

Université de Montréal

**A mixed method review and quality criteria analysis: Towards improving  
decision aids and informing care models in prenatal testing**

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## Résumé

**Introduction:** Les incertitudes des pronostics cliniques et les dilemmes moraux associés aux technologies des tests prénataux affectent les expériences et les processus décisionnels des femmes et des couples. D'une part, la validité des normes relatives au 'consentement autonome' et au conseil 'non directif' est remise en question. D'autre part, les aides à la décision sont prônées pour rehausser la prise de décision éclairée. L'objectif de ce mémoire est de construire un modèle de l'expérience des femmes et des couples qui font face aux tests prénataux afin d'identifier les facteurs qui amélioreraient les expériences, la prise de décision et le rôle des aides à la décision et informeraient le modèle de soin.

**Méthodologie:** La modélisation et l'analyse des expériences des femmes et des couples qui affrontent les tests prénataux reposent sur une méta-ethnographie des études qualitatives et sur une analyse narrative thématique des études quantitatives. La critique d'un outil (PT) en matière de tests prénataux est également effectuée en ayant recours aux critères de qualité de l'*International Patient Decision Aid Standards* (IPDAS).

**Résultats:** Un cadre conceptuel décrivant les expériences vécues est construit et l'analyse thématique le complète en soulignant que la prise de décision n'est que rarement éclairée. Les normes d'une 'décision autonome' et d'un 'conseil non directif' sont problématiques pour les femmes. Les aides à la décision amélioreraient les scores de connaissances, sans pour autant modifier la perception du risque, ni les niveaux d'anxiété. L'outil PT favorise une prise de décision basée sur les préférences, mais les critères IPDAS sont difficilement applicables et leur rôle dans une décision de qualité est incertain.

**Discussion et conclusion:** Les résultats éclairent les facteurs macro, méso et micro pouvant améliorer les expériences vécues des femmes et des couples et affecter la prise de décision et l'utilisation des aides à la décision. Un changement de paradigme préconisant le concept d'autonomie relationnelle dans le modèle de soins est suggéré. Dans le contexte des avancées en matière de test prénataux, une réévaluation des normes de pratique et de modèles de soin est requise. Le rôle des aides à la décision devra être élucidé.

**Mots-clés :** Dépistage anténatal, dépistage prénatal, méta-ethnographie, prise de décision éclairée, aide à la décision, autonomie relationnelle

## **Abstract**

**Introduction:** The clinical prognostic uncertainties and moral dilemmas associated with technological advances of prenatal testing impact the experiences and decision-making of women and couples. While the validity of the norms of 'autonomous consent' and 'non-directive' counseling is being questioned, decision aids are promoted to enhance informed decision-making. The goals of this thesis are to develop a model of the experiences of women and couples in prenatal testing so as to identify factors that may improve experiences, decision-making, the role of decision aids and inform the care model.

**Methods:** A model of the experiences of prenatal testing is developed through a meta-ethnography of qualitative studies and a narrative synthesis of the themes explored in quantitative studies. A prenatal testing (PT) decision tool is critically assessed using the International Patient Decision Aids Standards (IPDAS) quality criteria for decision aids.

**Results:** A conceptual framework of the experiences of women and couples in prenatal diagnosis is constructed and complemented by a narrative thematic analysis showing that decision-making is rarely informed and that the norms of an 'autonomous decision' and a 'non-directive' counselling are problematic for women. Decision aids improve knowledge scores, but do not modify risk perception or anxiety levels. A PT tool increases preference based informed decision-making, but quality criteria are not always applicable and their role in quality decision-making is unclear.

**Discussion and conclusion:** The results highlight macro, meso and micro-level factors that may improve the experiences of women and couples and inform decision-making processes as well as the use of decision aids. A paradigm shift towards the concept of relational autonomy in the prenatal diagnosis model of care is suggested. Advances in prenatal testing require a re-evaluation of the norms of practice and care model. The role of decision aids requires further elucidation.

**Key words:** Prenatal testing, meta-ethnography, informed decision-making, decision aids, relational autonomy

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## **List of acronyms and abbreviations**

AFP : Alpha feto protein

B HCG : beta subunit of human chorionic gonatotropin

CVS : Chorionic villus sampling

CMA : Chromosome micro arrays

DIA : Dimeric inhibin A

DA : Decision aids

DS : Down's syndrome

HCP : Health care professional

HTA : Health Technology Assessment

IPDAS: International Patient Decision Aid Standards

MMIC : Multidimensional measure of informed consent

MSM : Maternal serum markers

NIPT : Noninvasive prenatal test NT

NT: Nuchal translucency

PPV : Positive predictive value

SDM : Shared decision-making

SOGC : Society of obstetrics and gynecology of Canada

uE3 : Unconjugated estriol

US : Ultrasound or sonography

VUS : Variants of unknown significance

WE : Whole exome

WG : Whole genome

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## **Introduction**

The goal of this thesis is to synthesize and analyze the experiences of prenatal testing from a Western culture parental perspective with the aim of providing criteria that can inform and improve the quality of care at the level of the patient-physician encounter in the context of a prevalent technologically and medically driven imperative to expand prenatal diagnosis. This clinical practice includes, as will be explained in more detail below, a combination of screening (non-diagnostic) tests performed by ultrasound measurements and a series of maternal serum blood tests.<sup>1,2</sup> Ultrasounds can screen for congenital malformations known or not to be associated with genetic anomalies.<sup>1,2</sup> The results of these tests are combined with the mother's age to produce a probability that the fetus has a chromosomal anomaly or incomplete neural tube closure. In the case of "high risk," the pregnant woman can then choose to undergo or not an "invasive" diagnostic test, such as amniocentesis or chorionic villus sampling, to confirm a diagnosis.<sup>1,2</sup>

The field of prenatal diagnosis is being revolutionized by the introduction of a single screening test in the first trimester: the cell free fetal DNA test<sup>3</sup> or so called non-invasive prenatal test 'NIPT,' which could eliminate the need for ultrasound and maternal serum markers (MSM) for the genetic conditions that have been typically screened: triploidies trisomy 21,13 and 18.<sup>4</sup> With NIPT, it is additionally possible to uncover sex aneuploidies and the sex of the foetus.<sup>5 6</sup> There are few in-utero treatments for the conditions detected. For most women, the information provided by prenatal screening will be used to consider the options to do invasive testing and or to consider pregnancy continuation or termination.

## **Health Technology Assessment (HTA) and the perspective adopted in this thesis**

Over the last fifteen years, experts in Health Technology Assessment (HTA) have come to recognize that the ethical analysis in HTA cannot only be equated with effectiveness and safety of the technology. There are ethical, social and organizational implications to the development, diffusion and use of health technologies.<sup>7-9</sup> For Hofmann and collaborators,<sup>10,11</sup> HTA is by and large a process in value judgments, which are part of the basic elements of HTA.

Prenatal diagnosis requires the use of highly sophisticated technologies whose perceived usefulness is very much dependent on multiple factors which include the goals for their use, the expertise required for interpretation and application and the perceived values outside of the domain of the technologies

per se.<sup>11,12</sup> In the clinical context, ethical norms impose that in the application of any investigation or treatment —and particularly in the context of interpretations of results— informed consent is required to protect the autonomy of individuals when they make decisions<sup>13</sup>. In addition, decision aids and tools considered technologies in and of themselves can be analyzed with regards to their impact on the process of obtaining an informed consent and on the care model.<sup>14</sup>

The author of this thesis is a clinician that has had to counsel pregnant women or couples on the neurological prognosis of a future child in the presence of fetal and/or genetic malformations and parents of children with presumed genetic mutations associated with encephalopathies of various severities. It is her experience that the process of informing and obtaining consent for genetic screening is complex. The complexities include understanding the technical aspects and the efficacy rate of various testing procedures and deciding on the appropriate test and explaining the limitations of the testing results to the parents. The low diagnostic yield and the uncertainties in the prognosis are associated with disappointment for unfulfilled expectations in the parents that have hopes in ‘a last resort’ response to their queries. In addition, there are difficulties in the interpretation of results for which a clinical correlation has not yet been ascertained.

It thus seemed pertinent and timely to review issues related to the practice of prenatal diagnosis given that in the future a greater number of decisions of whether to terminate or not a pregnancy will be based on incomplete information, related to the uncertain prognosis of the conditions that will be detected. It is important that the women understand that the new genetic testing will open a Pandora’s box. Clinicians and the population at large believe that they are well informed of the clinical spectrum of Trisomy 21 (Down’s syndrome: DS), but the majority of the information that will be obtained by the new testing procedures will result in information of which the clinical significance will be unknown.<sup>15,16</sup> The rapid expansion of knowledge in genetics, moral dilemmas and issues related to informed consent in the context of difficult decision-making has practical implications for the structuring of services, various professional roles and, ultimately, calls into question the aim of the health care relationship and goal of the health care system.

### **Objectives, epistemology and outline of the thesis**

Several aspects of HTA in prenatal testing have led to the analysis of the ethical, legal and social implications of the genetic screening methods as applied in research or expert clinical practice.<sup>17</sup>

Other scholars have focused on the scientific accuracy, safety, effectiveness, clinical validity of molecular tests<sup>18</sup> and the organizational aspects underlying the practice and delivery of prenatal testing and diagnosis.<sup>19</sup>

This thesis instead will aim to conceptualize the lived experience of women and couples undergoing prenatal testing with the goal to inform patient care models and ultimately through knowledge translation lead to improving delivery of services. More specifically, there are three objectives to this thesis. The first is to clarify the perception and experiences of women and couples who undergo screening and diagnosis in pregnancy. The second is to understand whether parents undergo informed decision-making in prenatal diagnosis and the factors that could improve this process from their perspective. The third is to identify the role of decision aid tools in this domain.

This thesis, more broadly, calls for a transformation in the way that women and couples are educated in prenatal testing and for improved decision-making and quality of care. Theories of social interaction and understanding can shed light on how the health care relationship is conceived and how evidence is collected, understood and used.<sup>20</sup> The theory on which knowledge about relationships in clinical work and research are considered in this thesis draws on Alderson's description of social construction and critical theory. In particular, it pays attention to the way minorities may be socially "constructed" as inadequate or disabled and the way such socially shared understandings often reify the prejudices these minorities experience.<sup>20</sup> According to this theoretical framework, sick and disabled people should be valued as a source of relevant knowledge, uniquely gained through adversity and a particular position in the social world. The potential for bridging professional and lay knowledge is thus emphasized.<sup>20,21</sup>

A constructionist epistemology uses an inductive approach to analyzing data and is congruent with an interdisciplinary approach.<sup>20</sup> Discourse and interaction constitute means to a collective generation and transmission of meaning.<sup>22</sup> Discourse in the Foucauldian sense is conceived as a set of institutionalized statements about a topic that functions socially by forming that topic.<sup>23,24</sup> The critical social theory perspective is at the center of several inter related concepts, which include geneticization, normalization, risk as a form of social control, power of and in knowledge and governmentality.<sup>25,26</sup> These are the broad epistemological considerations underpinning the approach adopted in this thesis.

The methodology is a mixed method approach. A meta ethnography of qualitative studies using a thematic content analysis strategy to arrive at a conceptual framework<sup>27</sup> of the experiences of women and couples undergoing prenatal diagnosis is performed. The results of a narrative summary of specific themes related to decision-making in prenatal testing investigated by a quantitative approach are compared to the results of the qualitative analysis in order to augment, contrast or clarify the issues identified in the qualitative studies<sup>28</sup>. In addition, using the International Patient Decision Aid Standards (IPDAS) quality criteria, the role of decision aids is addressed through a critique of a prenatal testing tool used in a clinical trial.<sup>29-31</sup>

The structure of the thesis is as follows. An introductory section will familiarize the reader with the different prenatal testing techniques and their evolution and expose the complex clinical, ethical and social issues pertaining to the development and use of this technology. These issues require a deeper understanding of the value systems that have sustained the development of prenatal diagnosis. The second part of the introduction presents a limited, but albeit pertinent body of social scientific literature on the acceptance of prenatal testing. The third part of the introduction addresses the norms of clinical practice that impact on the relationship between the patient and physician and the informed consent process. This section also covers recent developments in decision aids and their quality that may shed some light as to how to improve the clinical care process from the parental perspective.

In the Methods chapter, it is argued that qualitative research is an effective way to inform health service policies and organizational issues including changes in resource allocation, management practices at the micro-level. It is also used to understand complex behaviors, attitudes and interactions in ways that quantitative studies cannot inform.<sup>20</sup> Similar to grounded theory for primary studies, the goal of our interpretative synthesis is the integration of concepts to enable understanding rather than just a description of prenatal diagnosis experiences.<sup>28,32</sup> Such a synthesis avoids specifying concepts in advance. Meta ethnography synthesizes grounded theory and phenomenological qualitative studies<sup>33-35</sup> by building third order constructs from comparing and contrasting first order construct (quotes from the patient) and second order constructs (author's interpretations of first order constructs) from different articles. Interpretation is a strength of the conceptual model that is developed through the third order constructs, which do not supplant, but add to the rich details obtained through studies conducted in different contexts and cultures.<sup>36,37</sup> In this chapter, we also describe how a thematic analysis of the quantitative studies relying on validated

measures such as the multidimensional measure of informed consent (MMIC)<sup>38</sup> and measures for knowledge, decisional conflict and anxiety<sup>39</sup> as a has a high level of explanatory value.<sup>28</sup>

In the Findings chapter, the qualitative and quantitative findings are compared for concordance and/or discordance and together enrich the analysis of the experiences of women in prenatal testing. Lastly, decision aids and tools that have the goal of improving informed decision-making in prenatal testing are critiqued drawing on a quality criteria analysis. The discussion summarizes the key findings, draw policy and practical implications and highlight further research areas.

