about the presence of Down syndrome in an unborn child (true)* | 76.6 | 60.2 | < 0.01 |
| What to do after further examination | *Should a major physcial abnormality be found in the fetal anomaly scan, termination of the pregnancy would be a possibility (true)* | *Should Down syndrome be diagnosed during the first four months of pregnancy, it is possible for a pregnant woman to terminate pregnancy (true)* | 66.2 | 85.3 | < 0.01 |
| Voluntariness of the test | *Every pregnant women in the Netherlands is obliged to have a fetal anomaly scan (not true)* | *Prenatal screening for Down syndrome is compulsory for every pregnant woman in the Netherlands (not true)* | 86.4 | 98.6 | < 0.01 |

mended by professionals in the field of prenatal screening and pregnant women [25]. Therefore, we expect the questionnaire to assess knowledge on the domains of second-trimester ultrasound screening that are essential for informed decision-making.
The group of responding women on the informed decision-making questionnaire was relatively small and consisted mainly of higher educated, ethnic Dutch women. This should be kept in mind when interpreting the results of this study.

**Knowledge, attitude, uptake and informed decision-making on fetal anomaly scan in other studies**

Although overall knowledge about the fetal anomaly scan was adequate, relatively large numbers of women had inadequate knowledge about the fact that the results of the fetal anomaly scan may lead to difficult choices (for example termination of the pregnancy). In addition, less women (as compared with first-trimester screening for Down syndrome with the combined test [23]) were aware that participating in the fetal anomaly scan is not obligatory. These findings are in keeping with other studies investigating the perception of pregnant women on the fetal anomaly scan [6,40]. Whereas first-trimester screening for Down syndrome with the combined test is perceived by pregnant women as being primarily focused on the detection of 'abnormalities', the second-trimester ultrasound scan is perceived as aiming to confirm 'normality' [26,41]. If abnormalities are observed, these may create strong emotional reactions that could have been alleviated by prior information about potential findings [42].
Consistent with previous findings [6,40], pregnant women had a very positive attitude about participating in the fetal anomaly scan, which is reflected in high uptake rates. Attitudes of pregnant women about participating in the fetal anomaly scan were considerably more positive than attitudes about participating in first-trimester screening for Down syndrome using the combined test [23] The same applies to uptake rates for these screening programs; almost all women had the intention to participate in the fetal anomaly scan, whereas only a minority of the pregnant women (32.8% [23]) had the intention to participate in first-trimester screening for Down syndrome with the combined test. Uptake rates of second-trimester ultrasound screening comparable with those determined in our study, are reported in international studies [43]. In England, uptake rates of between 88-100% were observed in a recent report [8]. However, if almost all women participate in the screening program, it can be questioned whether women perceive the fetal anomaly scan as voluntary.

Decisions on participating in prenatal screening as reported in the literature are often not informed decisions [22,44,45]. Most studies on informed decision-making about prenatal screening focus on first-trimester screening for Down syndrome with the combined test. In the Netherlands as well as internationally, informed-decision making about second-trimester ultrasound screening for fetal anomalies has not been investigated previously. Some studies focused on knowledge of pregnant women participating in the fetal anomaly scan [26,41,42,46-53]. Most of these studies identified gaps in women's understanding of ultrasound. Kohut et al. showed that 46% of pregnant women did not view ultrasound as a screen for anomalies and less than one third of the women participating in the fetal anomaly scan recalled having been given a choice about participating. In other words, these women participated in the screening program, but did not perceive having a right to choose whether or not to undergo this procedure [26]. In another study, also about one third of pregnant women were not aware of the right to refuse an ultrasound assessment [49]. In our study, a number of women was not aware of the fact that participating in second-trimester screening is a choice. However, the large majority knew that participating is voluntary. We may conclude that the standard offer

of information about the screening program, which was introduced in the Netherlands in 2007, did not result in 'forced participation' in pregnant women feeling overtaken by the offer and actually not willing to participate. Furthermore, our data do not support a 'normalisation' or 'routinisation' effect of prenatal screening, resulting in low levels of informed decision-making as was expected to appear with the introduction of a standard information offer.

## Conclusions

Participating in second-trimester ultrasound screening for fetal anomalies may lead to emotional distress and difficult choices. Although high levels of informed decision-making about participating in the fetal anomaly scan were determined in this study, we believe that, in the information provision procedure, special attention should be paid to reaching adequate levels of knowledge on the possible negative consequences of participating in this screening program. The high number of pregnant women intending to participate in second-trimester ultrasound screening currently, should be associated with adequate knowledge on the consequences of a decision to participate.

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*Details of Ethics Approval*
The procedures of this study received ethics approval from the Medical Ethics Research Committee Erasmus MC (MEC-2007-166).

# Appendix 1; Attitude measure used in the present study.

**Participating in second-trimester ultrasound screening: What is your opinion?**

What is your opinion of participating in second-trimester ultrasound screening? Please indicate this in the following four questions by marking for each line one of the boxes under the numbers one through seven.

**Example**

If you are of the opinion that participating second-trimester ultrasound screening would be 'a bad idea' for you, mark box 1 in the first line. If your opinion is that it is not such a bad idea, then you should choose one of the numbers more towards the right when making the assessment. If your opinion is that participating in second-trimester ultrasound screening is 'not a bad idea' for you, you should then mark box 7. The other three questions should be answered in the same way.

Participating in second-trimester ultrasound screening is, in my opinion:

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| A bad idea | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 | ☐ 6 | ☐ 7 | Not a bad idea |
| Useful | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 | ☐ 6 | ☐ 7 | Not useful |
| Harmful | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 | ☐ 6 | ☐ 7 | Not harmful |
| A good idea | ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 | ☐ 6 | ☐ 7 | Not a good idea |

Source: [15]

# References


[1] Lee K, Khoshnood B, Chen L, Wall SN, Cromie WJ, Mittendorf RL. Infant mortality from congenital malformations in the United States, 1970-1997. Obstet.Gynecol. 2001;98:620-627.

[2] Petrini J, Damus K, Russell R, Poschman K, Davidoff MJ, Mattison D. Contribution of birth defects to infant mortality in the United States. Teratology 2002;66 Suppl 1:S3-6.

[3] Georges E. Fetal ultrasound imaging and the production of authoritative knowledge in Greece. Med.Anthropol.Q. 1996;10:157-175.

[4] Larsen T, Nguyen TH, Munk M, Svendsen L, Teisner L. Ultrasound screening in the 2nd trimester. The pregnant woman's background knowledge, expectations, experiences and acceptances. Ultrasound Obstet.Gynecol. 2000;15:383-386.

[5] Harris G, Connor L, Bisits A, Higginbotham N. "Seeing the baby": pleasures and dilemmas of ultrasound technologies for primiparous Australian women. Med.Anthropol.Q. 2004;18:23-47.

[6] Garcia J, Bricker L, Henderson J, Martin MA, Mugford M, Nielson J, Roberts T. Women's views of pregnancy ultrasound: a systematic review. Birth 2002;29:225-250.

[7] Wertz DC, Fletcher JC. A critique of some feminist challenges to prenatal diagnosis. J.Womens Health 1993;2:173-188.

[8] Healthcare Commission. Towards better births. A review of maternity services in England 2008.

[9] Georgsson Ohman S, Waldenstrom U. Second-trimester routine ultrasound screening: expectations and experiences in a nationwide Swedish sample. Ultrasound Obstet.Gynecol. 2008;32:15-22.

[10] Statham H, Solomou W. Antenatal screening for Down's syndrome. Lancet 1998;352:1862.

[11] Bijma HH, van der Heide A, Wildschut HI. Decision-making after ultrasound diagnosis of fetal abnormality. Reprod.Health Matters 2008;16:82-89.

[12] Kirwan D, NHS Fetal Anomaly Screening Programme (NHS FASP). NHS Fetal Anomaly Screening Programme 2010 2010.

[13] RCOG. Report of the RCOG Working Party on Ultrasound Screening for Fetal Abnormalities 1997.

[14] Dutch National Institute for Public Health and the Environment (RIVM). Policy; timely information about possible disorders;2010.

[15] Marteau TM, Dormandy E, Michie S. A measure of informed choice. Health Expect 2001;4:99-108.

[16] Dormandy E, Hooper R, Michie S, Marteau TM. Informed choice to undergo prenatal screening: a comparison of two hospitals conducting testing either as part of a routine visit or requiring a separate visit. J Med Screen 2002;9:109-14.

[17] Dormandy E, Michie S, Hooper R, Marteau TM. Informed choice in antenatal Down syndrome screening: a cluster-randomised trial of combined versus separate visit testing. Patient Educ Couns 2006;61:56-64.

[18] Gourounti K, Sandall J. Do pregnant women in Greece make informed choices about antenatal screening for Down's syndrome? A questionnaire survey. Midwifery 2008;24:153-62.

[19] Jaques A, Sheffield L, Halliday J. Informed choice in women attending private clinics to undergo first trimester screening for Down syndrome. Prenatal diagnosis 2005;25:656-664.

[20] van den Berg M, Timmermans DR, ten Kate LP, van Vugt JM, van der Wal G. Informed decision making in the context of prenatal screening. Patient Educ Couns 2006;63:110-7.

[21] van den Berg M, Timmermans DR, Ten Kate LP, van Vugt JM, van der Wal G. Are pregnant women making informed choices about prenatal screening? Genet Med 2005;7:332-8.

[22] Fransen M, Essink-Bot ML, Vogel I, Mackenbach JP, Steegers E, Wildschut H. Ethnic differences in informed decision-making about prenatal screening for Down syndrome. J Epidemiol Community Health 2009.

[23] Schoonen HM, Wildschut HIJ, Essink-Bot ML, Peters IA, Steegers E, de Koning HJ. Evaluating the provision of information and informed decision-making on prenatal screening for Down's syndrome: a questionnaire and register-based survey in a non-selected population. Submitted, 2011.

[24] Statistics Netherlands. Gebieden in Nederland 2007 http://statline.cbs.nl/StatWeb/publication/?DM=SLNL&PA=71377NED&D1=2,48&D2=a&HDR=T&STB=G1&VW=T Accessed on 14/05/2010

[25] Schoonen HM, Essink-Bot ML, Van Agt HM, Wildschut HI, Steegers EA, De Koning HJ. Informed decision-making about the fetal anomaly scan: what knowledge is relevant? Ultrasound Obstet. Gynecol. 2011;37:649-657.
[26] Kohut RJ, Dewey D, Love EJ. Women's knowledge of prenatal ultrasound and informed choice. J Genet Couns 2002;11:265-76.
[27] Zapka JG, Geller BM, Bulliard JL, Fracheboud J, Sancho-Garnier H, Ballard-Barbash R, Group ICW. Print information to inform decisions about mammography screening participation in 16 countries with population-based programs. Patient Educ Couns 2006;63:126-37.
[28] Council of Europe. Council of Europe, Committee of Ministers, Recommendation No. R (90) 13 of Prenatal Genetic Screening, Prenatal Genetic Diagnosis and Associated Genetic Counselling 1990;R (90) 13.
[29] UK National Screening Committee. Antenatal screening- Working Standards Incorporating those for the National Down Syndrome Screening Programme for England 2003;2010.
[30] Dutch National Institute for Public Health and the Environment (RIVM). Information about screening for Down's Syndrome and the 20-week ultrasound http://www.rivm.nl/pns_en/down_ultrasound/information/ Accessed on 21/01/2011
[31] Dutch Association of Obstetrics and Gynaecology (NVOG). Kwaliteitsnorm 6- Prenatale screening op foetale afwijkingen (2005) http://www.knov.nl/docs/uploads/pns-kwn_06_pren_screening_op_foetale_afwijkingen_1.pdf Accessed on 06/03/2010
[32] Michie S, Dormandy E, Marteau TM. The multi-dimensional measure of informed choice: a validation study. Patient Educ Couns 2002;48:87-91.
[33] Dormandy E, Tsui EY, Marteau TM. Development of a measure of informed choice suitable for use in low literacy populations. Patient Educ Couns 2007;66:278-95.
[34] Schoonen HMHJD, van Agt HME, Essink-Bot ML, Wildschut HI, Steegers EAP, de Koning HJ. Informed decision-making in prenatal screening for Down's syndrome: What knowledge is relevant. Patient Educ Couns 2011:265-270.
[35] Stronks K, Kulu-Glasgow I, Agyemang C. The utility of 'country of birth' for the classification of ethnic groups in health research: the Dutch experience. Ethn.Health 2009;14:1-14.
[36] Statistics Netherlands. Beroepsbevolking; behaalde onderwijs naar herkomst geslacht en leeftijd 2009 http://statline.cbs.nl/StatWeb/publication/?DM=SLNL&PA=71822NED&D1=0&D2=l&D3=1-3&D4=0&D5=a&D6=0&D7=l&VW=T Accessed on 29/04/2010
[37] Statistics Netherlands. Geboorte; herkomstgroepering en leeftijd moeder (op 31 december) 2009 http://statline.cbs.nl/StatWeb/publication/?VW=T&DM=SLNL&PA=37884&D1=0-2,8-9-&D2=0&D3=0-2&D4=l&HD=100429-1135&HDR=T&STB=G2,G1,G3 Accessed on 29/04/2010
[38] Statistics Netherlands. Geboorte naar diverse kenmerken 2009 http://statline.cbs.nl/StatWeb/publication/?DM=SLNL&PA=37422NED&D1=40-44&D2=l&HDR=T&STB=G1&VW=T Accessed on 29/04/2010
[39] Green JM, Hewison J, Bekker HL, Bryant LD, Cuckle HS. Psychosocial aspects of genetic screening of pregnant women and newborns: a systematic review. Health Technol Assess 2004;8:iii, ix-x, 1-109.
[40] Bricker L, Garcia J, Henderson J, Mugford M, Neilson J, Roberts T, Martin MA. Ultrasound screening in pregnancy: a systematic review of the clinical effectiveness, cost-effectiveness and women's views. Health Technol.Assess. 2000;4:i-vi, 1-193.
[41] Santalahti P, Aro AR, Hemminki E, Helenius H, Ryynanen M. On what grounds do women participate in prenatal screening?. Prenat.Diagn. 1998;18:153-165.
[42] Ahman A, Runestam K, Sarkadi A. Did I really want to know this? Pregnant women's reaction to detection of a soft marker during ultrasound screening. Patient Educ.Couns. 2010;81:87-93.
[43] Georgsson Ohman S, Waldenstrom U. Second-trimester routine ultrasound screening: expectations and experiences in a nationwide Swedish sample. Ultrasound Obstet.Gynecol. 2008;32:15-22.
[44] van den Heuvel A, Chitty L, Dormandy E, Newson A, Deans Z, Marteau TM. Informed choice in prenatal testing: a survey among obstetricians and gynaecologists in Europe and Asia. Prenat.Diagn. 2008;28:1238-1244.

[45] van den Berg M, Timmermans DR, Knol DL, van Eijk JT, de Smit DJ, van Vugt JM, van der Wal G. Understanding pregnant women's decision making concerning prenatal screening. Health Psychol 2008;27:430-7.
[46] Goel V, Glazier R, Holzapfel S, Pugh P, Summers A. Evaluating patient's knowledge of maternal serum screening. Prenat Diagn 1996;16:425-30.
[47] Basama FM, Leonard B, Leighton M. Audit: women's perception and knowledge of the 20 weeks anomaly scan. J.Obstet.Gynaecol. 2004;24:44-46.
[48] Lalor JG, Devane D. Information, knowledge and expectations of the routine ultrasound scan. Midwifery 2007;23:13-22.
[49] Chan LW, Chan OK, Chau MC, Sahota DS, Leung TY, Fung TY, Lau TK. Expectation and knowledge of pregnant women undergoing first and second trimester ultrasound examination in a Chinese population. Prenat.Diagn. 2008;28:739-744.
[50] Larsen T, Nguyen TH, Munk M, Svendsen L, Teisner L. Ultrasound screening in the 2nd trimester. The pregnant woman's background knowledge, expectations, experiences and acceptances. Ultrasound Obstet.Gynecol. 2000;15:383-386.
[51] Smith RP, Titmarsh S, Overton TG. Improving patients' knowledge of the fetal anomaly scan. Ultrasound Obstet Gynecol 2004;24:740-4.
[52] Mulvey S, Wallace EM. Women's knowledge of and attitudes to first and second trimester screening for Down's syndrome. BJOG 2000;107:1302-1305.
[53] Lalor J, Begley C. Fetal anomaly screening: what do women want to know? J.Adv.Nurs. 2006;55:11-19.

# PART 3
# ETHNIC DIFFERENCES IN PARTICIPATION IN PRENATAL SCREENING FOR DOWN SYNDROME

# Chapter 6 Ethnic differences in participation in prenatal screening for Down syndrome: A register-based study

Ethnic differences in participation in prenatal screening for Down syndrome: a register-based study. Fransen, M.H., Schoonen, H.M.H.J.D., Mackenbach, J.P., Steegers, E.A., de Koning, H.J., Laudy, J.A., Galjaard, R.J., Looman, C.W., Essink-Bot, M.L., Wildschut, H.J.
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**Abstract**

*Objective:* To assess ethnic differences in participation in prenatal screening for Down syndrome in the Netherlands.

*Methods:* Participation in prenatal screening was assessed for the period 1 January 2009 to 1 July 2009 in a defined postal code area in the southwest of the Netherlands. Data on ethnic origin, socio-economic background and age of participants in prenatal screening were obtained from the Medical Diagnostic Centre and the Department of Clinical Genetics. Population data were obtained from Statistics Netherlands. Logistic regression models were used to assess ethnic differences in participation, adjusted for socio-economic and age differences.

*Results:* The overall participation in prenatal screening was 3865 out of 15 093 (26%). Participation was 28% among Dutch women, 15% among those from Turkish ethnic origin, 8% among those from North-African origin, 15% among those from Aruban/Antillean origin and 26% among women from Surinamese origin.

*Conclusions:* Compared to Dutch women, those from Turkish, North-African, Aruban/Antillean and other non-Western ethnic origin were less likely to participate in screening. It was unexpected that women from Surinamese origin equally participated. It should be further investigated to what extent participation and nonparticipation in these various ethnic groups was based on informed decision-making.

# Introduction

Studies in several countries have documented ethnic differences in participation in prenatal screening for Down syndrome. Women from ethnic minority groups are generally less likely to participate in prenatal screening (Ford *et al.*, 1998; Chilaka *et al.*, 2001; Khoshnood *et al.*, 2004; Rowe *et al.*, 2004; Dormandy *et al.*, 2005; Kuppermann *et al.*, 2006; Rowe *et al.*, 2008). This article addresses the question whether such differences also exist in the Netherlands, where 20% of the population presently consists of individuals from non-Dutch ethnic origin. More than half of this group originates from non-Western countries including Mediterranean (Turkey and Morocco) and Caribbean countries (Surinam, Dutch Antilles and Aruba) (Statistics Netherlands, 2009). In the 1960s and 1970s, men from Mediterranean came to the Netherlands as manual labour migrants and later brought their families to stay permanently. The Caribbean countries are former colonies of the Netherlands. After the 1980s, large groups from these populations migrated to the Netherlands, mostly due to economic recession in their home country.

Presently available tests for prenatal screening for Down syndrome can be classified into risk assessment tests and diagnostic tests. Risk assessment tests give an estimate of the probability that the fetus has Down syndrome. Commonly used risk assessment tests are first trimester maternal serum screening (MSS) that involves the assessment of free *ß*-hCG and PAPPA in maternal blood between 9 and 14 weeks, and the ultrasound assessment of fetal nuchal translucency thickness between 11 and 14 weeks' gestation. The individual probability of carrying a child with Down syndrome is subsequently estimated on the basis of the biochemical and ultrasound findings, where the pre-test risk of maternal age is included in the algorithm. If this probability exceeds an *a priori* specified threshold at the time of testing, the woman is offered diagnostic testing with chorionic villus sampling (CVS) or amniocentesis (AMN) that provides certainty about whether or not the fetus has Down syndrome (National Institute for Public Health & Environment, 2009).

The prenatal screening programme based on risk assessment has only recently (since 2007) been implemented in standard prenatal practice in the Netherlands (Health Council of the Netherlands, 2007; Ministry of Health Welfare and Sports, 2007). Since then, gynaecologists and midwives are legally obliged to inform each pregnant woman about the options for prenatal screening at the booking visit (Ministry of Health Welfare and Sports, 2007). The goal of providing information about prenatal screening to pregnant women is not to maximise participation in prenatal screening, but to enable women and their partners to make an autonomous informed decision whether or not to participate in prenatal screening for Down syndrome (Health Council of the Netherlands, 2001; Health Council of the Netherlands, 2004; Ministry of Health Welfare and Sports, 2004; Health Council of the Netherlands, 2006; National Institute for Public Health & Environment, 2009).

An informed decision needs to be based on sufficient and relevant knowledge about the benefits and limitations of the possible courses of action to take and should be in accordance with the individual values and beliefs (Bekker *et al.*, 1999; Green *et al.*, 2004). Women aged 36 years or over have an age-based indication for prenatal testing and may directly choose CVS or AMN. Women under 36 years of age are initially only eligible for risk assessment tests and have to pay for these tests themselves, unless they have a listed indication for diagnostic testing. If the test result indicates an increased risk of Down syndrome, the costs of diagnostic testing are reimbursed (Ministry of Health Welfare and Sports, 2008). As it is unknown

whether participation in prenatal screening differs between ethnic groups in the Netherlands, the objective of this study was to assess ethnic and socio-economic differences in participation in the prenatal screening programme for Down syndrome as set out above. Our research questions were as follows:

1. How many women from various ethnic backgrounds participate in prenatal screening in the southwest of the Netherlands?
2. To what extent do women from various ethnic groups differ in participation in prenatal screening?
3. Is participation in prenatal screening related to pregnant women's ethnic background, after adjustment for differences in socio-economic background and age?

# Methods

**Population and data collection**

Participation in first trimester MSS and maternal agebased CVS and AMN was assessed over the period 1 January 2009 to 1 July 2009 in the southwest of the Netherlands. The total number of live-born children in the southwest of the Netherlands comprises 18% of the total population live-born children in the Netherlands.
Address and date of birth of pregnant women who participated in MSS were obtained from STAR Medical Diagnostic Centre. Since 1 January 2009, all maternal serum screening tests that are performed in the southwest of the Netherlands are analysed in this centre. Data on women of advanced maternal age who had AMN or CVS were obtained from the Department of Clinical Genetics, Erasmus University Medical Centre Rotterdam. Women whose postal code did not fit in the defined postal code area of the southwest of the Netherlands were excluded from the study.

The denominator for our set of observations was estimated, because we did not have information about the number of pregnant women who were eligible to participate in the prenatal screening programme in 2009 (all women living in the assigned area in the 10th–13th week of pregnancy). On the basis of the data on women who gave birth in 2007 and the total population of women of fertile age (between 15 and 45 of age) in the defined postal code area in the same year, we calculated fertility rates per ethnic, socio-economic and age group. These fertility rates were applied to the population of women of fertile age in the defined postal code area in 2009 to estimate the ethnic and socio-economic background and age of the denominator.

**Measures**

Data on *ethnic origin* of the study population were obtained from the Dutch National Office of Statistics (Statistics Netherlands). In the Netherlands, ethnic origin is defined by country of birth of a person's parents. A woman is considered to be from non-Dutch ethnic origin when at least one of her parents was born abroad. A woman is considered to be from 'non-Western' ethnic origin when at least one of her parents was born in Turkey or countries in Africa (including Morocco), South America (e.g. Aruba, Dutch Antilles and Surinam) or Asia. However, Statistics Netherlands apply a rather odd exception for individuals who originate from Indonesia and Japan. Based on their socio-economic and social cultural position, they

are considered to be from Western ethnic background. In the Netherlands, these groups merely consist of individuals who were born in the former Dutch East Indies and employees of Japanese companies and their families. A woman is considered to be from 'other-Western' (non-Dutch) ethnic origin when at least one of her parents was born in a country in Europe, North America, Oceania or Indonesia or Japan (Statistics Netherlands, 2009).
Individual data (date of birth and address) of the women who participated in the prenatal screening programme were linked to the Population Registers of the respective municipalities in the southwest of the Netherlands. These individually linked records were delivered anonymously to the researchers. Data on ethnic origin of the women who gave birth to a live-born child in 2007 were obtained from the national birth records, available from the electronic database of Statistics Netherlands 'StatLine'. Data on ethnic origin of the women of fertile age in the southwest of the Netherlands were obtained for 2007 and 2009 from the Population Registers as available in StatLine.

Data on *socio-economic background* of the study population were obtained via Statistics Netherlands and based on the average disposable income in the neighborhood where the women lived. The disposable income was dichotomized into lower or higher than the average disposable income per Dutch citizen in the same year. Statistics Netherlands linked data on postal codes of the women who participated in prenatal screening to the Population Registers to add neighborhood codes to the dataset. These neighborhood codes were then linked to StatLine and delivered anonymously to the researchers.

Data on *age* of the study population were obtained via Statistics Netherlands and based on women's date of birth. Age was categorised as 'younger than 26 years of age', 'between 26 and 31 years of age', 'between 31 and 36 years of age' and '36 years of age or over'.

*Participation in the prenatal screening programme* was first of all measured by data on women who participated in MSS. As women of 36 years and older could also choose directly for AMN or CVS and therefore would unjustly be considered as non-participants, we also obtained data on participation in maternal age-based AMN or CVS. The number of women who directly chose for AMN or CVS was calculated by subtracting those who participated in both tests from the total number of participants in AMN or CVS. The women who participated in MSS as well as the diagnostic test AMN or CVS were counted as participants in MSS. The overall participation in the prenatal screening programme was calculated by adding women who participated in MSS to those who directly participated in AMN or CVS.

**Statistical analyses**

Multiple logistic regression analyses were used to assess ethnic and socio-economic differences in participation in maternal age-based prenatal screening. Three models were analysed with participation in the prenatal screening programme (yes/no) as dependent variable. The first model concerned unadjusted analyses for the independent variable ethnic origin. The second model concerned unadjusted analyses for socio-economic background as independent variable. The third model contained the independent variables ethnic origin, socio-economic background and age to adjust for each other.

Since the denominators in these logistic regression models were only estimates and not real numbers of women eligible for prenatal screening, we performed a parametric bootstrap. Simulated participant and nonparticipant counts were generated for each cell by independ-

ent Poisson sampling. Simulated participants were drawn from a Poisson distribution with the observed number of participants as a mean. Simulated nonparticipants were drawn from a Poisson distribution with the estimated population minus the observed participants as a mean. Simulated participants and non-participants were added up to obtain the simulated denominator, univariate and multivariate logistic regressions were performed for each of 1000 replicas, and we calculated the 2.5 and 97.5% quantile of the odds ratios (ORs) to reach 95% confidence intervals (CIs) and *p* values which were thereby corrected for the uncertainty of the denominator.

## Results

Table 1 shows that the overall participation in the prenatal screening programme for Down syndrome in the total population was estimated at 26%. The participation in MSS among women of all ages was 24% and the participation in direct AMN or CVS among women of 36 years and older was 8%. The participation was highest among women who originate from other (non-Dutch) Western countries (33%) and lowest among women from North-African (Moroccan) ethnic origin (8%). The participation was 20% among the women from low socioeconomic background and 33% among the women from high socio-economic background. The highest participation was measured among women aged 36 years or over; 42% participated in the prenatal screening programme. With the exception of Moroccan women, all women aged 36 years or over more often participated in direct age-based AMN or CVS than Dutch women of advanced maternal age.

Table 2 shows that women from North-African (Moroccan), Turkish, Aruban/Antillean and other non- Western ethnic origin were less likely to participate in the prenatal screening programme than Dutch women, whereas those from other Western (non-Dutch) ethnic origin were more likely to participate in the prenatal screening programme. Women from Moroccan origin differed most from Dutch women, followed by women from Turkish origin. No significant differences were found between women from Surinamese and Dutch ethnic origin. Women from high socio-economic background were more likely to participate in the prenatal screening programme than women from low socioeconomic background. This difference remained statistically significant after adjustment for ethnic origin and age. After adjustment for socio-economic background and age, the ORs for the Moroccan, Turkish and Aruban/Antillean groups remained statistically significant, indicating that the ethnic differences in participation were not attributable to differences in socioeconomic background or age. The difference between women from other non-Western ethnic origin and Dutch women was not significant anymore after adjustment for differences in socio-economic background and age.

## Discussion

This register-based study showed that participation in the prenatal screening programme for Down syndrome in the Netherlands is related to pregnant women's ethnic background, even after adjustment for differences in socio-economic background and age. Women from North-African (Moroccan), Turkish and Aruban/Antillean ethnic origin were less likely to participate in the prenatal screening programme than Dutch women, whereas those from other Western (non-Dutch) ethnic origin were more likely to participate in the prenatal screening programme. Most findings of this study are in keeping with previous international studies that

**Table 1:**
Participation in the prenatal screening programme for Down syndrome, according to ethnic origin, socio-economic background and age n (%) in the southwest region of the Netherlands

| | Total population | Women of 36 years and older | AMN/CVS among women of 36 years and older[a] | MSS among women of all ages[b] | Participation in prenatal screening[b] |
|---|---|---|---|---|---|
| Ethnic origin | | | | | |
| Dutch | 9904 (66) | 1785 (18) | 127 (7) | 2620 (26) | 2747 (28) |
| North African (Moroccan) | 846 (6) | 162 (19) | 5 (3) | 66 (8) | 71 (8) |
| Turkish | 756 (5) | 94 (12) | 8 (9) | 104 (14) | 112 (15) |
| Aruban / Antillean | 370 (2) | 51 (14) | 7 (14) | 50 (14) | 57 (15) |
| Surinamese | 572 (4) | 99 (17) | 16 (16) | 135 (24) | 151 (26) |
| Other non-Western | 1119 (7) | 170 (15) | 22 (13) | 205 (18) | 227 (20) |
| Other Western (non-Dutch) | 1526 (10) | 307 (20) | 28 (9) | 472 (31) | 500 (33) |
| Socio-economic background | | | | | |
| Low | 8509 (56) | 1348 (16) | 108 (8) | 1587 (19) | 1695 (20) |
| High | 6584 (44) | 1320 (20) | 105 (8) | 2065 (31) | 2170 (33) |
| Age | | | | | |
| <26 | 2554 (17) | 0 | Not applicable | 310 (12) | 310 (12) |
| 26-31 | 4942 (33) | 0 | Not applicable | 1005 (20) | 1005 (20) |
| 31-36 | 4930 (32) | 0 | Not applicable | 1429 (29) | 1429 (29) |
| ≥36 | 2668 (18) | 2668 (100) | 213 (8) | 908 (34) | 1121 (42) |
| Total | 15093 (100) | 2668 (18) | 213 (8) | 3652 (24) | 3865 (26) |

CVS, chrorionic villus sampling; AMN, amniocentesis; MSS, maternal serum screening.
[a] The percentages in this column are based on the population of women of 36 years and older.
[b] The percentages in the column are based on the total population per ethnic, socio-economic or age group.