### **Prenatal testing and contexts**

#### Background of prenatal screening and diagnosis

A recent Canadian HTA report on prenatal testing including testing for open neural tube defects and DS was performed in order to determine whether to implement a prenatal screening program in Alberta (the FAST report).<sup>19</sup> An international data set registries quotes annual prevalence medians in 2006 for Trisomy 21 at 17 cases per 10,000 births, for Trisomy 18 at 2.8 cases per 10,000 births and for Trisomy 13 at 1.4 cases per 10,000 births.<sup>19</sup> Neural tube defects are prevalent at 3.9 cases per 10,000 births and are associated with elevated serum maternal levels of alpha foetal protein (AFP).<sup>19</sup> In the last 40 years, screening has evolved. Initially performed in the second trimester screening for the detection of DS, it was associated with a detection rate of 30%, a false positive rate at 5%, and a diagnostic amniocentesis fetal loss risk of 0.5-1%.<sup>19</sup>

First trimester screening with nuchal translucency (NT) and maternal serum markers (MSM) has now a detection rate of about 85-90%, a false positive rate of 3-5% and chorionic villus sampling fetal loss risk of 1%.<sup>19</sup> The fetal ultrasound (US) features that have come to be recognized as associated with a 'high risk' pregnancy are increased fetal NT thickness, absence of nasal bone, regurgitant flow across the tricuspid valve (TR regurgitation) and a reversed wave in the ductus venosus.<sup>19</sup>

The serum markers tested in the first trimester consist of pregnancy associated plasma protein A (PAPP-A) and free beta subunit of human chorionic gonadotropin (b-HCG).<sup>19</sup> In the second trimester, MSM consist of AFP, b-HCG), unconjugated estriol (uE3), and dimeric inhibin A (DIA).<sup>19</sup> The biophysical profile or fetal ultrasound and, maternal serum markers along with the age of the woman are combined to estimate the patient specific risk for Trisomies 21, 18 and 13. First trimester screening strategies have included NT alone, MSM alone, or combined testing.<sup>19</sup> Second trimester screening



options have consisted of either double MSM (AFP, b-HCG) or triple serum markers (AFP, uE3, b-HCG) or quadruple serum markers (AFP, b-HCG, uE3, DIA) and ultrasound.<sup>19</sup>

From a couple of large cohort prospective studies,<sup>40</sup> it has been predicted that of 10,000 women screened for DS, 96% (n=9585) will be in the low risk category and two of these pregnancies will be affected by DS. Of the 4% that screened in the high-risk category (n=415), only 15 pregnancies will be affected with DS, thus overall only 0.15% of fetus will be affected with DS. One fetus in this group will be lost due to the diagnostic intervention provoked miscarriage and, in some cases, the risk of provoked fetal loss is equal to or greater than the risk of DS.<sup>40</sup>

A number of practical approaches are recommended for determination of the risk assessment. In the integrated approach, the results of the first trimester screening are withheld until second trimester test results are obtained.<sup>19</sup> The sequential approach, which is stepwise and represents a contingent screening using intermediate results is the most resource intensive. Moreover, it places high demands on the women and is not common practice in Canada.<sup>19</sup> The integrated screening test, which combines the results of first and second trimester maternal serum markers and nuchal translucency (NT) measurement to calculate the risk score is the most accurate.<sup>19</sup> Screening values that are greater than a risk cut off point express the probabilities that a fetus at term or mid trimester will express the condition suggesting the need for further tests to confirm or refute the diagnosis.

The diagnostic procedures otherwise known as invasive testing in the literature include chorionic villus sampling (CVS) and amniocentesis. CVS consists in obtaining an aspirated sample of the placenta and is performed between 11-13 weeks whereas amniocentesis is performed at 15 weeks and consists of a needle aspiration to obtain a sample of amniotic fluid.<sup>19</sup> Both procedures yield a diagnosis with greater than 99% confidence for Trisomy 13, 18 and 21 and amniocentesis for spina bifida with the same accuracy.<sup>19</sup> The frequency of the related pregnancy loss due to the procedures are reported somewhere between 0.3 and 1%.<sup>19</sup>

Recommendations for patient and health care workers for prenatal screening, diagnosis and management of neural tube defects and for fetal Trisomy 21, 18 and 13 in singleton pregnancies have been published as clinical practice guidelines by The Society for Obstetrics and Gynecology of Canada (SOGC).<sup>1</sup> The recommendations are to offer non-invasive prenatal screening for aneuploidy to all pregnant women and invasive testing for diagnosis to women with a higher score than the set risk score cut off level on the non-invasive testing or whose history places them at an increased risk. It is

important to note that the evidence on which are based their recommendations, which draws on the Canadian Task Force for Preventative Health Care, were for the most part either fair or contradictory.<sup>1</sup>

The guidelines by the SOGC suggest prenatal screening with a second trimester fetal ultrasound for dating and growth monitoring, and to verify for congenital malformations.<sup>1,2</sup> The screening programs and approaches adopted vary by geographic areas.<sup>19</sup> Prenatal screening programs are funded provincially and offered population wide in many provinces in Canada including Quebec.<sup>19</sup> Practices differ across the country and provinces rely on the regulation of practitioners to govern the use of different prenatal screening tests with different standards of care being used.<sup>19</sup> The FAST report underscored the absence of studies reporting the impact of screening results on physician decision-making and on maternal or fetal outcomes.<sup>19</sup> The authors concluded that before implementing a prenatal screening program in Alberta, the utility of the test results to support decision-making was considered crucial to investigate.<sup>19</sup>

#### Whole exome/genome sequencing and chromosomal microarrays

The technique of shotgun massive parallel sequencing using disease focused multigene panels and diagnostic exome sequencing to interrogate the coding regions of nearly all genes is now possible for the detection of Mendelian inherited disorders.<sup>41-43</sup> These new sequencing methods can analyze the genome at an increasingly rapid resolution. Chromosome microarrays (CMA) are genetic analyses that are possible following invasive diagnostic testing for conditions that are different from those usually screened and they provide a genome wide screen for microscopic and submicroscopic deletion, duplications and copy number changes which can occur.<sup>43</sup> This form of testing is less labor-intensive and has a shorter turnaround time compared to previous cell culture for karyotyping.<sup>43</sup> In a study of over 4000 women, 6 % and 1.7% of women with abnormal ultrasound findings and advanced maternal age or abnormal screening test results had fetuses with CMA anomalies respectively.<sup>44</sup>

These testing procedures are currently being carried out by clinicians for children with malformations, learning disabilities and mental retardation.<sup>44</sup> Some of these genetic anomalies are associated with anatomical malformations that are detected during the 'routine' ultrasound (US) visit of prenatal care. In the case where the fetus is sonographically and chromosomally normal, but carries a deletion or duplication abnormality that is less known or not yet reported in the literature, counseling of postnatal morbidity related to this 'variant of unknown clinical significance' (VUS) is uncertain and

potentially anxiety producing. Furthermore, obtaining a normal result on microarray does not rule out an US abnormality, nor the presence of genetic conditions or postnatal morbidity.<sup>44</sup>

#### The development of NIPT

Circulating cell free fetal DNA comprises 3-13% of maternal cell free DNA thought to be derived from the placenta and is cleared from the maternal blood within hours of childbirth.<sup>42,43</sup> Next generation sequencing or massively parallel genomic sequencing using a highly sensitive assay to quantify millions of DNA fragments was reported to accurately detect trisomy 13, 18 and 21 as early as the 10<sup>th</sup> week of pregnancy.<sup>4,42</sup> Although the cell free fetal DNA originating from placental DNA is often identical with that of the fetus, there can be differences thereby explaining some of the false positive results.<sup>4</sup> Test performance is affected by a number of factors including maternal body mass index, fetal fraction, the presence of a vanishing twin and singleton as opposed to multiple pregnancies.<sup>43</sup> It is also affected by practical technique and test performance factors that require quality control in order to produce reliable risk values to clinicians.<sup>43</sup>

A review of the different genetic technologies to detect fetal DNA aneuploidy from maternal serum and the results of clinical validation studies performed for the NIPT of aneuploidies has been reported.<sup>42,45-47</sup> A description of the new genetic testing and its application with clinical validity in prenatal diagnosis is reviewed by Babkina and Graham.<sup>44</sup> A committee report by The American College of Obstetrics and Gynecology (ACOG) on the use of cell free DNA testing was published as a practice guideline.<sup>48</sup>

Several large-scale validation studies using archived blood samples from women with a high risk for aneuploidy have reported detection rates of greater than 99% with very low false positive rates (0.5%).<sup>45,49</sup> The advantages of this technique compared to the usual screening techniques described above are that the results for NIPT are highly sensitive and specific (greater than 98-99%). However, it is important to recognize that given the incidence of Trisomy 21 in the USA, the positive predictive value (PPV) of the NIPT for a woman 35 years of age with no other risk factors is somewhere between 28 and 80%. Given the rare prevalence of Trisomy 13 and 18, the PPV for these anomalies in the same woman is approximately 10%.

Although at the time of the early publications no prospective trials were available, the ACOG stated that NIPT was the most effective screening test for aneuploidy in high risk women. The committee report considered the use of NIPT cell free DNA for the “high risk” women, but it did specify that this

test could not replace invasive testing and recommended that the women should have pretest counseling before undergoing the test.<sup>48</sup> A report on the use of NIPT, at the time when only one prospective study had been performed, reported on 8 cases in which there was discordance between the cell free DNA results and the cytogenetic testing.<sup>50</sup> The authors conclude that before this test is offered widely to the low risk obstetrics population, additional evaluation of cell free DNA in clinical practice with a mechanism for systematic reporting of false positive and false negative results will be important.<sup>50</sup> “In the meantime, incorporating information about the positive predictive value in the pretest counseling and clinical laboratory reports is recommended”.<sup>50</sup>

Using cell free DNA testing, Nicolaides et al.<sup>51</sup> reported a low false positive rate in a prospective cohort of 2049 pregnant women undergoing first trimester routine screening. The false positive rate for trisomy 21 and 18 in their population was 0.1%.<sup>51</sup> In their analysis, the screening method resulted in a detection rate and false positive rate for Trisomy 21 and 18 improved compared to older methods. In the conclusion, the authors do not do away with other screening tests such as the ultrasound at 11-13 weeks or the MSM as they are relevant for the discovery of other ploidyies.<sup>51</sup> Nor do the authors recommend not performing invasive diagnostic procedures according to the screening results and in the cases of positive NIPT.<sup>51</sup>

The commentary by Reiss and Cherry<sup>52</sup> on the work of Nicolaides et al.<sup>51</sup> highlights how NIPT is being aggressively marketed to clinicians and general public as companies sell the high sensitivity and specificity. Yet, this performance may be misleading because of the common confusion between high specificity and high positive predictive value. With the perception that NIPT is highly accurate, there may be the real danger that the test results are considered diagnostic. There is much optimism in the development of different assays and the necessary clinical conditions to obtain the “biotechnology pot of gold”.<sup>42</sup>

### **Ethical, legal and psychosocial implications of prenatal diagnosis expansion**

It is interesting to reflect on the term ‘NIPT’ specifically for cell free DNA testing given that ultrasound testing and MSM could also be considered non-invasive testing as compared to the diagnostic procedures. Might it be that the terminology has been adopted for this procedure exactly so that it could be contrasted with the invasive diagnostic procedures and eventually be adopted to replace the diagnostic procedures? As the sensitivity and specificity are high, professionals will be tempted to use

it to avoid invasive testing or other screening procedures even though test performance varies by condition. The guidelines issued by a number of clinical societies stress that NIPT is still to be considered a screening test in women at high risk for fetal aneuploidy that require pre- and post-test genetic counseling.<sup>1,48</sup> However, the recommendation for use of NIPT comes before a regulation and oversight framework is implemented to deal with ethical issues such as sex selection and VUS and incidental findings.

In the USA, there are many clinical practices that have adopted NIPT and four independent companies offer the test and several others offer it on the international markets.<sup>15</sup> NIPT is considered a highly lucrative technology. The global NIPT market is projected to be an estimated 3.62 billion in the USA by 2019.<sup>15</sup> In the USA, payers have reimbursed only those women considered 'high risk'.

Commentators argue that when more data for PPV for average risk women will be available, NIPT will then be offered to all women, perhaps replacing first trimester screening. Yet, the feasibility for provision based on the obstetricians' abilities to master the complexity and content of genetic information, cost and equity issues for provision of universal prenatal genetic counseling and testing is undoubtedly challenging.<sup>15,53</sup>

The test panels available for NIPT include detection for Trisomy 21, 18, 13, fetal sex, and sex chromosome aneuploidy Turner 45X and sex chromosome triploidy Klinefelter 47XXY. Expanded test panels may include Trisomies 9, 16, and 22 frequently implicated in miscarriages and microdeletion syndromes. The latter include 22q11.2 deletion (DiGeorge or Velo cardio facial syndrome), as well as 1p36 deletion, 5P- (Cri du chat), 15q11.2 Angelman/Prader-willi syndromes, 4p- (Wolf-Hirschhorn syndrome), 8q deletion (Langer-Giedion syndrome) and 11q deletion (Jacobson syndrome).<sup>15</sup>

Although all these conditions are indeed associated with severe physical and intellectual disturbances, the rarity of these conditions are such that the PPV for the most common 22q11.2 is only 2-4%.<sup>15</sup>

The ethical and social challenges related to the expansion of fetal genome wide sequencing (WGS/WE) are numerous.<sup>54,55</sup> The first of these is the financial cost to society and to the individual. Although these latest genetic tests have greater diagnostic capabilities than previous ones, they have at best an approximate incremental 25% increase in mutation detection rate.<sup>54</sup> Expectations can be high and when no causative mutation is found, parents or individuals can be disappointed or falsely reassured.

The enormous information analysis and lengthy and complex pre-test counseling required is impossible with the present number of health professionals and will thus require a reorganization of genetic counseling, which is presently individualized.<sup>54</sup> Virtual and interactive genetic counseling will need to be developed to reach a larger number of individuals and to standardize the information given in the pre-test counseling. The risk is that the individualized counseling required in many instances will not occur.<sup>54</sup>

The meaning of informed consent will have to be revisited as it will not be possible to list all the conditions and possible meanings and outcomes so that the consent process will have to be based on broad categories of results and outcomes.<sup>54</sup> The clinical and ethical issues related to incidental findings (mutations found for which testing was not performed is much higher for WGS/WE) are many. The first issue related to whole genome screening is categorization, that is stipulating if these mutations are pathogenic or not and knowledge in this area is debatable and evolving. The question remains: “should the actionable mutation be reported to patients?” In a context where the patient has refused to receive that information, is minor or for mutations in which the symptomatology is of adult onset, knowing what to do is extremely difficult.

Mutations in which there is little or no data for correlation with a defined functional consequence (VUS) in known disease genes are high and constitute the largest challenge in prenatal diagnosis.<sup>15,16</sup> It is difficult for physicians to determine the effects if any of VUS on the pregnancy outcome, postnatal prognosis for the fetus and to convey the reproductive risks of such findings when observed prenatally. In addition, because mutations can be inherited, professionals may be compelled to warn individuals at risk whose wishes can be in conflict with the child affected or with a parent’s desire for confidentiality.

These concerns are associated with ethical and policy issues of stigmatization, privacy and confidentiality in record keeping and insurability.<sup>15</sup> There are persistent debates about how best to store the genetic data, who should store the data and for how long. Reinterpretation of results is also necessary for ongoing knowledge acquisition and entails re-contacting individuals to explore their interest in the reanalysis of their genetic sequence data, which depends on coordination and infrastructure.<sup>54</sup>

In a prospective study in the UK, obstetricians and midwives anticipated giving significantly less counseling and decision-making time for NIPT than they would for invasive testing.<sup>15</sup> Meanwhile a

survey of genetic counselors in the USA felt that a written separate informed consent should be used for NIPT as patients have emphasized the need to make considered decisions.<sup>15</sup> Signing a consent form is a moment where patients can exercise a measure of control through shared decision-making.<sup>15</sup> However, given the expansion caused by offering the test to “lower risk” women and the increasing number of conditions tested for, conveying the information in a reliable and accurate way is next to impossible.

The unprecedented pace of expansion of technology into clinical translation has made it difficult for provider education to keep pace and the rapid commercialization with aggressive marketing to patients and providers has exacerbated the challenges to informed decision-making.<sup>15</sup> This has resulted in testing being offered even before clinical validation. Educational and consent material do not always meet the clinical and ethical standards.<sup>15</sup> Patients and providers have an increased awareness of the availability of the test without education regarding its correct use. Meanwhile, genetic counselors have reported provision of genetic tests by uninformed non-specialists leading to medical mismanagement, loss of trust in medical providers, unnecessary use of healthcare resources and inadequate counseling.<sup>15</sup>

Another barrier to informed decision-making is created by providers who do not provide their patients with educational materials. More complete and accurate information about the genetic conditions and their severity could help to alleviate concerns that parents may choose to terminate an affected fetus based on misinformation about raising a child with disability.<sup>15</sup> This is especially pertinent in the context of a sex aneuploidy as this anomaly occurs in 1/400 pregnancies and is associated with a milder affected phenotype.<sup>15</sup> Educational limitations of the providers thus need to be addressed.