**Table 2:**
OR for participation in the prenatal screening programme for Down syndrome by ethnic origin and socio-economic background

| | Participation | Unadjusted OR (95% CI; *p*) | Adjusted ORs (95% CIs; *p*) |
|---|---|---|---|
| Ethnic origin | | | |
| Dutch | 2747 (28) | 1.00 | 1.00 |
| North African (Moroccan) | 71 (8) | 0.24 (0.18-0.31; $p < 0.001$) | 0.28 (0.20-0.36; $p < 0.001$)[a] |
| Turkish | 112 (15) | 0.45 (0.35-0.56; $p < 0.001$) | 0.63 (0.48-0.78; $p < 0.001$)[a] |
| Aruban / Antillean | 57 (15) | 0.47 (0.31-0.63; $p < 0.001$) | 0.67 (0.45-0.90; $p = 0.01$)[a] |
| Surinamese | 151 (26) | 0.93 (0.72-1.18; $p = 0.52$) | 1.18 (0.90-1.52; $p = 0.23$)[a] |
| Other non-Western | 227 (20) | 0.66 (0.55-0.80; $p < 0.001$) | 0.83 (0.68-1.01; $p = 0.07$)[a] |
| Other Western (non-Dutch) | 500 (33) | 1.27 (1.10-1.49; $p < 0.001$) | 1.30 (1.10-1.55; $p < 0.001$)[a] |
| Socio-economic background | | | |
| Low | 1695 (20) | 1.00 | 1.00 |
| High | 2170 (33) | 1.98 (1.81-2.18; $p < 0.001$) | 1.62 (1.46-1.80; $p < 0.001$)[b] |
| Age | | | |
| <26 | 310 (12) | 1.00 | 1.00 |
| 26-31 | 1005 (20) | 1.85 (1.60-2.17; $p < 0.001$) | 1.64 (1.41-1.94; $p < 0.001$)[c] |
| 31-36 | 1429 (29) | 2.96 (2.53-3.48; $p < 0.001$) | 2.48 (2.12-2.95; $p < 0.001$)[c] |
| ≥ 36 | 1121 (42) | 5.25 (4.42-6.25; $p < 0.001$) | 4.58 (3.82-5.48; $p < 0.001$)[c] |

ORs, odds ratios; CIs, confidence interval.
[a] Adjusted for differences in age and socio-economic background.
[b] Adjusted for differences in age and ethnic origin.
[c] Adjusted for differences in ethnic origin and socio-economic background

also showed lower participation rates among women from non-Western ethnic background and women from lower socio-economic background (Ford *et al.*, 1998; Chilaka *et al.*, 2001; Khoshnood *et al.*, 2004; Dormandy *et al.*, 2005; Kuppermann *et al.*, 2006; Rowe *et al.*, 2004; Rowe *et al.*, 2008). However, an unexpected finding was that women from Surinamese ethnic origin participated equally in the prenatal screening programme.

As published results on participation in the prenatal screening programme in the Netherlands are not yet available, this provides important information for the evaluation of the recently introduced prenatal screening programme for Down syndrome. International studies on ethnic variations in participation in first trimester prenatal screening for Down syndrome are scarce. As far as we know, this is the first study to assess ethnic differences in participation in prenatal screening for Down syndrome in an unselected large population. This study has limitations as well. First, we did not have exact numbers of pregnant women who were living in the southwest of the Netherlands in the first half of 2009. The number of women giving birth in 2009 and their ethnic and socio-economic background had to be estimated from the population of women who gave birth to a living child in 2007 in the same postal code area. Since the comparison of the population of women of fertile age in 2007 and 2009 showed that the population sizes and the ethnic and socio-economic distribution did not change much in these two years, it is unlikely that the estimations for 2009 considerably deviate from the actual number and distribution in pregnant women in the first half of 2009. Second, we have to take into account that there will be differences between the number of women giving birth and the number of women being pregnant at the time of the screening, as not all pregnant women will reach delivery of a liveborn child. The percentage of fetal loss is generally estimated at less than 2% (Alfirevic *et al.*, 2003). As we had no reason to assume that this small percentage differs considerably per ethnic group, we do not expect this detracts from our results on ethnic differences in prenatal screening.

An important finding of this study was that especially women from Turkish and Moroccan ethnic origin were less likely to participate in prenatal screening for Down syndrome. These differences could partly be explained by their socio-economic background and age. As Dutch inhabitants from Turkish and Moroccan origin generally have a low household income, the need to pay for prenatal screening under the age of 36 could form a substantial barrier to participate among these groups (Statistics Netherlands, 2007). Another possible explanation is that women were less often aware of this relatively new screening test for Down syndrome or that prenatal screening was not offered to them. Our previous interview study among pregnant women from Turkish, Surinamese and Dutch ethnic origin showed that 85% of the women reported to have received information about prenatal screening for Down syndrome. In contrast to other studies, (Rowe *et al.*, 2004., 2008), we did not find significant differences in reported offer of information between Turkish, Surinamese and Dutch women. However, we did find that women from Turkish origin were less often aware of prenatal screening tests for Down syndrome, less often read written information material, had only little knowledge about Down syndrome and prenatal screening and less often made an informed decision whether or not to participate in prenatal screening compared to women from Dutch and Surinamese ethnic origin (Fransen *et al.*, 2009a; Fransen *et al.*, 2010).

These ethnic differences could especially be attributed to language barriers and educational attainment level. Studies in Australia and the United States also showed that language barriers play an important role in women's comprehension of information about prenatal screening for Down syndrome (Browner *et al.*, 1996; Jaques *et al.*, 2004). Higher awareness of the

recently introduced prenatal screening programme may also explain why Dutch women of advanced maternal age in our study were less likely to directly choose for diagnostic tests, but more often participated in first trimester serum screening compared to women from other ethnic origin. A Dutch study on late booking for prenatal care showed that women from non-Western ethnic origin generally book later for prenatal care than women from Dutch origin, which also diminishes their possibility of participating in first trimester prenatal screening. This especially counts for Moroccan women; 22% did not arrive for prenatal care before 18 weeks' gestation, this was 18% among Turkish women and 5% among Dutch women. These differences could mostly be explained by poor Dutch language skills, low education and more teenage pregnancies (Alderliesten *et al.*, 2007). Another explanation for the relatively low participation among Turkish and Moroccan women is that they more often chose not to participate because of their religious beliefs. Almost all people from Turkish and Moroccan ethnic origin in the Netherlands consider themselves as Muslims. Our previous study on pregnant women's considerations whether or not to participate in prenatal screening showed that Turkish women often reported not to participate in prenatal screening because they accept what God gives. However, this was not significantly associated with non-participation in this study (Fransen *et al.*, 2009b). Further research is needed to investigate if and how religious beliefs influence participation in prenatal screening.

An unexpected finding was that women from Surinamese ethnic origin participated equally in the prenatal screening programme. A potential explanation is the relatively low participation in prenatal screening among the Dutch women compared to women from other countries (Khoshnood *et al.*, 2004; Rowe *et al.*, 2004; Van den Berg *et al.*, 2005; Rowe *et al.*, 2008). Another explanation may be that the cultural distance between women from Surinamese origin and the Dutch host population is relatively small. Surinamese women generally do not experience language barriers, have a higher educational attainment level than women from Turkish or Moroccan ethnic origin and more often participate in the labour market (Oudhof *et al.*, 2008). It is therefore likely that they experience fewer barriers in access to prenatal screening. The results from our previous study among pregnant women from Dutch, Turkish and Surinamese ethnic origin indeed showed that women from Surinamese origin scored higher on informed decision-making than women from Turkish origin. However, compared to the level of informed decision-making among the Dutch women in our study population, other populations in the Netherlands and other countries, the level of informed decision-making among the Surinamese women that we interviewed was poor (Michie *et al.*, 2003; Dormandy *et al.*, 2005; Jaques *et al.*, 2005; Van den Berg *et al.*, 2005; Fransen *et al.*, 2010). It is therefore questionable whether the similar participation between Surinamese and Dutch women in this registered-based study also implies equal knowledge about Down syndrome and prenatal screening.

## Conclusion

This study showed that participation in prenatal screening is related to pregnant women's ethnic background. Women from Turkish, North-African (Moroccan) and Aruban/Antillean ethnic origin in the southwest of the Netherlands were less likely to participate in the prenatal screening programme than women from Dutch ethnic origin. It was unexpected that women from Surinamese origin equally participated in the programme. This is the first study on ethnic variations in participation in prenatal screening and therefore generates a starting point for further research and clinical practice. It should be further investigated to what extent

pregnant women are offered prenatal screening, whether they are interested in the provided information and to what extent they actually understand and use the information to make an informed decision whether or not to participate in prenatal screening. It would be interesting to study how variables such as ethnic background, religious beliefs, language barriers, educational level and health literacy contribute to informed decision-making and participation in a diverse population of pregnant women.

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# References


Alderliesten ME, Vrijkotte TG, van der Wal MF, Bonsel GJ. 2007. Late start of antenatal care among ethnic minorities in a large cohort of pregnant women. Br J Obstet Gynaecol 114: 1232–1239.

Alfirevic Z, Sundberg K, Brigham S. 2003. Amniocentesis and chorionic villus sampling for prenatal diagnosis. Cochrane Database Syst Rev CD003252.

Bekker H, Thornton JG, Airey CM, *et al.* 1999. Informed decision making: an annotated bibliography and systematic review. Health Technol Assess 3: 1–156.

Browner CH, Preloran M, Press NA. 1996. The effects of ethnicity, education and an informational video on pregnant women's knowledge and decisions about a prenatal diagnostic screening test. Patient Educ Couns 27: 135–146.

Chilaka VN, Konje JC, Stewart CR, Narayan H, Taylor DJ. 2001. Knowledge of Down syndrome in pregnant women from different ethnic groups. Prenat Diagn 21: 159–164.

Dormandy E, Michie S, Hooper R, Marteau TM. 2005. Low uptake of prenatal screening for Down syndrome in minority ethnic groups and socially deprived groups: a reflection of women's attitudes or a failure to facilitate informed choices?. Int J Epidemiol 34: 346–352.

Ford C, Moore AJ, Jordan PA, *et al.* 1998. The value of screening for Down's syndrome in a socioeconomically deprived area with a high ethnic population. Br J Obstet Gynaecol 105: 855–859.

Fransen MP, Wildschut HIJ, Vogel I, Mackenbach JP, Steegers EAP, Essink-Bot ML. 2009a. Information about prenatal screening for Down syndrome Ethnic differences in knowledge. Patient Educ Couns 77: 279–288.

Fransen MP, Wildschut HIJ, Vogel I, Mackenbach JP, Steegers EAP, Essink-Bot ML. 2009b. Ethnic differences in considerations whether or not to participate in prenatal screening for Down syndrome. Prenat Diagn 29: 1262–1299.

Fransen MP, Essink-Bot ML, Vogel I,Mackenbach JP, Steegers EAP, Wildschut HIJ. 2010. Ethnic differences in informed decisionmaking about prenatal screening for Down syndrome. J Epidemiol Community Health 64(3): 262–268.

Green JM, Hewison J, Bekker HL, Bryant LD, Cuckle HS. 2004. Psychosocial aspects of genetic screening of pregnant women and newborns: a systematic review. Health Technol Assess 8: 1–109.

Health Council of the Netherlan ds. 2001. Prenatal Screening: Down's syndrome, neural tube defects, routine-ultrasonography. Publication no. 2001/11.Health Council of the Netherlands: The Hague.

Health Council of the Netherlands. 2004. Prenatal Screening (2); Down's syndrome, neural tube defects. Publication no. 2004/06. Health Council of the Netherlands: The Hague.

Health Council of the Netherlands. 2006. Population screening act: inition of a national programme for prenatal screening;Down's syndrome and neural tube defects. Publication no 2006/03WBO. Health Council of the Netherlands: The Hague.

Health Council of the Netherlands. 2007. Population screening act: prenatal screening for Down's syndrome and neural tube defects. Publication no 2007/05WBO. Health Council of the Netherlands: The Hague.

Jaques AM, Halliday JL, Bell RJ. 2004. Do women know that prenatal testing detects fetuses with Down syndrome?. J Obstet Gynaecol 24: 647–651.

Jaques AM, Sheffield LJ, Halliday JL. 2005. Informed choice in women attending private clinics to undergo first-trimester screening for Down syndrome. Prenat Diagn 25: 656–664.

Khoshnood B, Blondel B, de Vigan C, Breart G. 2004. Socioeconomic barriers to informed decision-making regarding maternal serum screening for down syndrome: results of the French National Perinatal Survey of 1998. Am J Public Health 94: 484–491.

Khoshnood B, De Vigan C, Vodovar V, Goujard J, Goffinet F. 2004. A population-based evaluation of the impact of antenatal screening for Down's syndrome in France, 1981–2000. Br J Obstet Gynaecol 111: 485–490.

Kuppermann M, Learman LA, Gates E, *et al.* 2006. Beyond race or ethnicity and socioeconomic status: predictors of prenatal testing for Down syndrome. Obstet Gynecol 107: 1087–1097.

Michie S, Dormandy E, Marteau TM. 2003. Informed choice: understanding knowledge in the context of screening uptake. Patient Educ Couns 50: 247–53.

Ministry of Health Welfare and Sports. Standpunt prenatale screening (2). 2004. http://www.minvws.nl/kamerstukken/ibe/standpunt_prenatale_screening_2.asp.[22 October 2009].

Ministry of Health Welfare and Sports. Stand van zaken prenatale screening, perinatale sterfte en perinatale audit. 2007. http:// www.minvws.nl/kamerstukken/cz/2007/stand-van-zaken-prenatale-screening-perinatale-sterfte-en-perinatale-audit.asp [22 October 2009].

Prenatale tests alleen gratis voor 36+. 2008. http://www.minvws.nl/nieuwsberichten/ibe/prenatale_tests_alleen_gratis_voor_36ers.asp [22 October 2009].

National Institute for Public Health & Environment. Prenatal screening; Down and ultrasound. 2009. http://www.rivm.nl/pns_en/down_ultrasound/ [22 October 2009].

Oudhof K, Vliet Rvd, Hermans B. 2008. Annual report on integration 2008. Statistics Netherlands: The Hague.

Rowe R, Puddicombe D, Hockley C, Redshaw M. 2008. Offer and uptake of prenatal screening for Down syndrome in women from different social and ethnic backgrounds. Prenat Diagn 28: 1245–1250.

Rowe RE, Garcia J, Davidson LL. 2004. Social and ethnic inequalities in the offer and uptake of prenatal screening and diagnosis in the UK: a systematic review. Public Health 118: 177–189.

Rowe RE, Magee H, Quigley MA, Heron P, AskhamJ, Brocklehurst P. 2008. Social and ethnic differences in attendance for antenatal care in England. Public Health 122: 1363–1372.

Statistics Netherlands. Statline databank: average income on household level according to diverse characteristics. 2007.

Statistics Netherlands. Themes; Dossiers; People with a foreign background. 2009. http://www.cbs.nl/nl-NL/menu/themas/dossiers/allochtonen/cijfers/default.htm. [23 February 2009].

Van den Berg M, Timmermans DR, Kleinveld JH, Garcia E, van Vugt JM, van der Wal G. 2005. Accepting or declining the offer of prenatal screening for congenital defects: test uptake and women's reasons. Prenat Diagn 25: 84–90.

Van den Berg M, Timmermans DR, Ten Kate LP, van Vugt JM, van der Wal G. 2005. Are pregnant women making informed choices about prenatal screening?. Genet Med 7: 332–338.

# PART 4
# OFFERING INFORMATION ON PRENATAL SCREENING FOR DOWN SYNDROME PRIOR TO CONCEPTION

# Chapter 7 Informing on prenatal screening for Down syndrome prior to conception: An empirical and ethical perspective

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*Submitted*

**Abstract**

*Purpose:* In most Western countries, information on prenatal screening for Down syndrome is provided in the first-trimester of pregnancy. We investigate whether this information should additionally be provided before pregnancy to improve the informed decision-making process.

*Methods:* In an empirical study we obtained data from pregnant women with respect to their preferences regarding information on prenatal screening preconceptionally. In an ethical analysis we elaborated on these preferences by weighing pros and cons.

*Results:* Questionnaire data (n=510) showed that 55.7% of responding women considered participating in prenatal screening for Down syndrome before pregnancy. 28.0% of women possessed information on prenatal screening preconceptionally. 84.6% preferred not to receive information preconceptionally in retrospect. We considered two arguments against the provision of information on prenatal screening preconceptionally: women's preferences to receive information in a step-by-step manner, and the risk of providing a directive message. We identified three reasons supporting its provision preconceptionally: the likelihood of making an informed decision could, firstly, be increased by 'unchaining' the initial information from possible subsequent decisions, and, secondly, by providing women sufficient time to deliberate. Thirdly, the probability of equal access to prenatal screening may increase.

*Conclusion:* We propose to incorporate an information *offer* regarding prenatal screening for Down syndrome in preconception care consultations. By offering information, instead of providing information, prospective parents are enabled to either accept or decline the information, which respects both their right to know and their right not-to-know.

# Introduction

Preconception care is a set of primary interventions that identify and modify biomedical, behavioral and social risks to a woman's health and future pregnancies [1]. Preconception care aims to optimize the health of the future child and to improve maternal health [2]. Information on prenatal screening for Down syndrome is commonly provided after conception, during the first-trimester of pregnancy. Many Western countries have policies or recommendations for prenatal screening for Down syndrome, in which either women of advanced age are offered invasive diagnostic testing (chorionic villus sampling or amniocentesis), or in which women, irrespective of their age, are offered non-invasive risk-assessment tests in the first-trimester of pregnancy (nuchal scan, often combined with maternal serum evaluation) [3,4]. The latter screening tests provide an individual risk estimate of carrying a child with Down syndrome, and may be followed by diagnostic testing to confirm whether or not the fetus is affected.

## Practice of prenatal screening in the United States

In the United States, professional guidelines recommend that, ideally, all women regardless of maternal age should be offered screening for fetal chromosomal abnormalities before 20 weeks' gestation [5-8]. According to these guidelines, the decision to screen or test for Down syndrome in a pregnancy is a personal one, and patients should have the option to have a diagnostic test regardless of maternal age after being informed on the risks, benefits, and limitations of both screening and diagnostic tests [5].
In practice, the majority of prenatal health care professionals offers first-trimester screening for Down syndrome by the combined test (nuchal translucency and serum markers plasma protein-A; PAPP-A, and ß- human chorionic gonadotrophin [hCG]) [9]. However, since there is no national screening program, also other approaches are used, both in the first- and second trimester of pregnancy. Offering the integrated test is also a common procedure; with this test, the results from first-trimester screening tests are not analyzed until the results from second trimester tests are evaluated, when both sets are assessed together [10]. It happens as well, that women who began prenatal screening in the first trimester, but were not counseled on first-trimester screening, are referred to a gynecologist with an abnormal quadruple test at 17 weeks. They typically will not seek a termination in the current United States environment (C.P. Weiner, personal communication, September 10, 2011).
Concerning the provision of information on prenatal screening, usually a nurse hands out a standard brochure and no one speaks to the patient directly (C.P. Weiner, personal communication, September 10, 2011). In Figure 1 we describe the decisional steps on prenatal screening for Down syndrome in the United States.

## Practice of prenatal screening in the Netherlands

In the Netherlands, a national screening program for Down syndrome exists as of January 1, 2007 [11]. In this program, all pregnant women (regardless of age) are offered information on the possibility of having a screening test for Down syndrome, with the first-trimester combined test as the test of choice. Before 2007, only women aged 36 years or above, or women with a medical indication, were offered prenatal screening for Down syndrome [12].
An important aspect of the Dutch national screening program is the distinction between the information offer, and the actual provision of information. In the Netherlands, prenatal screening falls under specifications of the Dutch medical treatment agreement (WGBO), laid down in the civil code. The 'right not-to-know' is one of the concepts formulated in the WGBO

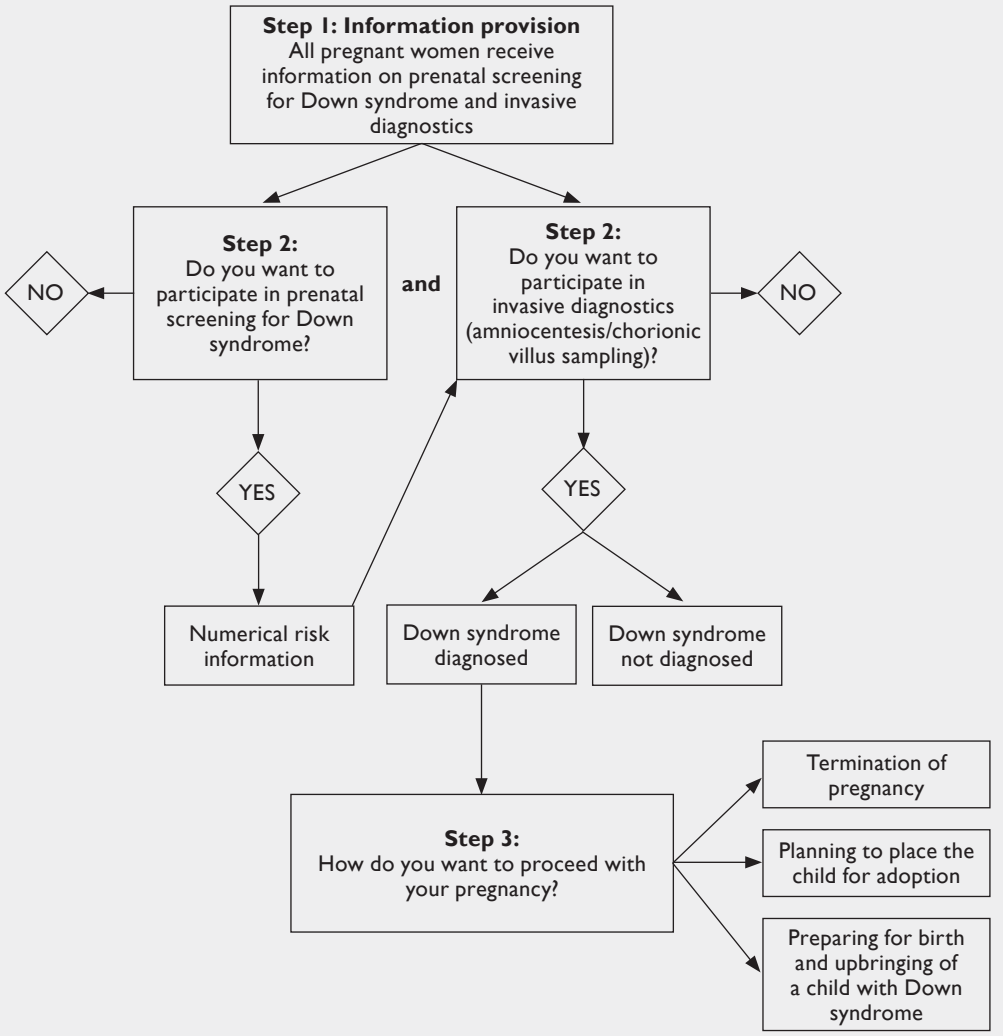


**Figure 1:** Decisional steps on prenatal screening for Down syndrome in United States

(art 7:449; Civil code of the Netherlands). In this context, the right not-to-know implicates that women are allowed to refuse receiving information about prenatal screening. However, in order to be able to refuse something, it should be offered first. When information is provided (instead of offered), which currently is the standard procedure in the United States (Figure 1), women are faced with the information, without having received the opportunity to reject. Therefore, in the Netherlands, women are first *offered* to receive information. Then, only if a woman indicates she is interested in receiving this information, the actual *provision* of information takes place (Figure 2).

To the best of our knowledge, this 'Dutch distinction' (between offering and providing), as an embodiment of the right not-to-know, is unique from an international perspective; in the United States and anywhere else, the right not-to-know has not been applied in order to make it possible to reject an information offer on prenatal screening. In the United States, the concept is mainly used (and criticized) in debates in the context of genetic screening [13].

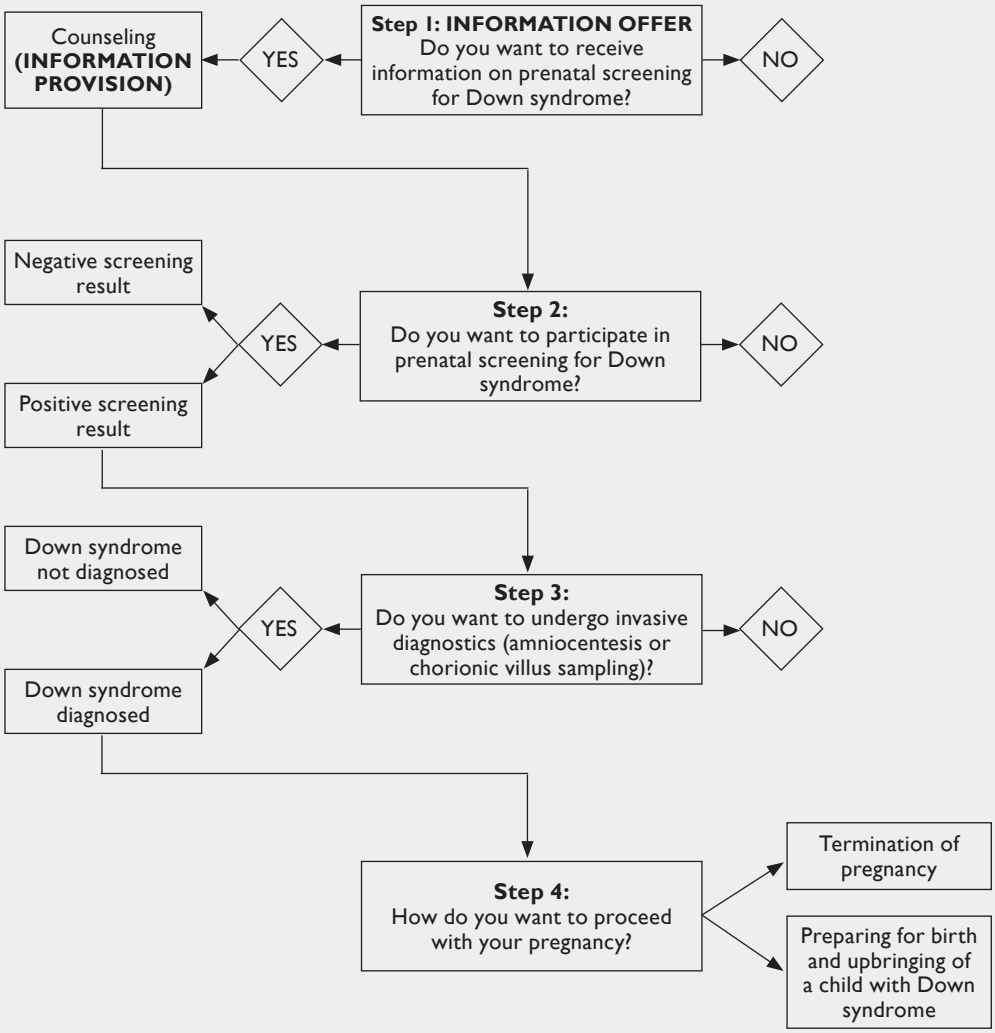


**Figure 2:** Decisional steps on prenatal screening for Down syndrome in the Netherlands

In this paper we consider the right not-to-know as an essential element of the framework of informed decision-making. This is why we started our study from the international situation in which information is provided instead of offered.

## Informed decision-making

Facilitating informed choice on participation in prenatal screening is a fundamental part of international guidelines [5,11,14-19].

An informed choice is based on relevant knowledge. In addition, actual behavior (in this case, participating or non-participating in prenatal screening for Down syndrome) should be consistent with the decision-maker's attitudes [20].

The optimal screening window, in terms of test performance, for first-trimester screening on Down syndrome is from 11 to 14 weeks gestation [21]. Recently, it was reported that

improvement in the first-trimester combined test performance might be reached through collection of the serum at two different time points in pregnancy, one before 11 weeks gestation [22]. Thus the time that pregnant women have to make a decision about participating in prenatal screening is limited. This time window will become even shorter when new prenatal screening programs are introduced that can be performed as early as five weeks gestation [23,24]. Time constraints are a key obstacle to informed decision-making [25,26]. Some women indicate wishing more time to consider their decision, stating that information is needed earlier in pregnancy. As the information about screening is usually given at the booking visit, it is difficult to provide it earlier in pregnancy. Therefore, there may be a need for information about prenatal screening tests before pregnancy [27] .

**Information provision on prenatal screening for Down syndrome prior to conception?**

The objective of this paper is to investigate whether information on prenatal screening for Down syndrome should be provided prior to conception, in addition to the prenatal information provision, in order to increase the likelihood of informed decision-making about participation in the screening. First, we performed an empirical study of women's preferences for receiving information about prenatal screening for Down syndrome prior to conception. We used the results of this empirical study as a starting point for an ethical analysis, presented in the second part of this paper. In the ethical analysis, we considered the pros and cons of providing information preconceptionally in addition to the provision during the initial prenatal visit. Using the results of our empirical study and ethical analysis, we conclude with an advice on information about prenatal screening for Down syndrome prior to conception.

## Materials and methods

### Empirical study

We used a self-completion questionnaire to investigate whether pregnant women wished to receive information on prenatal screening prior to conception. Questions were part of a larger instrument to measure informed decision-making on prenatal screening for Down syndrome [28].

*Data collection*

Twenty community midwifery practices in the Southwest region of the Netherlands agreed to participate in this study. In the period May 2008 to May 2009, midwives provided questionnaires to pregnant women during the initial prenatal visit, after being offered and possibly having received information about prenatal screening for Down syndrome, but prior to possible participation in the screening. Hence, the participants in this study consisted of women who wished and received information on prenatal screening for Down syndrome during their pregnancy, as well as women who did not wish and therefore did not receive the information during their pregnancy.

*Questionnaire*

A translated version of the questions used for this study is represented in an online appendix to this journal article (Appendix 1). Pregnant women were asked the following: (1) whether they had considered participating in prenatal screening for Down syndrome before pregnancy,

(2) whether they possessed any information on prenatal screening prior to conception, (3) whether they wished and received information on prenatal screening during their current pregnancy and (4) whether and why they would (not) have liked to receive such information preconceptionally.

*Analyses*
Data were analyzed for frequency distribution tables and percentages, using SPSS 15.0

*Ethical Approval*
The Ethical Committee of the Erasmus University Medical Centre (Rotterdam, The Netherlands) approved the empirical part of this study (MEC-2007-166).

# Results

## Empirical study

Table I provides background characteristics of the study participants (n=510). The response rate from pregnant women on the questionnaires that were distributed was estimated to be 30-35%. We had to rely on estimates regarding the response rate because of the anonymous nature of the questionnaires.

Table II reports results of the questionnaire. Overall, 55.7% of respondent women considered prenatal screening for Down syndrome before pregnancy. Of all respondents, 28.0% reported

**Table I:** Background characteristics of women participating in the questionnaire study (N=510)

| Variable | Mean (SD) | N | % | % of Dutch population |
|---|---|---|---|---|
| Age (years) | 30.8 (4.2) | | | |
| Low (<36) | | 433 | 87.7 | |
| High (≥36) | | 61 | 12.3 | |
| Educational attainment level | | | | |
| Low | | 223 | 44.1 | 72.2 |
| High | | 283 | 55.9 | 27.8 |
| Ethnic origin | | | | |
| Non-Dutch | | 40 | 7.8 | 26.3 |
| Dutch | | 470 | 92.2 | 73.7 |
| Residence | | | | |
| Suburban | | 230 | 46.3 | |
| Urban | | 267 | 53.7 | |
| Religious affiliation | | | | |
| Religious | | 205 | 40.8 | |
| Not religious | | 297 | 59.2 | |
| Religious activity | | | | |
| Often | | 65 | 13.3 | |
| Seldom/never | | 423 | 86.7 | |

**Table II:** Results of questionnaire measuring interest in receiving information about prenatal screening for Down syndrome, before pregnancy

| Question | Yes (%) | No (%) | Do not know (%) | Total (N) | Missing (N) |
|---|---|---|---|---|---|
| Considered participating in prenatal screening for Down syndrome before pregnancy? | 55.7 | 41.7 | 2.6 | 508 | 2 |
| Possessed any information on prenatal screening before pregnancy? | 28.0 | 68.7 | 3.3 | 508 | 2 |
| Accepted information offer during pregnancy (initial prenatal visit)? | 65.3 | 33.3 | 1.5 | 475 | 35 |
| Received information during pregnancy? | 83.5 | 15.5 | 1.0 | 510 | |
| Looking back, would have liked to receive information before pregnancy? | 9.8 | 84.6 | 5.6 | 500 | 10 |
| ...of the women that considered participating in prenatal screening before pregnancy | 13.8 | 80.0 | 6.2 | 275 | 8 |
| ... of the women that possessed any information before pregnancy | 21.6 | 68.7 | 9.7 | 134 | 8 |
| ... of the women that accepted information offer during pregnancy (initial prenatal visit) | 11.8 | 82.0 | 6.2 | 306 | 4 |
| ...of the women that did not accept the information offer during pregnancy (initial prenatal visit) | 6.5 | 89.6 | 3.9 | 154 | 4 |
| ...of the women that received information during pregnancy | 10.1 | 83.9 | 6.0 | 417 | 9 |
| ...of the women that considered information before pregnancy but did not possess any information before pregnancy | 6.1 | 91.2 | 2.7 | 147 | |
| Wanted information before conception because: | | | | 510 | |
| ...would have been easier to make a decision | 1.4 | 98.6 | | | |
| ...would have made a better decision | 0.4 | 99.6 | | | |
| ...not having to worry during my pregnancy | 1.6 | 98.4 | | | |
| ...more time to discuss my choice with others | 3.1 | 96.9 | | | |
| ...appreciated being timely informed about what to expect | 7.1 | 92.9 | | | |
| Other | 1.2 | 98.8 | | | |
| Did not want information before conception because: | | | | 510 | |
| ...had not given any thought to prenatal screening for Down Syndrome | 45.9 | 54.1 | | | |
| ...did not know that prenatal screening for Down syndrome was possible | 4.9 | 95.1 | | | |
| ...did not want to be informed because I wanted to become pregnant first | 14.7 | 85.3 | | | |
| ...would have been concerned for no reason | 4.7 | 95.3 | | | |
| ...don't think I would have understood it well enough, because I was not concerned about it | 2.9 | 97.1 | | | |
| ...I would have received too much information | 2.0 | 98.0 | | | |
| ...think it's better not to know everything beforehand | 20.6 | 79.4 | | | |
| ...just want to concentrate on my pregnancy without having to think about what could go wrong | 15.9 | 84.1 | | | |
| Other | 11.2 | 88.8 | | | |

possessing any information (not necessarily provided by a health care professional) on prenatal screening for Down syndrome prior to conception. Of all women in this study, 84.6% would not have liked receive information on prenatal screening for Down syndrome before pregnancy. During pregnancy, the information offer was declined by 33.3% of women. Of these women 89.6% did not wish to receive information (in retrospect) before pregnancy.
The most important reason for women to desire information prior to conception was an appreciation of being timely informed of what they could expect. The most common reasons for not wishing information prior to pregnancy were 'not have been giving any thought to prenatal screening for Down syndrome' and the opinion that 'it's better not to know everything beforehand'.

*Strengths and limitations - empirical study*
The results of the empirical study were obtained from an unselected group of women; all women presenting for their initial prenatal visit at 20 midwifery practices in the Southwest region of the Netherlands were asked to fill out the questionnaire. This group consisted of both participants and non-participants in prenatal screening for Down syndrome. This is a major strength of the study.
The retrospective character of the questions on women's preferences could be considered a limitation. However, we also consider this as an important strength; at the moment of filling out the questionnaires, women were deciding to participate, or not, in prenatal screening and therefore this was a good moment to reflect on when (before or during pregnancy) they would most prefer to receive the information.

A limitation of our empirical study is that it only focuses on women's preferences; despite their role as important actors in the decision-making process, partners were not included in our questionnaire study. In future studies, we would highly recommend including perspectives of the partners as well.
Another limitation is that we do not know precisely how the participants understood 'information on prenatal screening for Down syndrome'. They might have understood it as information on the screening program solely (e.g. combined test, invasive diagnostics) or as information on the screening program and on the condition Down syndrome itself. In future studies we recommend to distinguish and explicate these two interpretations.

We cannot exclude the possibility of selection bias occurring in our study; women completing the questionnaires might have been more motivated to do so because they were willing to participate in prenatal screening for Down syndrome or because they were more opinionated due to worse previous experiences.
We pretested the items used in this study in a small sample, and concluded that these were comprehensible. In future studies, psychometric testing of items on validity and reliability needs to be performed and if necessary, items need to be adapted. For now, these items, although not extensively tested on validity and reliability, provide us a relevant first insight in pregnant women's preferences on receiving information about prenatal screening for Down syndrome before conception.

**Ethical analysis**

We investigate whether information on prenatal screening for Down syndrome should be provided prior to conception, in addition to the prenatal information provision, in order to increase the likelihood of informed decision-making about participation in the screening. In

the empirical study we investigated women's preferences and concluded that the majority preferred not to receive information on prenatal screening for Down syndrome preconceptionally. Although women's preferences play an important role in our analysis, we will show that there is more to say with regard to the question whether it is desirable to provide this information before conception. In the ethical analysis, we elaborate on the reasons mentioned by the women for preferring not to receive this information before pregnancy.
In the ethical analysis, we explicitly chose to focus only on the arguments concerning the proposed timing of the information provision. We did not consider the pros and cons of (providing information on) prenatal screening for Down syndrome in general, as previous studies have done [29-41], nor did we elaborate on the ethical aspects related to preconception care.

*The concept of informed decision-making as framework*

There is consensus in ethical guidelines published in Europe and the United States that health professionals providing prenatal screening services should give prospective parents the information and support they need to make autonomous, informed decisions [5-8]. We will use the concept of informed decision-making as a framework for our study.
A process of informed decision-making results in informed decisions, also termed informed choices. To define informed decision-making, many different terms are used, often interchangeably [20,42-46]. However, there is an emerging consensus that an informed decision has two core characteristics. First, it is based on relevant, high quality information, resulting in adequate knowledge. Second, the actual choice should reflect the decision-maker's attitudes [20,47]. Following this definition, an informed choice to participate in screening occurs when relevant knowledge about the test is accompanied with a positive attitude towards participating. An informed choice to decline a test, on the other hand, occurs when relevant knowledge about the test is accompanied with a negative attitude towards participating in the screening [20]. Relevant knowledge includes information on different screening domains, e.g. the purpose of screening, the meaning of a positive or negative test result and the condition being screened for [48].

Sometimes an additional element is included in the definition: 'deliberation', the process of evaluating the alternatives and weighing their pros and cons [44,45,49]. We consider this third element as part of the decision-making process. In the context of screening for Down syndrome it is essential to be aware of alternatives, especially with regard to the final decision. For example, a couple considering any child to be welcome, regardless of its disabilities, might not want to participate in screening. Many couples, however, did not yet reflect on the possibility of having a child with Down syndrome. In our view, deliberation on the aspects and possible subsequent steps of a decision is necessary.
The concept of informed decision-making is embedded in the principle of respect for autonomy [50]. To respect a person as autonomous is "first, to recognize a person's capacities and perspectives, including his or her right to hold views, to make choices, and to take actions based on personal values and beliefs. But respect involves more than taking this attitude. It involves treating agents so as to allow or to enable them to act autonomously" [51]. Respecting one's autonomy most of the time means that a patient should be informed thoroughly. However, debate exists on whether provision of information is a prerequisite for autonomy, or that the principle of respect for autonomy sometimes prescribes to protect people from unwarranted disclosures of information [52]. The latter is conceptualized in the patient's 'right not-to-know' [53]. In this paper we consider the right not-to-know as an essential element of the framework of informed decision-making.

Despite the relevance ascribed to the concept of informed decision-making in the field of prenatal screening, it can be disputed whether informed decision-making is something every individual is willing to reach. Recently, it was argued that, because the perceived importance of parental choice and of the significant other's views with regard to prenatal screening differs among nations, the concept of informed choice is more meaningful to practices in societies that are individualistically oriented than those that are more collectively oriented [54]. Hence, people vary in their preferred degree of involvement in health decisions [55]. Finally, more information does not always lead to better, more informed decisions, and increased autonomy. It can be difficult for individuals to deal systematically with large amounts of information, often resulting in decisions being made from the context rather than from the content of the information [56].

We are aware of these limitations in the concept of informed decision-making. However, as this concept, in its current form, is dominant in most Western countries, and as both prenatal screening and preconception care are, until now Western developments, we accept the concept of informed decision-making as a framework for this study. In the next section, we will consider pros and cons with regard to informing on prenatal screening for Down syndrome *prior to conception,* in addition to the *prenatal* information provision.

*Con: Step by step approach*

In the empirical study, the majority of respondents preferred not to receive information on prenatal screening prior to conception. The reasons mentioned most often were 'not yet being engaged in this topic' and 'not wishing to know everything beforehand'. This means that these women wish to approach their pregnancy in a step-by-step manner: they first wish information on getting pregnant, and once being pregnant they wish to receive the information on prenatal screening (among other things).

If information on prenatal screening was provided prior to conception, irrespective of women's preferences, a large number of women would have received information against their will (in our sample, 84.6% of women reported –retrospectively- not wish to receive this information before pregnancy). In fact, these women would not even have been able to express their reluctance. This means that, by a standard information provision before pregnancy, the right not-to-know would have been disregarded. In addition, focusing on the possibility of becoming pregnant with a child having Down syndrome, the risk appears that this unwanted information spoils the (unconcerned) process of getting pregnant [57].

*Con: A perceived directive*

In addition to individual preferences, informed decision-making is dependent upon the availability and accessibility of choices and alternatives [58,59]. It is important that the decision to participate or not is made *autonomously,* without undue manipulation by others [60]. Repeating the provision of information on prenatal screening (i.e. providing it not only during the initial prenatal visit but also preconceptionally) may conflict with the core principle of genetic counseling; non-directiveness. Caregivers may communicate, unintentionally, a perceived directive; prospective parents may regard the choice for prenatal screening as the right thing to do and may perceive choosing against prenatal screening as imprudent. Some women seem to accept testing during pregnancy, just because these tests are offered [61,62]. As a consequence, although people *are* in fact free to choose one of both options, the prospective parents may not *feel* free to choose against participation in prenatal screening. In terms of the framework of informed decision-making, repeating the provision of information will fulfill the condition of providing adequate knowledge, but if pregnant women feel pressure to participate, choosing against participation is no longer an equivalent alternative. Hence, women may

feel that their choice would no longer be voluntary [51]. Based on these perceptions, repeatedly providing information on prenatal screening increases the possibility of communicating a perceived directive.
Careful, non-directive counseling is essential in providing information about prenatal screening and it can prevent the message from being perceived as directive. However, the non-directive content of the information provided might acquire a directive character due solely to the fact that it is provided more than once. This would hinder the informed decision-making process and therefore argues against the provision of information before pregnancy.
In conclusion, women's lack of interest and the risk of spreading a perceived directive are reasons not to provide information on prenatal screening prior to conception. In the following, we will present three possible benefits of the provision of information on prenatal screening before pregnancy, in addition to during the initial prenatal visit.

*Pro: Preventing a gradual trap*
Based on several international evaluations, a large proportion of pregnant women appear to not make informed decisions about prenatal screening [20,42,63,63-68], and are unaware of the decisive implications of participation in screening [69,70]. Making the decision to participate or not in prenatal screening is difficult; the decisions to be made and the chain of reasoning behind them are complex and can produce emotional burden. Prospective parents should receive information and should decide whether to participate in screening; if an increased risk of Down syndrome is detected, they must choose whether to receive invasive testing; and, if an abnormality is diagnosed, the parents must decide whether to terminate or continue pregnancy. Continuing pregnancy is bifurcated into two options; raising the child or planning to place the child for adoption.
Women may perceive the first step, the provision of information, as innocent. Having accepted the first step, it may seem rational to accept the second step as well. The same is true for the following steps, and, as a result, one can feel trapped. With regard to the last step in the chain of events, this may be most unfortunate: 'I've accepted the information, the participation in screening, the invasive testing, and now the fetus appears to have Down syndrome, I need to terminate pregnancy.' The Dutch Health Council explicitly warns against participation in screening without considering the consequences of this decision, and refers to this process as a 'gradual trap' [71]. With regard to the final step, the American College of Obstetricians and Gynaecologists (ACOG) recognizes the difficulty and recommends: "non-directive counseling before prenatal diagnostic testing does not require a patient to commit to pregnancy termination if the result is abnormal" [6].

The non-directive, step-by-step procedure should make it clear for women that they are not required to choose "b" because of choosing "a", and so further. In the meanwhile they should be aware of the final decision they may ultimately have to make if the fetus is diagnosed with Down syndrome: prepare for the birth and upbringing of this child with special needs, planning to place the child for adoption, or deciding to terminate the pregnancy.
Also in the United States, non-directive counseling is an important prerequisite of prenatal screening. In the American National Society of Genetic Counselors Code of Ethics genetic counselors are recommended to 'enable clients to make informed decisions, free of coercion, by providing or illuminating the necessary facts and clarifying the alternatives and anticipated consequences' [72]. In the United States all women are offered screening and all women may opt for diagnostic testing, regardless of their personal risk estimation retrieved from screening. The ACOG regards this as a decision that is based on personal values, and therefore patients should be provided with their numerical risk rather than a positive versus negative

screening result using an arbitrary cutoff [5,73] as is common practice in the Netherlands. The ACOG recommends that all women should be counseled about the risks and benefits of invasive testing compared with screening tests [5].
Providing information on screening for Down syndrome preconceptionally may be helpful to 'unchain' the choice for prenatal screening. Because prospective parents are not confronted immediately with the subsequent decisions to be confronted, they would have time to understand the complexity of the screening process and to think, discuss, and rethink about their decision when confronted with subsequent steps in the testing process.

*Pro: Time is pressing*
Time is limited in the current procedure for presenting and performing prenatal screening. It is common practice that the prospective parents are informed about the options for prenatal screening for the first time during the initial prenatal visit. In that case, there is on average only one week remaining during which they have to decide on participating in the screening program. The healthcare professional informs the couple about the screening and needs an immediate response concerning their choice, because the test must be performed in a diagnostic center within a short time frame. When prospective parents are undecided, the healthcare professional attempts to keep all possibilities open -as a good antenatal care professional should do – by making an appointment for the test. The prospective parents are told to cancel the appointment in case of deciding not to participate in the screening. This way, an 'opt-in' screening procedure changed to an 'opt-out' screening. In fact, such cases do not conform to the model of informed decision-making. There is not enough time to process the information and the choice is not free: since an appointment has already been made, participating may appear to women 'the thing one just has to do'. Deciding to opt out may result in a woman feeling like a 'bad' patient.

In the United States, the existence of quadruple screening makes it possible to start screening in the second trimester, which provides pregnant women with additional time to make a decision. However, quadruple screening is not an equal alternative for integrated-, sequential- or contingent-screening that all three start in the first trimester. First, performance of quadruple screening, in terms of the detection of Down syndrome, is considered less optimal when compared to screening that combines first-and second trimester testing [5,74].Therefore, to guarantee optimal and timely screening test results, women should decide in the first trimester about prenatal testing and therefore the time frame continues to be 'short'.
Another disadvantage of suspending screening for Down syndrome until the second trimester of pregnancy, is that results are available as late as the second trimester, which could create undue anxiety. In addition, choosing to terminate the pregnancy may be even more intrusive in the second trimester. The fact that waiting for a quad screen is still common in the United States may well reflect the opinion of those who do not favor early diagnosis and termination.

*Pro: Equal access*
One of the benefits of initiating antenatal care during early pregnancy is the possibility of a timely provision of information on prenatal screening for Down syndrome. However, Alderliesten et al. found a disturbing delay in the timing of the initial prenatal visit among women from several ethnic groups in the Netherlands: more than 10% of these women had their initial visit at 18 weeks of gestation or later [75]. This excludes them from the possibility of participating in prenatal screening for Down syndrome. In the United States in 2007, 18% of all mothers did not have prenatal care in the first-trimester. These percentages are even higher

for most ethnic minorities, on the upper side of the scale 31.7% for American Indian or Alaska Native [76]. These women are excluded from first-trimester screening as well.
Participation rates for prenatal screening are lower in minority ethnic groups and in socially underserved groups, as compared with white and socioeconomically advantaged women with a higher socio-economic status [63]. In another study, lower participation rates did not reflect more negative attitudes toward screening, but rather low rates of informed choice [64]. In addition, women of Turkish and South Asian or Afro-Caribbean origin more often reported difficulties in understanding the information, and had less knowledge about Down syndrome, prenatal screening, and amniocentesis [77].

What exactly causes the delay in the initial prenatal visit and the low rate of participation in prenatal screening is unknown. One possibility could be that women's knowledge is inadequate; this could be improved by providing information about prenatal screening not only during the initial prenatal visit, but also before pregnancy. In addition, women's awareness of the importance of a timely initial prenatal visit and hence equal access to the opportunity of prenatal screening for Down syndrome could be improved. We realize that it might be 'wishful thinking' to assume that women arriving too late for prenatal care, will be in time for preconception care. We acknowledge that reaching these women is a challenge, but we want to emphasize that there is no reason not to accept this challenge. Past experiences and practices to adequately reach these groups [78-81] should be implemented and research should continue.
Preventing a 'gradual trap of choices', providing sufficient time to make an informed decision and increasing the probability for equal access to prenatal screening are three arguments in favor of the provision of information about prenatal screening for Down syndrome before pregnancy.

## Discussion

We empirically investigated women's preferences and identified arguments against and in favor of providing information about prenatal screening for Down syndrome preconceptionally. In our view, providing this information additionally before pregnancy has serious drawbacks including acting against many women's wishes and an increased possibility of communicating a directive message. Improving the informed decision-making process by unchaining the initial information offer and by providing sufficient time together with increased probability for equal access, however, constitute important benefits.
In our opinion, these drawbacks and benefits of preconceptional information provision on prenatal screening are valid and should be considered seriously. Regarding the drawbacks, we consider providing information on prenatal screening before conception not to be a desirable option. However, we showed that informing women on prenatal screening before conception does also bring forward important benefits. We believe that these benefits should not be ignored, but instead be acted upon. To bypass the drawbacks and maintain the benefits as considered in this paper, we suggest a different approach based on the Dutch information procedure about prenatal screening for Down syndrome: *offering* information instead of *providing*.

### Offering information on prenatal screening before conception

Our proposal is to copy the first step of the Dutch information process on prenatal screening (The information offer; see Figure 2) to the period before pregnancy. This means that, before

pregnancy, the information on prenatal screening for Down syndrome should be *offered* instead of *provided.* By offering information, instead of providing information, the prospective parents are free to accept or decline the offer. In this procedure, women are given the opportunity to express their right not-to-know. Meanwhile, their right to know is respected. Regardless of women's (non-) acceptance of the offer, the information offer should be repeated during the initial prenatal visit.

**An information offer; will it work?**

In our view, offering information instead of directly providing it, partly bypasses the drawbacks considered in this paper. The finding of our empirical analysis, that most women prefer not to receive information on prenatal screening before pregnancy, is an important argument against the provision of information before pregnancy. However, in that analysis, we asked women whether they would have preferred the *provision* of information before pregnancy. We did not ask whether they would have preferred to receive an *offer* to hear the information. The essential difference between these two questions is that if information is offered, women could choose to decline the offer when they did not wish to receive information.
Unfortunately, we cannot deduce these differences from the questionnaire. We can, however, compare our proposal to the current procedure of offering information about prenatal screening in the Netherlands. In the research population of our empirical study, all women were offered information and a substantial group (33.3%) declined the offer. Of these women, 89.6% reported not wishing information on screening before pregnancy. Based on the fact that one-third of the women were able to refuse the information offer on prenatal screening during pregnancy, we assume that women will understand the difference between offering and providing information and we believe that they will be also be able to refuse the offer before pregnancy.

Given new non-invasive prenatal diagnostic tests that become available, biotechnology companies may advertise for laboratory-developed prenatal tests for example on the Internet, in commercials on television, or in magazines. If pregnant women are casually picking up a magazine, or turning on their television, and are confronted with prenatal testing about Down syndrome, this may violate their right not-to-know: they may receive information unwillingly, information that they might have rejected if their physician offered the option of receiving it. On the other hand, keeping women ignorant by poor information provision by gynecologists and by not providing information in public domains may violate women's 'right to know'. In either case, it is important that information is provided in a non-directive way, and that women are by no means pressured to undergo screening. In case of providing information by companies, it is the question while being commercially driven, the information presented is balanced enough to make an informed choice [82]. It may be hard to regulate all information provision 'in the open' and to check on reliability and non-directiveness. A thorough discussion of pros and cons on this issue is needed, however, such a discussion falls beyond the scope of this manuscript.
With regard to the increased likelihood of communicating a perceived directive, we acknowledge that this likelihood is still increased in our proposal, because of the repeated offer for testing. However, women need not to receive the information twice. With our proposal, we give women the opportunity to decide whether they wish to receive information on prenatal screening before conception, *in addition to* the current prenatal information offer (in the Netherlands) or provision (internationally). Since women are allowed to decline the offer, this limits the risk of communicating a perceived directive. It is important to emphasize that

the information on prenatal screening should be offered explicitly as an *option* and should not be perceived as an unwanted offer of excessive or unnecessary information. Therefore, health care professionals offering information on prenatal screening should be trained in non-directiveness, and in communication skills required for counseling on this topic, including an awareness of women's diverging values [83].

The benefits discussed in this paper for providing information on prenatal screening prior to pregnancy are still valid when the information is offered instead of provided. Offering the information before pregnancy may unchain the first decisional step from the numerous decisions that may follow, thereby preventing a gradual trap of choices. Furthermore, the offer of information before pregnancy provides prospective parents who accept the offer a sufficient time window to accept or decline participation in prenatal screening. Additionally, equal access to antenatal care may be improved, at least among women accepting the preconceptional information offer, because many women currently present for their initial prenatal visit too late for the opportunity to participate in prenatal screening for Down syndrome.

**Implications for practice**

In this study, we propose to give women the opportunity to decide whether to receive information on prenatal screening for Down syndrome to prospective parents before pregnancy, in addition to the current prenatal information offer (in the Netherlands) or provision (internationally). This proposal is based on an empirical study and ethical analysis. We believe that giving women the opportunity to decide whether to receive information on prenatal screening for Down syndrome prior to conception (by introducing the information *offer* at that time) would increase the likelihood of making an informed decision, with minimal disadvantages.
The *offer* of information concerning prenatal screening could be incorporated in a preconception care consultation, which is part of general preconception care that is increasingly regarded as an approach to improve reproductive health [81]. In the Netherlands, the Health Council advised to provide preconception care in a single-package consultation. In the United States the general view is that preconception care should be placed in a continuum of women's health-care strategies, with the aim to 'catch' women with reproductive potential at any time they meet with a health-care provider. To enhance awareness and health promotion, it might be possible to extend the target population and provide information to high school students [81].

Awareness among health care providers should be increased as well. In the United States the Centers for Disease Control and Prevention (CDC), the March of Dimes, the American College of Obstetricians and Gynecologists and an Expert Panel convened by the CDC published recommendations on preconception care. These recommendations are designed to promote optimal health throughout the lifespan for women, children, and families by using both clinical care and population-focused public health strategies. They are a starting point to make comprehensive preconception care a standard of care in the United States and to provide a more universal, comprehensive, evidence-based model of preconception care. The recommendations will promote the development and practice of preconception care that will be flexible to meet persons' changing reproductive care needs and address risks throughout their lifespan [84-87].
An offer of information that is not in accordance with the goals of preconception care could result in reduced public support. The goals of preconception care are to optimize the health of the future child and mother through primary intervention and to increase reproductive

autonomy by providing information on reproductive options [11,88]. The offer of prenatal screening information during this counseling could be regarded as a reproductive option, thereby serving the second goal. In our view, the information offer would therefore fit appropriately in a preconception care consultation.

Also, the expert panel convened by the CDC recommended that everyone should be encouraged to have a reproductive life plan and that educational and health promotion counseling should be provided to all women of childbearing age, including information regarding the importance of early prenatal care [84-87]. Although not mentioned explicitly by the committee, these recommendations seem to be not inconsistent with our viewpoint that the information on prenatal screening for Down syndrome should be incorporated in preconception care.
By extending the content of preconception care consultations, there is a risk of "information overload". This may lead to wrongly prioritizing the information on prenatal screening for Down syndrome in lieu of on the other important preconception information. Therefore, appropriate prioritizing by the counselors is required. We recommend elaboration on this and other practical aspects of incorporating the information offer in preconception care consultations, prior to its implementation in clinical practice.

**Recommendations for practice and further research**

Preconception care consultations should be carefully monitored and process evaluations should be performed regularly. Monitors and evaluations should contain at least the various aspects that were pointed at in this paper: women's preferences with regard to the *offer* of information on prenatal screening, the fear of communicating a perceived directive by repeatedly offering/providing information, adequate prioritization, and the risk of information overload. Furthermore, monitoring and evaluation should be performed to determine if the provision of this information prior to pregnancy would indeed increase the likelihood of informed decision-making by lengthening time for contemplation and by unchaining the offer from the other decisional steps with regard to prenatal screening. Finally, it should be monitored and evaluated whether this offer would improve equal access to opportunities to participate in prenatal screening for Down syndrome.
Practices of preconception care are developing rapidly and new methodologies for prenatal screening will be introduced allowing testing very early in pregnancy. These developments require a rapid implementation of information about prenatal screening for Down syndrome in preconception care consultations.

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# Appendix 1: Self-completion questionnaire*

1. Before you became pregnant, did you consider participating in prenatal screening for Down syndrome for this particular pregnancy?
   - ☐ Yes
   - ☐ No
   - ☐ I don't remember

2. Were you given any information about prenatal screening for Down syndrome before you became pregnant?
   - ☐ Yes
   - ☐ No
   - ☐ I don't remember

3. How did you respond when your midwife or obstetrician asked you, during this particular pregnancy, if you wanted to be informed about prenatal screening for Down syndrome? (1 answer only)
   - ☐ Yes, I wanted information about prenatal screening for Down Syndrome
   - ☐ No, I did not want any information about prenatal screening for Down Syndrome
   - ☐ I don't remember

4. Did you receive information about prenatal screening for Down syndrome from your midwife or obstetrician, during this particular pregnancy? (1 answer only)
   - ☐ Yes, I received information about prenatal screening from my midwife / obstetrician
   - ☐ No, I did not receive information about prenatal screening from my midwife / obstetrician
   - ☐ I don't remember

5. Looking back in retrospect, do you wish you had received information about prenatal screening for Down syndrome before you became pregnant?
   - ☐ Yes
   - ☐ No (continue to question 7)
   - ☐ I don't remember (>end questionnaire)

6. You indicated that you wish you had received information about prenatal screening for Down syndrome before you became pregnant. What are the most important reasons for this? (multiple answers allowed)
   - ☐ I think it would have made it easier for me to make a decision
   - ☐ I think I would have made a better decision
   - ☐ I would not have had to worry about this during my pregnancy
   - ☐ I would have had more time to discuss my choice with other people
   - ☐ I appreciate being timely informed about what to expect
   - ☐ Other

(End questionnaire)

7. You indicated that you did not want to receive information about prenatal screening for Down syndrome before you became pregnant. What are the most important reasons for this? (multiple answers allowed)
   - ☐ I had not given any thought to prenatal screening for Down Syndrome before I became pregnant
   - ☐ I did not know that prenatal screening for Down Syndrome was possible
   - ☐ I did not want to receive information about prenatal screening for Down's Syndrome because I wanted to become pregnant first
   - ☐ I would have been concerned for no reason
   - ☐ I don't think I would have understood it well enough, because I was not concerned about it.
   - ☐ I would have received too much information
   - ☐ I think it's better not to know everything beforehand
   - ☐ I just want to concentrate on my pregnancy without having to think about what could go wrong
   - ☐ Other

* As this study has been performed in the Netherlands, the original self-completion questionnaire was formulated in Dutch. The authors indicate that the version translated to American English, as represented in this Appendix, is not suitable for use as a questionnaire for the United States population. This is mainly due to the fact that this translated version has not been tested on feasability and psychometric properties in an American-English population.

# References


[1] Centers for Disease Control and Prevention (CDC). National Center on Birth Defects and Developmental Disabilities. Preconception Health and Care, 2006

[2] Health Council of the Netherlands. Preconception care: a good beginning 2007; 2007/19E.

[3] Boyd PA, Devigan C, Khoshnood B, Loane M, Garne E, Dolk H, EUROCAT Working Group. Survey of prenatal screening policies in Europe for structural malformations and chromosome anomalies, and their impact on detection and termination rates for neural tube defects and Down's syndrome. BJOG 2008;115:689-696.

[4] EUROCAT. Special Report: Prenatal Screening Policies in Europe, 2010.

[5] American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 77, January 2007: screening for fetal chromosomal abnormalities. Obstet.Gynecol. 2007;109:217-227.

[6] American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 88, December 2007. Invasive prenatal testing for aneuploidy. Obstet.Gynecol. 2007;110:1459-1467.

[7] Palomaki GE, Bradley LA, McDowell GA, Down Syndrome Working Group, ACMG Laboratory Quality Assurance Committee. Technical standards and guidelines: prenatal screening for Down syndrome. Genet.Med. 2005;7:344-354.

[8] Consensus Group Statement (National Down Syndrome Society-NDSS, National Down Syndrome Congress-NDSC, American College of Obstetricians and Gynecologists-ACOG, American College of Medical Genetics-ACMG, National Society of Genetic Counselors-NSGC). Toward concurrence: Understanding Prenatal Screening and Diagnosis of Down Syndrome from the Health Professional and Advocacy Community Perspective, 2009.