Many practitioners, including genetic counselors, do not feel comfortable counseling patients on microarray results.<sup>15</sup> Women receiving test results experienced limited professional guidance and found the use of microarray testing complex and burdensome.<sup>56</sup>

The ethical issues and counseling challenges of ambiguous results, incidental findings and results that show non-paternity or consanguinity are still underestimated.<sup>55</sup> A HTA report examined the cultural, social, psychological and emotional aspects underlying the decision to undergo prenatal diagnosis.<sup>57</sup> It highlighted that although parents are favorable to screening, women report conflicting evaluations of the role of screening and thus questioned the information it provides to the individual and to

society.<sup>57</sup> Women value the opportunity to make decisions, but few women who were enrolled in a study of genetic testing deliberated about the testing before making their choice and between 10-42% of them found the choices hard to make and wanted more support and/or time to do so.<sup>57</sup> Women were relying on reassurance and or recommendations from health professionals and 3-30 % of women who screened positive expressed regret about their screening decision.<sup>57</sup> Those who were satisfied with their choice were also more falsely reassured and made their choices less systematically.<sup>57</sup>

On the other hand, those women who made their choices more systematically also rated higher on the worry scale. The psychological distress found in women who screened false positive is likely a product of inadequate understanding and might be reduced if there were more effective means of communicating the information.<sup>57</sup> The alternative is to better identify the personal factors or those related to service provision that predict those women that are more vulnerable. The authors of the above study suggest an informed model of patient -professional interaction to improve the parental experience of prenatal diagnosis.<sup>57</sup>

A qualitative study<sup>58</sup> of parental perspectives on prenatal testing from the United Kingdom reported that parents found the information excessive and complex. There seemed to be a lack of understanding underpinning the screening decision in some cases. Although printed material was appreciated, the parents perceived there was not enough personalized discussion with the health professional. Women preferred a joint decision-making process with their partner, a view not shared by the professional who perceived it to be predominantly the responsibility of the women.<sup>58</sup>

If used to make decisions about termination of pregnancy, the increased use of genetic information in the prenatal context will raise the moral and philosophical concern of the role of genetic determinism in influencing parental decisions about pregnancy termination.<sup>59-61</sup> Broader, societal-wide ethical concepts include eugenics and justice, whereas issues at the individual level include autonomy and non-maleficence, which could include the “right not to know”<sup>62</sup>. This latter view seems to be held by a minority and becomes threatened by the opposing group that claim that parents have a “responsibility to prevent handicap”. With the expansive growth in the use of diverse screening technologies, patients will inevitably be confronted with physicians that will propose the use of these tests on the basis of autonomy of choice and prevention of disease. Hence, the normative standards for ethical analysis will shift from choice to obligation<sup>60</sup>. How parents will react to the pressure to



comply to this new norm needs exploration and analysis. In question also are the future autonomy of the child and the confidentiality of the child's genetic information<sup>60</sup>.

Two recent qualitative reports of parental perceptions, acceptance and values associated with NIPT, microarrays and sex aneuploidy testing are informative with regards to the perceptions and experiences of women on expanded testing.<sup>63,64</sup> Women who were pregnant or had recently been, viewed NIPT as favorable to the regular screening methods as they appreciated the accuracy, early timing and test ease as well as the possibility to detect the fetal sex using a non-invasive procedure.<sup>63</sup> The women also stressed the importance of being informed of all conditions assessed by NIPT prior to testing. However, they were uncertain about the test's utility and "actionability" upon receiving information about microdeletion syndromes with VUS.<sup>64</sup> In another qualitative study, the participants did see a risk that a perceived ease of testing could lead to uncritical use or even pressure to use the test.<sup>65</sup> The participants were in favor of limiting the test for only those suspected of having a severe fetal abnormality, but admitted that it would be difficult to draw the line between severe and minor abnormalities.<sup>65</sup> Parents in an exploratory qualitative interview study recognized the difficulties in accepting unexpected results and in communication of the prognosis surrounding the discovery of a sex aneuploidy during prenatal diagnosis.<sup>66</sup> Questions that parents wanted answered as to the future of the pregnancy and the life of the child after birth were not answered and remained unanswered even after birth.

As part of a research study of prenatal cytogenetic diagnosis using microarray analysis a prospective study investigating experiences of women found five key themes that dominated the experiences of women.<sup>67</sup> These consisted of 'an offer to good to pass off', 'blindsided by the results', 'uncertainty and unquantifiable risks', 'need for support' and 'toxic knowledge'.<sup>67</sup> These authors report that women were initially shocked, anxious, confused and overwhelmed at hearing the result of the microarray.<sup>67</sup> They reported getting conflicting messages about the significance of the result and found decision-making very difficult when they realised that there were no definite answers to their questions about prognosis.<sup>67</sup> All the women needed support to manage, understand and act upon the microarray results. They complained that they did not get as much decision-making support as they wanted regarding the continuing or terminating of the pregnancy.<sup>67</sup> Although most women understood that the microarray analysis could uncover anomalies not detected by other cytogenetic analysis, most women could not recall having been told during the informed consent process that they could receive results that are uninterpretable and/or of uncertain significance.<sup>67</sup> This is

knowledge the women wished they did not have, i.e., ‘toxic knowledge,’ which caused constant anxiety during the pregnancy and lingering worries after the pregnancy about the child’s development.<sup>67</sup>

These early qualitative reports suggest that NIPT will easily replace the need for invasive testing even though the guidelines specifically state that, at this point, it should not negate the need for invasive testing. More importantly, understanding the implications of the testing procedures, experiencing the uncertainties and facing moral dilemmas with the newer genetic testing raise similar issues for women and couples compared to those undergoing the established screening and invasive procedures.<sup>57,58,67</sup>

## **An overview of the literature: Psychosocial and cultural factors affecting the development of prenatal testing**

### **Women centered critiques: Lost opportunity for a relational autonomy?**

One of the earlier writings about fetal imaging and monitoring<sup>68</sup> used a women centered critique to demonstrate how birthing technologies lead us to ignore human stories and relationships. Arguing from the perspective of the social nature of human life and the dynamic character of the moral self, this author showed by example how the use of a birthing monitor “can inappropriately replace the interaction between the woman and the nurse” and is seen as trivializing the birthing mother as clinical material, robbing her of her agency and her opportunity to act on behalf of her baby”.<sup>68</sup> Whitbeck states “that concern with the development of people within and through their relationships reflects a perspective that is distinct from both modern individualism and traditional patriarchy”.<sup>68</sup>

Similarly, Lippman who uses a critical feminist social justice and constructionist lens to examine prenatal screening has explored issues of genetics and ethics.<sup>69-71</sup> She examines the ways in which prenatal screening has been socially constructed and the impact that this construction has had on the status of women, children and people with disabilities.<sup>69</sup> Lippman recognizes that constructions around the themes of reassurance, control and choice are in tension with each other, and often occur together. The discourse on prenatal screening consists in constructing a “need” for prenatal diagnosis and the promotion of “choice”.<sup>69</sup> Lippman decries this discourse as a marketing strategy, one which hides other facets of prenatal screening, by not asking questions such as how risk groups are

generated, why reassurance is sought and how eligibility for obtaining this kind of reassurance is determined.<sup>69</sup>

Also adopting a critical theory feminist perspective, Gregg<sup>72</sup> concludes from a qualitative study of women's perspectives on pregnancy, technology and choice, with a participant's quote: "how to behave like a pregnant woman is like a double edge sword".<sup>72</sup> In her study, women welcomed the freedom to make prenatal choices, but discovered that these choices were accompanied by internal and social pressures and feelings of ambivalence and guilt. Hence, with women's freedom to choose comes "the 'freedom' to be blamed, censured or sanctioned for making choices deemed inappropriate or dangerous".<sup>72</sup>

For Lippman, despite its insistence on objectivity and neutrality, the Western biomedical system is grounded in particular social and cultural assumptions. These assumptions shape the way that disease, malady and disorders are constructed by biomedicine.<sup>69,71</sup> "There is no value-free view of disease, rather, scientists give biological processes different forms in different people, thereby creating disorders and disabilities as social products".<sup>71</sup> As a result, "technology used by biomedicine reinforces and reflects social norms and standards that exist within power relationships in our society. Just as disease cannot be value-free, neither can technology."<sup>71</sup>

### **Risk and disabilities**

Risks in prenatal testing have been discussed in different contexts including risk of physical affliction and statistical risk. In this section, risk will be viewed in its socially constructed nature. Indeed, prenatal screening takes place in a particular historical and cultural context where risk dominates pregnancy.

Lippman notes that pregnant women are immediately labeled high-risk or low-risk, but never no-risk.<sup>70</sup> The risk identified by authorities is never external and never the result of possible occupational or social environmental effects on the baby.<sup>70</sup> Risk is always internal and sets up the pregnant woman as the party worthy of blame regarding behavior she may have engaged in during pregnancy.<sup>70</sup> After attaching a risk label, medicine reconstructs a normal experience, i.e., one that requires health care professional's supervision. Lippman had predicted that the discourse of reassurance with prenatal screening would eventually be associated with removal of the "high-risk" age category, thereby making all pregnancies high risk and encouraging physician surveillance and control over all pregnant

women”.<sup>70</sup> Lippman questions what choice really means when the pregnant woman is forced to choose from options constructed by others. “Why is genetic testing more reassuring than allocating funds for home care, for children with needs and is bearing a child with Down Syndrome really a choice when society does not truly accept children with disabilities or provide assistance for their care”?<sup>70</sup>

In a qualitative study exploring women’s experience entering, living and exiting higher risk status, the authors discuss the preoccupation of a risk-oriented way of looking at the world, which shapes health care delivery and practice and the meaning of higher risk status to women undergoing prenatal maternal screening for chromosomal anomalies.<sup>73</sup> When pregnancy came to be considered as a period of risk, prenatal screening programs in the late 20<sup>th</sup> century became a way to reduce the risk of unwanted diseases and disabilities.<sup>73</sup> By submitting to screening, women are implicitly offered a healthy baby.<sup>74</sup> Western culture’s fascination with the control over one’s life has resulted in the popularization of the concept of risk to explain deviations from the norm and misfortune and as such it behooves us to recognize that something must be done to prevent misfortunes.<sup>75</sup>

Saxton<sup>76</sup> criticizes the concept that a pregnancy should be based on the assurance that no deviances are present and that fetuses are liabilities. She supports proponents of disability rights arguing that disabilities are not problems to be eliminated, but differences to be supported responsibly by the collective society.<sup>76</sup> Prenatal screening programs are open to critiques from the disabilities movements arguing against the eugenic mentality indirectly promoted by these programs<sup>77</sup>. The assumption is that screening reduces the incidence of disability and improves quality of life. There needs to be a questioning of the concept. ‘quality of life’ and acknowledgement of the social value of people with disabilities.<sup>76</sup>

Saxton through her own experiential knowledge of disabilities offers new perspectives to women and couples for the decision-making process regarding abortion.<sup>76</sup> In a recent review of the difficulties with genetic counseling in this modern era, the author reports: “surprisingly there are few empirical data reporting on public opinion about DS” considering that “the issues about DS and disability are complex and conflicted”.<sup>15</sup> Public misconceptions about the nature of the disability may affect the decision to perform prenatal testing and to terminate pregnancy.<sup>15</sup> Whereas people with DS overwhelmingly report being happy with their lives, 64% of Dutch women felt that raising a child with Down syndrome would be a burden.<sup>15</sup> Women who opted to terminate a fetus affected with DS

feared that these children would lead excessively burdensome lives because of the condition and due to the perception of low societal respect for people with disabilities<sup>15</sup>. Nevertheless, another study indicates that parents of children with Down syndrome reported feeling love and pride for their child with DS and only 4% expressed regret over having that child".<sup>15</sup>

### **"Ordinary testing"**

The institutional uptake and the 'routinisation' of maternal serum alpha fetoprotein (MSAFP) testing as well as the promoters impact on women's discourse and thinking were investigated in a qualitative study.<sup>78</sup> MSAFP was initially used to screen open neural tube defects (ONTD), but clinicians soon realized that it was correlated with other fetal anomalies and quickly the test was offered for "off label" screening. California physicians felt that the mandating by the state left them no option, but to force all women to get tested for fear of liability for medical negligence. However, this rapid 'routinisation' did not acknowledge seemingly contradictory and limiting factors to the adoption of this practice. The most important factor was the absence of any treatments for the anomalies detected by this screening procedure. A decision for termination had to be made quickly by the women before the legally accepted 24 weeks of gestation. Furthermore, a positive screen test with actual fetal anomalies applied to only 0.1-0.2% of women, whereas 8-13% screened positive so that a significant proportion of women underwent subsequent testing procedures with additional monetary and psychosocial costs. Finally, there were concerns related to the lack of genetic counseling to palliate for uninformed decision-making and parental anxieties in certain geographical areas.<sup>78</sup> The results of the authors' qualitative study are rather striking. The following is a quote from one of the participants:

I went back and forth...I should do this; I don't know why I'm going to do this...  
[interviewer introduces the topic of a possible positive result]. So then you get this positive and you're panicked because you think that there is some kind of problem...and if there is no problem you feel better but there's been a lot of undue stress. (But) if there is a problem, well—you're already 24 weeks pregnant. So then you have to make a choice and I can't make that choice. For me the choice has already been made. We're going to have this child... So now I've gone through all of this to find out something is wrong but I'm not going to do anything about it anyhow. So then I figure, why am I taking this test? I don't know, and then I say I'm not going to take it

and then I come down to it and I go, 'Fine, here's my arm, take my blood' ... (In the end) it was a matter of needing to know everything you can and do everything you can.<sup>78</sup>

For the authors, this participant's statement clearly describes the pressures that led her to accept the test.

Her objections revolve around the increased anxiety created by testing, the high rate of false positive results, and her rejection of the option of late term abortion. These are precisely the concerns one finds in the theoretical literature about MSAFP testing. Yet the participant appears to have carried on her cogent conversation quite apart from the provider of the testing procedure where MSAFP screening exists not in a world of bioethical concerns but rather as part of standard medical practice. So although she had decided not to be tested, once at Health Pride, the routine flow of prenatal care took over and led to the action she describes as 'fine, here's my arm, take my blood.'<sup>78</sup>

The authors<sup>78</sup> underscore that "something even more than "going with the flow" appears to have informed" this participant's action: "By the time she acquiesced to testing, its meaning had been transformed." MSAFP was no longer perceived as a test that could diagnose untreatable birth defects and prompted a decision "she did not want to have to make." Her comment about the need to "know everything you can, and do everything you can" is highlighted as an excellent summation of their informants' quest for routine prenatal care, not necessarily prenatal diagnosis. This study showed that the new screening test became 'absorbed' under the rubric of ordinary non-controversial routine prenatal care. According to the authors, "when it is just about another blood test, it ceases to be something for which a deliberate patient decision needs to be made." Testing henceforth becomes imbued with meaningful care, that is, additional information, reassurance for a normal pregnancy and prevention of fetal harm.

Another participant's statement highlights the way women confronted the issue of abortion: "The benefits of having the test would be if you could find out that something was wrong you might be able to fix it, or make your decision early"<sup>78</sup>. For the authors, "while it seems reasonable to assume that the 'decision' referred to is abortion, it seems added on as a secondary consideration" since it follows the hope that the problem could be solved. The contested nature of abortion in America, the

purposeful omission of the mention of abortion in patient education by providers and the promotion of fetal health linked with prenatal care are factors that influence the way women think of prenatal diagnosis and it “appears to be deeply confusing to women to think about testing and abortion decision-making together”.<sup>78</sup>

### **“Governmentality” and the media**

The routinization of prenatal testing can be understood through Foucault’s delineation of the way in which power operates in modern societies.<sup>79</sup> As Foucault explained, since the 18<sup>th</sup> century, authorities have increasingly taken on the task of managing life by enhancing the health, welfare, prosperity and happiness of the population as a whole.<sup>23</sup> Based on Foucault’s theorization of the power/knowledge relationship, “the study of governmentality looks at the production of truth and knowledge and its impact on conduct or regimes of practices”.<sup>25</sup> Knowledge developed through science is reflected in different discourses that have come to be regarded as representing the right ways of acting and thinking. Foucault defined discourse as “practices that systematically form the objects of which they speak”.<sup>24</sup> Individuals in modern liberal societies are not forced or coerced to behave in a certain way. Rather, they are governed through their freedom; “by voluntary self-discipline we behave in the ‘correct’ way”.<sup>26</sup> Those who deviate from the norm and do not adopt the expected behavior are indeed said to be at risk.

By studying the various discourses that developed among different social groups on fetal screening, Gottfredsdottir et al. have tried to uncover the sometimes hidden and multi-dimensional operations of power that influence the decision to offer and undergo fetal screening<sup>80</sup>. Women make decisions about first-trimester screening before their initial visit to the prenatal clinic. The inference is that the media are of key importance in providing prospective parents with the knowledge for prenatal testing, typically emphasizing the positive findings and avoiding the downsides of the technology. In Iceland, the use of NT was initially limited to women with high risk pregnancies, but by 2005 it was offered to all pregnant women.<sup>80</sup> The authors contend that in the absence of a collective responsibility parents have become responsible for the implications of screening and for ethical dilemmas such as disabilities and the value of the disabled.<sup>80</sup> In their conclusion, they state that parents are not forced to behave in a particular way, nor to comply with any laws or rules. Nonetheless, they behave in a suggested way, which is understood as “governmentality” since it is through their free choice that parents make the “right “ decision.<sup>80</sup>

### **The therapeutic gap: From the logic of choice to the logic of care**

An ethnographic study of prenatal ultrasound was reported by Mirlesse and Ville in the context of generalized access, but restrictive legislation and social inequalities.<sup>81</sup> The underscore that “the increased performance of imaging techniques combined with the computerisation of measurement produce new forms of knowledge, both expert and lay, that transform the experience of maternity and perception of the fetus”.<sup>82</sup> The world-wide diffusion of these technologies encounters, however, local historical, cultural and political particularities.<sup>81</sup>

In the Brazilian context, the physicians working in the public fetal medicine center are just as concerned with objectifying the anomaly and understanding the etiological process as their colleagues from the northern hemisphere. However, this logic is not easily assimilated by the women they are treating. The latter are far more concerned with their role as mothers and with the well-being of their babies. “Only when the diagnostic sequence has been completed and when it is clear that there is no chance that the baby will survive can the question of abortion be raised by professionals, very gradually, as the anticipation of an inevitable death”.<sup>81</sup> The fragmentation of the fetus through images that take place during the diagnostic phase creates a distance that dehumanizes the fetus, making it easier to discuss the possibility of its death. The following quote from an obstetrician in this ethnographic study exemplifies the point:

The problem is the kidneys; the kidneys have not developed properly, they don't work. They will never work. The baby cannot pee, there is no liquid in the pouch. We won't be able to see the sex. And it won't be able to breathe. It will not survive.<sup>81</sup>

The possibility of an abortion is nevertheless very slim. Young doctors trained at the center thus express their unease with what they consider to be a paradoxical situation, which offers diagnostic opportunities without allowing for pregnancy termination when there are severe non-lethal fetal malformations. This has been framed as a therapeutic gap, which is viewed as a source of psychological distress for women.<sup>83</sup> When the malformations are not fatal, the women are confronted by attitudes from the physicians that are diverted from a logic of choice to a logic of care; in the process, the fetus initially ‘dehumanized’ by undergoing detailed analysis for diagnosis becomes ‘rehumanized’ by the physician.<sup>81</sup>



## **The effects of socio-technological settings on prenatal testing uptake**

A review of the evolution of policy implementation and the organization of health service delivery effects on the manner in which prenatal testing is experienced by women in three European countries was investigated.<sup>84,85</sup> In England, prenatal diagnosis is state funded, centrally organized with a network of practitioners that are coordinated locally. Pregnant women have a unique health care path, making it easier to coordinate and train personnel.<sup>84</sup> The screening policy for prenatal testing consists of lengthy consultations presumably aiming to reduce the position of inequality between the patient and the healthcare provider.<sup>84</sup> Prenatal testing information is provided to women before and during the consultation. However, the information that is given is not easily accessible and women are pressured into giving an answer as to their decision for testing immediately even though they may change their minds at a subsequent visit.<sup>84</sup>

In France, the ‘medicalisation’ of pregnancy is very strong. Health care professionals in both public and private clinics have the responsibility of implementing screening and the obligation to obtain a signed consent form without having at their disposal the necessary additional resources needed to obtain such consent.<sup>84,85</sup> The screening procedure occurs in a highly medicalized environment, after a brief consultation where the pregnant woman is required to digest the information and make a decision for testing the same day.<sup>84,85</sup> Women experience pressure if not imposition by health care professionals to perform the screening tests and have to argue their decision to opt out of screening.<sup>84,85</sup>

In the Netherlands, a screening policy was not developed for a long time as there was a *prima facie* rule against it.<sup>84</sup> After an initial limitation of the use of screening to ‘high risk’ women, it became available to all women later than in other European countries.<sup>84</sup> Practitioners need to be trained to respect the rights of people not to be informed. Women under the age of 36 pay for the testing procedure as they are considered low risk.<sup>84</sup> The screening procedures involve lengthy interactions in a low medicalised setting with information provided during and after the consultation mostly by midwives.<sup>84</sup> The decision-making occurs at a different time, hence it can be described as an opt in screening procedure.

Vassy et al. argue that the testing “script” in England encourages its uptake, it takes the form of an expectation in France and it is framed as optional in The Netherlands. Public policies and health care organizations thus influence the interactions between health care providers and women, indirectly

shaping the choice for prenatal screening.<sup>84</sup> These findings suggest that the ideology of freedom of choice for the patients in prenatal testing in some European countries is seriously compromised.

To summarise, the first two introductory sections explored the clinical and ethical complexities raised by the explosion of genetic information and technology in prenatal testing. Many factors explain the adoption of new genetic technologies in prenatal diagnosis, which favors an expansion even before the difficult ethical and organizational issues have been analyzed at an institutional or societal level. A limited body of social scientific knowledge from some western cultures highlights important concepts and values that have influenced all of society in the acceptance and diffusion of prenatal testing. Pregnancy in the western biomedicalised culture has become conceptualized as a state of risk wherein the norm for pregnant women is to 'minimize harm' and protect the fetus, which can only be achieved through prenatal testing.<sup>86</sup> Prenatal testing is promoted as a way to give women more control over their own bodies, presumably protecting them from risk and providing positive feelings for the women.

This optimistic framing of a new technology facilitates its acceptance. The absence of relational autonomy pushes, however, pregnant women into the individualization of the decisions related to the ethical dilemmas facing them, but also of the responsibilities underpinning these decisions. For Rapp, pregnant women who were "at once conscripts of techno-scientific regimes of quality control and normalisation, and explorers of the ethical territory its presence produces", "have become moral philosophers of the private".<sup>87</sup>

The effects of "governmentality" together with the evidence of the practices and experiences of women in different "socio-technological settings" reviewed above leads one to question whether the ideal of freedom of choice for prenatal testing is, can or should be realized. Freedom of choice presupposes an autonomous informed decision-making process. This first section of the introduction thus contextualized the first objective of this thesis, which is to understand the experiences of women and couples who undergo prenatal diagnosis.

The next section discusses currently accepted norms of practice such as autonomy, informed choice and shared decision-making. These concepts and practice norms have been linked with the development of decision aids that are promoted as favoring the shared decision-making paradigm. We present the conceptual and pragmatic difficulties related to this paradigm that is key to our

second objective, which is to understand whether women undergo an informed consent process in prenatal diagnosis.

## **Informed choice and shared decision-making**

### **Autonomy, informed choice and culture**

In accordance with the policies of the Directorate of Health UK<sup>88</sup> and of NICE 2008 guidelines on prenatal screening<sup>89</sup>, the main role of health professionals is to inform prospective parents in a way that encourages their autonomy and informed choice.<sup>90</sup> Yet 'routinization' as discussed above can be seen to reduce, rather than expand choice. An informed choice is considered present when the decision is based on relevant knowledge, is consistent with the decision maker's values and is behaviorally implemented. It is embedded in the principle of autonomy, which can be defined as self governance<sup>79</sup>. Informed choice is internationally recognized and accepted as an important aspect of ethical health care<sup>91</sup>. Informed choice is important because greater patient involvement in making choices can lead to better patient outcomes.<sup>92</sup> In the UK, antenatal screening policies state that their aim is to facilitate reproductive informed choices. In practice and in accordance with guidelines, professionals are required to offer screening in a non-directive way to enable pregnant women and their partners to make prenatal screening decisions independently<sup>89</sup>.

Before pursuing with the discussion on the link between autonomy, informed decision-making, and the role of culture, a few clarifications are required. Autonomy in the bioethical literature relates to the patient's right to decide the course of investigations or treatments based on his or her particular situation, cultural or religious beliefs as long as the individual is deemed cognitively competent. This concept differs from the notion of autonomy as derived from the psychological theory of self-determination, which is defined as behavior willingly enacted, or a state in which the action or the values expressed through that act are fully endorsed. Furthermore, autonomy is not equal to independence although both are aspects of individualism<sup>93</sup>. Autonomy is of central importance to personality function and wellness and is salient across development, life domains and cultures<sup>93</sup>. Individuals can be dependent (reliant on others for guidance and support) and simultaneously autonomous<sup>93</sup>. It is comprehensible that autonomous choice is not the same as independence of a decision-making process. The UK antenatal screening policy can be critiqued in so far as information

giving by professionals and the prenatal screening process cannot be neutral; the aim should be for informed decision-making and not independent (or “autonomous”) decision-making by the parents.

This thesis does not aim to analyze the customs or modes of behavior related to prenatal testing amongst cultural groups of women. An individual culture is constructed through various personal experiences, including cultural background and histories that influence an individual’s views, values and understanding of health and illness. For instance, Chirkov et al.<sup>93</sup> adopted a psychological perspective on culture using Triandis’ conceptualization of cultural choices and norms built around two dimensions: interchangeability vs. hierarchy and individualism vs. collectivism<sup>93</sup>. They reported cultural practices amongst university students in four different countries. They found that individuals from different cultures internalize different practices, but any type of cultural practice can be engaged in by the participant autonomously, which predicts the wellbeing of individuals in all four countries. For these authors, studies that report a cultural perspective should acknowledge that “one cannot presume that a person truly endorses cultural practices or values just because she is surrounded by them or because she resides in a given country”<sup>93</sup>. Within this perspective, cultural aspects are presented below as per the authors’ descriptions, assumptions and definitions of culture. An analysis of the key criteria for defining cultural dimensions that characterize the experiences or decision-making processes in prenatal testing surpass the scope of this thesis.

To identify to what extent the guidelines aimed at facilitating informed choice reflect values in the general population, van den Heuvel and collaborators performed a population based survey of some European and Asian countries.<sup>94</sup> In their introductory remarks, the authors stress that autonomy conceived of as self-governance is not compatible with the concept of independence. Autonomy can be considered a universal need, but its expression can vary according to the culture and religious views. Some of these views promote interdependence and privilege the interests of society over that of the individual.<sup>94</sup> The concept of relational autonomy allows for the influence of interpersonal relationships or social organizations to influence decisions. Social context shapes individual choices, characteristics and aspirations.<sup>94</sup> These authors found that people in Northern European countries valued parental choice more than significant other’s views. In comparison, in the southern European and Asian countries only a minority of people advocated parental choice and significant other’s views were considered more important by the women.<sup>94</sup>

NICE stipulated concept of informed choice is seen as deriving from culturally specific set of western ideologies that are not valued by others from different cultures.<sup>95,96</sup>

Western societies have been characterized as 'individualistic' where individuals see themselves as independent from their social group, in contrast with the Asian countries often described as 'collectivists' where individuals may value the wishes of the group over their own.<sup>95</sup>

Research shows that in collectivist cultures the family often plays a more important role in health care decisions.<sup>95</sup> In this study, the diversity in the value attached to autonomous informed choice in genetic disorders and the similarities and differences in this value in women from different ethnic origins were explored. All women claimed they wanted the right to retain the ultimate decision. While many women valued informed choice as conceptualized in the policy definition this was not universal. Women that conceived the choice as in the policy intention and those who were pro-choice for the right to follow their religious convictions thought that professionals were health information providers that had little role to play in the decision-making process.<sup>95</sup>

Other groups of women wanted professionals to be involved in the decision-making process to a varying extent. Some women valued decision-making in the family context and, in most groups, the partner would be involved in the decision. These characteristics were not culture specific. Some women of the minority ethnic groups, particularly those who did not speak English and or had recently migrated to the UK, wanted advice from health professionals when making choices. Furthermore, ethnicity and religious held beliefs were not a proxy for individual values and didn't mean that the person would not seek the health professional's advice. More importantly, about half of the women did not want to actively use the information they were given to make a choice. Some women wanted direct advice and recommendation from the health care professional. Many women did not see advice giving by professionals as incompatible with autonomous choice, but rather as a process to support informed choice by engaging in discussion and thus raising ethical concerns as to the policy directive that stipulates that health care professionals are to practice non-directiveness.<sup>95</sup> The authors found that screening is valued by most women regardless of their ethnic origin or country. While personal acceptability varies within groups, the reasons for uptake or decline of screening are strikingly similar across groups.<sup>95</sup>

Acknowledging that people ascribe to different value systems yet can still make informed decisions about prenatal testing suggests that the test providers should try to assist the making of informed decisions in a manner relevant to the individual. If other's views are highly valued, then the tests should be presented to facilitate action in accordance with the social opinion by example encouraging discussion with significant others.<sup>95</sup>

Ahmed concludes that policy definition and implementation of informed choice may support the needs of individuals from individualistic societies, but they may not meet the needs of those with cultural norms and practices of a collectivist approach.