[9] Driscoll DA, Morgan MA, Schulkin J. Screening for Down syndrome: changing practice of obstetricians. Am.J.Obstet.Gynecol. 2009;200:459.e1-459.e9.

[10] Gekas J, Gagne G, Bujold E, Douillard D, Forest JC, Reinharz D, Rousseau F. Comparison of different strategies in prenatal screening for Down's syndrome: cost effectiveness analysis of computer simulation. BMJ 2009;338:b138.

[11] Health Council of the Netherlands. Population Screening Act. Prenatal screening on Down's syndrome and neural tube defects. Health Council of the Netherlands 2007;2007/05.

[12] Health Council of the Netherlands. Prenatal Screening (2); Down's syndrome, neural tube defects. Health Council of the Netherlands 2004;2004/06.

[13] Weaver KD. Genetic screening and the Right not to Know. Issues Law Med 1997;13:243-279.

[14] World Health Organization. Statement of WHO expert advisory group on ethical issues in medical genetics,1998.

[15] General Medical Council. Seeking patients' consent: the ethical considerations, 1999.

[16] Joint Working Party of the Royal College of Obstetricians and Gynaecologists and the Royal College of Paediatrics and Child Health. Fetal abnormalities- guidelines for screening, diagnosis and management: report of a joint working party of the Royal College of Obstetricians and Gynaecologists and the Royal College of Paediatrics and Child Health. RCOG Press 1997.

[17] Royal College of Obstetricians and Gynaecologists. Amniocentesis and chorionic villus sampling 2005.

[18] National Screening Committee. Second report of the UK National Screening Committee 2000.

[19] The Royal Australian and New Zealand College of Obstetricians and Gynaecologists. College Statement: Prenatal screening tests for trisomy 21 (Down syndrome), trisomy 18 (Edwards syndrome) and neural tube defects 2010;C-Obs 4.

[20] Marteau TM, Dormandy E, Michie S. A measure of informed choice. Health Expect 2001;4:99-108.

[21] Nicolaides KH. Screening for chromosomal defects. Ultrasound Obstet Gynecol 2003;21:313-321.

[22] Kuc S, Koster MP, Visser GH, Schielen PC. Performance of first-trimester serum screening for trisomy 21 before and from 11 + 0 weeks of gestational age in The Netherlands. Prenat.Diagn. 2010;30:906-908.

[23] Wright CF, Burton H. The use of cell-free fetal nucleic acids in maternal blood for non-invasive prenatal diagnosis. Hum.Reprod.Update 2009;15:139-151.

[24] de Jong A, Dondorp WJ, de Die-Smulders CE, Frints SG, de Wert GM. Non-invasive prenatal testing: ethical issues explored. Eur.J.Hum.Genet. 2010;18:272-277.
[25] Barry MJ. Health decision aids to facilitate shared decision making in office practice. Ann.Intern. Med. 2002;136:127-135.
[26] Holmes-Rovner M, Wills CE. Improving informed consent: insights from behavioral decision research. Med.Care 2002;40:V30-8.
[27] Skirton H, Barr O. Antenatal screening and informed choice: a cross-sectional survey of parents and professionals. Midwifery 2009.
[28] Schoonen HM, Wildschut HIJ, Essink-Bot ML, Peters IA, Steegers E, de Koning HJ. Evaluating the provision of information and informed decision-making on prenatal screening for Down's syndrome: a questionnaire and register-based survey in a non-selected population. Submitted, 2011.
[29] Parens E, Asch A. Disability rights critique of prenatal genetic testing: reflections and recommendations. Ment.Retard.Dev.Disabil.Res.Rev. 2003;9:40-47.
[30] Chervenak FA, McCullough LB. Ethical considerations in first-trimester Down syndrome risk assessment. Curr.Opin.Obstet.Gynecol. 2010;22:135-138.
[31] Chervenak FA, McCullough LB, Chasen ST. Clinical implications of the ethics of informed consent for first-trimester risk assessment for trisomy 21. Semin.Perinatol. 2005;29:277-279.
[32] Lindeman R. Take Down syndrome out of the abortion debate. CMAJ 2008;179:1088.
[33] Reynolds TM. Down's syndrome screening is unethical: views of today's research ethics committees. J.Clin.Pathol. 2003;56:268-270.
[34] Reynolds TM. Down's syndrome screening: a controversial test, with more controversy to come!. J.Clin.Pathol. 2000;53:893-898.
[35] Garcia E, Timmermans DR, van Leeuwen E. Reconsidering prenatal screening: an empirical-ethical approach to understand moral dilemmas as a question of personal preferences. J.Med.Ethics 2009;35:410-414.
[36] Garcia E, Timmermans DR, van Leeuwen E. The impact of ethical beliefs on decisions about prenatal screening tests: searching for justification. Soc Sci Med 2008;66:753-64.
[37] Buckley F, Buckley S. Wrongful deaths and rightful lives - screening for Down syndrome. Downs Syndr.Res.Pract. 2008;12:79-86.
[38] Zindler L. Ethical decision making in first trimester pregnancy screening. J Perinat Neonatal Nurs 2005;19:122-31; quiz 132-3.
[39] Savulescu J, Kahane G. The moral obligation to create children with the best chance of the best life. Bioethics 2009;23:274-290.
[40] Alderson P. Prenatal screening, ethics and Down's syndrome: a literature review. Nurs.Ethics 2001;8:360-374.
[41] Bombard Y, Miller FA, Hayeems RZ, Avard D, Knoppers BM. Reconsidering reproductive benefit through newborn screening: a systematic review of guidelines on preconception, prenatal and newborn screening. Eur.J.Hum.Genet. 2010.
[42] Green JM, Hewison J, Bekker HL, Bryant LD, Cuckle HS. Psychosocial aspects of genetic screening of pregnant women and newborns: a systematic review. Health Technol Assess 2004;8:iii, ix-x, 1-109.
[43] Kohut RJ, Dewey D, Love EJ. Women's knowledge of prenatal ultrasound and informed choice. J Genet Couns 2002;11:265-76.
[44] Rimer BK, Briss PA, Zeller PK, Chan EC, Woolf SH. Informed decision making: what is its role in cancer screening?. Cancer 2004;101:1214-1228.
[45] Bekker HL, Hewison J, Thornton JG. Applying decision analysis to facilitate informed decision making about prenatal diagnosis for Down syndrome: a randomised controlled trial. Prenat Diagn 2004;24:265-75.
[46] Summers AM. Informed choice in prenatal screening. Can.Fam.Physician 1994;40:1688-91, 1694-7.
[47] O'Connor A, O'Brien Pallas LL,. Decisional conflict. In: McFarlane GK, McFarlane EA eds.,. Nursing diagnosis and intervention. Toronto: Mosby, 1989;486-96.
[48] Schoonen HMHJD, van Agt HME, Essink-Bot ML, Wildschut HI, Steegers EAP, de Koning HJ. Informed decision-making in prenatal screening for Down's syndrome: What knowledge is relevant. Patient Educ Couns 2011:265-270.

[49] van den Berg M, Timmermans, D.R.M., ten Kate, L.P., van Vugt, J.M.G., van der Wal, G. Informed decision making concerning prenatal screening. Patient Education and Counseling 2006:110-117.
[50] Seavilleklein V. Challenging the rhetoric of choice in prenatal screening. Bioethics 2009;23:68-77.
[51] Beauchamp, T., Childress, J.,. Principles of Biomedical Ethics. Oxford: Oxford University Press, 1989.
[52] Laurie G,. Genetic privacy: a challenge to medico-legal norms. Cambridge: Cambridge University Press, 2001.
[53] Andorno R. The right not to know: an autonomy based approach. J.Med.Ethics 2004;30:435-9; discussion 439-40.
[54] van den Heuvel A, Chitty L, Dormandy E, Newson A, Attwood S, Ma R, Masturzo B, Pajkrt E, Marteau TM. Is informed choice in prenatal testing universally valued? A population-based survey in Europe and Asia. BJOG 2009;116:880-885.
[55] Ende J, Kazis L, Ash A, Moskowitz MA. Measuring patients' desire for autonomy: decision making and information-seeking preferences among medical patients. J.Gen.Intern.Med. 1989;4:23-30.
[56] Bekker H, Thornton JG, Airey CM, Connelly JB, Hewison J, Robinson MB, Lilleyman J, MacIntosh M, Maule AJ, Michie S, Pearman AD. Informed decision making: an annotated bibliography and systematic review. Health Technol Assess 1999;3:1-156.
[57] Katz Rothman B. The tentative pregnancy. New York: Viking, 1986.
[58] Guadagnoli E, Ward P. Patient participation in decision-making. Soc.Sci.Med. 1998;47:329-339.
[59] Goldberg H. Informed Decision Making in Maternity Care. J.Perinat.Educ. 2009;18:32-40.
[60] Stiggelbout AM, Molewijk AC, Otten W, Timmermans DR, van Bockel JH, Kievit J. Ideals of patient autonomy in clinical decision making: a study on the development of a scale to assess patients' and physicians' views. J.Med.Ethics 2004;30:268-274.
[61] Hartley NE, Scotcher D, Harris H, Williamson P, Wallace A, Craufurd D, Harris R. The uptake and acceptability to patients of cystic fibrosis carrier testing offered in pregnancy by the GP. J.Med. Genet. 1997;34:459-464.
[62] Williams C, Sandall J, Lewando-Hundt G, Heyman B, Spencer K, Grellier R. Women as moral pioneers? Experiences of first trimester antenatal screening. Soc.Sci.Med. 2005;61:1983-1992.
[63] Dormandy E, Michie S, Hooper R, Marteau TM. Low uptake of antenatal Down syndrome screening in ethnic and socially deprived groups: a reflection of women's attitudes or a failure to facilitate informed choices? Int J Epidemiol 2005:346-352.
[64] Fransen MP, Essink-Bot ML, Vogel I, Mackenbach JP, Steegers EA, Wildschut HI. Ethnic differences in informed decision-making about prenatal screening for Down's syndrome. J.Epidemiol.Community Health 2010;64:262-268.
[65] Michie S, Dormandy E, Marteau TM. The multi-dimensional measure of informed choice: a validation study. Patient Educ Couns 2002;48:87-91.
[66] Gourounti K, Sandall J. Do pregnant women in Greece make informed choices about antenatal screening for Down's syndrome? A questionnaire survey. Midwifery 2008;24:153-62.
[67] Gekas J, Gondry J, Mazur S, Cesbron P, Thepot F. Informed consent to serum screening for Down syndrome: are women given adequate information?. Prenat Diagn 1999;19:1-7.
[68] Al-Jader LN, Parry-Langdon N, Smith RJ. Survey of attitudes of pregnant women towards Down syndrome screening. Prenat.Diagn. 2000;20:23-29.
[69] Seror V, Costet N, Ayme S. Prenatal screening for trisomy 21 with maternal serum markers: information for decision-making in pregnant women. J.Gynecol.Obstet.Biol.Reprod.(Paris) 2000;29:492-500.
[70] Roelofsen EE, Kamerbeek LI, Tymstra TJ, Beekhuis JR, Mantingh A. Women's opinions on the offer and use of maternal serum screening. Prenat.Diagn. 1993;13:741-747.
[71] Health Council of the Netherlands. Prenatal screening: Down's syndrome, neural tube defects, routine-ultrasonography 2001;11.
[72] National Society of Genetic Counselors. The NSGC Code of Ethics. Journal of Genetic Counseling 1992;1:41-44.
[73] Tapon D. Prenatal testing for Down syndrome: comparison of screening practices in the UK and USA. J.Genet.Couns. 2010;19:112-130.

[74] Gekas J, Gagne G, Bujold E, Douillard D, Forest JC, Reinharz D, Rousseau F. Comparison of different strategies in prenatal screening for Down's syndrome: cost effectiveness analysis of computer simulation. BMJ 2009;338:b138.
[75] Alderliesten ME, Vrijkotte TG, van der Wal MF, Bonsel GJ. Late start of antenatal care among ethnic minorities in a large cohort of pregnant women. BJOG 2007;114:1232-1239.
[76] National Center for Health Statistics. Health, United States, 2010 2011;Library of Congress Catalog Number 76-641496.
[77] Fransen MP, Hajo W, Vogel I, Mackenbach J, Steegers E, Essink-Bot ML. Information about prenatal screening for Down syndrome: ethnic differences in knowledge. Patient Educ.Couns. 2009;77:279-288.
[78] Hesselink AE, Verhoeff AP, Stronks K. Ethnic health care advisors: a good strategy to improve the access to health care and social welfare services for ethnic minorities?. J.Community Health 2009;34:419-429.
[79] Flanagan SM, Hancock B. 'Reaching the hard to reach'--lessons learned from the VCS (voluntary and community Sector). A qualitative study. BMC Health Serv.Res. 2010;10:92.
[80] Livingood WC, Brady C, Pierce K, Atrash H, Hou T, Bryant T,3rd. Impact of pre-conception health care: evaluation of a social determinants focused intervention. Matern.Child Health J. 2010;14:382-391.
[81] van der Zee B, de Beaufort I, Temel S, de Wert G, Denktas S, Steegers E. Preconception care: An essential preventive strategy to improve children's and women's health. J.Public Health Policy 2011;32:367-379.
[82] Borry P, Henneman L, Lakeman P, ten Kate LP, Cornel MC, Howard HC. Preconceptional genetic carrier testing and the commercial offer directly-to-consumers. Hum.Reprod. 2011;26:972-977.
[83] Williams C, Alderson P, Farsides B. Dilemmas encountered by health practitioners offering nuchal translucency screening: a qualitative case study. Prenat.Diagn. 2002;22:216-220.
[84] Johnson K, Posner SF, Biermann J, Cordero JF, Atrash HK, Parker CS, Boulet S, Curtis MG, CDC/ATSDR Preconception Care Work Group, Select Panel on Preconception Care. Recommendations to improve preconception health and health care--United States. A report of the CDC/ATSDR Preconception Care Work Group and the Select Panel on Preconception Care. MMWR Recomm Rep. 2006;55:1-23.
[85] Freda MC, Moos MK, Curtis M. The history of preconception care: evolving guidelines and standards. Matern.Child Health J. 2006;10:S43-52.
[86] American College of Obstetricians and Gynecologists. ACOG Committee Opinion number 313, September 2005. The importance of preconception care in the continuum of women's health care. Obstet.Gynecol. 2005;106:665-666.
[87] Broussard DL, Sappenfield WB, Fussman C, Kroelinger CD, Grigorescu V. Core state preconception health indicators: a voluntary, multi-state selection process. Matern.Child Health J. 2011;15:158-168.
[88] de Weerd S, Steegers EA. The past and present practices and continuing controversies of preconception care. Community Genet. 2002;5:50-60.

# Chapter 8 General discussion

This chapter begins by addressing each of the research questions. This is followed by a general discussion focusing on methodological considerations, interpretation of the findings, main conclusions, and recommendations for further research. The chapter ends with recommendations for policy and practice.

# 1. Answers to research questions

This section is organised around the four research topics and associated research questions, as described in the introduction of this thesis *(Chapter 1)*.

## Knowledge

*What is the content of relevant knowledge needed to make an informed decision about (non-) participation in first-trimester prenatal screening for Down syndrome with the combined test / in second-trimester ultrasound screening for fetal anomalies?*
Based on expert opinions and literature we defined the domains and items considered representative for decision-relevant knowledge required for informed decision-making on screening participation (Table 1). The resulting questionnaires *(Chapter 2, Figure 1; Chapter 3, Figure 2)* are now ready for large-scale implementation.

*What are differences between the content of decision-relevant knowledge for informed decision-making about second-trimester ultrasound screening (b) and decision-relevant knowledge for informed decision-making about first-trimester prenatal screening for Down syndrome with the combined test (a)?*
In the expert consultation, all domains were scored as very important for both screening programs. For both screenings, the domains ranked as most important were 'The meaning of an abnormal test result' (termed 'The meaning of an increased probability for DS test result' in the Down syndrome screening), 'Disorders being screened for and purpose of the screening' ('Purpose of the screening' in the Down syndrome screening), and the voluntary nature of the test. The domains ranked as least important in both screening programs were 'Test procedure', 'Prevalence in the population' (the theoretical risk that the disorder that is tested is present), and 'Expected percentage of detection'. The domain 'what to do in the event of a positive test result' received a higher expert ranking in first-trimester screening than in second-trimester screening. The meaning of a positive test result was considered as less important knowledge (to make an informed decision) in second-trimester ultrasound screening for fetal anomalies than the meaning of a positive test result in first-trimester screening for Down syndrome *(Chapter 3, Figure 3)*. There was a positive correlation between the importance ranking orders of the domains for the two screening programs ($r = 0.71$, $n = 11$, $p = 0.015$) *(Chapter 3, Figure 4)*.

## Quality assurance of the information process

### *First-trimester prenatal screening for Down syndrome with the combined test*

*Are all pregnant women offered information about prenatal screening for Down syndrome? How many women accept the information offer and, of these women, how many do actually receive the information?*

**Table 1:** Knowledge domains, and items representing these domains, in knowledge measure on first-trimester prenatal screening with the combined test and second-trimester prenatal screening for congenital anomalies

| Knowledge domain | Item in knowledge measure first-trimester screening | Item in knowledge measure second-trimester screening |
|---|---|---|
| 1. Purpose of the screening | (1) The probability that your child has Down syndrome can be determined through prenatal screening in the early stages of pregnancy (true) | (1) The fetal anomaly scan is aimed at examining the unborn child for certain physical abnormalities (true) |
| 2. Disorder (s) being screened for | (3) All children with Down syndrome are mentally handicapped (true)<br>(4) Heart defects in children with Down syndrome can generally be treated effectively (true) | *No item* |
| 3. Prevalence in the population (theoretical risk that the disorder is present) | (2) The probability that an unborn child has Down syndrome is generally very slight (less than 1%) (true) | (4) The chance that a child has a congenital abnormality is generally relatively small (less than 5%) (true) |
| 4. Test procedure | (5) The combined test consists of a measurement of the thickness of the nuchal fold of the unborn child (a nuchal ultrasound) and a blood test on the mother (true) | (5) Repeatedly performing a scan is dangerous for the unborn child (not true) |
| 5. The meaning of an 'abnormal' / increased probability test result (incl. possibility of false positives) | (6) Should the result of the combined test be unfavorable, this means that the child has Down syndrome (not true) | (6) If the result of the fetal anomaly scan is 'abnormal', further examination is usually required to obtain more certainty (true) |
| 6. The meaning of a 'normal' / decreased probability test result (incl. possibility of false negatives) | (7) Should the result of the combined test be favorable, the child may still prove to have Down syndrome when born (true) | (7) If the result of the fetal anomaly scan is 'no abnormality', there is still the possibility of the child having an abnormality when it is born (true) |
| 7. The expected percentage of detection | *No item* | (3) Spina bifida is usually clearly recognized using the fetal anomaly scan (true) |
| 8. What to do in the event of an 'abnormal' / increased probability test result | (8) Amniocentesis or chorionic villus sampling may induce a miscarriage (true) | No item |
| 9. Possible findings resulting from a further examination | (9) Both amniocentesis and chorionic villus sampling provide certainty about the presence of Down syndrome in an unborn child (true) | (8) Further examination after an abnormal result on the fetal anomaly scan may reveal that the child does not have any major physical abnormalities (true) |
| 10. What to do after a further examination | (10) Should Down syndrome be diagnosed during the first four months of pregnancy, it is possible for a pregnant woman to terminate the pregnancy (true) | (9) Should a major physical abnormality be found in the fetal anomaly scan, termination of the pregnancy would be a possibility (true) |
| 11. Possible side effects of the test procedure | (11) The result of prenatal screening for Down syndrome may lead to difficult choices (true) | (2) The result of prenatal screening with the fetal anomaly scan may lead to difficult choices, for example termination of the pregnancy (true) |
| 12. Voluntary nature of the test | (12) Prenatal screening for Down syndrome is compulsory for every pregnant woman in the Netherlands (not true) | (10) Every pregnant woman in the Netherlands is obliged to have a fetal anomaly scan (not true) |

As we showed in *Chapter 4,* midwives reported offering information to almost all pregnant women. Of these women, 62.6% wished to receive information, 81.9% of the women who wished to receive information, actually received the information.

*Is pregnant women's knowledge adequate? What is a pregnant woman her attitude towards undergoing prenatal screening for Down syndrome herself? To what extent is decision-making regarding (non-) participation in prenatal screening for Down syndrome based on an informed decision? What are the determinants of informed decision-making?*
Decision-relevant knowledge about prenatal screening for Down syndrome was adequate in 89.0% of responding women. Knowledge about the condition Down syndrome was less adequate than knowledge about the screening program. Almost half of responding women had a negative attitude towards their own participation in prenatal screening for Down syndrome. A minority of women (35.8%) intended to participate in the screening program. A total of 75.5% of women made an informed decision; 94.3% of women participating in the screening program, and 64.9% of women not participating. Religious activity was associated with lower levels of knowledge, a more negative attitude towards one's own participation, and a lower intention to participate. In multivariate analysis, educational level was the only significant determinant of informed decision-making. Adequate knowledge on prenatal screening for Down syndrome, and a positive attitude towards one's own participation, were associated with a positive intention to participate *(Chapter 4).*

***Second-trimester ultrasound screening for fetal anomalies***
*Are all pregnant women offered information about second-trimester ultrasound screening? How many women accept the information offer and, of these women, how many do actually receive the information?*
As we showed in *Chapter 5,* almost all pregnant women were asked whether they wanted information. Of these women, 92.3% wished to receive information. Of the women that wished to receive information, 94.3% actually received the information.

*Is pregnant women's knowledge adequate? What is a pregnant woman her attitude towards undergoing second-trimester ultrasound screening herself? To what extent is decision-making regarding (non-) participation in second-trimester ultrasound screening based on an informed decision? What are the determinants of informed decision-making?*
Decision-relevant knowledge about second-trimester ultrasound screening, was adequate in 93.5% of responding women. Pregnant women had relatively little knowledge on the fact that the result of the fetal anomaly scan may lead to difficult choices, and on the chance that a child has a congenital anomaly.
A positive attitude towards one's own participation in second-trimester ultrasound screening for fetal anomalies was reported by 90.4% of pregnant women. 87.7% of pregnant women had the intention to participate in second-trimester ultrasound screening.
Of all women, 88.0% made an informed choice, and 95.7% of these were informed choices to participate. Out of 12.0% uninformed choices, 72.5% were choices to participate *(Chapter 5).*

***Comparison between first- and second-trimester prenatal screening***
*Do knowledge, attitude and uptake in second-trimester ultrasound screening for fetal anomalies, differ from knowledge, attitude and uptake in first-trimester screening for Down syndrome with the combined test? Does decision-making about participating in prenatal screening for Down syndrome differ from that for participating in the fetal anomaly scan?*

**Table 2:** Comparison of knowledge levels on second-trimester ultrasound screening, with first-trimester prenatal screening for Down syndrome (N=214)

| **Domains on which women had *higher* knowledge levels for second-trimester prenatal screening as compared to first-trimester prenatal screening** | **Domains on which women had *lower* knowledge levels for second-trimester prenatal screening as compared to first-trimester prenatal screening** |
|---|---|
| Meaning of a normal test-result (termed 'meaning of a decreased probability test-result, in first-trimester prenatal screening) | Test procedure |
| Possible findings resulting from a further examination | Possible negative side effects of the test procedure |
| | What to do after a further examination |
| | Voluntariness of the test |

In Table 2, differences in knowledge level of pregnant women on second-trimester ultrasound screening, as compared to first-trimester prenatal screening for Down syndrome are represented, organised per knowledge domain.
Women had a more positive attitude towards their own participation in second-trimester ultrasound screening as compared to their own participation in first-trimester screening for Down syndrome.
Almost all women had the intention to participate in the fetal anomaly scan, whereas only a minority of pregnant women (32.8%) had the intention to participate in first-trimester screening *(Chapter 5).* Both for first-and second-trimester prenatal screening, high levels of informed decision-making were observed.

## Ethnic differences in participation in prenatal screening for Down syndrome

*How many women from various ethnic backgrounds participate in prenatal screening in the southwest of the Netherlands?*
The overall participation in the prenatal screening program for Down syndrome in the total population (Southwest of the Netherlands) was estimated at 26%. The participation was highest among women who originate from other (non-Dutch) Western countries (33%) and lowest among women from North African (Moroccan) ethnic origin (8%).

*To what extent do women from various ethnic groups differ in participation in prenatal screening?*
Women from North-African (Moroccan), Turkish, Aruban/Antillean and other non-Western ethnic origin were less likely to participate in the prenatal screening program than Dutch women, whereas those from other Western (non-Dutch) ethnic origin were more likely to participate in the prenatal screening program. Women from Moroccan origin differed most in uptake rate from Dutch women, followed by women from Turkish origin. No significant differences were found between women from Surinamese and Dutch ethnic origin.

*Is participation in prenatal screening related to pregnant women's ethnic background, after adjustment for differences in socio-economic background and age?*
After adjustment for differences in socio-economic background and age, participation in the prenatal screening program for Down syndrome in the Netherlands was related to pregnant women's ethnic background. Women from North-African (Moroccan), Turkish, and Aruban / Antillean ethnic origin were less likely to participate in the prenatal screening program than Dutch women, whereas those from other Western (non-Dutch) ethnic origin were more

likely to participate in the prenatal screening program. The difference between women from other non-Western ethnic origin and Dutch women was not significant anymore after adjustment for differences in socio-economic background and age. Women from Surinamese ethnic origin participated equally as Dutch women in the prenatal screening program.

**Offering information on prenatal screening for Down syndrome prior to conception**

*Do pregnant women wish to receive information on prenatal screening for Down syndrome prior to conception?*
Of all women completing questions on receiving information on prenatal screening prior to conception, 55.7% considered prenatal screening for Down syndrome before pregnancy. 28.0% of respondents reported possessing any information (not necessarily provided by a health care professional) on prenatal screening for Down syndrome prior to conception. Of all responding women in this study, 84.6% would not have liked to receive information on prenatal screening for Down syndrome before pregnancy. During pregnancy, the information offer was declined by 33.3% of responding women. Of these women 89.6% in retrospect did not wish to receive this information before pregnancy.

*What are the pros and cons of providing information on prenatal screening for Down syndrome preconceptionally, in addition to during the initial prenatal visit, from an ethical point of view?*
We identified three reasons supporting provision of information about prenatal screening before conception, in addition to during the initial visit for prenatal care; the likelihood of making an informed decision could, firstly, be increased by 'unchaining' the initial information from possible subsequent decisions, and, secondly by providing women sufficient time to deliberate. Thirdly, the probability of equal access to prenatal screening may increase.
Despite two arguments against the provision of information about prenatal screening for Down syndrome before conception (women's preferences to receive information in a step-by-step manner, and the risk of providing a directive message), we propose to implement an information *offer* on prenatal screening for Down syndrome to prospective parents before pregnancy. By *offering* the information (instead of providing), prospective parents are given the opportunity to decide whether to receive information on prenatal screening for Down syndrome in addition to the current prenatal information offer (in the Netherlands) or provision (internationally).

## 2. Methodological considerations

Methodological considerations will be discussed in order of the four research topics as described in the introduction of this thesis (Chapter 1).

**Knowledge**

Strengths and limitations of the method we used to empirically determine the content of decision relevant knowledge needed for informed decision-making about first-and second-trimester prenatal screening *(see also Chapter 3, Figure 1),* and to develop knowledge measures, include:

***Strength- Inclusion of all knowledge domains considered relevant for screening***
In both of the knowledge measures we developed, we included all eight areas of which participants should be aware when making prenatal screening choices. Although there is currently no 'gold standard knowledge questionnaire', professional guidelines [1] outline eight areas of which participants should be aware of when making prenatal screening choices. Knowledge about prenatal screening for Down syndrome is not assessed adequately in most studies, as none of them systematically assesses issues related to each of the eight information areas [2]. By including all of these areas in our studies, we think we covered all aspects of relevant knowledge needed for informed decision-making on prenatal screening, which we consider as a major strength of this part of the thesis.

***Limitation- Small, selected pre-test sample***
We pretested the knowledge measures among a small group of pregnant women, showing that the questionnaire was easy to fill out and that completion did not require much time. Unfortunately, in the execution of the pretesting, although all women were selected at random, the majority had a high educational level. This might be considered as a potential weakness of this part of the study.

**Quality assurance of the information process**

Strengths and weaknesses in evaluating the process of providing information on first- and second-trimester prenatal screening programs, and in measuring informed decision-making as a quality indicator of the information provision procedure of these two screening programs, include;

***Strength- Evaluation in a non-experimental setting***
Our results arise from a real-life setting including all pregnant women in a defined area. At the start of this research project, informed decision-making on prenatal screening for Down syndrome had only been investigated on a small scale and/or in a selected group of pregnant women (e.g. single centre studies, trials) [3-9]. To the best of our knowledge, informed decision-making on second-trimester ultrasound screening was not investigated before.

***Strength- Data from participants and from non-participants***
Data on informed decision-making were obtained both for women participating in prenatal screening and women not participating. This unselected inclusion is a major strength of this study compared to other studies on informed decision-making that have often failed to obtain data from non-participants in screening because of low response rates in this group [10-12].

***Limitation- Absence of information on the denominator; estimation of response rate***
To determine the response rate for the questionnaires on informed decision-making, information on the total number of women that received a questionnaire was needed. Unfortunately, we did not receive this information from midwives that were asked to distribute these questionaires. Therefore, the denominator for this part of the study was unknown. It had to be estimated from the number of questionnaires we distributed to midwives, assuming that all of these questionnaires were handed out to pregnant women.

***Limitation; anynomous questionnaire data; no specific information regarding response***

It would have been interesting to obtain background characteristics (e.g. age, partity, socio-economic status, ethnicity) of women not responding to the questionnaire study, in order to improve response in future evaluation studies. Unfortunately, due to the anonymous nature of the questionnaire study, we did not have this data.

***Limitation; low (estimated) response rate***

Because questionnaire data were collected anonymously, reminding pregnant women to fill out and return the questionnaire was not feasible. The (estimated) low response rate is a threat for external validity. The group of responding women on the questionnaire study was relatively small. In addition, this group consisted mainly of higher educated, ethnic Dutch women. Therefore, concerning the external validity, conclusions we have drawn on informed decision-making are only applicable to this selective group of responding women. We cannot generalise our results to the Dutch population, which has a larger number of ethnic minorities and lower educated women, which makes the external validity of our study low.

Midwifery practices were contacted after the study period to examine possible reasons for the low response of pregnant women. They expected that women who did not participate in the screening program would also be less interested in completing the questionnaire. This is in agreement with the literature regarding other screening programs [10-13]. In our study on first-trimester prenatal screening for Down syndrome, the questionnaire response among non participants was relatively high, and most data on informed decision-making (64.2%; n=285/444) were from women not participating in the prenatal screening program for Down syndrome. Despite the relatively high number of non-participants in the prenatal screening program for Down syndrome participating in the questionnaire study, it is still possible that the questionnaire response is lower among non-participants in the screening program as compared with participants in the screening. Therefore, we cannot ignore the possibility of a bias in the results on informed decision-making, which is again a threat for external validity. Furthermore, a lower response for non-participants in the screening program would imply an overestimation of the uptake rate in prenatal screening for Down syndrome in this study.

***Limitation: No data on actual participation***

A final limitation of these quality assurance studies is that only *intention* participate (and not actual participation) was known. Reason for this was that questionnaires on informed decision-making were handed out before a final decision on actual participation in prenatal screening for Down syndrome / ultrasound screening was made. This was done because information on what women know and understand needs to be collected after efforts have been made to inform them, but before any decision has been enacted. If information on knowledge is collected before that, it may provide insight into levels of lay understanding, but that is a separate question, as what matters is the woman's understanding at the time the decision was made. If information on knowledge is collected later, after tests have been taken by some women, then knowledge about procedural aspects of testing is likely to have increased in the group as a whole because of direct experience and possibly because of further information imparted at the time of testing by the professional performing the procedure. Knowledge measures taken after testing cannot be interpreted as evidence of women's knowledge at the time they made the uptake decision [2]. We were not able to determine actual participation retrospectively, because questionnaires were filled out anonymously.

The fact that we did not obtain data on actual participation might be a threat for the internal validity of this study. However, screening intention was highly predictive of actual screening

behavior in a recent study on prenatal testing choices [14] the comparison of intention to participate as provided by pregnant women themselves with uptake information as provided by midwives for a subset of the women in our sample showed broad agreement between these two data sources. Therefore, we expect that this weakness of our study design had minimal influence on the results.

**Ethnic differences in participation in prenatal screening for Down syndrome**

***Limitation: Possibility of residual confounding***
A limitation of this study is that, although we controlled for various background variables (age, socio-economic background), residual confounding could have influenced the association between ethnic origin and uptake of prenatal screening.

**Offering information on prenatal screening for Down syndrome prior to conception**

***Strength: Combination of an empirical analysis with an ethical reflection***
Most important strength of this study is the combination of an empirical analysis with an ethical reflection. We first performed our empirical analysis. Since we observed that women were not willing to receive this information, this might have resulted in concluding that information on prenatal screening for Down syndrome should not be provided before pregnancy. However, we had to acknowledge that information provision on prenatal screening before pregnancy might have important advantages, especially with regard to a longer time frame to deliberate, possibly resulting in higher levels of informed decision-making. We wondered whether we would violate any ethical principles if information would be offered preconceptionally, even though women indicated not to prefer this. This way, the results of our empirical analysis were a starting point for our research study, and not a final result. By an ethical analyses on the question whether women should receive this information prior to conception, we elaborated on the findings of the empirical study and we came to the advice that an information offer on prenatal screening should be implemented in preconception care.
Although we tried to consider all aspects related to our proposal, it might be possible that additional drawbacks occur when offering information on prenatal screening for Down syndrome before pregnancy is actually implemented in practice. Therefore, evaluations should be constantly alert to the possible downsides of this new procedure.

## 3. Interpretation of the findings, and going beyond.

In this section we will take a broader look at observations we did in this thesis, that are associated with the Dutch information provision procedure and informed decision-making on prenatal screening.

**Measuring knowledge; how much is enough, and how much... of what?**

Adequate decision-relevant knowledge is an essential component in the concept of informed decision-making. A distinction can be made between subjective (or perceived) knowledge (e.g. 'I know how an ultrasound scan is performed' and 'I feel I was given enough information about the scan') or objective (or factual) knowledge. Existing knowledge measures on first-trimester prenatal screening for Down syndrome and second-trimester ultrasound screening,

often measure subjective knowledge. In this thesis, objective knowledge for these two types of screening was assessed. Which type of knowledge should be measured depends on the specific research question addressed; measuring subjective knowledge is reasonable if the main interest is in anxiety, since feeling that one knows too little – or indeed too much- may well be a more important determinant of anxiety than the actual level of knowledge a woman possesses. For evaluation of informed decision-making, objective knowledge is the relevant variable. Objective knowledge can be quite different from subjective knowledge; a woman may be satisfied with very little information, and she may think she understands something fully, when in fact she has incomplete or indeed even incorrect understanding. Some studies have reported both objective and subjective knowledge data and have shown the extent to which the two may be discrepant [2,15].

The definition of informed choice that we used in our studies, was adapted from the Multidimensional Measure of Informed Choice (MMIC) [16], and is based on the definition from O'Connor and O'Brien Pallas definition of an effective decision; 'An informed choice is one that is based on relevant knowledge, consistent with the decision-maker's values and behaviourally implemented' [17]. In this definition and the knowledge measures based upon this definition, knowledge is quantified as the amount of information that can be recalled correctly. However, according to Beauchamp and Faden, a choice is informed 'if the person receives a thorough disclosure about the procedure, comprehends the disclosed information, acts voluntarily, is competent to act, and consents' [18]. According to this definition, understanding is central to the 'informed' element of an informed choice. The assessment of knowledge through the recall of information does not specifically provide evidence on the requirement of understanding; tests of recall do not reveal whether the implications of screening are understood. At best any answers deemed to be 'correct' serve only to give evidence of the individual's memory [19] Indeed, the contrary may be true, the ability to actually recall information, says nothing of whether that information was used in the decision-making process, and so whether the decision was informed [20]. In a recent paper on informed choice and newborn screening, it is stated that measures which rely on parents remembering specific pieces of technical information are inadequate if one wishes to consider wider notions of understanding, and consequently, whether parents are making informed choices. Therefore, the author argues that we should move away from knowledge assessment through the recall of specific, often technical pieces of information, and instead take a more nuanced approach to evaluating understanding, that is, the ability to place knowledge in context and to appreciate the implications of the screening [21]. However, if understanding of factual information is to be examined, the question arises as to how understanding is to be assessed. Some studies have used open-ended questions. The knowledge measures developed and used in our thesis, were constructed with the ultimate aim of use in large-scale program monitoring, to measure knowledge as an outcome-indicator of the quality of the information procedure. Therefore, they had to be short, and easy to understand. This condition made us focus on the recall of information, instead of on understanding.

In our view, the measurement of knowledge has an indicative function; nationwide monitoring of informed decision-making about prenatal screening should be performed, to assure that the condition of an informed choice is sufficiently met. Each item of the knowledge measures needs to be regarded as an indicator, drawn from a larger sample of other potential indicators, for the content of its domain. When remarkable differences, for instance on a regional or practice level, are observed, further evaluation should be organised to gather insight in the causes of these differences. As an example, when relatively low levels of informed decision-

making are caused by inadequate levels of knowledge, a closer look should be taken at the information provision procedure; the content of the oral and written information provided to prospective parents, and the way this provision takes place in practice. Are the essential topics needed to make an informed decision included in the counseling of the parents to be? Is the time that is allocated to this counseling process satisfactory? Does adequate prioritisation of topics in the counseling procedure take place, to prevent an information overload?
Looking at levels of informed decision-making by paying attention to regional differences is one way to handle the matter; this way, relative differences are reason for a more detailed evaluation. However, levels of informed decision-making can also be treated on their own; this way, absolute levels of informed decision-making are what counts. In the latter case, a threshold is needed, and 'action' when levels below this threshold are observed. As no accepted yardstick of knowledge is available, scores on derived measures, or even simple total scores, cannot be interpreted without reference to the original questionnaire [2]. In the absence of an a priori threshold to determine whether the amount of knowledge was sufficient for making informed decisions, Marteau and colleagues at first used a distribution based criterion (the median score of the scale) as a cut-off point to make a distinction between good and poor knowledge. This way, a relative standard was used; knowledge was judged as good or poor within the context of the sample [16]. However, in later papers of (partly) the same research group, it was decided to use the scale (midpoint) as a cut-off rather than the sample (median), 'because there are no agreed external criteria for 'good' and 'poor' knowledge, and 'positive' and 'negative' attitudes' [22]. The same method was applied in more recent studies of this group [4,23]. Two Dutch studies used the guess-corrected midpoint as a cut-off [7,8]. In our knowledge measure, we considered a standard correction for random guessing as inadequate, since 'do not know' was one of the answer options provided. This way, we tried to prevent guessing, which does not mean that we can exclude the possibility that guessing the correct answer did still occur.

To conclude with, much of the way in which knowledge should be assessed, depends on the research question to be answered. For informed decision-making, objective knowledge should be assessed rather than subjective knowledge. We focused on recall rather than understanding, as our knowledge measure had to be short and suitable for large-scale program monitoring of knowledge as an outcome indicator of the quality of the information procedure. If desired, the monitoring of informed decision-making can be followed by an evaluation of understanding in smaller samples, using open-ended questions. The midpoint of the scale was used as an objective threshold, instead of the median that is considered distribution-specific. Scores derived from the knowledge measure (e.g. a knowledge score of 8.3) cannot be interpreted outside the context of the study. In other words, the content of the knowledge measure should be taken into account and a comparison of these derived scores between different knowledge measures is not adequate. However, basic descriptive information on levels of knowledge (e.g. 57.3% of women know that both amniocentesis and chorionic villus sampling provide certainty about the presence of Down syndrome in an unborn child) can be valuable too and is interpretable outside the context of the study.

**Counseling; provision of information on prenatal testing**

One of the conditions that should be met to reach the goal of informed decision-making is the provision of information and options within time limits, to ensure that those options are indeed available [24]. When pregnant women accept the initial information offer, actual information on prenatal screening is provided. The aim of this information provision about prenatal

screening is informed decision-making. Careful, non-directive counseling is essential in providing information about prenatal screening. Therefore, health care professionals offering information on prenatal screening should be trained in non-directiveness, and in communication skills required for counseling on this topic, including an awareness of women's diverging values [25]. Quality assurance of this aspect can take place retrospectively (after the provision of information) by measuring informed decision-making of pregnant women about (non-) participation in prenatal screening. Alternatively, subjective experiences of pregnant women can be measured (i.e. how satisfied are they with the information provided). However, prospectively, quality should be assured by guidelines on the information provision procedure.
In order to conclude an agreement with a regional centre for prenatal screening, health care professionals need to have completed a course in which counseling skills are trained. These skills and theoretical knowledge needed to provide counseling on prenatal screening are described in a program for digital individual education (DIN), developed by the Dutch Organisation of General Practitioners (NHG) and the Royal Dutch Midwives Organisation (KNOV), in close cooperation with the Dutch Association of Obstetrics and Gynaecology (NVOG) and the Dutch Association for Clinical Genetics (VKGN).

The practice of counseling has only been investigated on a small scale in the Netherlands, for instance in the so called PreNT study, that is performed in the Southern part of the country. In this project, client experiences with prenatal counseling are measured by questionnaires that are filled out by pregnant women after the counseling has taken place. From the data, a feedback report is developed for the health care professional, in which the personal result is reported together with the mean of a total group. Aim of the project is to improve the counseling by the provision of personalised feedback.
Recently, Stichting Downsyndroom (SDS; see also introduction of this thesis) investigated experiences of women who gave birth to a child with Down syndrome after participation in prenatal screening during pregnancy. Of the women in this study who participated in prenatal screening program for Down syndrome or invasive testing (n=78), only 32% (n=25) reported having received information about the condition Down syndrome. Of these 25 women, 75% (n=19) indicated that the information was adequate. In total, 76% of 78 parents reported having received no information, or inadequate information on prenatal screening and/ or invasive diagnostic testing. Of women who continued their pregnancy after a positive diagnosis and hence were delivered of a child with Down syndrome, 64% supports the idea of receiving education and counseling about Down syndrome by parents of children having this disorder, under the condition that the information has an objective character [26]. Therefore, the authors conclude that counseling on Down syndrome is not adequate [27].

**Measurement of attitude; on participating in general, or on your own participation?**

Attitude was measured with a translation of the Multidimensional Measure of Informed Choice (MMIC) [16]. The MMIC evaluates an informed choice on the basis of knowledge, attitudes and test uptake. In retrospect it can be questioned whether pregnant women understood the attitude scale as it was intended; in the study in which we focused upon prenatal screening for Down syndrome, the mode of the attitude scores was 10, whereas a majority of non-informed choices (55.9%) related to women deciding not to participate in spite of adequate levels of relevant knowledge and a positive attitude. This might imply that the attitude items were perceived by respondents different to our intention, e.g. as measuring attitude of pregnant women concerning the test in general, instead of measuring attitude of pregnant

women towards their own participation in prenatal sceening. A study investigating informed decision-making on prostate specific antigen screening, reported the same limitation with the MMIC [28].

**First-and second-trimester prenatal screening: comparable goals, different viewpoints?**

Prospective parents in the Netherlands can have their unborn child tested for Down syndrome and other congenital disorders using prenatal screening for Down syndrome and ultrasound screening. Both screening opportunities are different entities, performed in different stages of pregnancy; the combined test in the first-trimester of pregnancy, ultrasound screening for congenital anomalies in the second-trimester. However, despite these screening programs having different entities and characteristics, they have one goal in common; the detection of fetal malformations.
In our study, in which we compared experts their rankings for importance of knowledge domains between first- and second-trimester screening, we observed a high correlation between these rankings. It seems as if experts were aware of the comparable goals both screening programs have, namely the early detection of fetal anomalies.

Pregnant women attribute different goals to first- and second-trimester prenatal screening, and also perceive them as substantially different [29]. They often wish to undergo an ultrasound scan for nonmedical reasons, such as to see the baby, to make the pregnancy seem more real, and to discover the sex of the baby [29-31]. Hence, women expect ultrasound to be a positive and pleasant event [29,31-33]. In contrast, pregnant women show ambivalence towards screening for Down syndrome. They associate participating in prenatal screening for Down syndrome with abortion and often cite unwillingness to have an abortion as a reason for not participating in the screening program [2]. To summarise, it seems that first-trimester screening for Down syndrome is perceived by pregnant women as being primarily focused on the detection of 'abnormalities', whereas the second-trimester ultrasound is perceived as aiming to confirm 'normality' [29-31].
Comparing results of both quality assurance studies (on the information procedures of first- and second-trimester prenatal screening), we recognise these different perceptions of pregnant women for both screening programs. Although mean knowledge scores of pregnant women on first-trimester prenatal screening with the combined test and on second-trimester ultrasound screening were comparable (8.1 versus 8.3), attitude scores differed considerably, with women having a much more negative attitude towards their own participation in screening for Down syndrome than on their own participation in ultrasound screening (6.1 versus 8.8). This difference was especially present for non-participants in these screening programs, with non-participants in screening for Down syndrome having a mean attitude score towards their own participation of 4.8 and non-participants in ultrasound screening having a mean attitude score towards their own participation of 5.9.

Differences in attitude on one's own participation in first- and second-trimester prenatal screening, as observed in this thesis are in accordance with existing literature on these screening programs and were reflected in different uptake rates. In our study, almost all women had the intention to participate in the fetal anomaly scan, whereas only a minority of the pregnant women (32.8%) had the intention to participate in first-trimester screening. Uptake rates of second-trimester ultrasound screening comparable with those determined in our study, are

reported in international studies [34]. In England, uptake rates of between 88-100% were observed in a recent report [35].

**Screening is offered, but participation is not always free of charge**

In the Netherlands, an apparent contradiction is observed concerning the offer and practice of prenatal screening for Down syndrome; although every pregnant women is offered information on this screening program, some women have to pay to actually participate in this screening; women younger than 36 years of age willing to participate in risk assessment tests must pay the costs themselves, unless they have an additional insurance, or a listed indication for invasive testing. If the test result indicates an increased risk of Down syndrome, the costs of invasive testing are reimbursed. Women aged 36 years or over have an age-based indication for prenatal diagnostic testing, and may choose for amniocentesis or chorionic villus sampling, without first having the combined test. Invasive testing is free of charge. Hence, for younger women, an offer to participate is followed by a request to pay for participation. In a recent study on ethnic differences in participating in prenatal screening, it was reported that Surinamese women (as compared to Turkish and ethnic Dutch women) more often mention the costs of screening, as a reason not to participate [36]. In another small-scale study, authors reported that costs of participating in the combined test hardly play any role of importance [27]. On a national scale, it is not known to which extent these costs are a reason not (being able) to participate for pregnant women, or to which extent they result in unequal access.

**The 'Dutch distinction'**

An important aspect of the Dutch national screening program is the distinction between the information offer, and the actual provision of information. In the Netherlands, prenatal screening falls under specifications of the Dutch medical treatment agreement (WGBO), laid down in the civil code. The 'right not to know' is one of the concepts formulated in the WGBO (art 7:449; Civil code of the Netherlands). In this context, this right implicates that women are allowed to refuse receiving information about prenatal screening [37]. However, in order to be able to refuse something, it should be offered first. When information is *provided* (instead of *offered),* which currently takes place internationally in the context of prenatal screening, women are faced with the information, without having received the opportunity to reject. Therefore, in the Netherlands, an information offer on prenatal screening is provided. This is performed in practice by asking pregnant women whether they want to receive information. Health care providers are allowed to provide information, only if the pregnant woman indicates she is interested in receiving this information.
As far as we know, this 'Dutch distinction' (between offering and providing), as an 'embodiment' of the right not to know, is unique from an international perspective. Despite the theoretical soundness of this distinction, to date, practical effectiveness has not been investigated. Is it unknown whether the qualitative difference between an information offer, and the provision of information, is experienced as such by pregnant women. In addition, the feasibility of the 'right not to know', which forms the basic principle behind this distinction, can be questioned, when women do not know anything about prenatal screening at all. After all, they can only reject an offer deliberately if they know where the offer is about. In other words, in order to decide not to receive some information, women should previously be informed of prenatal screening. Now, this is precisely what these women wanted to avoid [38].

**International differences between uptake levels**

In this thesis, we reported a minority of women (35.8%; n=159/444) having the intention to participate in the prenatal screening for Down syndrome. Of all women filling out questionnaires on informed decision-making about second-trimester prenatal screening, 87.7% (n=412/470) had the intention to participate. For first-trimester prenatal screening, the uptake rate we observed (35.8%) is low compared with international studies [39] and in accordance with previous evaluation studies in the Netherlands, performed before the implementation of the national screening program [8,40,41].
Uptake rates in the Netherlands for second-trimester prenatal screening are comparable with European uptake rates. For first-trimester prenatal screening however, the uptake rate is relatively low, as compared with other European countries. In Denmark, uptake rates of 99% have been observed [42], whereas in the United Kingdom, for which the prenatal screening program for Down syndrome resembles the Dutch one, uptake rates of 66% have been reported [14].
The Dutch program for prenatal screening for Down syndrome is not directed at achieving high uptake rates. Therefore, the relatively low number of women participating in this screening, as compared with other European countries, is not a matter of concern, at least as long as these uptake rates are based on informed decision-making. However, it would be interesting to gain insight in causes of these differences. In addition, it might be investigated whether the extreme high uptake rates as observed in for example Denmark, are based on informed decision-making. Future studies should be directed at factors that can explain the international variance in uptake of Down syndrome screening.

**Prenatal screening for trisomy 13 and 18**

Edwards syndrome (trisomy 18) and Patau syndrome (trisomy 13) are the second and third most common autosomal trisomies after Down syndrome. They are associated with severe malformations, mental retardation and a very high rate of intrauterine death [43].
Screening for Down syndrome using ultrasound and biochemical markers can also be applied to trisomy 13 and trisomy 18; for all of these trisomies, similar markers are taken into account; maternal age, fetal nuchal translucency thickness and maternal serum PAPP-A and maternal serum free ß-hCG. Recently, a prediction was made of the consequences for the Dutch Down syndrome screening program in terms of detection rate and false positive rate if trisomy 18 and 13 screening would be introduced, using the algorithm and retrospective data of the Dutch program, collected between 2004 and 2008. It was concluded that an algorithm for trisomy 18 significantly improves the detection rate for trisomy 18 and 13 within the Dutch Down syndrome screening program, implying a cost effective introduction [44].

The government licence for the national screening program for Down syndrome, as implemented in 2007, was strictly confined to screening for trisomy 21. Therefore, health care providers were not allowed to report on the risks for trisomy 18 and 13. However, since an increasing number of health care providers know the potential role of serum screening for trisomy 18 and 13, including some who already counsel their patients on these anomalies, and since these trisomies are associated with early maternal complications, it was recently decided to extend the government license to Edwards and Patau syndrome.
Including trisomy 18 and 13 in the prenatal screening program for Down syndrome, has important consequences for the information provision procedure. Health care professionals are expected to offer prospective parents information about these disorders, the risks on false

positive and false negative outcomes and the implications of (not) participating in the screening program. If the information offer is accepted, this information should be provided, in addition to the information about Down syndrome.

**Informed decision-making and the future of prenatal screening**

Concerns about the impending introduction of non-invasive prenatal diagnosis upon informed decision-making have been expressed [45]. As non-invasive prenatal diagnosis removes the need to discuss procedure related risks, the decision-maker may fail to adequately consider the remaining implications of test outcomes. These include discussion of the option of pregnancy termination if test results indicate an affected fetus. The widespread introduction of non-invasive procedures may also lead to a 'routinization' of prenatal testing. Evidence was provided to suggest that practitioners will view the consent process for prenatal diagnostic testing differently depending upon whether it is an invasive or non-invasive test. This has the potential to undermine women making informed choices about non-invasive testing based on the assumption that separating in time test offer and test procedure facilitates informed choices, as might the process of seeking written consent [46].

# 4. Main conclusions

1. We developed specific measures to determine decision-relevant knowledge about first-trimester prenatal screening with the combined test, and second-trimester ultrasound screening for fetal anomalies. These measures are short and suitable for self-completion, and are ready now to be used for routine application in large-scale program evaluations of the quality of the information provision procedure on these prenatal screening programs.

2. Both in first-trimester prenatal screening for Down syndrome with the combined test, and in second-trimester ultrasound screening for fetal anomalies, high levels of informed decision-making were observed in our study sample. Therefore, we conclude that current information provision procedures on prenatal screening are of good quality, and the standard offer of information as it currently exists, has not resulted in 'routinisation' of participating.

3. Participants as well as non-participants in prenatal screening for Down syndrome have lower levels of knowledge on the condition being screened for than on the screening program. As information on the presence of Down syndrome is the ultimate result of the screening program on which should be acted upon (deciding to continue pregnancy and prepare for the birth of the child with the condition, or deciding to terminate pregnancy), knowledge on this condition should be improved.

4. Although high levels of informed decision-making about participating in the fetal anomaly scan were determined in this study, we believe that, in the information provision procedure, special attention should be paid to reaching adequate levels of knowledge on the possible negative consequences of participating in this screening program.

5. Both first-trimester prenatal screening for Down syndrome and second-trimester ultrasound screening aim at the detection of fetal malformations. However, pregnant women have a considerably more positive attitude towards their own participation in ultrasound screening than towards their own participation in screening for Down syndrome. This is reflected in

higher uptakes rates for second-trimester ultrasound screening, compared to first-trimester screening for Down syndrome.

6. Future quality assurance studies on information provision are essential in nation-wide programs on prenatal screening. Our evaluations of informed decision-making about first-trimester prenatal screening for Down syndrome and second-trimester ultrasound screening for fetal anomalies may serve as pilot studies for quality monitoring studies at national levels

7. Participation in the prenatal screening program for Down syndrome in the Netherlands is lower in specified non-western ethnic minorities. These ethnic variations may be related to barriers in access to information on prenatal screening and barriers in the informed decision-making process.

8. In addition to the current information offer on prenatal screening for Down syndrome during the initial prenatal visit, this information offer should also take place prior to conception, in a preconception care consultation. This is especially relevant regarding the expected introduction of new prenatal screening programs that can be performed as early as five weeks gestation. With a preconceptional information offer, the likelihood of informed decision-making could be increased by lengthening time for contemplation and by unchaining the offer from other decisional steps with regard to prenatal screening.

## 5. Recommendations for further research

In this thesis, a number of questions on informed decision-making about prenatal screening were addressed. However, more questions were raised and remain unanswered until now. This section will address recommendations for future research with respect to the measurement of informed decision-making and the observation that large international differences in levels of uptake in prenatal screening for Down syndrome do exist.

1. We recommend refinement of the attitude measure as used in this thesis. It should be directed more explicitly to a woman's attitude towards her own participation in prenatal screening (instead of being open to misinterpretation as attitude towards the general availability of prenatal screening). In addition, it should be investigated whether attitude for the test procedure as a whole (screening, possibly followed by diagnostics and termination of the pregnancy) can be measured with only oneitem, as is currently done [14]. Maybe, attitude should be measured for all these different phases of the screening program separately. The current attitude measure does not include affective components. Adding these components to the attitude measure might be essential to measure this concept more adequately. To conclude with, it should be investigated whether measuring attitude towards the target of the screening (in this case, Down syndrome or other congenital anomalies) is a better predictor of actual participation than the measurement of attitude towards (participating in) the screening [14].

2. Knowledge measures specific to prenatal screening for trisomy 18 and 13 should be developed and it should be investigated whether attitude towards one's own participation in this extended screening program can be measured with (refinement of) the current attitude measure.

3. We recommend to evaluate whether the costs of participating in prenatal screening for Down syndrome (for women younger than 36 years of age) are a barrier in actual participation. Not being able to pay these costs, or not willing to do this, may result in attitude uptake inconsistencies (with women not participating in prenatal screening for Down syndrome, despite having a positive attitude towards their own participation in this screening program).

4. It would be interesting to gain more insight in factors attributing to the low number of participants in prenatal screening for Down syndrome internationally, as compared to the Netherlands.

5. Future evaluation studies should take into account the question whether the theoretical difference between the offer and provision of information on prenatal screening, is experienced as such in practice by pregnant women, and whether this information offer provides a realistic opportunity for these women to express their right not to know. To the best of our knowledge, the offer of information about prenatal screening, as a basic principle in the information process in the Dutch screening program, has not been investigate to date.

## 6. Recommendations for policy and practice

The results of this study lead to several recommendations for the practice of prenatal screening.

1. The measurement of informed decision-making as an outcome measure for the quality of the information provision procedure on first- and second-trimester prenatal screening in The Netherlands should become standard practice. Our evaluations of informed decision-making about first-trimester prenatal screening for Down syndrome and second-trimester ultrasound screening for fetal anomalies, may serve as pilot studies for these quality monitoring studies at national levels.

2. An implementation trajectory is needed, directed at all actors and stakeholders, to make future quality assurance studies on information provision being perceived as an integral part of prenatal care. Currently, these groups are not used to participate regularly in evaluations of informed decision-making, to monitor the quality of the screening program. They should be convinced of the relevance of these evaluations. In addition, strategies to improve response rates should be applied. No one solution to improve response rates and perception of quality assurance as standard part of care is available; for each of the actors, a different approach is needed. The model of Grol & Wensing [47] can be used to implement changes, aiming at quality assurance being perceived as a regular aspect of daily practice in prenatal care

3. Quality assurance by regular monitoring should include a measurement of knowledge about trisomy 13 and 18, attitude towards one's own participation in the screening program, and choosing to participate in screening for Down syndrome, with or without choosing to accept personalised risk information on trisomy 18 and 13.

4. Monitoring of the procedure for providing information about prenatal screening for Down syndrome and for fetal anomalies is a way to assess whether the objective of informed decision-making is fulfilled. We recommend using resulting insights in levels of informed decision-making to generate further investigations (evaluation) into the underlying causes of these dif-

ferences between regions or groups (e.g. hospitals versus midwifery practices) and to provide a starting point for improvements in the (procedure of the offer of) information.

5. In addition to determining levels of informed decision-making, we recommend to investigate whether careful, non-directive counseling on first- and second-trimester prenatal screening is provided. All of the knowledge domains we identified as relevant in informed decision-making on these prenatal screening programs, should be present in the counseling session.

6. It should be investigated whether information on first-trimester prenatal screening for Down syndrome is provided together with information on second-trimester ultrasound screening for fetal anomalies in one counseling session, or whether information on these programs is provided in different sessions, at different moments in time. We expect major practice variation and suggest, for informed decision-making to be reached, counseling at two different points in time; one counseling session in the first-trimester of pregnancy (before deciding about participating in screening with the combined test) and one in the second-trimester of pregnancy (before deciding about participating in ultrasound screening).

7. An information offer on prenatal screening for Down syndrome should be implemented in preconception care consultations.

## 7. Work in progress

Recently, the Dutch National Institute for Public Health and the Environment (RIVM) has been developing a national digital database (Peridos), in which information on prenatal screening can be registered. All healthcare professionals (midwives, sonographers, gynaecologists), associated with the eight regional centres for prenatal screening in the Netherlands, are expected to register data on the counseling procedure (for first- and second-trimester prenatal screening) and on the outcome of the pregnancy. In addition, data that are used for quality assurance should be registered by these health care professionals. To data, Peridos is being implemented and tested in all regions in the Netherlands.
Peridos is expected to offer a range of possibilities for the national quality assurance of prenatal screening. When informed decision-making is measured using questionnaires for pregnant women, these data on informed decision-making can be linked with data as filled out by the health care professionals in Peridos (i.e. data on the information provision procedure, participation and outcome of the screening, outcome of the pregnancy). This is a solution to a number of the problems we experienced in measuring informed decision-making. By using data as registered in Peridos, actual participation in the screening program can be used as a variable in informed decision-making, instead of the intention to participate, that was used in this thesis. In addition, linkage between the use of the questionnaires on informed decision-making and data in Peridos, gives more insight into background characteristics of respondents and non-respondents in these questionnaire study. In this thesis, we had information on only a few background characteristics of the respondents was known, we did not obtain background characteristics of non-respondents in the questionnaire study.