It appears that understanding of autonomous decision-making is ambiguous and associated with misconceptions of independence. There is an apparent contradiction in the NICE directive for neutral advice giving and the goal of independent decision-making by the parents, which lends support to Ahmed's view according to which policy developers should revisit these concepts for clarification and perhaps adoption of new policy directives. The removal of the word 'autonomous' linked to the 'informed choice' terminology and 'non-directive' counseling could clarify and facilitate the decision-making process.<sup>95</sup>

### **Shared decision-making**

Patient centered care emphasizes the importance of facilitating the engagement of patients in their own health care decisions and is the new norm for clinical practice.<sup>14</sup> Shared decision-making (SDM) is conceived as a process in which the patient and family members arrive, through an interactive approach, at quality decisions that are evidence based and patient centered.<sup>97</sup> Charles and collaborators define shared treatment decision-making in the context of the physician-patient encounter as follows: "the information exchange is two ways" and the deliberation between the physician and the patient or potential others is interactional, "both parties work towards reaching an agreement and both parties have an investment in the ultimate decision made"<sup>97</sup>.

Shared information about values and likely treatment outcomes is an essential prerequisite, but the process also depends on a commitment from both parties to engage in the decision-making process. The clinician has to be prepared to acknowledge the legitimacy of the patient's preferences and the patient has to accept shared responsibility for the treatment decision.<sup>97</sup> A detailed discussion of the

philosophical, historical and ethical perspectives and arguments for or against this concept can be found in other publications.<sup>98,99</sup>

Sepucha and colleagues<sup>100</sup> point out that since there is no gold standard for the measurement of SDM, establishing the validity of the tools to evaluate the process will be a problem.<sup>100</sup> Few studies have shown construct validity or discriminate validity of the decision-making processes.<sup>100</sup> There is also little information available as to the role of the measurements with regards to the health outcomes or the use of health care services.<sup>100</sup> It is worth noting that patient participation in decision-making is viewed differently by patients than what is typically conceived by health care professionals.<sup>101</sup> Patients view decision-making as an ongoing process in which their participation may change over time.<sup>101</sup> Patients with higher education view their role as gathering information and weighing the consequences of each alternative, which is exactly what experts advocate to promote high quality decision-making.<sup>101</sup> It also means that more vulnerable patients need adequate support to participate in decision-making.

For the patients, it is important that the decisions be made within an extended social unit emphasizing the need to include all relevant stakeholders since for practical reasons extended family are implicated in the care of the patient.<sup>101</sup> The decisions patients report being involved in are not those traditionally studied (such as treatment or screening strategies), but rather have to do with the choice of the physician or to follow or not the physician's recommendation.<sup>101</sup> The response of patient involvement in decision-making occurs in response to physician's recommendations and patients make choices in their specific illness perspectives.<sup>101</sup> The differences in the perception of roles in decision-making between the patient and the physician may be related to the dominant medical disease model that focuses on symptoms, testing, diagnosis and treatment, whereas patients' illness perception focuses on how they interpret and cope with the effect of their symptoms on their quality of life.<sup>101</sup>

An example of shared decision-making occurring at an ultrasound clinic in Denmark during the first trimester prenatal risk assessment identifies the difficulties with the expected informed decision-making model and non-directive counseling policy and the boundaries of shared decision-making.<sup>102</sup> Drawing on ethnographic material and interviews with health professionals, these authors identified grey zones that required adaptation of professional attitudes and actions necessary for the communication and understanding of risk figures. The radiologist is responsible for 'attuning' the

hopes and expectations related to fetal ultrasound and remaking of boundaries of risk and life in their interaction with the pregnant woman.<sup>102</sup> First, the radiologist feels the need to identify the gap between the woman's expectation of the scan as a technology for confirmation of life and not as a screening tool. The radiologist knows that women labelled "high risk" experience shock and grief. Hence, to protect the women, the radiologist attempts to reduce the 'gap' by trying to reach a shared understanding of and expectations about the fetal ultrasound. The radiologist tries actively to engage in how risk will be understood and reacted upon. Instead of using the word risk, he may refer to 'two groups of results' only one of which those women will be offered further testing. The radiologist also acts to "attune life" knowing that seeing the image of the fetus on the screen has the potential of escalating the identities of fetal subjecthood and maternal responsibility<sup>102</sup>. The radiologist tries to accommodate his body language to the interpretation of the image on the screen. If an anomaly is detected, he will distance himself from the woman and not comment the image. The aim is to avoid contributing to the enactment of the image as a living child, whereas in the context of a "low risk" image, he will be engaged in the enactment of the fetus as life by saying things like 'this one is active'<sup>102</sup>.

Women are "left in limbo in the face of complex risk knowledge and to appease their anxiety they continually search for tools they could use to make the risk figure meaningful and thus actionable".<sup>102</sup> To the question 'what would you do in my situation?,' the radiologist tries to reconcile non-directive counseling with not leaving the woman "behind," navigating "a sea of information." The radiologist thus provides statistics of what the majority of women with the same situation do in that context.<sup>102</sup> The radiologist also uses knowledge taking into account the particular woman's situation in an attempt to support the woman in reaching a meaningful decision.<sup>102</sup> Some argue that conscious knowledge differentiation works against the principle of non-directiveness and autonomous decision. Nonetheless, such practices may be understood as what makes decision-making possible in a situation where complex risk knowledge is experienced as basically meaningless by the pregnant women<sup>102</sup>. The authors conclude that "if acknowledged that meaningful decisions are made through interrelations then a shared responsibility for decision-making and the decision would allow for influence and advice which is an act of care if the woman deciding is simultaneously capable of challenging the advice"<sup>102</sup>.



## **Decision aids and the International Patient Decision Aids Standards (IPDAS)**

### **Fundamental concepts, goals and outcome measures**

A “decision aid” is a general label that has been applied to different tools or instruments used to inform patients about various treatment options, their benefits and risks, and to structure the decision-making process in order to encourage patients to express their treatment preferences.<sup>103</sup> Their development and evaluation derives from a number of different domains including educational, clinical, decision sciences, psychology and health economics.<sup>104,105</sup> They are meant to be used in situations in which there is enough ambiguity, rendering a choice not self-evident. They are intended to supplement and not replace patient-physician interaction. These aids may be leaflets, videos, audio or interactive media. These tools can personalize the information by allowing patients to clarify scientific uncertainties, potential benefits and harms of the options and their personal values. Decision aids can also help patients to communicate their values to their health care provider and acquire skills in collaborative decision-making.<sup>29</sup>

However, fundamental questions that ultimately have an impact on the types of decision aids developed and the ultimate goals for their use remain. First, decision scientists disagree about the processes by which people make decisions, the quality of these decisions and what a “good” decision entails.<sup>105</sup> The ultimate goals of these aids and their role in decision-making are also under scrutiny.<sup>97,106</sup> For Charles and collaborators,<sup>97</sup> such tools have to be adapted to the mode of decision-making adopted (i.e., “shared vs informed”) and should be context and time sensitive. The potential other sequences of actions subsequent to an initial decision should also be known.<sup>97</sup>

These tools clearly need to be founded on solid theoretical constructs. An example of a problematic mismatch between the goal of a tool and its measure is found with the construct of decision regret. Such regret typically stems from a non-optimal health status outcome, which the patient assumes (perhaps incorrectly) as a result of the decision. However, the scale used to measure decisional regret relies on the patient’s perception of the rightness of the decision rather than to its outcome, thereby not matching the conceptual definition.<sup>97</sup> Finally, there should be a conceptual plausibility for the decision aid that can inform particular design features for the tool to fulfill the stated aim.<sup>97</sup>

For Charles et al., the value assumptions underpinning the goals of decision aids need to be made explicit.<sup>97</sup> The first assumption is that patients agree to a normative approach to decision-making.

Only then should a decision aid be considered. However, there is no classification available to summarize and compare the range and type of value assumptions of currently available tools. For instance, explicitly informing patients in an understandable way and using a decision tree analysis refer to the conceptual framework of expected utility theory, which is a normative approach to decision-making. Both the clinician “offering” this tool and the patient should ascribe to the value assumptions underlying the tool and feel that the tool and the underlying theory are the best way to arrive at the right decision. Similarly, the limited options being considered and a focus on risks and benefits characterize many decision aids<sup>97,98</sup>. Finally, assumptions are also key to the specific measures being used to assess the outcomes of decision aids: “the more the outcome is positively influenced by a decision aid, the more the tool is considered positively, regardless of whether the tool was designed to affect change in those areas”<sup>97</sup>.

Decision aids often include values clarification exercises, which represent another area of contention.<sup>106,107</sup> O’Connor and colleagues suggest that a primary outcome measure of decision aid use should be the congruence between the patients’ decision and their values.<sup>92</sup> However, values clarification exercises aimed at helping a patient reveal his or her true preference entail certain “trade-offs” that may distort or prove inconsistent with the way this person usually makes decisions. Rather than allowing the patients to clarify and articulate their own values in their own way, decision aids impose a pre-defined information processing framework.<sup>97</sup> For O’Connor and colleagues, the fact that these aids are used implies that patients have difficulty making decisions that are consistent with their values and that these tools do help them to identify and articulate significant values.<sup>92</sup>

Nelson and collaborators provide a critical examination of the theoretical basis and appropriateness of values clarification exercises and decisional conflict measures.<sup>99</sup> They enumerate several reasons for excluding values clarification exercises. The first consists in the unreliability and doubtful validity of utility measurements in individual decision-making. These measurements are linked with logic and discrimination errors and procedural variance in elicitation. One study found that individuals with low numeracy had the most inconsistent utilities, hence invalid preferences.<sup>99</sup> Values clarification relies on the problematic assumption that values elicited for unfamiliar health states are a reliable and valid measure of long term preferences.<sup>99</sup> This assumption is challenged by research.

As Nelson and collaborators underscore, the concept of decisional conflict is a normative question, not an empirical one. In principle, decisional conflict may represent an undesirable state that may be

detrimental to decision-making. Hence, promoting deliberation of different choices, personal goals and an ongoing engagement in the decision-making process may prove positive. However, decision aids that seek to decrease decisional conflict “may be doing a disservice to people and physicians by ‘pathologizing’ decisional conflict”<sup>99</sup>. Patients may incorrectly assume that decision-making needs to be clearly circumscribed and the decision irrevocable. This is in sharp contrast with natural situations where individuals experience ambivalence and where revisiting a decision may be beneficial and should be possible. Nelson and collaborators hence call for a cautious approach and warn about the potential of decision aids to cause harm.

For users of decision aids, the most promising design feature of a decision aid is that of explicitly showing the implications of one’s values by displaying the extent to which each decision option aligns with what matters to the user.<sup>108</sup> In practice though, no framework explicitly requires that physicians help their patients to understand the connections between what matters to them and which option is thus better suited.<sup>108</sup> According to a systematic review of 110 decision aids,<sup>108,109</sup> the majority were used in cancer for screening and diagnostic decisions, less than a third explicitly showed users the implications of their stated values, and only 38% asked the users’ preferences. The actual decision made by the individual was recorded in only 16% of the tools and few tools explicitly stated the possibility of using the tool iteratively. Few of the studies used theories, frameworks or previous designs as a foundation for the design of the values clarification exercises.<sup>110</sup>

### **The criteria of International Patient Decision Aids Standards (IPDAS)**

Decision aids can modify the use of a treatment or procedure not only because of their stated goal, but also because of their inherent bias. The work of IPDAS has thus sought to establish consensus around the evaluation of their importance, quality and effects.<sup>111</sup> To identify quality criteria for decision aids and tools, the group produced a framework with supporting empirical evidence of the different components and processes required to produce a decision aid. The value of the criteria was scored amongst different stakeholders which included researchers, policy makers, practitioners and patient groups. The criteria were scored according to the level of importance as perceived by the stakeholder when, in fact, the usefulness of the criteria should have also been considered considering the feasibility of their measurement.<sup>30</sup> The development process for the criteria were scrutinized<sup>112</sup> and an evaluation of the evolution of the IPDAS collaboration was published.<sup>31</sup> The latest version of the IPDAS criteria consists of six qualifying criteria and ten certification criteria, the latter being

considered necessary to avoid risk of harmful bias<sup>113</sup> (see Appendix 1). The quality criteria (28 items) were adapted from the original framework<sup>29</sup> (see Appendix 2).

In a Cochrane review of a convenience sample of patient decision aids investigating the application of the IPDAS 4, it was reported that most of the tools met the qualifying criteria, but only 10% met the certification criteria (predominantly for failure to disclose policy update and funding sources or lack of acknowledgement about the uncertainties related to the risks and benefits of various options).<sup>114</sup>

Considerable inter rater variability was found even using experienced raters suggesting additional training and standardization is required for use of decision aids.<sup>114</sup>

### Critique of quality criteria

Bekker contests the unquestioned application of the IPDAS checklist<sup>101</sup>. According to her, using this checklist “should mean that interventions designed to help patients make treatment decisions have a comparable level of quality, thereby reducing variations in health service delivery”<sup>105</sup>. However, using a checklist effectively implies that investigators know what information is pertinent to patients to make a decision and have sufficient knowledge to appraise critically the decision aid, its evaluation and implementation.<sup>105</sup>

Bekker lists several reasons for problems with the criteria. The IPDAS checklist is informed by several theoretical and health service policy areas. As a result, there are many criteria to fulfil and it is implied that all the criteria need to be met and/or have equal weight in decision facilitation.<sup>105</sup> Second, many of the statements require significant expertise to operationalise and this is problematic since many developers lack the abilities required for proper operationalization. For example, how should one ‘provide steps to make a decision’, ‘use visual diagrams to present probabilities of outcomes’ and ‘present information in a balanced manner enabling people to compare positive and negative features’?<sup>105</sup> Thirdly, the IPDAS checklist was informed by expert opinion and the evidence-base for each IPDAS domain was weak.<sup>105</sup> Unlike other evidence-based checklists, there is no distillation of evidence to suggest which criteria or technique results in a more effective patient decision aid.<sup>105</sup> For Bekker, IPDAS criteria are not to be considered as a theory about informed decision-making. To develop, evaluate and implement a decision aid is challenging as it requires multiple expertise and shared goals and philosophies among experts.<sup>105</sup>

From a decision theory perspective, good decisions should be about decisions made well, which remains difficult to evaluate.<sup>105</sup> For Bekker, indirect measures of decision processes are currently

used, including measures of knowledge, attitudes, values, preferences, utilities, risk perception and reasons for and against options chosen. Other measures, such as decisional conflict, satisfaction and regret, refer to users' perception. While decision aids may facilitate patient participation, there is no evidence, according to Bekker, that the IPDAS criteria support the development of more effective interventions: "data is needed to show how better decisions improve shared decision-making or patient centered care"<sup>105</sup>.