Currently, Erasmus MC (on behalf of the Centre for Population Research [CvB] of the Dutch National Institute for Public Health and the Environment [RIVM]) performs a first national monitor of informed decision-making on prenatal screening, using both hard-copy (Figure 1-3) and digital versions of the questionnaires (in Dutch, Turkish and standard-Arabic) for

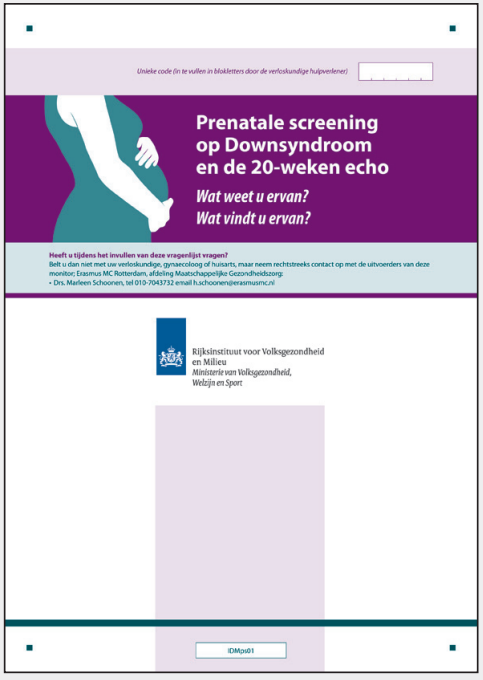


**Figure 1:** Dutch version of questionnaire to measure informed decision-making in a national monitor

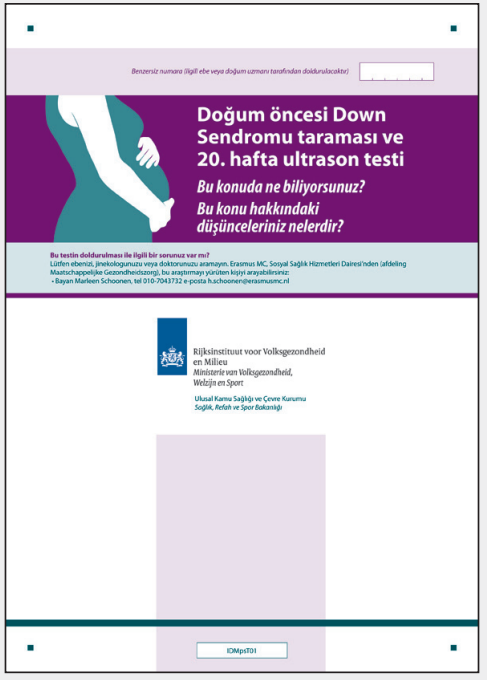


**Figure 2:** Turkish version of questionnaire to measure informed decision-making in a national monitor


**Figure 3:** Arabic version of questionnaire to measure informed decision-making in a national monitor

pregnant women, and the linkage of data with Peridos. This monitoring should become a regular procedure to assure a satisfactory organisation of prenatal screening. When gaps in knowledge are observed (e.g. knowledge on the condition Down syndrome, knowledge on the voluntary nature of first- and second-trimester prenatal screening) this should contribute to the development of improved information provided through oral and/or written communication to pregnant women and their partners about prenatal screening, in order to make informed decision-making possible.

# References


[1] Royal College of Obstetricians and Gynaecologists. Report of the working party on biochemical markers and the detection of Down's syndrome. RCOG Press 1993.

[2] Green JM, Hewison J, Bekker HL, Bryant LD, Cuckle HS. Psychosocial aspects of genetic screening of pregnant women and newborns: a systematic review. Health Technol Assess 2004;8:iii, ix-x, 1-109.

[3] Dormandy E, Hooper R, Michie S, Marteau TM. Informed choice to undergo prenatal screening: a comparison of two hospitals conducting testing either as part of a routine visit or requiring a separate visit. J Med Screen 2002;9:109-14.

[4] Dormandy E, Michie S, Hooper R, Marteau TM. Informed choice in antenatal Down syndrome screening: a cluster-randomised trial of combined versus separate visit testing. Patient Educ Couns 2006;61:56-64.

[5] Gourounti K, Sandall J. Do pregnant women in Greece make informed choices about antenatal screening for Down's syndrome? A questionnaire survey. Midwifery 2008;24:153-62.

[6] Jaques A, Sheffield L, Halliday J. Informed choice in women attending private clinics to undergo first trimester screening for Down syndrome. Prenatal diagnosis 2005;25:656-664.

[7] van den Berg M, Timmermans DR, ten Kate LP, van Vugt JM, van der Wal G. Informed decision making in the context of prenatal screening. Patient Educ Couns 2006;63:110-7.

[8] van den Berg M, Timmermans DR, Ten Kate LP, van Vugt JM, van der Wal G. Are pregnant women making informed choices about prenatal screening? Genet Med 2005;7:332-8.

[9] Fransen M, Essink-Bot ML, Vogel I, Mackenbach JP, Steegers E, Wildschut H. Ethnic differences in informed decision-making about prenatal screening for Down syndrome. J Epidemiol Community Health 2009.

[10] Eborall HC, Griffin SJ, Prevost AT, Kinmonth AL, French DP, Sutton S. Psychological impact of screening for type 2 diabetes: controlled trial and comparative study embedded in the ADDITION (Cambridge) randomised controlled trial. BMJ 2007;335:486.

[11] Nijs HG, Essink-Bot ML, DeKoning HJ, Kirkels WJ, Schroder FH. Why do men refuse or attend population-based screening for prostate cancer?. J.Public Health Med. 2000;22:312-316.

[12] van den Bergh KA, Essink-Bot ML, van Klaveren RJ, de Koning HJ. Informed participation in a randomised controlled trial of computed tomography screening for lung cancer. Eur.Respir.J. 2009;34:711-720.

[13] Sutton S, Bickler G, Sancho-Aldridge J, Saidi G. Prospective study of predictors of attendance for breast screening in inner London. J.Epidemiol.Community Health 1994; 48:65-73.

[14] Bryant LD, Green JM, Hewison J. The role of attitudes towards the targets of behaviour in predicting and informing prenatal testing choices. Psychol.Health 2009:1-20.

[15] Sepucha KR, Fagerlin A, Couper MP, Levin CA, Singer E, Zikmund-Fisher BJ. How does feeling informed relate to being informed? The DECISIONS survey. Med.Decis.Making 2010;30:77S-84S.

[16] Marteau TM, Dormandy E, Michie S. A measure of informed choice. Health Expect 2001;4:99-108.

[17] O'Connor A, O'Brien Pallas LL,. Decisional conflict. In: McFarlane GK, McFarlane EA eds.,. Nursing diagnosis and intervention. Toronto: Mosby,1989; 486-96.

[18] Beauchamp T, Faden R,. Meaning and Elements of Informed Consent. In: Reich W ed.,. Encyclopedia of Bioethics. New York: MacMillan, 1995; 1238-41.

[19] Beauchamp, T., Childress, J.,. Principles of biomedical ethics. Oxford: Oxford University Press, 2001.

[20] Bekker H, Thornton JG, Airey CM, Connelly JB, Hewison J, Robinson MB, Lilleyman J, MacIntosh M, Maule AJ, Michie S, Pearman AD. Informed decision making: an annotated bibliography and systematic review. Health Technol Assess 1999;3:1-156.

[21] Nicholls SG. Knowledge or Understanding? Informed Choice in the Context of Newborn Bloodspot Screening. Public Health Ethics 2010;3:128-136.

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

[23] Dormandy E, Tsui EY, Marteau TM. Development of a measure of informed choice suitable for use in low literacy populations. Patient Educ Couns 2007;66:278-95.
[24] Dutch National Institute for Public Health and the Environment (RIVM). Policy; timely information about possible disorders (2010) http://www.rivm.nl/pns_en/down_ultrasound/policy/ Accessed on 05/03/2010
[25] Williams C, Alderson P, Farsides B. Is nondirectiveness possible within the context of antenatal screening and testing?. Soc Sci Med 2002:339-347.
[26] de Graaf G, van Os C, Borstlap R, de Graaf E. Ervaringen van ouders met prenatale screening. Down Update, Bijlage bij Down+Up 2010;91:37-48.
[27] de Graaf G, van Os C, Borstlap R, de Graaf E. Voorlichting over Down syndroom ver onder de maat. Persbericht 016. Stichting Downsyndroom 2010.
[28] van Vugt HA, Roobol MJ, Venderbos LD, Joosten-van Zwanenburg E, Essink-Bot ML, Steyerberg EW, Bangma CH, Korfage IJ. Informed decision making on PSA testing for the detection of prostate cancer: an evaluation of a leaflet with risk indicator. Eur.J.Cancer 2010;46:669-677.
[29] Santalahti P, Aro AR, Hemminki E, Helenius H, Ryynanen M. On what grounds do women participate in prenatal screening?. Prenat.Diagn. 1998;18:153-165.
[30] Stephens MB, Montefalcon R, Lane DA. The maternal perspective on prenatal ultrasound. J.Fam. Pract. 2000;49:601-604.
[31] Ahman A, Runestam K, Sarkadi A. Did I really want to know this? Pregnant women's reaction to detection of a soft marker during ultrasound screening. Patient Educ.Couns. 2010;81:87-93.
[32] Bricker L, Garcia J, Henderson J, Mugford M, Neilson J, Roberts T, Martin MA. Ultrasound screening in pregnancy: a systematic review of the clinical effectiveness, cost-effectiveness and women's views. Health Technol.Assess. 2000;4:i-vi, 1-193.
[33] Garcia J, Bricker L, Henderson J, Martin MA, Mugford M, Nielson J, Roberts T. Women's views of pregnancy ultrasound: a systematic review. Birth 2002;29:225-250.
[34] Georgsson Ohman S, Waldenstrom U. Second-trimester routine ultrasound screening: expectations and experiences in a nationwide Swedish sample. Ultrasound Obstet.Gynecol. 2008;32:15-22.
[35] Healthcare Commission. Towards better births. A review of maternity services in England 2008.
[36] Fransen MP, Wildschut HI, Vogel I, Mackenbach JP, Steegers EA, Essink-Bot ML. Ethnic differences in considerations whether or not to participate in prenatal screening for Down syndrome. Prenat. Diagn. 2009;29:1262-1269.
[37] Andorno R. The right not to know: an autonomy based approach. J.Med.Ethics 2004;30:435-9; discussion 439-40.
[38] Wertz DC, Fletcher JC. Privacy and disclosure in medical genetics examined in an ethics of care. Bioethics 1991;5:212-232.
[39] Spencer K, Spencer CE, Power M, Moakes A, Nicolaides KH. One stop clinic for assessment of risk for fetal anomalies: a report of the first year of prospective screening for chromosomal anomalies in the first trimester. BJOG 2000;107:1271-1275.
[40] Health Fransen M, Essink-Bot ML, Vogel I, Mackenbach JP, Steegers E, Wildschut H. Ethnic differences in informed decision-making about prenatal screening for Down syndrome. J.Epidemiol. Community Health 2010; 64 (3): 262-8
[41] Fransen MP, Wildschut HI, Vogel I, Mackenbach JP, Steegers EA, Essink-Bot ML. Ethnic differences in considerations whether or not to participate in prenatal screening for Down syndrome. Prenat. Diagn. 2009.
[42] Ekelund CK, Jorgensen FS, Petersen OB, Sundberg K, Tabor A, Danish Fetal Medicine Research Group. Impact of a new national screening policy for Down's syndrome in Denmark: population based cohort study. BMJ 2008;337:a2547.
[43] Morris JK, Savva GM. The risk of fetal loss following a prenatal diagnosis of trisomy 13 or trisomy 18. Am.J.Med.Genet.A. 2008;146:827-832.
[44] Koster MP, Stoutenbeek P, Visser GH, Schielen PC. Trisomy 18 and 13 screening: consequences for the Dutch Down syndrome screening programme. Prenat.Diagn. 2010;30:287-289.
[45] Wright CF, Burton H. The use of cell-free fetal nucleic acids in maternal blood for non-invasive prenatal diagnosis. Hum.Reprod.Update 2009;15:139-151.

[46] van den Heuvel A, Chitty L, Dormandy E, Newson A, Deans Z, Attwood S, Haynes S, Marteau TM. Will the introduction of non-invasive prenatal diagnostic testing erode informed choices? An experimental study of health care professionals. Patient Educ.Couns. 2010;78:24-28.

[47] Grol R, Wensing M,. Implementation, effective changes in patient-care [in Dutch]. Maarsen: Elsevier Gezondheidszorg, 2001.

# Summary

# Introduction

## Congenital anomalies

Congenital anomalies are the leading cause of death and morbidity in children under 1 year of age. During the last decades, an increasing number of congenital anomalies have been diagnosed prenatally by prenatal screening. In this thesis, we will take a closer look at the information provision procedure, informed decision-making and participation in the prenatal screening program for Down syndrome and neural tube defects. Down syndrome and neural tube defects are chromosomal and structural congenital anomalies respectively, that can both be diagnosed before birth. Down syndrome and neural tube defects are the primary focus of the Dutch national prenatal screening program for congenital anomalies.

## Prenatal screening for Down syndrome and strucural congenital anomalies in the Netherlands

In the Netherlands, a national screening program for Down's syndrome, open to all pregnant women, exists as of 2007. Before, offering a pregnant woman information on a risk estimation test for Down's syndrome was only allowed upon her explicit request. Only invasive diagnostic testing to women aged 36 years or over, in high-risk categories, or with medical indications was actively offered. In the current program, all pregnant women are actively offered information on the possibility of having a screening test for Down's syndrome. Only if the pregnant woman indicates she wants to be informed, the consultation is followed up with a counseling appointment. Although every pregnant women is offered information on this screening program, some women have to pay to actually participate in this screening; women younger than 36 years of age willing to participate in risk assessment tests must pay the costs themselves, unless they have an additional insurance, or a listed indication for invasive testing. If the test result indicates an increased risk of Down syndrome, the costs of invasive testing are reimbursed. Women aged 36 years or over have an age-based indication for prenatal diagnostic testing, and may choose for amniocentesis or chorionic villus sampling, without first having the combined test. Invasive testing is free of charge.
Second-trimester ultrasound screening for fetal anomalies has become a standard part of prenatal care in the Netherlands. Similar to prenatal screening for Down syndrome, the aim of ultrasound screening is defined as informing pregnant women and their partners in a timely manner about any possible disorder(s) their child may have and to allow them to choose the best course of action if the child is affected. To achieve this goal, requirements are set concerning the offer of information. Provision of relevant, good quality information about prenatal screening, aims at informed decision-making by pregnant women about (non-) participation in the screening.

## Informed decision-making

An informed decision has two core characteristics. First, it is based on relevant, good quality information, resulting in adequate decision-relevant knowledge. Secondly, an informed decision should reflect the decision-maker's values. As high quality information provision to those who want to be informed is an essential element in the Dutch program on prenatal screening, the level of informed decision-making can be used as an indicator of the quality of information provision procedure.

In the Netherlands, experimental and small-scale observational studies reported informed decision-making about prenatal screening for Down syndrome in 51%-68% of pregnant women. However, these studies were performed before the current national screening program, with the routine offer of information to all pregnant women, was implemented. In a recent Dutch study, performed after the implementation of the routine offer of information on prenatal screening in 2007, substantial ethnic differences in informed decision-making on prenatal screening for Down syndrome were reported.

**This thesis**

To date, no evaluations have been performed of the quality of the information provision procedure on prenatal screening, in the real life setting of a national screening program for Down syndrome and congenital anomalies. At the start of the research underlying this thesis, no data were available on the information process, informed decision-making and participation in prenatal screening for Down syndrome and congenital anomalies.
The objective of this thesis was to evaluate the information provision, informed decision-making and participation, in the context of the Dutch program for prenatal screening. The following research questions were formulated and classified in three central themes.

# Research questions

**Part 1- Knowledge**

*1a. What is the content of relevant knowledge needed to make an informed decision about (non-) participation in first- trimester prenatal screening for Down syndrome with the combined test?* (Chapter 2).
*1b. What is the content of relevant knowledge needed to make an informed decision about (non-) participation in second- trimester ultrasound screening for fetal anomalies?* (Chapter 3).
*1c. What are differences between the content of decision-relevant knowledge for informed decision-making about second- trimester ultrasound screening (b) and decision-relevant knowledge for informed decision-making about first- trimester prenatal screening for Down syndrome with the combined test (a)?* (Chapter 3).

**Part 2 - Quality assurance of the information process**

***First- trimester prenatal screening for Down syndrome with the combined test***
2a. The process of providing information about first- trimester prenatal screening for Down syndrome with the combined test: *Are all pregnant women offered information about prenatal screening for Down syndrome? How many women accept the information offer and, of these women, how many do actually receive the information?* (Chapter 4).
2b. Informed decision-making as quality-indicator of the information provision procedure about first-trimester prenatal screening for Down syndrome with the combined test; Is pregnant women's knowledge adequate? *What is a pregnant woman her attitude towards undergoing prenatal screening for Down syndrome herself? To what extent is decision-making regarding (non-) participation in prenatal screening for Down syndrome based on an informed decision? What are the determinants of informed decision-making?* (Chapter 4).

***Second-trimester ultrasound screening for fetal anomalies***

2c. The process of providing information about second-trimester ultrasound screening for fetal anomalies: *Are all pregnant women offered information about second- trimester ultrasound screening? How many women accept the information offer and, of these women, how many do actually receive the information?* (Chapter 5).

2d. Informed decision-making (outcome of the information provision), as quality-indicator of the information provision procedure about second-trimester ultrasound screening for fetal anomalies; *Is pregnant women's knowledge adequate? What is a pregnant woman her attitude towards undergoing second-trimester ultrasound screening herself? To what extent is decision-making regarding (non-) participation in second- trimester ultrasound screening based on an informed decision? What are the determinants of informed decision-making?* (Chapter 5).

***Comparison between first-and second-trimester screening***

*2e. Do knowledge, attitude and uptake in second- trimester ultrasound screening for fetal anomalies, differ from knowledge, attitude and uptake in first-trimester screening for Down syndrome with the combined test? Does decision-making about participating in prenatal screening for Down syndrome differ from that for participating in the fetal anomaly scan?* (Chapter 5).

**Part 3- Ethnic differences in participation in prenatal screening for Down syndrome**

*3a. How many women from various ethnic backgrounds participate in prenatal screening in the southwest of the Netherlands?* (Chapter 6).

*3b.To what extent do women from various ethnic groups differ in participation in prenatal screening?*

*3c. Is participation in prenatal screening related to pregnant women's ethnic background, after adjustment for differences in socio-economic background and age?* (Chapter 6).

**Part 4 – Offering information on prenatal screening for Down syndrome prior to conception**

*4a. Do pregnant women wish to receive information on prenatal screening for Down syndrome prior to conception?* (Chapter 7).

*4b. What are the pros and cons of providing information on prenatal screening for Down syndrome preconceptionally, in addition to during the initial prenatal visit, from an ethical point of view?* (Chapter 7).

## Answers to research questions

**Part 1- Knowledge**

Chapter 2 and 3 provide answers to the research questions of the first part of this thesis. Based on expert opinions and literature we defined the domains and items considered representative for decision-relevant knowledge required for informed decision-making on screening participation. (Question 1a and 1b). This resulted in a knowledge questionnaire for determining levels of decision-relevant knowledge needed for informed decision making on prenatal screening for Downsyndrome, and a knowledge questionnaire for determining those levels in the context of second trimester ultrasound screening for fetal anomalies.

In Chapter 3, differences between the content of decision-relevant knowledge for informed decision-making about second- trimester ultrasound screening and decision-relevant knowledge for informed decision-making about first- trimester prenatal screening for Down syndrome with the combined test are investigated (question 1c). In the expert consultation, all domains were scored as very important for both screening programs. There was a positive correlation between the importance ranking orders of the domains for the two screening programs. Both the domains 'what to do in the event of a positive test result' and 'the meaning of a positive test result' received a higher expert importance ranking in first-trimester screening than in second-trimester screening.
Questionnaires we developed for this part of the thesis, are now ready for large-scale implementation to determine informed decision-making on prenatal screening.

**Part 2- Quality assurance of the information process**

Chapter 4 and 5 provide answers to the research questions of the second part of this thesis.
As we showed in Chapter 4, midwives reported offering information on first-trimester prenatal screening for Down syndrome to almost all pregnant women. Of these women, 62.6% wished to receive information, 81.9% of the women that wished to receive information, actually received the information (question 2a).
Decision-relevant knowledge about prenatal screening for Down syndrome was adequate in 89% of responding women. Knowledge about the condition Down syndrome was more often inadequate than knowledge about the screening program. Almost half of responding women had a negative attitude towards participating in prenatal screening for Down syndrome. A minority of women (35.8%) intended to participate in the screening program. A total of 75.5% of responding women made an informed decision; 94.3% of participants in the screening and 64.9% of non-participants. Self reported religious activity was associated with lower levels of knowledge on prenatal screening for Downsyndrome, a more negative attitude towards own participation and a lower intention to participate. In multivariate analysis, educational level was the only significant determinant of informed decision-making. Adequate knowledge and a positive attitude were associated with a positive intention to participate (question 2b).

As we showed in *Chapter 5,* almost all pregnant women were asked whether they wanted information. Of these women, 92.3% wished to receive information. Of the women that wished to receive information, 94.3% actually received the information (question 2c).
Decision-relevant knowledge about second- trimester ultrasound screening, was adequate in 93.5% of responding women. Pregnant women had relatively little knowledge on the fact that the result of the fetal anomaly scan may lead to difficult choices, and on the chance that a child has a congenital anomaly. A positive attitude towards participating in second- trimester ultrasound screening for fetal anomalies was reported by 90.4% of pregnant women. 87.7% of pregnant women had the intention to participate in second- trimester ultrasound screening. Of all women, 88.0% made an informed choice, and 95.7% of these were informed choices to participate. Out of 12.0% uninformed choices, 72.5% were choices to participate (question 2d).

Pregnant women in our study group had higher knowledge levels for second-trimester ultrasound screening as compared to first-trimester prenatal screening for Down syndrome for the domains 'Meaning of a normal test-result' (termed 'meaning of a decreased probability test-result in first-trimester prenatal screening for Down syndrome), and for the domain 'Possible findings resulting from a further examination'. Pregnant women in our study group

had lower knowledge levels for second-trimester ultrasound screening as compared to first-trimester prenatal screening for Down syndrome for the domains 'Test procedure', 'Possible negative side effects of the test procedure', 'What to do after a further examination', and 'Voluntariness of the test'. Women had a more positive attitude towards participating in second-trimester ultrasound screening as compared to participating in first-trimester screening for Down syndrome. Almost all women had the intention to participate in the fetal anomaly scan, whereas only a minority of pregnant women (32.8%) had the intention to participate in first-trimester screening. Both for first-and second-trimester prenatal screening, high levels of informed decision-making were observed (question 2e).

**Part 3- Ethnic differences in participation in prenatal screening for Down syndrome**

Chapter 6 provides answers to the research questions of the third part of this thesis.
The overall participation in the prenatal screening program for Down syndrome in the total population (Southwest of the Netherlands) was estimated at 26%. The participation was highest among women who originate from other (non-Dutch) Western countries (33%) and lowest among women from North African (Moroccan) ethnic origin (8%) (question 3a).
Women from North-African (Moroccan), Turkish, Aruban/Antillean and other non-Western ethnic origin were less likely to participate in the prenatal screening program than Dutch women, whereas those from other Western (non-Dutch) ethnic origin were more likely to participate in the prenatal screening program. Women from Moroccan origin differed most in uptake rate from Dutch women, followed by women from Turkish origin. No significant differences were found between women from Surinamese and Dutch ethnic origin (question 3b).

After adjustment for differences in socio-economic background and age, participation in the prenatal screening program for Down syndrome in the Netherlands was related to pregnant women's ethnic background. Women from North-African (Moroccan), Turkish, and Aruban / Antillean ethnic origin were less likely to participate in the prenatal screening program than Dutch women, whereas those from other Western (non-Dutch) ethnic origin were more likely to participate in the prenatal screening program. The difference between women from other non-Western ethnic origin and Dutch women was not significant anymore after adjustment for differences in socio-economic background and age. Women from Surinamese ethnic origin participated equally as Dutch women in the prenatal screening program (question 3c)

**Part 4 – Offering information on prenatal screening for Down syndrome prior to conception**

Chapter 7 provides answers to the research questions of the fourth part of this thesis.
Of all women completing questions on receiving information on prenatal screening prior to conception, 55.7% of respondent women considered prenatal screening for Down syndrome before pregnancy. 28.0% of respondents reported possessing any information (not necessarily provided by a health care professional) on prenatal screening for Down syndrome prior to conception. Of all women in this study, 84.6% would not have liked to receive information on prenatal screening for Down syndrome before pregnancy. During pregnancy, the information offer was declined by 33.3% of women. Of these women 89.6% in retrospect did not wish to receive this information before pregnancy (question 4a).
We identified three reasons supporting provision of information about prenatal screening for Down syndrome before conception, in addition to during the initial visit for prenatal care; the

likelihood of making an informed decision could, firstly, be increased by 'unchaining' the initial information from possible subsequent decisions, and, secondly by providing women sufficient time to deliberate. Thirdly, the probability of equal access to prenatal screening may increase. Despite two arguments against the provision of information about prenatal screening for Down syndrome before conception (women's preferences to receive information in a step-by-step manner, and the risk of providing a directive message), we propose to implement an information *offer* on prenatal screening for Down syndrome to prospective parents before pregnancy. By *offering* the information, prospective parents are given the opportunity to decide whether to receive information on prenatal screening for Down syndrome in addition to the current prenatal information offer (in the Netherlands) or provision (internationally) This way, both the right to know and the right-not-to know of pregnant women are respected. (question 4b).

## Discussion

The general discussion of this thesis starts with a summary of the main findings per research question. Strengths and limitations that should be considered when interpreting the results, are discussed.
The knowledge measures we developed include all domains considered as relevant by experts (professionals in the field of prenatal screening and pregnant women themselves) for screening. However, they have only been tested in a small selected sample.

Our quality assurance studies, in the second part of this thesis, were performed in a non-experimental setting. Contrary to previous studies, investigating informed decision making on a small scale and/or in a selected group of women, our results arise from a real-life setting including all pregnant women (both participants and non-participants) in a defined area. Concerning the internal validity, absence of data on actual participation are a limitation. The small and selected response threatens external validity of these studies. Response had to be estimated due to the anonymous nature of our questionnaire study.
A limitation of the third part of this thesis (determination of ethnic differences in participation in prenatal screening for Down syndrome) is that, although we controlled for various background variables (age, socio-economic background), residual confounding could have influenced the association between ethnic origin and uptake of prenatal screening.
In the fourth part of this thesis, we combine an empirical analysis with an ethical reflection, to find out whether information on prenatal screening should be provided prior to conception. The results of our empirical analysis were a starting point for our research study, instead of a final result.

### Interpretation of the findings, and going beyond

The knowledge measures developed and used in our thesis, were constructed with the ultimate aim of use in large-scale program monitoring, to measure knowledge as an outcome-indicator of the quality of the information procedure. In our view, the measurement of knowledge has an indicative function; nationwide monitoring of informed decision-making about prenatal screening should be performed, to assure that the condition of an informed choice is sufficiently met. Each item of the knowledge measures needs to be regarded as an indicator, drawn from a larger sample of other potential indicators, representative for the content of its domain. When remarkable differences, for instance on a regional or practice level, are

observed, further evaluation should be organised to gather insight in the causes of these differences.
To date, not much is known about the quality of the information provision procedure on prenatal screening in the Netherlands. Available data indicate that counseling should be improved, especially regarding information provision about the condition Down syndrome. In the current study, we performed a determination of levels of informed decision-making, as an indicator of the quality of information provision on prenatal screening. Several considerations were made regarding the measurement of knowledge and attitude. Knowledge measures we developed can be used in national monitoring of informed decision-making. The attitude measure we used in this thesis should be refined.

Prenatal screening for Down syndrome and ultrasound screening are different entities, performed in different stages of pregnancy; the combined test in the first-trimester of pregnancy, ultrasound screening for congenital anomalies in the second-trimester. However, despite these screening programs having different entities and characteristics, they have one goal in common; the detection of fetal malformations. Pregnant women attribute different goals to first- and second-trimester prenatal screening, and also perceive them as substantially different. Comparing results of both quality assurance studies (on the information procedures of first-and second-trimester prenatal screening), we recognize these different perceptions of pregnant women for both screening programs. These different perceptions were reflected in different uptake rates.
For younger women, an offer to participate in prenatal screening for Down syndrome is followed by a request to pay for participation. On a national scale, it is not known to which extent these costs are a reason not (being able) to participate for pregnant women, or (and to which extent)they result in unequal access.

An important aspect of the Dutch national screening program is the distinction between the information offer, and the actual provision of information. In the Netherlands, prenatal screening falls under specifications of the Dutch medical treatment agreement (WGBO), laid down in the civil code. The 'right not to know' is one of the concepts formulated in the WGBO (art 7:449; Civil code of the Netherlands). In this context, this right implicates that women are allowed to refuse receiving information about prenatal screening. However, in order to be able to refuse something, it should be offered first. When information is *provided* (instead of *offered),* which currently takes place internationally in the context of prenatal screening, women are faced with the information, without having received the opportunity to reject. Therefore, in the Netherlands, an information offer on prenatal screening does exist. This is performed in practice by asking pregnant women whether they want to receive information. Health care providers are allowed to provide information, only if the pregnant woman indicates she is interested in receiving this information. As far as we know, this 'Dutch distinction' (between offering and providing), as an 'embodiment' of the right not to know, is unique from an international perspective. Despite the theoretical soundness of this distinction, to date, practical effectiveness has not been investigated.
Uptake rates in the Netherlands for second-trimester prenatal screening are comparable with European uptake rates. For first-trimester prenatal screening however, the uptake rate is relatively low, as compared with other European countries. The Dutch program for prenatal screening is not directed at achieving high uptake rates. Therefore, the relatively low number of women participating in this screening, as compared with other European countries, is not a matter of concern, at least as long as these uptake rates are based on informed decision-making. However, it would be interesting to gain insight in causes of these differences in uptake.

The government licence for the national screening program for Down syndrome, as implemented in 2007, was strictly confined to screening for trisomy 21. Therefore, health care providers were not allowed to report on the risks for trisomy 18 and 13. However, since an increasing number of health care providers know the potential role of serum screening for trisomy 18 and 13, including some who already counsel their clients on these anomalies, and since these trisomies are associated with early maternal complications, it was recently decided to extend the government license to Edwards and Patau syndrome.
Concerns about the impending introduction of non-invasive prenatal diagnosis upon informed decision-making have been expressed. As non-invasive prenatal diagnosis removes the need to discuss procedure related risks, the decision-maker may fail to adequately consider the remaining implications of test outcomes.

**We conclude…**

- The knowledge measures we developed in this thesis are ready now to be used for routine application in large-scale program evaluations of the quality of the information provision procedure on these prenatal screening programs.
- Both in first-trimester prenatal screening for Down syndrome with the combined test, and in second-trimester ultrasound screening for fetal anomalies, high levels of informed decision-making were observed in our study sample. Therefore, we conclude that current information provision procedures on prenatal screening are of good quality, and the standard offer of information as it currently exists, has not resulted in 'routinisation' of participating in prenatal screening.
- Participants as well as non-participants in prenatal screening for Down syndrome have lower levels of knowledge on the condition being screened for than on the screening program.
- Pregnant women have a considerably more positive attitude on participating in ultrasound screening than on participating in screening for Down syndrome, despite these screening programs having comparable aims. This is reflected in higher uptakes rates for second-trimester ultrasound screening, compared to first-trimester screening for Down syndrome.
- Our evaluations of informed decision-making about first-trimester prenatal screening for Down syndrome and second- trimester ultrasound screening for fetal anomalies may serve as pilot studies for quality monitoring studies at national levels.
- Participation in the prenatal screening program for Down syndrome in the Netherlands is lower in specified non-western ethnic minorities, as compared with native Dutch people.
- In addition to the current information offer on prenatal screening for Down syndrome during the initial prenatal visit, this information offer should also take place prior to conception, in a preconception care consultation.

**For further research, we recommend...**

- Refinement of the attitude measure as used in this thesis. It should be directed more explicitly to a woman's attitude towards her own participation in prenatal screening (instead of being open to misinterpretation as attitude towards the general availability of prenatal screening). In addition, it should be investigated whether attitude for the test procedure as a whole (screening, possibly followed by diagnostics and termination of the pregnancy) can be measured with only one item, as is currently done.
- Development of knowledge measures specific to prenatal screening for trisomy 18 and 13. In addition, it should be investigated whether attitude about participating in this extended screening program can be measured with (refinement of) the current attitude measure.