Ultimate considerations on the use of decision aids and criteria

O'Connor et al<sup>115</sup> report on a systematic review of randomized control trials of the effectiveness of decision aids, using measures of quality decisions that included knowledge, improved value congruence with the chosen option and accuracy of risk perception. Decision aids improved knowledge scores, lowered decisional conflict scores and increased patient participation in the decision-making. Complex decision aids were better at reducing decisional conflict scores than the simpler versions, but did not affect satisfaction. The decision aids had variable effects on the decisions and the link between the tool and its outcomes such as long term persistence of choice, regret and quality of life remained uncertain.<sup>115</sup>

In a Cochrane systematic review of randomized controlled trials of decision aids, the primary outcomes of interest included the choice made and the decision-making process attributes following the IPDAS criteria.<sup>116,117</sup> Secondary outcomes of interest were behavioral, health and health system effects.<sup>117</sup> As per the 'choice made', knowledge after the use of a decision aid was increased when compared to usual care and a more detailed aid was significantly associated to knowledge.<sup>117</sup> Accurate risk perception was higher with decision aids that expressed probabilities. Exposure to a decision aid with explicit values clarification resulted in a higher proportion of patients choosing an option congruent with their values.<sup>117</sup> With regards to the 'decision-making process', patients who used decision aids experienced lower decisional conflict when compared to usual care.<sup>117</sup> The proportion of patients who were passive in decision-making or undecided after the intervention was reduced.<sup>117</sup> In many studies, decision aids improved patient-physician communication and patient satisfaction.<sup>117</sup>

For prenatal testing, research shows that pregnant women want to participate in the decision-making. Nevertheless, according to a recent environmental scan, few decision aids were made public or evaluated even when shown effective.<sup>118</sup> A content analysis of educational leaflets on DS available

in Canada showed that few of them were adequate: many lacked basic information about the risks and benefits of each option and less than half of them provided practical decision support methods and values clarification exercises. Only 25% of the aids presented a method for evaluating women's understanding of the information regarding the testing options and their outcomes.<sup>118</sup> These tools were developed for the most part after 2011: hence when the 47 criteria IPDAS tool was already available, one may wonder why the majority of the tools did not incorporate the IPDAS criteria.<sup>118</sup>

In summary, the multidisciplinary bodies of knowledge reviewed in the second section of the introduction raised fundamental issues as to the value and practicality of an informed, shared and non-directive decision-making model. While several organizations are in favour of this norm in patient care, the concept of autonomous decision-making that lies at its centre is called into question by women experiencing prenatal diagnosis. Women want to make the decision, but find the information complex and feel they are not sufficiently supported when seeking to make an informed choice. For women, choice is not incongruent with the participation of the health care professional in decision-making. Rather, many women welcome the care provider's opinion. This attitude seems compatible with the concept of relational autonomy and contradicts the non-directive model of decision-making.

Shared decision-making and patient centred care may be conceived as providing the context for a relational autonomy approach to decision-making. Nevertheless, a number of foundational issues with regards to the development and use of decision aids have been highlighted. The notion that decision-making is deemed to be improved with the use of decision aids is contested by scholars because of the underlying normativity (e.g., measures laden with discrimination and logic errors potentially inducing errors in decision-making). Despite the fact that quality criteria have been established, few decision aids fulfill IPDAS certifying criteria. Furthermore, there is no clear correlation between the type of decision tool and the outcomes of the decision, either with value congruence or health care outcomes. The use of prenatal testing decision aids is at its beginnings and the tools suffer from the same limitations as reported for other tools. How the congruence between personal values and the decision made should be measured—which the proponents argue is the major goal of the tools—is not explicitly identified and was not included in the revised version of the IPDAS criteria.

Thus, from the perspective of the shared decision-making model of care, it would seem reasonable to accept that prenatal testing and diagnosis occurs with a less than ideal informed consent process.

Within an increasingly complex context of information load, ethical, social and legal requirements, the degree of uninformed decision-making is likely to augment. To date, there is a lack of evidence on ways to improve patient decision-making and the theoretical basis upon which the stated process and outcomes of decision aids rely is weak.

## **Methodology**

In order to identify potential direction for improvements in the development and use of patient-oriented prenatal testing tools, this thesis relies on a combined analysis of the qualitative and quantitative studies that have examined women and couples' prenatal experiences and decision-making and on a structured critique of an existing decision aid.

### **Meta-ethnography of qualitative studies**

A meta ethnography refers to a structured synthesis methods in which only qualitative studies are included. These are analyzed following a qualitative thematic content analysis strategy with the aim of constructing a conceptual framework of an empirical phenomenon. In our case, the phenomenon of interest refers to the experiences of women and couples undergoing prenatal diagnosis.

#### Literature search

Bibliographic searches were conducted in PubMed, Medline, PsycINFO, CINAHL, EMBASE and EMBASE reviews. Appendix 3 describes the full search strategy for each of these databases. The medical subject headings included prenatal diagnosis, informed consent, ethics, decision-making, congenital, genetic, chromosomal abnormalities, foetal screening and diagnosis, ultrasonography, and variant thereof. These were combined with text words and terms such as maternal, parental, attitudes, paternity, behavior, morality, qualitative research, narrative, interviews, questionnaires, focus groups, experience and variants thereof.

The search period was from 1970 or since inception of the data base until July 2015. The searches were launched in June 2014 and relaunched in July 2015 for an update. The reference list of relevant studies and reviews were also searched. There was no geographical restriction. Language was limited to English given the concern about translating qualitative data. Eligibility criteria were decided by title and abstract and confirmed by reading the methodology section of each article.

#### Article selection process and criteria

To be included, articles had to have used a qualitative or mixed qualitative and quantitative methodology and reported empirical data (such as interviews or focus groups). Findings may refer to psychosocial, cultural, emotional and or ethical themes, as reported by women or couples who underwent or considered undergoing screening or diagnostic interventions during pregnancy for the



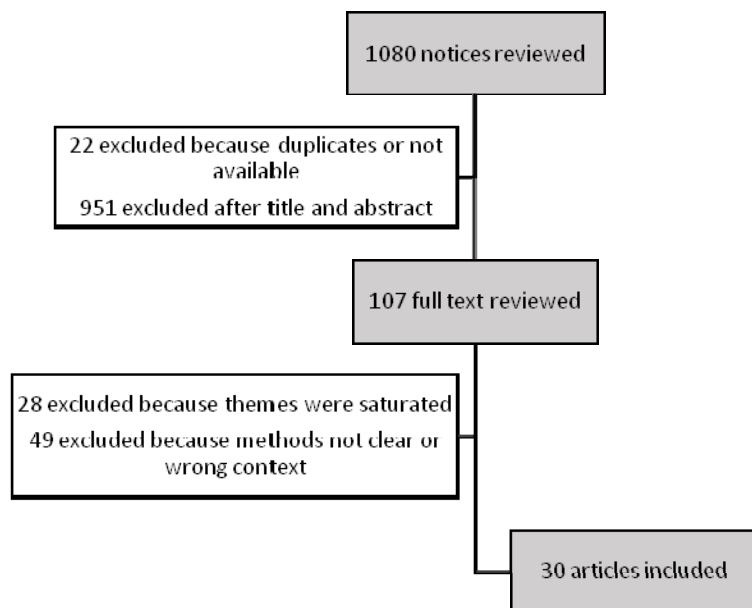
purpose of detecting a foetal malformation or genetic abnormality. The search was not limited to a particular medical condition, subset of women, testing procedure, trimester of pregnancy, or congenital or genetic condition. Radiological and genetic screening interventions could include fetal US, MSM, fetal MRI and cytological genetic screening tests for specific conditions including microarray, cell free DNA and whole genome sequencing.

The studies were considered eligible if they reported on at least one of the following outcomes or themes: knowledge, ethics of prenatal diagnosis, diagnostic and prognostic uncertainties, informed consent, emotional aspects, side effects and long term effects of screening and or diagnosis, concept of disability and quality of life in disabled children. Studies included would have had to describe the primary research question, context of the research, study sample and methods used for data collection and analysis.

Studies providing only data from health care providers' perspective were excluded. Only the qualitative data from mixed methods studies fulfilling the inclusion criteria were included. The data collected were from women only or women and couples, the latter often interviewed separately. A few studies involved men only. The testing pertained to AFP, MSM, NT and ultrasound. None of the studies related to the newer testing procedures. Semi-structured interviews of individual women were the most commonly applied data collection strategy; some studies consisted of focus groups and others included both.

Figure 1 summarizes the number of articles that were retrieved for the meta-ethnography as well as those that were excluded and included. The electronic database identified 1080 notices. The first author screened the abstracts and titles and retrieved 107 full articles. Of these, 58 fulfilled the inclusion criteria. Nonetheless, the analysis and conceptual framework was almost entirely articulated with 30 articles. The analysis of the key themes extracted from these articles provided a sense of saturation in that they covered all key aspects of the phenomenon. The analysis of the remaining 28 articles identified themes that were either an already described or additional subtheme, but did not modify the overall conceptual framework.

**Figure 1. Flow chart of the studies included in the meta-ethnography**



The details of the study setting, testing procedure, population analyzed, methodology, and goals of each of the individual studies are presented in Table 1 (at the end of this thesis). In most studies, information was related to experiences, emotions and decisions obtained at the time or shortly after the presentation of the testing or decision to undergo diagnosis. Concepts explored consisted of expectations, beliefs and attitudes related to testing. Factors important for decision-making related to invasive testing and the meaning of high risk status. Key social influences and the impact of women’s personal ethical beliefs on decision-making in addition to men’s experiences of screening and diagnosis were explored. Several studies interviewed women between 21-32 weeks of gestation, but many interviewed the women several months after the decision had been taken (and less often years later). Several studies specifically reported on the experiences of women of certain ethnicities or cultural background.

#### Analysis of the qualitative study findings

The findings were analyzed following a thematic analysis derived from a grounded theory approach. More specifically, drawing on the principles of meta-ethnography, we iteratively analyzed and interpreted the study findings to construct a conceptual framework of the experiences of women and couples. Key concepts within each study were systematically identified and common and disparate

concepts within and across studies were noted using first and second order constructs. First order constructs are the expressions or insights shared by study participants. Second order constructs are the interpretative themes developed by the original researchers. Several themes are described similarly by many authors. Third order constructs are derived from multiple studies by analyzing and interpreting second order constructs. Table 2 (at the end of this document) contains second and first order constructs for all of the studies included in this meta-ethnography.

Table 2 also indicates a judgement over the quality of the studies. Quality appraisal for qualitative studies is a matter of scholarly debate. There are many criteria suggested, but no consensus about what makes a study good.<sup>34</sup> For Toye and colleagues, a study should be excluded from a synthesis if it does not present a reflexive account of the research process. Reflexivity allows the reader to make a sound judgment about the author's interpretation. In this thesis, this recommendation was used as a reference point for deciding whether to include or exclude a specific study.

### **Narrative summary of quantitative studies on prenatal testing and decision-making**

#### Literature search

A systematic review of studies reporting quantitative data of various aspects of decision-making in prenatal testing was performed using the medical subject headings of prenatal diagnosis and related terms in combination with text words such as tools, decision aids, informed and parental consent. The database searched was Pub Med and Appendix 4 describes the full search strategy.

The search period was from 1970 until February 2015. The articles chosen were not restricted by geographical location and the languages included English and French. Reference lists of relevant studies were also searched.

#### Article selection process and criteria

Eligibility criteria were assessed by a review of the title and abstract and confirmed by reading the methodology section. Studies included had to define a primary research question, the study context, the study sample and the methods used for data collection and analysis. Studies providing only data from a health care providers' perspective were excluded. Only the quantitative data from mixed methods studies fulfilling the inclusion criteria were included. Figure 2 (next page) details the flow chart of the studies retained for the quantitative review. A total of 1258 articles were found, of which 50 were read and 18 included.

**Figure 2. Flow chart of the studies included in the quantitative review**

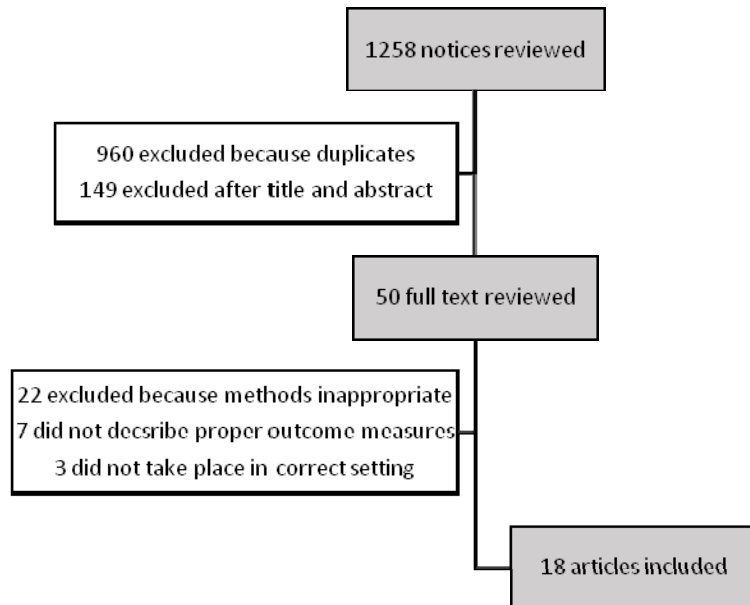


Table 3 (at the end of this document) provides details on each study retained (e.g., location, context, population of women studied, goals of the study). The articles contained quantitative or mixed quantitative and qualitative data in which decision-making processes were evaluated prior, during or after the decision for prenatal testing. The data were mostly collected by questionnaires using case control or longitudinal study design. The search was not limited to a particular congenital or genetic condition, trimester of pregnancy, subset of women, procedure or geographical location. Radiological and genetic screening interventions could include AFP, fetal US, MSM, fetal MRI and cytological genetic screening tests for specific conditions including microarray, cell free DNA and whole genome sequencing. The studies were considered eligible if they reported on at least one of the outcomes of interest. The outcome measures consisted of percentages and/or scores from validated scales such as a knowledge scale, a decisional conflict scale, anxiety scale or MMIC scale.

Women followed mostly in urban obstetrical centres or by midwives participating in screening programs were recruited. In some settings, women were interviewed and questionnaires completed after consent, but before testing was performed. Typically, a repeat questionnaire was completed after the testing either before or both before and after the test results were obtained. Some studies evaluated attitudes and others primarily the psychological state throughout the testing procedure and decision-making for invasive testing. The concept of risk was evaluated in women considered to

have higher risk pregnancies. While several studies addressed specifically the elements required for informed decision-making, only one study examined the usefulness of decision analysis. The studies used descriptive methods while others used control and intervention groups and randomized trial design. Interventions ranged from pamphlets, consultation with an expert, standardized educational group intervention to a computerized audio-visual decision aid.

#### Analysis of the quantitative study findings

The narrative synthesis consisted of tabulating themes that were found to be significant by the authors and using the measurements reported (e.g., percentages obtained on the questionnaires, statistics, scores on validated scales, etc.). These themes included attitudes, risk perception, decisional conflict, anxiety, knowledge acquired and level of informed decision-making. Some authors examined only one theme, whereas others examined several of these themes in the same population of women. The details of these findings are presented in Table 4 (at the end of this document). The quality of the studies was evaluated according to the CASP quantitative checklist tool<sup>119</sup> for randomized studies or otherwise based on the quantity and clarity of details given in the methodology section. The presence of bias and conflict was also noted. These results are included with the other characteristics of the studies in Table 3 (at the end of this document).

#### **Comparisons across the two reviews and integration of findings**

The findings between the two reviews were analyzed keeping in mind the similarities and differences between qualitative and quantitative research principles; although several themes partially overlap, the respective strengths and weaknesses of each type of methodology enables to derive a broad understanding of the phenomenon. The critique of the usefulness of the IPDAS criteria using a specific prenatal diagnosis tool builds on, and complements the review findings.

## Results

The first section of this chapter presents the findings of the meta-ethnography, which summarizes the themes and constructs of a conceptual framework of the experiences of women and couples surrounding prenatal diagnosis. The second section summarizes the key findings from the narrative review of the quantitative studies and concludes with the critique of a decision aid using IPDAS criteria.