- Evaluating whether the costs of participating in prenatal screening for Down syndrome (for women younger than 36 years of age) are a barrier in actual participation.
- Receiving more insight in factors attributing to the low number of participants in prenatal screening for Down syndrome in the Netherlands, as compared to other European countries.
- Taking into account, in future evaluation studies, the question whether the theoretical difference between the offer and provision of information on prenatal screening, is experienced as such in practice by pregnant women, and whether this information offer provides a realistic opportunity for these women to express their right not to know.

**For policy making and practice, we recommend...**

- The measurement of levels of informed decision-making as an outcome measure for the quality of the information provision procedure on first- and second-trimester prenatal screening in The Netherlands should become standard practice. Our evaluations of informed decision-making about first-trimester prenatal screening for Down syndrome and second-trimester ultrasound screening for fetal anomalies, may serve as pilot studies for these quality monitoring studies at national levels.
- An implementation trajectory is needed, directed at all actors and stakeholders, to make future quality assurance studies on information provision being perceived as an integral part of prenatal care.
- Quality assurance by regular monitoring should include a measurement of knowledge about trisomy 13 and 18, attitude towards participating in the screening program and choosing to participate in screening for Down syndrome, with or without choosing to accept personalised risk information on trisomy 18 and 13.
- Monitoring of the procedure for providing information about prenatal screening for Down syndrome and for fetal anomalies is a way to assess whether the objective of informed decision-making is fulfilled. We recommend using resulting insights in levels of informed decision-making to generate further investigations (evaluation) into the underlying causes of possible differences between regions or groups (e.g. hospitals versus midwifery practices) and to provide a starting point for improvements in the (procedure of the offer of) information.
- In addition to determining levels of informed decision-making, we recommend to investigate whether careful, non-directive counseling on first- and second-trimester prenatal screening is provided. All of the knowledge domains we identified as relevant in informed decision-making on these prenatal screening programs, should be present in the counseling session.
- It should be investigated whether information on first-trimester prenatal screening for Down syndrome is provided together with information on second-trimester ultrasound screening for fetal anomalies in one counseling session, or whether information on these programs is provided in different sessions, at different moments in time. We expect major practice variation and suggest, for informed decision-making to be reached, counseling at two different points in time; one counseling session in the first-trimester of pregnancy (before deciding about participating in screening with the combined test) and one in the second-trimester of pregnancy (before deciding about participating in ultrasound screening).
- An information offer on prenatal screening for Down syndrome should be implemented in preconception care consultations.

## Towards a national monitor of informed decision-making on prenatal screening

Currently, Erasmus MC (on behalf of the Centre for Population Research [CvB] of the Dutch National Institute for Public Health and the Environment [RIVM]) performs a first national monitor of informed decision-making on prenatal screening, using both hard-copy and digital versions of the questionnaires (in Dutch, Turkish and standard-Arabic) for pregnant women, and the linkage of data with Peridos. This monitoring should become a regular procedure to assure a satisfactory organisation of prenatal screening. When gaps in knowledge are observed (e.g. knowledge on the condition Down syndrome, knowledge on the voluntary nature of first- and second- trimester prenatal screening) this should contribute to the development of improved information provided through oral and/or written communication to pregnant women and their partners about prenatal screening, in order to make informed decision-making possible.

# Samenvatting

# Introductie

## Aangeboren afwijkingen

Aangeboren afwijkingen zijn de voornaamste oorzaak van sterfte en morbiditeit bij kinderen onder de leeftijd van 1 jaar. Sinds een aantal decennia is een toenemend aantal aangeboren afwijkingen al voor de geboorte te diagnosticeren door het gebruik van prenatale screening. In dit proefschrift zal nader worden gekeken naar de procedure van informatievoorziening, geïnformeerde besluitvorming en deelname aan prenatale screening op Downsyndroom en de 20-weken echo. Downsyndroom en neuralebuisdefecten zijn respectievelijk chromosomaal en structureel aangeboren afwijkingen, die voorafgaand aan de geboorte kunnen worden gediagnosticeerd. Downsyndroom en neuralebuisdefecten zijn de primaire focus van het Nederlandse programma voor prenatale screening op aangeboren afwijkingen.

## Prenatale screening op Downsyndroom en structureel aangeboren afwijkingen in Nederland

Sinds 2007 bestaat er in Nederland een nationaal screeningsprogramma voor Downsyndroom, beschikbaar voor alle zwangeren. Vóór 2007 was het alleen toegestaan informatie over een kans bepalende test voor Downsyndroom aan te bieden, als een zwangere daar zelf om vroeg. Er werd alleen invasieve diagnostiek aangeboden aan zwangeren boven de leeftijd van 36 jaar, met een hoog-risico of met een medische indicatie. In het huidige programma krijgen *alle* zwangere actief informatie aangeboden over de mogelijkheid tot deelname aan prenatale screening op Downsyndroom. Alleen als de zwangere aangeeft dat ze geïnformeerd wil worden, wordt het consult gevolgd door een counselingafspraak. Ondanks het feit dat iedere zwangere vrouw informatie aangeboden krijgt over het screeningsprogramma, dienen sommige vrouwen zelf te voorzien in de kosten die aan deelname zijn verbonden; vrouwen onder de leeftijd van 36 jaar dienen deze kosten zelf te betalen, tenzij ze hiervoor aanvullend zijn verzekerd of ze een geregistreerde medische indicatie hebben voor invasieve diagnostiek. Als er uit de screening een verhoogde kans uitslag op Downsyndroom blijkt, worden de kosten van invasieve diagnostiek vergoed. Vrouwen boven de leeftijd van 36 jaar hebben een leeftijd gerelateerde indicatie voor prenatale diagnostiek en kunnen zodoende kiezen voor een vruchtwaterpunctie of vlokkentest zonder eerst aan prenatale screening te hoeven deelnemen. Deelname aan invasieve diagnostiek is gratis.
Echoscopische screening op aangeboren afwijkingen in het tweede trimester van de zwangerschap (20-weken echo) is een standaard onderdeel van de zorg geworden in Nederland. Net zoals bij prenatale screening op Downsyndroom, is het doel van de 20-weken echo geformuleerd als 'het tijdig informeren van de zwangere vrouw en haar partner over mogelijke afwijking (en) die het kind zou kunnen hebben en het bieden van handelingsopties als het kind een afwijking heeft'. Om dit doel te bereiken zijn er voorwaarden gesteld aangaande het informatie aanbod. Het geven van relevante, kwalitatief goede informatie over prenatale screening heeft als doel geïnformeerde besluitvorming van de zwangere over (niet-) deelname aan het screeningsprogramma.

## Geïnformeerde besluitvorming

Een geïnformeerd besluit heeft twee kenmerken. Allereerst is het gebaseerd op relevante, kwalitatief goede informatie, resulterend in adequate beslissingsrelevante kennis. Daarnaast dient een geïnformeerd besluit overeen te komen met de waarden van de besluitvormer.

Omdat kwalitatief hoogwaardige informatievoorziening aan diegenen die geïnformeerd wensen te worden, een essentieel onderdeel is van het Nederlandse programma voor prenatale screening, kan de mate van geïnformeerde besluitvorming gebruikt worden als een indicator voor de kwaliteit van de informatievoorzieningsprocedure.
In Nederland heeft experimenteel en kleinschalig observationeel onderzoek geïnformeerde besluitvorming aangetoond bij 51 tot 68% van de zwangere vrouwen. Echter, deze onderzoeken werden uitgevoerd in de periode voorafgaand aan de implementatie van het huidige nationale screeningsprogramma, met daarin het routine informatieaanbod aan alle zwangere vrouwen. In een recente Nederlandse studie, uitgevoerd na de implementatie van het standaard aanbod van informatie over prenatale screening in 2007, werden aanzienlijke etnische verschillen in geïnformeerde besluitvorming over prenatale screening op Downsyndroom gerapporteerd.

**Dit proefschrift**

Tot op heden zijn er geen evaluaties uitgevoerd naar de kwaliteit van de informatievoorziening over prenatale screening, in de 'real life setting' van een nationaal screeningsprogramma voor Downsyndroom en structureel aangeboren afwijkingen. Bij aanvang van dit proefschrift waren er geen data beschikbaar over het informatieproces, geïnformeerde besluitvorming en deelname aan prenatale screening op Downsyndroom en aangeboren structurele afwijkingen.
Het doel van dit proefschrift was de evaluatie van de informatievoorziening, geïnformeerde besluitvorming en deelname, in de context van het Nederlandse programma voor prenatale screening. De volgende onderzoeksvragen zijn geformuleerd, onderverdeeld in drie centrale thema's.

# Onderzoeksvragen

**Deel 1- Kennis**

*1a. Wat is de inhoud van relevante kennis, noodzakelijk voor geïnformeerde besluitvorming over (niet-) deelname aan eerste- trimester prenatale screening op Downsyndroom?* (Hoofdstuk 2).
*1b. Wat is de inhoud van relevante kennis, noodzakelijk voor geïnformeerde besluitvorming over (niet-) deelname aan tweede trimester echoscopische screening op aangeboren afwijkingen (20-weken echo)?* (Hoofdstuk 2).
*1c. Wat zijn de verschillen tussen de inhoud van relevante kennis, noodzakelijk voor geïnformeerde besluitvorming over tweede-trimester echoscopische screening op aangeboren afwijkingen en eerste-trimester prenatale screening op Downsyndroom?* (Hoofdstuk 3).

**Deel 2: Kwaliteitswaarborging van het informatieproces**

***Eerste-trimester screening op Downsyndroom met de combinatietest***
2a. De informatievoorzieningsprocedure over eerste-trimester prenatale screening op Downsyndroom met de combinatietest: *Wordt aan alle zwangere vrouwen informatie aangeboden over prenatale screening op Downsyndroom? Hoeveel vrouwen accepteren dit informatieaanbod en hoeveel van deze vrouwen ontvangen daadwerkelijk informatie?* (Hoofdstuk 4).
2b. Geïnformeerde besluitvorming als indicator voor de kwaliteit van de informatievoorzieningsprocedure over eerste-trimester prenatale screening op Downsyndroom met de combinatietest: *Is de kennis van zwangere vrouwen voldoende? Wat is de attitude van zwangere vrouwen*

*over hun eigen deelname aan prenatale screening op Downsyndroom? In welke mate is het besluit om (niet-) deel te nemen aan prenatale screening op Downsyndroom, gebaseerd op een geïnformeerde keuze? Wat zijn de determinanten van geïnformeerde besluitvorming?* (Hoofdstuk 4).

***Echoscopische screening op aangeboren afwijkingen in het tweede trimester van de zwangerschap (20-weken echo)***

2c. De informatievoorzieningsprocedure over echoscopische screening op aangeboren afwijkingen in het tweede trimester van de zwangerschap *Wordt aan alle zwangere vrouwen informatie aangeboden over de 20-weken echo? Hoeveel vrouwen accepteren dit informatieaanbod en hoeveel van deze vrouwen ontvangen daadwerkelijk informatie?* (Hoofdstuk 5).

2b. Geïnformeerde besluitvorming als indicator voor de kwaliteit van de informatievoorzieningsprocedure over echoscopische screening op aangeboren afwijkingen in het tweede trimester van de zwangerschap *Is de kennis van zwangere vrouwen voldoende? Wat is de attitude van zwangere vrouwen over hun eigen deelname aan de 20-weken echo. In welke mate is het besluit om (niet-) deel te nemen aan de 20-weken echo, gebaseerd op een geïnformeerde keuze? Wat zijn de determinanten van geïnformeerde besluitvorming?* (Hoofdstuk 5).

***Vergelijking tussen eerste- en tweede trimester screening***

*2e Verschillen kennis, attitude en deelname aan echoscopische screening op aangeboren afwijkingen in het tweede trimester van de zwangerschap, van kennis, attitude en deelname aan eerste-trimester prenatale screening op Downsyndroom met de combinatietest? Verschilt besluitvorming over deelname aan eerste- trimester prenatale screening op Downsyndroom van besluitvorming over echoscopische screening op aangeboren afwijkingen in het tweede trimester van de zwangerschap?* (Hoofdstuk 5).

## Deel 3: Etnische verschillen in deelname aan prenatale screening op Downsyndroom

*3a. Hoeveel vrouwen van verschillende etnische herkomst nemen deel aan prenatale screening op Downsyndroom, in de regio Zuidwest Nederland?* (Hoofdstuk 6)

*3b. In welke mate verschillen vrouwen van diverse etnische groepen in deelname aan prenatale screening?* (Hoofdstuk 6)

*3c. Is deelname aan prenatale screening gerelateerd aan etniciteit, gecontroleerd voor verschillen in socio-economische status en leeftijd?* (Hoofdstuk 6)

## Deel 4 – Het informatieaanbod over prenatale screening op Downsyndroom, voorafgaand aan de conceptie

*4a. Wensen vrouwen informatie te ontvangen over prenatale screening op Downsyndroom, voorafgaand aan de conceptie?* (Chapter 7).

*4b. Wat zijn de voor- en nadelen van informatievoorziening over prenatale screening op Downsyndroom voorafgaand aan de conceptie, naast het bestaande aanbod tijdens het eerste prenatale consult, vanuit een ethisch perspectief?* (Chapter 7).

# Antwoorden op de onderzoeksvragen

## Deel 1- Kennis

In hoofdstuk 2 en 3 wordt antwoord gegeven op de onderzoeksvragen horend bij het eerste deel van dit proefschrift. Gebaseerd op expertopinie 's en wetenschappelijke literatuur, definieerden we de domeinen en items die als representatief worden beschouwd voor beslissingsrelevante kennis, noodzakelijk voor geïnformeerde besluitvorming over screeningsdeelname (Onderzoeksvraag 1a en 1b). Dit resulteerde in een kennisvragenlijst, geschikt voor het bepalen van de mate van beslissingsrelevante kennis, noodzakelijk voor geïnformeerde besluitvorming over deelname aan eerste- trimester prenatale screening op Downsyndroom met de combinatietest, en een kennisvragenlijst voor het bepalen van de mate van beslissingsrelevante kennis bij de 20-weken echo.
In hoofdstuk 3 onderzochten we verschillen tussen de inhoud van beslissingsrelevante kennis, noodzakelijk voor geïnformeerde besluitvorming over de 20-weken echo, en de inhoud van beslissingsrelevante kennis, noodzakelijk voor geïnformeerde besluitvorming over eerste-trimester prenatale screening op Downsyndroom met de combinatietest (Onderzoeksvraag 1c). In de consultatie van experts werden alle domeinen beoordeeld als zeer relevant voor beide vormen van screening. Er bestond een positieve correlatie voor de relevantie van de kennisdomeinen tussen beide vormen van screening. Zowel het kennisdomein 'Wat te doen bij een afwijkend test resultaat' als het kennisdomein 'De betekenis van een afwijkend test resultaat' werd door de deelnemende experts als belangrijker beoordeeld bij eerste-trimester screening op Downsyndroom dan de 20-weken echo.
De kennisvragenlijsten die we ontwikkelden voor het eerste deel van dit proefschrift, zijn geschikt voor grootschalige implementatie ter bepaling van de mate van geïnformeerde besluitvorming over prenatale screening.

## Deel 2: Kwaliteitswaarborging van het informatieproces

In hoofdstuk 4 en 5 wordt antwoord gegeven op de onderzoeksvragen horend bij het tweede deel van dit proefschrift. In hoofdstuk 4 toonden we aan dat verloskundig hulpverleners informatie over eerste- trimester prenatale screening op Downsyndroom met de combinatietest, aanbieden aan bijna alle zwangere vrouwen. Van deze vrouwen wenst 62,6% informatie te ontvangen, 81,9% van laatstgenoemde groep ontvangt ook daadwerkelijk informatie (Onderzoeksvraag 2a).
Beslissingsrelevante kennis over prenatale screening op Downsyndroom was voldoende bij 89% van de vrouwen die deelnamen aan ons onderzoek. Kennis over de aandoening Downsyndroom bleek vaker onvoldoende te zijn dan kennis over het programma voor prenatale screening op Downsyndroom. Bijna de helft van de zwangeren gaf aan een negatieve attitude te hebben over mogelijke eigen deelname aan prenatale screening op Downsyndroom. Een minderheid van de zwangeren (35,8%) had de intentie deel te nemen aan prenatale screening op Downsyndroom. In totaal werd door 75,5% van alle deelnemende vrouwen aan dit onderzoek een geïnformeerd besluit genomen over mogelijke deelname aan de combinatietest; dit was het geval bij 94,3% van de deelneemsters aan de screening en bij 64,9% van de niet-deelneemsters. Zelf-gerapporteerde religieuze activiteit bleek samen te hangen met lagere kennisniveaus over prenatale screening op Downsyndroom, een negatievere attitude ten aanzien van mogelijke eigen deelname en de intentie om niet deel te nemen. In een multivariate analyse was opleidingsniveau de enige significante determinant van geïnformeerde besluitvorming. Voldoende kennis over het screeningsprogramma en een positieve attitude ten aanzien

van eventuele eigen deelname, hingen samen met de intentie om deel te nemen aan prenatale screening op Downsyndroom (Onderzoeksvraag 2b).

In hoofdstuk 5 lieten we zien dat verloskundig hulpverleners informatie over de 20-weken echo aanbieden aan bijna alle zwangere vrouwen. Van deze vrouwen wenst 92,3% de informatie te ontvangen, 94,3% van laatstgenoemde groep ontvangt de informatie ook daadwerkelijk (Onderzoeksvraag 2c).
Beslissingsrelevante kennis over de 20-weken echo was voldoende bij 93,5% van de zwangeren die deelnamen aan dit onderzoek. Zwangeren hadden relatief weinig kennis over het feit dat deelname aan de 20-weken echo kan leiden tot moeilijke keuzes, en over de kans dat een kind een aangeboren afwijking heeft. Van de deelnemende zwangere vrouwen aan dit onderzoek, had 90,4% een positieve attitude over deelname aan de 20-weken echo, 87,7% had de intentie om deel te nemen. Door 88% van alle vrouwen die deelnamen aan dit onderzoek werd een geïnformeerd besluit gemaakt, en 95,7% van deze beslissingen was een besluit deel te nemen aan de 20-weken echo. Van de 12% niet- geïnformeerde keuzes, was 72,5% een keuze om deel te nemen aan de 20-weken echo.

Zwangere vrouwen in onze onderzoeksgroep hadden meer kennis over de 20-weken echo dan over prenatale screening op Downsyndroom met de combinatietest voor wat betreft de kennisdomeinen 'Betekenis van een normaal testresultaat' en 'Mogelijke bevindingen uit vervolgonderzoek'. Zwangere vrouwen in onze onderzoeksgroep hadden minder kennis over de 20-weken echo dan over prenatale screening op Downsyndroom met de combinatietest voor wat betreft de kennisdomeinen 'Test procedure', 'Mogelijke negatieve gevolgen van de test procedure', 'Wat te doen na vervolgonderzoek', en 'Vrijwilligheid van de test'. Zwangeren hadden een positievere attitude ten aanzien van eventuele eigen deelname aan de 20-weken echo dan ten aanzien van eventuele eigen deelname aan prenatale screening op Downsyndroom met de combinatietest. Bijna alle vrouwen wilden deelnemen aan de 20-weken echo, slechts een minderheid van de zwangeren wilde deelnemen aan prenatale screening op Downsyndroom. Zowel voor prenatale screening op Downsyndroom als voor de 20-weken echo vonden we hoge niveaus van geïnformeerde besluitvorming.

**Deel 3: Etnische verschillen in deelname aan prenatale screening op Downsyndroom**

In hoofdstuk 6 wordt antwoord gegeven op de onderzoeksvragen horend bij het derde deel van dit proefschrift. De algehele deelname aan prenatale screening op Downsyndroom in onze onderzoekspopulatie (regio Zuidwest Nederland) wordt geschat op 26%. De deelname is het hoogst onder vrouwen afkomstig uit andere (niet-Nederlandse) Westerse landen (33%) en het laagst onder vrouwen afkomstig uit Noord-Afrika (Marokko) (8%) (Onderzoeksvraag 3a).
Voor vrouwen van Noord-Afrikaanse, Turkse, Arubaans/Antilliaans en andere niet-Westerse etnische origine is het minder waarschijnlijk dat ze deelnemen aan prenatale screening op Downsyndroom dan voor Nederlandse vrouwen, terwijl het voor vrouwen van andere Westerse (niet- Nederlandse) origine waarschijnlijker is dat ze deelnemen aan prenatale screening op Downsyndroom dan voor Nederlandse vrouwen. Marokkaanse vrouwen verschillen het meest voor wat betreft deelname aantal van Nederlandse vrouwen, gevolgd door vrouwen van Turkse origine. Er werden geen significante verschillen gevonden tussen vrouwen van Surinaamse en Nederlandse afkomst (Onderzoeksvraag 3b).

Na het controleren voor verschillen in sociaal-economische status en leeftijd, bleek deelname aan prenatale screening voor Downsyndroom in Nederland gerelateerd aan de etniciteit van de zwangere vrouw. Voor vrouwen van Noord-Afrikaanse (Marokkaanse), Turkse en Arubaans/Antilliaanse etnische origine was het minder waarschijnlijk dat ze deelnamen aan prenatale screening op Downsyndroom dan voor Nederlandse vrouwen, terwijl het voor vrouwen van andere Westerse (niet- Nederlandse) origine waarschijnlijker is dat ze deelnemen aan prenatale screening op Downsyndroom dan voor Nederlandse vrouwen. Het verschil tussen vrouwen van andere niet-Westerse etnische origine en Nederlandse vrouwen was niet significant meer na controle voor verschillen in socio-economische status en leeftijd. Vrouwen van Surinaamse origine nemen even vaak deel aan prenatale screening op Downsyndroom als Nederlandse vrouwen (Onderzoeksvraag 3c).

**Deel 4 – Het informatieaanbod over prenatale screening op Downsyndroom, voorafgaand aan de conceptie**

In hoofdstuk 7 wordt antwoord gegeven op de onderzoeksvragen horend bij het vierde deel van dit proefschrift.
Van alle vrouwen die vragenlijsten invulden over het ontvangen van informatie over prenatale screening op Downsyndroom voorafgaand aan de conceptie, gaf 55,7% aan voorafgaand aan de zwangerschap na te hebben gedacht over prenatale screening op Downsyndroom. 28% van de respondenten gaf aan informatie te hebben gehad (niet noodzakelijk door een verloskundig hulpverlener gegeven) over prenatale screening op Downsyndroom voorafgaand aan de zwangerschap. Van alle vrouwen in dit onderzoek gaf 84,6% aan geen informatie te hebben willen ontvangen over prenatale screening op Downsyndroom voorafgaand aan de zwangerschap. Tijdens de zwangerschap werd het informatieaanbod geweigerd door 33,3% van alle zwangeren. Van deze zwangeren gaf 89,6% (retrospectief) aan ook geen informatie te hebben gewild voorafgaand aan de zwangerschap (Onderzoeksvraag 4a).

In dit proefschrift werden drie argumenten genoemd voor het geven van informatie over prenatale screening op Downsyndroom voorafgaand aan de zwangerschap, naast het bestaande informatieaanbod tijdens het eerste consult van de zwangerschap. Allereerst zou de kans op het maken van een geïnformeerd besluit kunnen worden vergroot door de aanvankelijke informatie los te koppelen van latere beslissingen, en door vrouwen voldoende tijd te geven om na te denken. Daarnaast zou de kans op gelijke toegang tot prenatale screening toenemen. Ondanks twee argumenten tegen het geven van informatie over prenatale screening op Downsyndroom voorafgaand aan de zwangerschap (vrouwen hun voorkeur om informatie stap voor stap te ontvangen en het risico op het geven van een directieve boodschap), stellen wij voor om een informatie *aanbod* ten aanzien van prenatale screening op Downsyndroom te implementeren in de periode voorafgaand aan de zwangerschap. Door de informatie *aan te bieden* wordt aan toekomstige ouders de mogelijkheid gegeven om te beslissen of ze informatie willen ontvangen over prenatale screening op Downsyndroom, in aanvulling op het huidige informatieaanbod (in Nederland) en de informatievoorziening (internationaal). Op deze manier wordt zowel het recht op weten als het recht op niet- weten van de zwangeren gerespecteerd (Onderzoeksvraag 4b).

# Discussie

De discussie van dit proefschrift begint met een samenvatting van de belangrijkste bevindingen per onderzoeksvraag. Sterke en zwakke punten van het onderzoeksdesign, die in overweging genomen moeten worden bij de interpretatie van de resultaten, worden besproken.
De kennisvragenlijsten die zijn ontwikkeld bevatten alle domeinen die door experts (professionals in het veld van de prenatale screening en zwangeren zelf) relevant werden bevonden. Echter, ze zijn slechts getest in een kleine, selectieve groep.

Onze kwaliteitsborgingsonderzoeken, beschreven in het tweede deel van dit proefschrift, werden uitgevoerd in een niet-experimentele setting. In tegenstelling tot voorgaande studies, waarin geïnformeerde besluitvorming werd onderzocht op kleine schaal en/of in een vooraf sterk geselecteerde groep, vloeien onze resultaten voort uit een 'real life' setting, met daarin alle zwangeren (zowel deelnemers als niet deelnemers aan de screening) in een bepaald gebied. De afwezigheid van data over daadwerkelijke deelname vormt een beperking op het vlak van de interne validiteit. De relatief lage en geselecteerde respons is een bedreiging voor de externe validiteit van het huidige onderzoek. De respons moest worden geschat vanwege het anonieme karakter van het vragenlijstonderzoek.

Een beperking van het derde deel van dit proefschrift (bepaling van etnische verschillen in deelname aan prenatale screening op Downsyndroom) is dat, ondanks het feit dat er gecontroleerd is voor verschillende achtergrondvariabelen (leeftijd, sociaale-conomische status), 'residual confounding' de relatie tussen etniciteit en deelname kan hebben beïnvloed.

In het vierde deel van dit proefschrift combineerden we een empirische analyse met een ethische reflectie, om te onderzoeken of informatie over prenatale screening op Downsyndroom voorafgaand aan de conceptie zou moeten worden gegeven. De resultaten van onze empirische analyse vormden een startpunt voor ons onderzoek, in plaats van een resultaat.

**Interpretatie en implicaties van de resultaten**

De kennisvragenlijsten die zijn ontwikkeld en gebruikt in dit proefschrift, zijn ontwikkeld met als uiteindelijke doel het gebruik bij grootschalige monitoring, voor het meten van kennis als een uitkomst indicator van de kwaliteit van de informatievoorzieningsprocedure. Het meten van kennis heeft een indicatieve functie; nationale monitoring van geïnformeerde besluitvorming over prenatale screening moet worden uitgevoerd om te waarborgen dat de aan de voorwaarde van geïnformeerde besluitvorming voldoende wordt voldaan. Ieder item van de kennisvragenlijst dient te worden beschouwd als een indicator, getrokken uit grotere steekproef aan andere potentiele indicatoren, representatief voor de inhoud van het kennisdomein. Als er opmerkelijke verschillen, bijvoorbeeld op regionaal- of op praktijkniveau worden geobserveerd, is er verdere evaluatie nodig om inzicht te krijgen in de oorzaak van deze verschillen.
Tot op heden is er weinig bekend over de kwaliteit van de informatievoorzieningsprocedure over prenatale screening in Nederland. Beschikbare data geven aan dat counseling verbeterd zou moeten worden, vooral met betrekking tot informatievoorziening over de aandoening Downsyndroom. In het huidige onderzoek stelden we niveaus van geïnformeerde besluitvorming vast, als een indicator voor de kwaliteit van de informatievoorzieningsprocecure. Verschillende overwegingen werden gemaakt aangaande het meten van kennis en attitude. De kennisvragenlijsten die we ontwikkelden kunnen worden gebruikt in nationale monitoring van

geïnformeerde besluitvorming. De attitude meting die we gebruikten in dit proefschrift dient te worden verfijnd.

Prenatale screening op Downsyndroom en de 20-weken echo zijn verschillende onderzoeken, uitgevoerd op verschillende momenten in de zwangerschap; de combinatietest in het eerste trimester, de 20-weken echo in het tweede trimester. Echter, ondanks deze verschillen hebben zij één gemeenschappelijk doel; het opsporen van aangeboren afwijkingen. Zwangeren kennen verschillende doelstellingen toe aan eerste- en tweede trimester prenatale screening en zij percipiëren deze als substantieel verschillend. Als we de resultaten van beide kwaliteitsborgingsstudies bekijken, zien we deze verschillende percepties van zwangeren terug. Deze uiteenlopende percepties worden weerspiegeld in sterk verschillende deelname percentages.

Voor jongere vrouwen geldt dat het aanbod om deel te nemen aan prenatale screening op Downsyndroom wordt gevolgd door het verzoek om te betalen als men daadwerkelijk wil deelnemen. Op landelijk niveau is het onbekend in hoeverre dit kostenaspect een reden vormt om niet (in staat te zijn) deel te nemen, of in welke mate dit mogelijk leidt tot ongelijke toegang tot prenatale screening.

Een belangrijk aspect van het Nederlandse programma voor prenatale screening is het onderscheid tussen het informatie aanbod, en de daadwerkelijke informatievoorziening. In Nederland valt prenatale screening onder de Wet op de Geneeskundige Behandelings Overeenkomst (WGBO), vastgelegd in het Burgerlijk Wetboek. Het 'recht op niet-weten' is een van de concepten geformuleerd in de WGBO (art 7:449). In de context van prenatale screening betekent dit recht dat vrouwen informatie over prenatale screening mogen weigeren. Echter, om iets te kunnen weigeren dient het je eerst te worden aangeboden. Als in informatie wordt gegeven (wat momenteel internationaal veelal gebeurt), in plaats van aangeboden, krijgen vrouwen de informatie zonder deze te hebben kunnen weigeren. Daarom bestaat er in Nederland een informatieaanbod. In de praktijk wordt dit uitgevoerd door zwangeren te vragen of zij informatie willen ontvangen over prenatale screening. Verloskundig hulpverleners mogen alleen informatie geven als de zwangere aangeeft deze te willen ontvangen. Vanuit een internationaal perspectief is dit 'Nederlands onderscheid' (tussen het aanbieden en het daadwerkelijk verstrekken van informatie), als belichaming van het recht op niet- weten, uniek. Ondanks de theoretische juistheid van dit onderscheid, is tot op heden de praktische effectiviteit nog niet onderzocht.

Nederlandse deelnamepercentages aan de 20-weken echo zijn vergelijkbaar met Europese deelnamepercentages. Echter, voor eerste-trimester prenatale screening op Downsyndroom is het deelnamepercentage in Nederland relatief hoog, in vergelijking met andere Europese landen. Het Nederlandse programma voor prenatale screening richt zich niet op het behalen van hoge deelnamepercentages. Daarom is het relatief lage aantal vrouwen dat deelneemt aan de screening, in vergelijking met andere Europese landen, geen probleem, als de deelnamepercentages maar gebaseerd zijn op geïnformeerde besluitvorming. Echter, het zou interessant zijn meer inzicht te verkrijgen in de oorzaken van deze verschillen in deelname.

De overheidsvergunning voor het nationale screeningsprogramma op Downsyndroom, zoals geïmplementeerd in 2007, was beperkt tot screening op Trisomie 21. Verloskundig hulpverleners mogen niet rapporteren over de risico's op Trisomie 13 en 18. Echter, aangezien een toenemend aantal zorgverleners het potentiele belang kent van serumscreening op Trisomie 13 en 18, inclusief enkele die hun cliënten al counselen over deze afwijkingen, en gezien het feit

dat deze trisomieën gerelateerd zijn aan vroege maternale complicaties, is recent besloten om de vergunning uit te breiden naar deze beide trisomieën.

Geïnformeerde besluitvorming kan lastiger worden als niet-invasieve prenatale diagnostiek wordt geïmplementeerd. Door niet-invasieve prenatale diagnostiek hoeven procedure gerelateerde risico's niet meer te worden besproken, waardoor de besluitvormer kan nalaten om de mogelijke implicaties van de deelname aan de test te overwegen.

**Conclusies**

- De kennisvragenlijsten zoals beschreven in dit proefschrift kunnen worden gebruikt voor routinematige toepassing in grootschalige programma-evaluaties over de kwaliteit van de informatievoorzieningsprocedure m.b.t. prenatale screening.
- Zowel bij eerste-trimester prenatale screening op Downsyndroom met de combinatietest, als bij tweede-trimester prenatale screening als bij de 20-weken echo, vinden we hoge niveaus van geïnformeerde besluitvorming in onze steekproef. Daarom concluderen we dat de huidige informatievoorzieningsprocedure over prenatale screening van goede kwaliteit is, en dat het standaard-aanbod van informatie zoals dat momenteel bestaat, niet geleid heeft tot 'normalisering' van deelname aan prenatale screening.
- Zowel bij deelnemers als bij niet-deelnemers aan prenatale screening op Downsyndroom, zijn de kennisniveaus over de aandoening waarop wordt gescreend, lager dan de kennisniveaus over het screeningsprogramma.
- Zwangere vrouwen hebben een beduidend positievere attitude over eventuele eigen deelname aan de 20-weken echo, dan over eventuele eigen deelname aan screening op Downsyndroom, dit terwijl beide screeningsprogramma's een vergelijkbaar doel hebben. Dit is terug te zien in hogere deelname aantallen voor de 20-weken echo, vergeleken met eerstetrimester screening op Downsyndroom.
- De evaluaties van geïnformeerde besluitvorming over prenatale screening op Downsyndroom en de 20-weken echo in Nederland, zoals uitgevoerd in dit proefschrift, kunnen dienen als pilotstudie voor kwaliteitsborgingsonderzoek op nationaal niveau.
- Deelname aan prenatale screening op Downsyndroom in Nederland ligt lager voor specifieke niet-Westerse etnische minderheden dan voor autochtone Nederlanders.
- Informatie over prenatale screening op Downsyndroom dient te worden aangeboden in een pre-conceptioneel consult, naast het huidige bestaande aanbod tijdens het eerste prenatale bezoek.

**Aanbevelingen voor verder onderzoek**

- Het meetinstrument dat in dit proefschrift is gebruikt voor het vaststellen van de attitude van zwangeren, dient te worden verfijnd. Het zou meer gericht moeten zijn op vrouwen hun attitude ten aanzien van hun eigen deelname aan prenatale screening (in plaats van dat het foutief kan worden geinterpreteerd als zijnde gericht op de attitude ten aanzien van het bestaan van prenatale screening in het algemeen). Daarnaast dient te worden onderzocht of attitude ten aanzien van de testprocedure als geheel (screening, mogelijk gevolgd door diagnostiek en afbreken van de zwangerschap) kan worden gemeten met 1 item, zoals momenteel wordt gedaan.
- Er dienen kennis vragenlijsten te worden ontwikkeld specifiek voor prenatale screening op trisomie 13 en 18. Daarnaast dient te worden onderzocht of attitude ten aanzien van het

uitgebreide screeningsprogramma kan worden gemeten met (verfijning van) het huidige attitude meetinstrument.
- Er dient te worden geëvalueerd of de kosten voor deelname aan prenatale screening (voor vrouwen van jonger dan 36 jaar) een drempel zijn om deel te nemen.
- Er dient meer inzicht verkregen te worden in factoren die bijdragen aan het relatief lage deelname cijfer aan prenatale screening op Downsyndroom in Nederland, in vergelijking met andere Europese landen.
- In vervolgonderzoek dient rekening gehouden te worden met de vraag of het theoretische onderscheid tussen het aanbod en de voorziening van informatie over prenatale screening, ook in de praktijk als zodanig wordt ervaren door zwangeren, en of dit informatie aanbod een realistische mogelijkheid biedt voor deze vrouwen om hun recht op niet- weten te uiten.

**Aanbevelingen voor beleidsvorming en praktijk**

- Het bepalen van de mate van geïnformeerde besluitvorming als een uitkomstmaat voor de kwaliteit van de informatievoorzieningsprocedure over eerste- en tweede trimester prenatale screening in Nederland, dient tot de standaard praktijk te gaan behoren. De evaluaties van geïnformeerde besluitvorming over eerste- trimester prenatale screening op Downsyndroom en de 20-weken echo, zoals uitgevoerd in dit proefschrift, kunnen dienen als pilotstudie voor deze kwaliteitsborgings onderzoeken op nationaal niveau.
- Er is een implementatietraject nodig, gericht op alle actoren en belanghebbenden, om toekomstige kwaliteitsborgingsonderzoeken over de informatievoorzieningsprocedure rondom prenatale screening als integraal deel van de prenatale zorg te laten worden beschouwd.
- Kwaliteitsborging door regelmatige monitoring moet een meting van kennis over trisomie 13 en trisomie 18 omvatten, attitude ten aanzien van deelname aan het screeningsprogramma en de keuze om (niet-) deel te nemen aan prenatale screening op Downsyndroom, met of zonder de keuze gepersonaliseerde risico-informatie over trisomie 13 en trisomie 18 te ontvangen.
- Monitoring van de informatievoorzieningsprocedure over prenatale screening op Downsyndroom en de 20-weken echo is een manier om te bepalen of het doel van geïnformeerde besluitvorming wordt vervuld. Wij bevelen aan om resulterende inzichten in niveaus van geïnformeerde besluitvorming te gebruiken voor verder onderzoek (evaluatie) naar de onderliggende oorzaken van mogelijke verschillen tussen regio's of groepen (bijv. ziekenhuizen versus verloskundigenpraktijk) en als startpunt voor verbeteringen in de informatievoorzieningsprocedure.
- Naast het bepalen van de mate van geïnformeerde besluitvorming, bevelen we aan te onderzoeken of in niet- directieve counseling over eerste- en tweede trimester screening wordt voorzien. Alle kennisdomeinen die wij identificeerden als relevant voor geïnformeerde besluitvorming over deze screeningsprogramma's, dienen aan bod te komen in de counseling.
- Het dient te worden onderzocht of informatie over eerste-trimester prenatale screening op Downsyndroom gelijktijdig wordt gegeven met informatie over de 20-weken echo (in 1 counselingsgesprek) of dat informatie over deze twee vormen van screening op verschillende momenten in de tijd (in meerdere counselingsgesprekken) wordt gegeven. We verwachten grote verschillen tussen praktijken en adviseren, voor het bereiken van geïnformeerde besluitvorming, counseling op twee verschillende momenten; één counselingsgesprek in het eerste trimester van de zwangerschap (voorafgaand aan een beslissing over deelname aan de combinatietest) en één in het tweede trimester van de zwangerschap (voorafgaand aan een beslissing over deelname aan de 20-weken echo).

- Het aanbod informatie te ontvangen over prenatale screening op Downsyndroom, dient te worden geïmplementeerd in een preconceptieconsult.

**Naar een nationale monitor van geïnformeerde besluitvorming over prenatale screening**

Op dit moment voert het Erasmus MC (in opdracht van het Centrum voor Bevolkingsonderzoek [CvB] van het Rijksinstituut voor Volksgezondheid en Milieu [RIVM]) een eerste nationale monitor uit naar geïnformeerde besluitvorming over prenatale screening, door middel van zowel een papieren als digitale versie van de vragenlijst voor zwangeren (Nederlandse, Turkse en Arabische versie) en de mogelijkheid tot het koppelen van vragenlijstdata aan Peridos. Deze monitor dient een reguliere procedure te worden. Als er hiaten in kennis worden geconstateerd (bijvoorbeeld over de aandoening Downsyndroom, of over de vrijwillige aard van deelnemen aan de combinatietest en 20-weken echo) dan dient dit bij te dragen aan de ontwikkeling van een verbeterde schriftelijke en / of mondelinge informatievoorzieningsprocedure over prenatale screening aan zwangere vrouwen en hun partners, om het doel van geïnformeerde besluitvorming voor zoveel mogelijk van hen te bewerkstelligen.

# Dankwoord

Vaak heb ik het moment voor me gezien waarop ik het dankwoord van mijn proefschrift zou schrijven. Dit is dat moment. De afgelopen vier jaar is er voor mij niet alleen op professioneel, maar ook op persoonlijk vlak, veel gebeurd. Tussen al die gebeurtenissen door liep steeds mijn proefschrift. En ook daarin liep niet alles zoals gepland. Toch is het er gekomen. Ik ben trots op mijn omgeving, die mij gemaakt heeft tot wie ik ben, en zonder wie ik dit proefschrift niet had kunnen schrijven. Deze laatste pagina's van mijn proefschrift bieden mij de mogelijkheid enkele mensen uit die omgeving persoonlijk te bedanken, maar helaas lang niet iedereen. Degenen die ik niet noem maar die wel deel uitmaken van mijn leven, weten hopelijk dat ik ook hen bedank voor de bijdrage die zij, ieder op hun eigen wijze, geleverd hebben.

Op de eerste plaats dank ik mijn promotor van de afdeling Maatschappelijke Gezondheidszorg, Harry de Koning, en mijn promotor van de afdeling Verloskunde en Vrouwenziekten, Eric Steegers. Harry, dank voor de mogelijkheid die je me hebt gegeven mijn promotieonderzoek uit te voeren. Ik heb op zowel inhoudelijk als persoonlijk vlak veel geleerd. Dat ik de laatste fase van mijn proefschrift mocht combineren met de ontwikkeling en uitvoering van de eerste landelijke monitor geïnformeerde besluitvorming prenatale screening waardeer ik; ik ben trots dat ik heb kunnen bijdragen aan de dataverzameling op nationaal niveau. Hoewel de data niet meer in mijn proefschrift zijn verwerkt, en op dit moment nog dienen te worden geanalyseerd en gepubliceerd, zie ik ze nu al als kroon op mijn promotieonderzoek. Eric, dank voor de begeleiding die jij me gedurende mijn proefschrift hebt geboden. Ik waardeer het dat je er was op de momenten dat het noodzakelijk was, en bewonder je om je kordate en professionele manier van handelen.

Frequent en steeds intensiever contact heb ik gehad met mijn beide copromotoren; Hajo Wildschut en Marie-Louise Essink-Bot. Zij haalden mij binnen in het Erasmus MC als hun 'jongste dochter'. Hajo, dank voor alles dat je me hebt geleerd. Ik wist dat ik altijd op je feedback kon rekenen, zowel schriftelijk; op de vele hoeveelheden papier die je steeds van mij ontving (ons eerste werkoverleg zei je me, terwijl je lachend wees op de agenda en stukken die ik je had gestuurd, dat mijn proefschrift al zo goed als af was), als mondeling; je wist me altijd in te plannen tussen je drukke spreekuren en andere werkzaamheden door. Ik heb genoten van je kwinkslagen, taalgevoel en enthousiasme. Ik heb veel geleerd van je rijke wetenschappelijke en klinische ervaring en het was steevast een plezier als ik samen met je brainstormde of discussieerde over de inhoud van onze artikelen, of de manier waarop iets het mooist kon worden opgeschreven.

Als 'jongste dochter' was het lastig om te gaan met 'gescheiden ouders'; Marie-Louise, toen jij je functie in het Erasmus MC verwisselde voor een baan in het AMC, heb ik moeten worstelen mijn proefschrift vorm te geven. Je zag het op een afstand, en kwam weer terug, althans, als begeleider van mijn proefschrift. Dat heeft voor mij het verschil gemaakt en me op moeilijke momenten het doorzettingsvermogen gegeven om gestaag verder te werken. Je kennis over geïnformeerde besluitvorming en prenatale screening heeft me verrijkt. Ik bewonder je kritische en scherpe blik, humor en relativeringsvermogen. Ik heb veel geleerd van je manier van werken en dank je voor het feit dat je altijd tijd voor me wist te maken, en vaak ook in de avonden en weekenden bereid was tot het lezen van stukken of het voeren van overleg. Je begeleiding was er even niet, maar had op alle momenten dat je er wel was, niet beter kunnen zijn. Dank daarvoor.

Ik dank de leden van de kleine commissie; Professor de Beaufort, Professor Reinders en Professor van Vugt voor het beschikbaar stellen van hun tijd en expertise door zitting te nemen in de commissie.

Voor de dataverzameling van mijn proefschrift heb ik nauw samengewerkt met de Stichting Prenatale Screening Zuidwest Nederland. Bij de start van mijn promotie was deze nog maar net opgezet, door Hajo en zijn stafadviseur Ingrid Peters. Ingrid, ik herinner me nog ons eerste werkoverleg, waarin we beiden als kersverse Erasmus medewerkers stonden te popelen om de Stichting en mijn onderzoek op de kaart te zetten. Wat hebben wij veel uren samengewerkt en wat heb ik een bijzondere band met je gekregen. Het is niet voor niets dat je tijdens mijn verdediging naast me staat als paranimf. Ook gedurende mijn proefschrift stond je naast en achter me; we deelden werk en privé tijdens de vele koffiemomentjes en je sleepte me door de moeilijke momenten heen. Ik was vereerd de geboorte van Veerle van zo dichtbij mee te mogen maken en ben jou en Gosling dankbaar dat ik haar nu mag zien opgroeien. Ik ben trots op je als moeder van Veerle, als collega en niet in de laatste plaats als vriendin, je was en bent er altijd. Dankjewel.

Ook de andere medewerkers van de Stichting Prenatale Screening, in het bijzonder Anne Marie en Mieke, wil ik bedanken voor hun meeleven, enthousiasme en hulp gedurende mijn promotie. Ton Verkerk, ik ben blij dat jij deel uit ging maken van de Stichting en daarmee van mijn promotieonderzoek. Door de ontwikkeling van een web applicatie heb je een onmisbare bijdrage geleverd aan de dataverzameling van mijn proefschrift. Dank voor je kritische blik en je geduld. Zoals Hajo het eens zei, 'voor een web applicatie heb je een Ton nodig'; niets is minder waar.

Een deel van mijn onderzoek werd uitgevoerd in opdracht van het Centrum voor Bevolkingsonderzoek van het Rijksinstituut voor Volksgezondheid en Milieu. In de laatste fase van mijn proefschrift voerde ik frequent en intensief overleg met Jantine Wieringa, in het kader van de eerste landelijke monitor. Jantine, dank voor de plezierige samenwerking, je enthousiasme en daadkracht. Het was een plezier de eerste landelijke monitor geïnformeerde besluitvorming onder jouw coördinatie te mogen uitvoeren. Op deze plaats wil ik ook Nico Ooms en Ronald Buit van Medical Phit bedanken, die de verantwoordelijkheid voor het ICT deel van de monitor op zich namen. Ook wij hebben vele overleggen gevoerd, die met name fijn waren door jullie enthousiasme en de concrete stappen die steeds, vaak op heel korte termijn, werden gezet.

Fop Smit, we kennen elkaar nog maar kort, des te meer waardeer ik het dat je de omslag van mijn proefschrift hebt willen ontwerpen. Ik ben me ervan bewust dat de voorkant het enige is dat veel mensen van mijn proefschrift zullen zien, daarom wilde ik een bijzondere voorkant. En dat is meer dan gelukt. Dank daarvoor!

Mijn collega's zorgden voor de nodige afwisseling tijdens de soms lange dagen in het Erasmus MC. Robine, Suzan, Ruben, Kevin, dank voor de gezellige gesprekken en koffiemomenten. Sander, dank voor je hulp aan ons 'internationale project'. Dank ook voor je geduld, het eindresultaat is er nog niet, maar komt er zeker! Heleen, wij zijn in de loop der jaren steeds meer gaan samenwerken. Dat was altijd fijn; je flexibiliteit, kritische blik en spontaniteit maakten dat de projecten die ik met jou deed voor mijn gevoel altijd 'vanzelf' gingen, hoe hard het soms ook werken was. Mirjam, je bent alweer even weg uit het Erasmus maar ons artikel maakt ook deel uit van dit proefschrift. Van onze tijd op MGZ herinner ik me van jou, mijn grote

zus, vooral je enthousiaste en daadkrachtige manier van werken waaruit ik, ook na ons artikel, nog veel motivatie heb gehaald. Onze afspraak nog eens te gaan stappen ben ik niet vergeten; komt zeker weten nog! Jesse, wij deelden bijna twee jaar een kamer. Dank voor de fijne gesprekken, qua inhoud uiteenlopend van dartpijlen tot chi-kwadraat toetsen, van iso-waarden tot de laddertheorie en nieuwe telefoons of sneakers. Ook jouw proefschrift gaat er komen, en in de tussentijd ga ik graag nog samen met je fotograferen of een biertje te drinken! Erdogan, wij hadden met name in het eerste jaar van mijn proefschrift veel contact. Als nieuwe medewerkers waren we op elkaar aangewezen bij het organiseren van de afdelingsborrel (gelukkig bestond er ook toen al een Albert Heijn website) en daarna was ik amper nog bij je weg te slaan. Ik heb enorm met je gelachen en ook voor serieuze gesprekken kon ik bij je terecht. Vroeg vertrekken naar het werk was een stuk gemakkelijker wetend dat er een stoere man op motor op me wachtte, die me achterop steeds weer veilig afleverde. Ik miste je toen je naar Australië vertrok, maar gelukkig kwam je terug, al was het op een andere afdeling. Helaas is ons contact wat minder geworden, zoals altijd zijn we allebei druk, maar ik hoop dat we elkaar blijven zien. Last but not least Boukje. Jij bent van een collega veranderd in een goede vriendin. De wetenschapsbesprekingen op woensdagochtend leken een stuk minder vroeg als we samen koffie en mijn ochtendhumeur konden delen. Ook jouw persoonlijke leven stond niet stil de afgelopen vier jaar, en ik ben blij dat ik daarin mocht delen, net zoals dat jij deel uit ging maken van mijn leven. Kroon op onze koffiepauzes is ons gezamenlijke artikel. Door jou leerde ik de overeenkomsten en met name de verschillen kennen tussen het 'medische' en 'filosofische' denken en zonder dat je het misschien merkte werd ik steeds enthousiaster over het laatste. Wie weet ga ik ooit nog eens verder in de ethiek, dan wordt dat jouw verdienste! Dankjewel voor je vrolijkheid, eerlijkheid, steun en humor, onze vriendschap is veel voor me gaan betekenen.

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Anne, jou bedanken is een boek schrijven. Wat heb jij veel meegemaakt de afgelopen jaren en wat ben ik trots op wie jij bent en hoe je je overal doorheen slaat. Je kent me zo goed, en je vertrouwen in het afronden van mijn proefschrift heeft me zo geholpen. We hebben al veel meegemaakt samen en er gaat vast nog heel veel komen, zolang wij in elkaars leven zijn heb ik er alle vertrouwen in. Dankjewel dat je er altijd bent!

Pa en Ma, ik was er vaker niet dan wel de afgelopen jaren, maar weet dat ik jullie dochter ben die van jullie houdt, waar ik ook ben. Dankjewel voor de mogelijkheid die jullie me hebben gegeven om me te ontwikkelen, ik weet dat jullie er enorm hard voor hebben gewerkt. Dankjewel voor de liefde en het geduld dat jullie met me hebben gehad. Zonder de kansen die jullie me hebben gegeven had dit boekje er nu niet gelegen. Jos en Angela, lieve broer en zus, al had ik zo vaak geen tijd, ik zie jullie graag. Jos, dankjewel voor die mooie dag in Antwerpen. Angela, voor de 'zussendagen'. Je bent een bijzonder zusje, daarom sta jij vandaag ook aan mijn zijde als paranimf.

Ingrid, lieve liefste jij bent mijn toekomst. Dankjewel voor alle mooie, speciale momenten die jij in mijn leven brengt, voor het leven samen met jou. Dankjewel voor al je geduld als ik weer eens in de stress zat vanwege mijn 'opstelletje'. Het ligt er nu, en wij gaan samen verder. Kom je mee? Er wacht een heel mooi leven op ons!

Marleen
6 Oktober 2011

# PhD Portfolio Summary

## Summary of PhD training and teaching activities

Name PhD student: Marleen Schoonen
Erasmus MC Department: Public Health
Research School: Nihes (Netherlands Institute for Health Sciences)
PhD period: 2007-2011
Promotors: Prof. dr. H.J. de Koning, Prof. dr. E.A.P. Steegers
Supervisors: dr. M.L. Essink-Bot (AMC), dr. H.I.J. Wildschut

| PhD training | Year | Workload (Hours / ECTS) |
|---|---|---|
| ***Research skills*** | | |
| Master of Public Health, Netherlands Institute for Health Sciences (NIHES) Rotterdam, The Netherlands | 2007-2010 | 70 |
| ***Presentations and national and international conferences*** | | |
| Researchmeeting afdeling Verloskunde en Vrouwenziekten<br>Landelijke evaluatie van een programma voor prenatale screening op Downsyndroom, (oral presentation) | 2007 | 0,6 |
| Nederlands Congres Volksgezondheid 2008, Groningen, The Netherlands<br>*Prenatale screening op Downsyndroom; voorlichting doorgelicht* (oral presentation) | 2008 | 0,6 |
| Lustrumsymposium Stichting Downsyndroom<br>*Prenatale screening op Downsyndroom; voorlichting doorgelicht* (oral presentation) | 2008 | 0,6 |
| Research meeting afdeling Public Health<br>*Prenatal screening for Down syndrome; a closer look at the process of offering information* (oral presentation) | 2008 | 0,6 |
| Society for Medical Decision Making (SDMD)<br>SMDM 2008, Engelberg, Switzerland<br>*Prenatal screening for Down syndrome; A closer look at the process of offering information* (oral presentation) | 2008 | 1 |
| Onderzoeksdag Verloskunde en Vrouwenziekten<br>*Landelijke evaluatie van een programma voor prenatale screening op Downsyndroom* (oral presentation) | 2008 | 0,6 |
| Tweede Landelijke Conferentie Pre- en Neonatale Screening; Centrum voor Bevolkingsonderzoek RIVM and Nederlandse Associatie voor Community Genetics (NACG), Utrecht<br>*Prenatale screening; keuzes in een kader* (oral presentation) | 2009 | 0,6 |
| RIVM, Bilthoven, The Netherlands<br>*Evaluatie aanbiedingsprocedure prenatale screening op Downsyndroom en het Structureel Echoscopisch Onderzoek* (oral presentation) | 2009 | 0,6 |
| Symposium Stichting Prenatale Screening Zuidwest Nederland Rotterdam, The Netherlands<br>Workshop dataverzameling counseling *(organisation workshop)* | 2009 | 1 |
| Satellietoverleg afdeling Verloskunde en Vrouwenziekten<br>*Prenatale screening op aangeboren afwijkingen en geinformeerde besluitvorming; eerste resultaten uit de regio Zuidwest Nederland* (oral presentation) | 2009 | 0,6 |

| | | |
|---|---|---|
| International Congress of the International Society of Psychosomatic Obstetrics and Gynaecology, Venice, Oct 2010<br>*Prenatal screening for Down's syndrome; low uptake rates are based on informed decision-making, A study in community midwifery practices in the Southwest region of the Netherlands* (oral presentation) | 2010 | 1 |
| Research meeting afdeling Public Health<br>*Prenatal screening for Down syndrome; a closer look at the process of offering information* (oral presentation) | 2008 | 0,6 |
| Researchmeeting afdeling Verloskunde en Vrouwenziekten<br>*Prenatal screening for Down's syndrome; low uptake rates are based on informed decision-making, A study in community midwifery practices in the Southwest region of the Netherlands* (oral presentation) | 2010 | 0,6 |
| Researchmeeting afdeling Verloskunde en Vrouwenziekten<br>Preconceptioneel aanbieden van informatie over prenatale screening op Downsyndroom, Een emprisch onderzoek en ethische reflectie (oral presentation) | 2010 | 0,6 |
| Middagseminar "Business Intelligence in de Zorg, ervaring met indicatoren" Medical PHIT<br>Evaluatie aanbiedingsprocedure prenatale screening op Downsyndroom en het Structureel Echoscopisch Onderzoek (oral presentation) | 2010 | 0,6 |
| Symposium Downsyndroom; Feiten en Fictie<br>Prenatale screening op Downsyndroom en geinformeerde besluitvorming (oral presentation) | 2011 | 0,6 |
| ***Seminars and workshops*** | | |
| Attending seminars at the Department of Public Health, Erasmus MC Rotterdam | 2007-2011 | 3,6 |
| Attending and organising meetings of the 'Risk perception-Informed decision making- Quality of life- club' at the department of Public Health, Erasmus MC, Rotterdam | 2009-2011 | 0,6 |
| Eerste Landelijke Conferentie Pre-en Neonatale Screening; Centrum voor Bevolkingsonderzoek RIVM and Nederlandse Associatie voor Community Genetics (NACG), Utrecht | 2007 | 0,2 |
| Prenatale Diagnostiek IX, Maastricht, The Netherlands International Society for Prenatal Diagnosis, Amsterdam, July 2010 | 2010 | 0,2 |
| Workshop Performing a systematic review of measurement properties<br>VUMC, Knowledgecenter Measurement instruments, | 2011 | 0,2 |

# List of publications

**International**

Schoonen HM, van Agt HME, Essink-Bot ML, Wildschut HI, Steegers EAP, de Koning HJ. Informed decision-making about prenatal screening for Down's syndrome: What knowledge is relevant?
Patient Education and Counseling 2011; **84** (2): 265-270

Schoonen HM, Essink-Bot ML, Van Agt HM, Wildschut HI, Steegers EA, De Koning HJ. Informed decision-making about the fetal anomaly scan: What knowledge is relevant?
Ultrasound in Obstetrics and Gynecology 2011; **27** (6): 649-657

Schoonen HM, Wildschut HI, Essink-Bot ML, Peters IA, Steegers EAP, de Koning HJ. Evaluating the provision of information and informed decision-making on prenatal screening for Down's syndrome: a questionnaire- and register- based survey in a non-selected population.
Patient Education and Counseling: in press

Schoonen HM, Wildschut HI, Steegers EAP, de Koning HJ, Essink-Bot ML. Informed decision-making on the fetal anomaly scan; evaluation of the process and quality of information provision, and comparison with Down syndrome screening.
Submitted

Fransen MP, Schoonen HM, Mackenbach JP, Steegers EA, de Koning HJ, Laudy JA, Galjaard RJ, Looman CW, Essink-Bot ML, Wildschut HI. Ethnic differences in participation in prenatal screening for Down syndrome: a register-based study.
Prenatal Diagnosis 2010; **30**: 988-994

Schoonen HM, van der Zee B, Wildschut H, de Beaufort I, de Wert G, de Koning H, Essink-Bot M.L, Steegers, E.A.P. Informing on Prenatal Screening for Down Syndrome Prior to Conception. An empirical and ethical perspective.
Submitted

**National**

Van Agt HME, Schoonen HMHJD, Wildschut HIJ, de Koning HJ, Essink-Bot ML. Voorlichting voor pre-en neonatale screeningsprogramma's: Vragenlijsten voor landelijke evaluatie van de aanbiedingsprocedure. Rotterdam: Maatschappelijke Gezondheidszorg, Erasmus MC 2007

Schoonen HMHJD, Wildschut HIJ, Steegers EAP, de Koning HJ. Evaluatie van de aanbiedingsprocedure van prenatale screening op Downsyndroom en het Structureel Echoscopisch Onderzoek. Rotterdam: Maatschappelijke Gezondheidszorg, Erasmus MC 2009

# About the author

Helena Maria Johanna Dymphina Hendrika (Marleen) Schoonen was born, on the 3th of July 1982, and raised in Roosendaal, The Netherlands. After graduating from secondary school at Norbertuscollege and obtaining her first year's degree in Journalism (Fontys Hogeschool Tilburg), she started studying Psychology at Tilburg University. She wrote her masters thesis at the department of Cardiothoracic surgery of the Leiden University Medical Center, and graduated Cum Laude in 2006 with a major in health psychology and a minor in neuropsychology. In 2007 she started with the PhD project resulting in this thesis, at the Department of Public Health of the Erasmus MC in Rotterdam. Meanwhile, she completed the Master of Science programme at the Netherlands Institute for Health Sciences (Nihes) and obtained her Master of Science in Health Sciences, in August 2010. Spring 2011, she combined finishing of her thesis with coordinating and executing the first national monitor of informed decision-making on prenatal screening for Down syndrome and for structural congenital anomalies, on behalf of the Centre for Population Research of the Dutch National Institute for Public Health and the Environment. End 2011, results of this monitor will be published.

Helena Maria Johanna Dymphina Hendrika (Marleen) Schoonen is geboren op 3 juli 1982, en opgegroeid in Roosendaal. Na haar middelbare school (Norbertuscollege) en het behalen van haar propedeuse Journalistiek (Fontys Hogeschool Journalistiek), begon ze met een studie Psychologie aan de Universiteit van Tilburg. Ze schreef haar masterscriptie aan de Afdeling Thoraxchirurgie van het Leids Universitair Medisch Centrum, en studeerde in 2006 Cum Laude af met een major Gezondheidspsychologie en een minor Neuropsychologie. Vanaf 2007 is zij als onderzoeker verbonden aan de afdeling Maatschappelijke Gezondheidszorg en de afdeling Verloskunde & Vrouwenziekten van het Erasmus MC, en voerde het promotieonderzoek uit dat resulteerde in dit proefschrift. In deze periode volgde ze de eveneens de opleiding Public Health bij de Netherlands Institute for Health Sciences (Nihes), die ze in augustus 2010 met een Master of Science afrondde. Voorjaar 2011 combineerde zij de afronding van haar proefschrift met de coördinatie en uitvoering van de eerste landelijke monitor naar geïnformeerde besluitvorming over prenatale screening op Downsyndroom en de 20-weken echo, in opdracht van het Centrum voor Bevolkingsonderzoek van het Rijksinstituut voor Volksgezondheid en Milieu. De resultaten van deze monitor worden eind 2011 verwacht.