### Findings from the meta-ethnography

An overview of the studies analyzed

Table 1 (at the end of this thesis) provides the details of each study included in the meta-ethnography. Below, a broad sketch of the characteristics of investigations covered in these 30 articles is presented for orientation. These included the role of the ultrasound and the experiences of women undergoing 1<sup>st</sup> trimester NT for DS and perception of risk assessment.<sup>82,120-126</sup> Other studies dealt specifically with the issue of decision-making for amniocentesis, which included investigating the meaning to higher risk and factors necessary for decisions related to amniocentesis by women of different cultures.<sup>73,120,125,127-131</sup> Several articles dealt with the meaning of informed choice and information sharing and support<sup>95,127,132-135</sup>, while others looked at the process of decision-making or perception of the decision-making process.<sup>136-141</sup> Men's place in fetal screening and their experiences were specifically investigated in several articles.<sup>126,142-144</sup> The long term effects following a procedure for testing of fetal anomalies were reported by several authors<sup>145-147</sup> as were the attitudes and experiences of parents who chose to continue with a pregnancy in which a fetal anomaly was detected.<sup>143,148,149</sup> The issue of why some women seek prenatal testing<sup>150</sup> and qualitative studies investigating the role of biomedical and experiential knowledge in their decision-making are reported.<sup>151-153</sup> Bioethical concepts such as autonomy, moral status and the meaning of nature and its impact on decision-making in prenatal diagnosis are dealt with in several reports.<sup>82,154-157</sup>

## Key constructs extracted for the qualitative studies

Initial reactions and perceptions to testing

No option for women and unclear role for men

Santalathi et al<sup>136</sup> and Gottfredsdottir et al<sup>124</sup> find that women do not perceive prenatal testing as an optional test, but rather “that’s what you do when you are pregnant”. Women perceive the testing as benign as it is often performed in the context of non-controversial routine antenatal care.

Ultrasounds are “harmless” in comparison to invasive testing. Most women and couples accept ultrasound screening in order to see their baby and seek reassurance by confirming its healthy state<sup>158</sup>. Yet, women lack knowledge and experience unpreparedness for testing<sup>58,123,159</sup>. In Williams’<sup>82</sup> study, the scan was a significantly powerful tool for men and women. Women and men perceive the ultrasound as a way to exclude a health problem for their foetus, reduce uncertainty or as a “rubber stamp” for normalcy. Women feel they are encouraged by obstetricians to see the image, to identify the gender and movements of the foetus. As Aune et al<sup>123</sup> point out, women recognize that it is about existential choices. Yet, a number of women are “ignorant” about the potential problematic information requiring moral judgments that a screening test could provide and report shock and disbelief to the possibility of abnormal findings.

Although the majority of the women want choice, they experience ambivalence about deciding. Even though a number of women have thought through issues and possibilities of what they might do in the case of abnormal test results, they experience unpreparedness to confront the issues raised by screening tests and eventual choice making. The women who decline screening perceive the information obtained with screening as insufficient and a cause for experiencing anxiety during the pregnancy.<sup>82</sup> Carolan et al<sup>120</sup> points to the altered view of pregnancy and difficulty adapting to the “at risk category”. “The improvement in US has led to a shifting of knowledge about fetal viability to a discussion of the ethical dilemma of termination of pregnancy”<sup>82</sup>. Technology allows the foetus to become a “social child,” but at the same time, if the scan detects an anomaly, it favors the perception of the fetus to patienthood and to personhood. The scan is simultaneously a tool that enables the development of a relationship with the fetus as a person, but if an anomaly is detected the relationship becomes tentative and the foetus is seen as a commodity. Williams’ comment on the “dragnet effect” related to the implementation of a screening program available to all women and not just to those falling in the high-risk category; it is intended to benefit everyone equally, but in so

doing treats all pregnancies as potentially pathological and needing to draw women into an anxious dependence for expert medical risk management. The universal access to prenatal screening is seen as beneficial and necessarily conflicts with respect for women's informed refusal as a rational choice.<sup>82</sup>

Men partners want to be involved in decision-making, information gathering and screening. They have an interest in their paternity and the ultrasound is important to help them realize their transition to fatherhood<sup>144</sup>. Locock et al found the degree of involvement of men in the prenatal screening process variable. Although they are not formally excluded from participating, their presence during the ultrasound is not formally acknowledged and are thus seen as "bystanders". During the procedure, they are not offered a chair and are in a separate location from their partners in the room. When an anomaly is detected, the men experience even more distance from their partner since the health care provider focuses more attention on the pregnant woman. Moreover, physician's subsequent decisions about the pregnancy as belonging predominantly the women. According to Dheensa et al<sup>142</sup>, men allow experts to take control, trusting that the tests pose no risk and, like women, view the ultrasound as a way to confirm fetal health.

#### Familiarity, tolerance for diversity and unreliable test

According to Gottfredsdottir et al<sup>143</sup>, refusal by prospective parents of prenatal screening is associated with familiarity with disability and acceptance that diversity and complexity of the different health conditions should be sustained in order to show care and respect for children with anomalies<sup>149</sup>. This tolerance for diversity is one approach, whereas other parents spoke predominantly of being realistic about the expectation of the abilities of these children. These parents feel that they have to justify their decisions to decline screening since they feel that family, friends, and health professionals lack flexibility and understanding.<sup>143</sup> For parents who do not have experience with disability, one reason to refuse testing was the uncertainty and unreliability of the testing and the presence of a certain mistrust of scientific probabilities.<sup>143,149</sup>

#### Reactions to a positive screening result

##### Information overload

Many parents felt overwhelmed with information overload being unable to prioritize the information received<sup>58</sup>, but at the same time felt there was an information gap in a context of time pressure and



anxiety.<sup>58</sup> The printed material was often not easily accessible. The partner's reactions were that of frustration at not being able to get answers to their questions immediately, leaving them worried and speculative about the possible consequences if the foetus was affected by Down's syndrome.<sup>124</sup>

Women's reactions are consistent with high expectations associated with unanswered questions causing uncertainty and anxiety.<sup>124</sup> The women receive anomalous results in disbelief or they perceive the messages they obtained from health care professionals as incongruent.<sup>124</sup> While receiving information that an anomaly has been detected, a woman may be reassured that it is unlikely to represent a malformation.<sup>124</sup> This sense of incongruence is likely related to the fact that most women have difficulty grasping the concept of screening and likely perceive the test result as diagnostic.

The study by Redlinger-Grosse et al<sup>148</sup> identifies how parents perceive professional attitudes. Parents perceive a lack of concern by the professionals for the fetus and their role as useful only insofar as they can deal with a "wrong" pregnancy by getting the woman 'unpregnant' as soon as possible.<sup>148</sup>

Stuck in the decision and gendered responsibility

Seeking information and dealing with incongruent messages is the first step to the rationalization process. As Hawthorne and Ahern<sup>158</sup> stress, a number of women feel that it is improper timing to divulge complex information such as false positive and false negative results at the time of the detection of an anomaly when the woman has not even considered the possibility of an abnormal result. Heyman et al<sup>73</sup> discuss how women perceive receiving the information during the examination as not having been given sufficient time to assimilate and understand the information and their subsequent need to seek more knowledge. The anxiety related with the threat to the pregnancy together with the risk linked to the advanced age, possible termination, regret and importance of making the right decision are factors associated with a sense of being "stuck in the decision". Subsequently, the women experience anxious waiting and adopt an attitude of "status quo" reserving emotional investment in the pregnancy, distancing themselves from the fetus<sup>82</sup>, but also avoiding contacts with persons who could wish for an explanation of the events.

Women suffer from emotional detachment with physical and psychological symptoms of anxiety while waiting for the diagnostic test results and they suffer from self-stigmatization related to the social relationships and social meanings of having a child with Down's syndrome within an Asian culture<sup>127</sup>.

Dheensa et al<sup>142</sup> found that men felt that midwives did not explain the information clearly and found that the midwives failed to address them and include them in the discussion. When complications in the pregnancy were detected, men wanted to be involved as they felt it was their parental responsibility to ensure that the foetus was safe.<sup>138</sup> The men persisted in the communication with the health care provider, but they got the impression that they were perceived as coercive. “In the process the men had to manage their anxieties and their roles as supporters and advocates while negotiating their place in a woman centred environment”.<sup>138</sup>

Ahman et al<sup>126</sup> and Gottfredsdottir et al<sup>124</sup> discuss how men focus on safety and risk language as a way to control the process. Men adopt a strategy of fact finding to gain a sense of control before they can decide how to deal with the situation including the risk assessment.<sup>120,122</sup> Men are anxious not to draw the wrong conclusion as they see their role as supporter of their partners.<sup>122</sup> Even according to Locock et al<sup>144</sup>, in cases of anomalies some of the men become “guardians and gatherers of facts”. “They are in search of clarity and certainty and are described by themselves and their partners as ‘analytical, factual, black and white, simple minded, detached’”.<sup>140</sup> This approach is used by men to remind their partners in times of confusion and to restore optimism. When a decision has to be made with regards to termination of the pregnancy, men developed the role of decider or enforcer, encouraging, hastening and/or ensuring that a decision is implemented.<sup>140</sup> Men felt that it was less of an emotional ordeal when the decision and action were done quickly.<sup>140</sup> Some men left the decision to the women and others were non-directive or even slowed down the process for more information gathering.<sup>144</sup>

Men learned appropriate and effective communication over time, but others disengaged from the process because of diminished amenability of the health care team and recognition of the limited reassurance that screening provides. Locock et al<sup>144</sup> found that the emotional distance that developed through the experience of complicated prenatal screening evolved to a sense of loss of parent status and of control of the ability to protect and support the women. Some men find it easier to choose to be bystander. In the study by Gottfredsdottir et al<sup>124</sup>, when considering whether to continue or not a pregnancy with an affected foetus, men were concerned with negative attitudes of society towards disability and the impact of the disability and attitudes on the future child.

## Guilt, concealment and isolation

Women experience guilty feelings of a different nature. Women fear or apprehend reactions by the health care providers if they refuse the test, fearful of being thought of as ignorant or that the refusal may convey a lack of trust in healthcare professionals.<sup>128</sup> Some women who intend to terminate the pregnancy feel guilty for “not being a saint”; they perceive themselves psychologically unable to parent a child with a handicap and feel guilty that “they are not the kind of woman that can accept that challenge”<sup>160</sup>.

Women experience anxiety and guilt stemming from moral conflict related to the universally upheld natural law of respect for life and the decision to proceed with invasive testing and termination of pregnancy due to a chromosomal defect.<sup>123</sup> Women feared opinions from friends and family as they viewed them as potentially influential in their own decision-making.<sup>160</sup> The women felt peer pressure “to fit in” concerned about doing the “right thing” for their baby.<sup>158</sup> Aune et al<sup>123</sup> showed that social pressure was associated with the perception by women that others had difficulty to accept the decision to continue a pregnancy in the presence of DS. Women feared the external influence that they perceived as being part of social norms in either the decision to have the test and later perform a termination or against disabled children.

Hawthorne and Ahern<sup>158</sup> state that women did not defend their view publicly, but chose to lie to avoid having to admit active termination. Yet, many women were seeking guidance for their decision-making as a way to deal with the anxiety and to strengthen their conviction in their decision<sup>149</sup>. Women felt isolated as they felt pressured by health care professionals to make a decision without discussing it with others.<sup>148</sup> Isolation was also experienced by those who decided to pursue pregnancy with an affected foetus. Some of these parents perceived a shift in attitude from the health care professional, attending to liability concerns to the detriment of the emotional support that parents felt they needed.<sup>148</sup>

## The experience of an unwanted burden and yet a woman’s responsibility

For the women interviewed by Gottfredsdottir et al,<sup>124</sup> decision-making was in principle a joint decision with their spouses. However, the men claimed that it was the women who decided for the screening procedure. Although women believe that the decision for testing and for termination of pregnancy is ultimately theirs, they experience overt or covert pressure from family and friends. The obligation to undergo testing and make the socially acceptable decision is palpable. When they are

undecided or think contrary to that decision, they feel the need to hide their decision for fear of reprisal. Many women expressed this unwanted burden of decision-making.

A number of articles<sup>82,123,158</sup> report women's overwhelming sense of responsibility for decision-making for prenatal testing under varying aspects. Aune and Moller<sup>123</sup> discuss the anxiety related to the thought of termination of the pregnancy and importance of making the right decision. Increased ambivalence was associated with unrealistic concerns, but also with a sense of guilt for possibly choosing to carry to term a foetus with Down's syndrome. According to these authors, the decision to continue with the pregnancy was the woman's and, hence, the outcome of her responsibility solely.

#### 'Being a good mother'

In western countries, the women express the prevailing attitude that it is their responsibility as a mother to prevent suffering, as motherhood begins in utero<sup>130,150</sup>. Hawthorne and Ahern<sup>158</sup> report that women felt responsible for the health of their child. Being a good mother was associated with the moral conclusion for some women that raising a child with DS was cruel. For women who refused the ultrasound, being a good mother was associated with a stronger sense of connection and these women had more positive attitudes towards Down's syndrome. For women of the Muslim faith, motherhood began during pregnancy and being a good mother meant accepting a child with handicap<sup>130</sup>.

#### Decision-making for amniocentesis and pregnancy outcome

##### Understanding risk and culturally sensitive decisions for amniocentesis

Knowledge about risk can be reassuring if the result is low or can be used as a reason to prepare for a child with handicap. A number of women have difficulty understanding the difference between a screening test result and a diagnostic test, perceiving the risk test as actually diagnostic<sup>123</sup>. According to Hawthorne and Ahern<sup>158</sup>, understanding low and high risk for women is irrelevant since a low risk category is perceived as a high risk and women who are considered from a medical perspective to be in the high-risk category experience greater anxiety than those in the low risk category. The calculated risk of carrying a foetus with DS was perceived to be higher than the actual higher risk of a miscarriage with invasive testing. Choosing for amniocentesis was a way to ease the worry that a malformation was actually present<sup>73</sup>. Women of many cultures were concerned with the risk of miscarriage caused by amniocentesis, but the women in the study by Pivetti et al<sup>161</sup> discussed the

indirect harmful effects on the development of the foetus related to the anxiety of undergoing amniocentesis.

Religious beliefs were accountable for women refusing amniocentesis. Women of Islamic faith of Moroccan descent deliberated and hesitated to do prenatal testing as they did not consider termination of a pregnancy for fetal anomaly an option<sup>130</sup>. Very few had testing, consenting to fetal anomaly scan only since it was an appropriate way to see the baby.

In the study by Remennick et al<sup>150</sup>, two opposite attitudes towards amniocentesis in women in the low risk category were found. The women that rejected the elective test explained their decision by moral and or religious attitudes to abortion, prohibitive costs and poor understanding of the meaning of the tests and their implications. However, those who sought elective testing viewed it as a normative test, and were more often educated middle class Ashkenazi women that feared having a sick or socially inflicted child in an unsupportive environment<sup>150</sup>. There is a predominance of popular and professional discourse of the common mutations found in the Ashkenazi culture causing “genetic anxiety” and there is a social pressure for genetic testing seen as an indispensable part of “good motherhood”<sup>150</sup>.

Experiential vs. biomedical knowledge and imagined futures

Markens categorizes American women of Mexican ethnicity according to their willingness to abort a foetus and willingness to perform amniocentesis linked with the women’s trust or lack of trust in their experiential and/or biomedical knowledge.<sup>153</sup> She categorized one group of women as being skeptical of technologies and physicians and trusting fully in their experiential knowledge otherwise known as embodied knowledge. These women are unwilling to abort and decline amniocentesis. A second category of women are willing to use biomedical knowledge such as ultrasound to bolster their experiential knowledge, which they trust. These women are willing to abort, but decline amniocentesis.<sup>153</sup> They consider amniocentesis as risky and these women are critical about advice from physicians although they don’t totally reject medicine. They look to differential familial experiential knowledge<sup>153</sup>. In a third category, women approach decision-making with complete faith in physicians and medicine and they use biomedical knowledge to assure themselves of their experiential sources<sup>153</sup>. These women “desired to be a good patient” and were unwilling to abort, but agreed to amniocentesis to ensure normality of the foetus. Lastly, one category of women was willing to abort and agreed to amniocentesis<sup>153</sup>. These women lack belief in their experiential sources, are

skeptical about such knowledge, seek other's knowledge, consider research important, view themselves as agents of choice and trust doctors<sup>153</sup>.

France et al examined the influence of familial experiential knowledge that's used in combination with biomedical knowledge to wield an internal coherence of the accounts for the decisions for prenatal testing over time and between pregnancies<sup>151</sup>. They did not find a clear pattern on how different perspectives of experiential knowledge interacted with biomedical knowledge to form an approach to testing. In another article, France et al discuss the experiential knowledge of disability in affecting the decision to continue or not a pregnancy in which the foetus is affected by a fetal abnormality.<sup>148</sup> The decisions were affected by "imagined fetuses" with issues that concerned the imagined scenarios consisting of physical and emotional suffering, day to day prognosis, nature of services for disabled children and the stigma associated with disability<sup>152</sup>. Quality of life was a concept that was raised by parents that felt the quality of life for DS was reasonable or poor, but these two views were not decisive for either continuing or terminating a pregnancy as both categories of perceptions were associated with both decisions<sup>157</sup>.

Decision to continue a pregnancy with an affected fetus

For Hickerton et al<sup>149</sup>, who studied women or couples who decline invasive testing prenatally in the context of having been screened in the higher risk category, their initial experiences are not any different from those who accept invasive testing. For couples who refused invasive testing, the reasons for consisted of being apprehensive about the risk of miscarriage, lack of knowledge of the conditions tested for and considering the decision of termination as a moral dilemma<sup>149</sup>.

The subsequent phase in the process consisted of coping and adjusting to a different life path, receiving valuable support and reframing original expectations to a broadened perspective<sup>149</sup>. The parents confirmed having to cope with changing nature of friendships and challenging attitudes especially those of health care providers.<sup>149</sup> The views and feeling emanating from the health care professionals that mattered most to parents in their encounter was exemplified by the statement "we are dealing with people first and not a diagnosis", which they felt reflected a positive attitude and respect for their choice<sup>149</sup>.

### Moral status of nature, quality of life and social ostracism

Garcia identifies through a qualitative study of women and couples two perceptions of nature. The first view is that nature ought neither to be changed, nor totally controlled. According to this view, some women find that the health status of the fetus is a matter of fate or that “we are not to modify nature as nature knows best”. One subgroup feels that disability belongs to life and accords value to it<sup>158</sup>. According to the contrasting view, humans are meant to use their rationality to help nature do its work well. The goal is thus to improve health. While the decision to test the fetus depends on the accuracy of the information, parents are aware of the limits of this information. They also recognize that there is no guarantee for a healthy child even when a test shows up “normal.” Testing is felt not to be necessary unless risks are increased or if experiential knowledge warrants it<sup>158</sup>.

Poor prognostication was the only concept that differentiated the women according to accepting or declining testing respectively.<sup>155</sup> Quality of life criteria was used by women who accepted prenatal diagnosis and refused abortion as well as by those who accepted abortion.<sup>155</sup> In some studies, women experienced the condition themselves and used their own experiential knowledge to reason against the worth of a “life full of pain”<sup>151</sup>. In a number of articles, parents raised the issue of suffering related to the social prejudice that the handicapped child would have to endure<sup>151,151</sup>.

### Loss and grief in termination for foetal anomalies

Women and men who decide to terminate a pregnancy for fetal anomaly disclosed the decision selectively to close family and friends. The reasons for partial concealment include guilt over the decision and wanting to avoid being judged or to protect other’s feelings<sup>138</sup>. Locock et al found that men subvert their own experience of grief by focusing on their work allowing them to be more available to deal with their partner’s grief.<sup>140</sup> The refusal to see the foetus after death or performing a funeral is a way to “get over it quickly” with the optic that it will also encourage their partner to do the same. More often men found it hard to access emotional support from social networks because it was expected that men should “deal with it”<sup>144</sup>.

### Long term effects of prenatal diagnosis

Several articles discussed the continued anxiety even after being reassured about the healthy state of the pregnancy. This anxiety persisted in time and altered the women’s perception of their child as being more vulnerable<sup>120</sup>. Carolan concludes that women do not experience a clear resolution to their

fears.<sup>116</sup> Many women continue to experience anger and concern for the future.<sup>116</sup> Some try to dispel this feeling by adopting the attitude that the screening process was “all for nothing”. The women also altered their views about future plans for childbearing.

Different experiential knowledge intermingles with biomedical knowledge over time so that women arrive at an internal coherence. This implies a constant process of knowledge building by the women, whereby decisions for prenatal diagnosis can differ in time<sup>152</sup>. Many parents recount their ethical dilemmas of having to choose for future pregnancies related to the prevalent societal attitudes of little tolerance for disabilities and emphasis on perfection and of women being accountable for reproductive decisions<sup>145</sup>. A few articles highlighted the disjuncture, for those who decided to accept a fetus and child with disability, between the biomedical view of genetic pathology and the parental life world experience of a different way of being in families<sup>143,149</sup>. Parents had learned to develop a new set of skills and interpretation of the phenomenon of impairment through their handicapped children that was not known to the health care professionals and which lead them to refuse prenatal diagnosis in future pregnancies<sup>130</sup>.

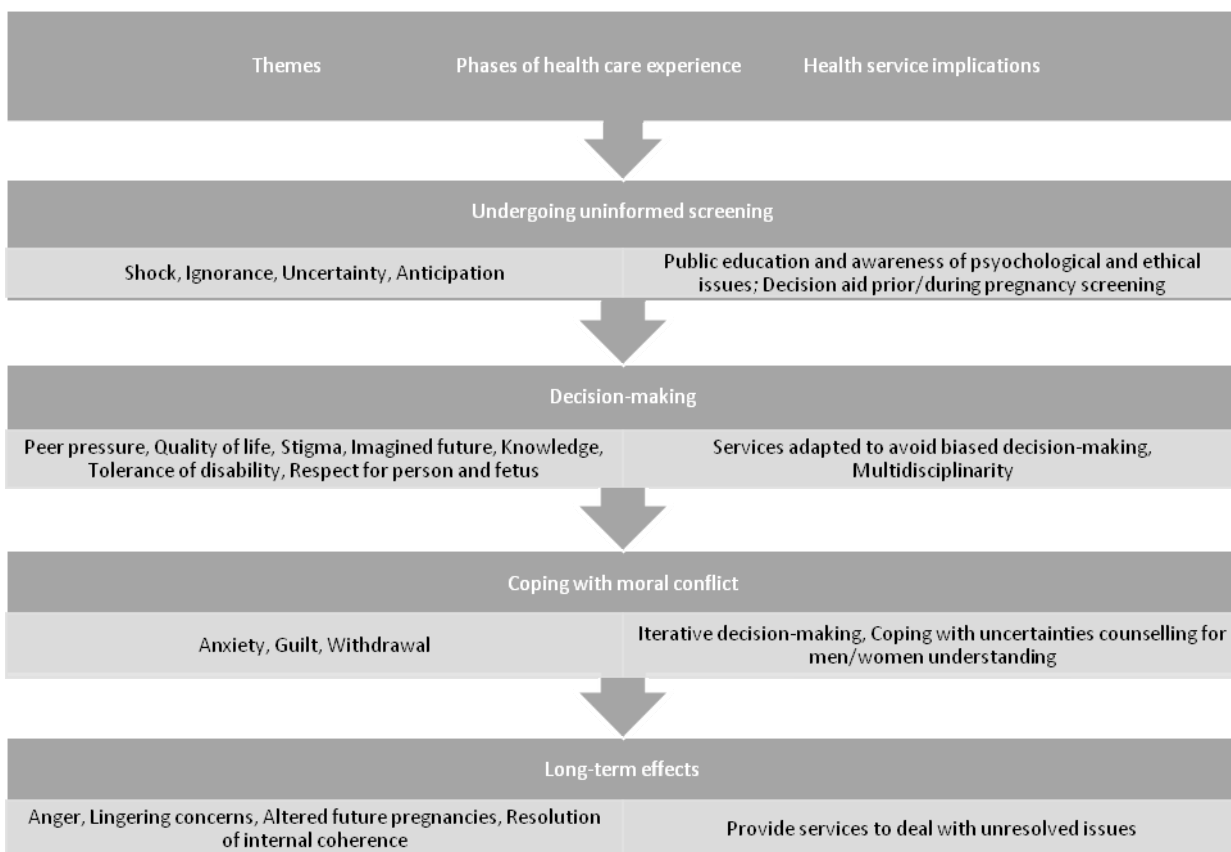
### **A conceptual framework to organize the constructs**

The key themes stemming from the meta-ethnography can be organized in a conceptual framework as shown in Figure 3 (next page). This framework summarizes along the various phases of the phenomenon of interest the themes that we reviewed above as well as their health service implications. The latter will be further examined in the discussion of this thesis.

The qualitative studies showed that women and men expect confirmation of a healthy fetus with prenatal screening and are dismayed when they are informed of a possible fetal abnormality. Both conceive of the ultrasound as a means to visualize their fetus and not simultaneously as a tool that can identify pathologies with ever increasing sensitivity. Even if women can anticipate potential conflicts with screening, the experience of receiving any screening results is cause for concern. Risk assessment is not perceived by women as it is conceived by health professionals. Women conceive of the risk of the fetus afflicted with DS as being higher than it actually is. In some cases, the risk of fetal loss associated with amniocentesis is higher than the actual risk of a fetal anomaly, but many women will proceed nonetheless with amniocentesis seeking reassurance for a normal infant.



**Figure 3. Conceptual framework of experiences of women and couples in prenatal testing**



Women identify incongruence between the attitude adopted by the health care professional who appears to minimize the screening result and their experience of incredulity and perceived severity. Moral conflict arises as a result of a sense of insufficient knowledge, lack of time with the physician and inappropriate timing of the presentation of the information. After receiving positive screening results or while awaiting amniocentesis results, patients suffer from anxious awaiting and they emotionally distance themselves from the foetus and from friends and family that they perceive could have an influence on their decision-making and could judge them.

Men experience a sense of physical distance and, like women, an emotional isolation from the health care provider particularly if a screening result is positive. Health care providers perceive that it is the women’s responsibility to make further decisions with regards to amniocentesis and termination of pregnancy and do not see a role for men in the process. Some men subsequently disengage from the

process, but, according to the health care providers' view, they seemingly impose themselves in the process. Men tend to see their role as gatherers of facts, ready to inform and support their spouse.

Contrary to their own perception of a joint decision with their partners and as confirmed by their partners, women make the screening decision alone. This decision is rationalized taking into account many concepts including quality of life, unbearable burden, inherent morality of nature, suffering, peer pressure, stigma, best interest and good mother. The women suffer moral grief for they stress the importance of making the "right decision," but they lose the sense of control and agency. They experience feelings of guilt and stigmatization either because they consider termination of pregnancy or they consider having a disabled child, either of which are perceived not to be in accordance with the opinions of their peers or family.

Women are left alone with the moral choice of the kinds of disabilities that can be avoided and the reasons that justify their decision. A number of women or couples who consider continuing a pregnancy with an affected fetus also experience isolation in decision-making, sometimes pressure to undergo testing and termination by health care professionals, and perceive a lack of respect for their choice.

Various types of experiential knowledge —that of the women, of friends or family members or that related to disabilities— are important elements that have an impact on an individual decision in a specific time during the history of childbearing and which evolves over time.

Despite reassurance following amniocentesis, worry lingers even after the birth of the child. This worry can potentially impact the relationship with the child and lingering concerns can affect childbearing plans. Societal negative attitudes toward disabilities influence some parents in not to reproduce, to put off the decision about testing in future pregnancies or in choosing to leave it to fate.

Overall, the qualitative studies explored the phenomenological experiences of women, couples and of men undergoing prenatal testing for DS with the use of ultrasound and or serum markers in the first and or second trimester. The meaning of high risk category and experiences in deciding to undergo an invasive procedure such as amniocentesis or CVS were also explored. Some would argue that these issues will be irrelevant in the near future as the implementation of cell free DNA diagnosis will make decision-making easier. Although these new procedures abolish the need to proceed to an invasive procedure, the issues of whether or not to undergo prenatal screening will nonetheless remain.

## Narrative summary of quantitative studies

The narrative summary of the quantitative studies focused on the themes and measures that are relevant to decision-making. The characteristics of these studies are presented in Table 3 (at the end of this document) and the themes extracted for the review are listed in Table 4 (at the end of this document) and explained below.

### Knowledge base, risk perception and decisional conflict

Several studies reported lack of sufficient baseline knowledge in 25-46% of the women about the role of US or MSM or NT<sup>162-167</sup>. The two studies reporting satisfactory knowledge levels were those of van den Berg<sup>168,169</sup> and referred to the same group of women. Not only do women experience surprise at a positive screening result, but they do not understand screening results and do not recognize that a decision for invasive testing would be required. The majority of the studies reported improvement in knowledge scores with an intervention compared to the controls. In both studies by Kupperman<sup>170,171</sup>, there was an increase in knowledge for age-adjusted and miscarriage related risk following the use of a decision aid compared to controls.<sup>170,171</sup>

The knowledge gained during a pre-test consultation influenced the amniocentesis rate, but did not appear to be associated with a decrease in indecisiveness.<sup>172</sup> The knowledge level seems to be associated with higher education in women<sup>173</sup> and the knowledge base seems to have variable effects on the decisional conflict depending on the study. In the study of Dahl<sup>174</sup>, a higher knowledge level seemed to be associated with a higher level of well-being and less decisional conflict, but it did not appear to affect the level of worry, either in general or that related with the status of the fetus.

While some women interpret a negative MSAFP result as falsely reassuring for a normal fetus and child<sup>166</sup>, other women apprehend the risk of a DS affected fetus and perceive the actual risk higher; the perception of risk could decrease after an intervention, but it still remains higher than the actual risk<sup>39,164,175</sup>. In Tercyak's study, interestingly the perceived risks were not associated with the uptake rate of amniocentesis.<sup>39</sup> In this study,<sup>39</sup> the women who had the highest perceived risk had the highest anxiety scores. In Kaiser's study, the women who received counseling with an adjusted risk score experienced a decreased risk perception.<sup>175</sup> Only one study reported potential factors that could contribute to the risk perception which included personal factors, the influence of media and of health care professionals<sup>164</sup>. Risk perception in one study was not associated with knowledge level or

satisfaction of the intervention and although the risk perception dropped with the intervention it still remained high compared to the actual risk.<sup>39</sup> Furthermore, the actual or perceived risk level was not associated with the uptake level of amniocentesis.<sup>39</sup> The only study using decision analysis to support decision-making reported an association with less perceived risk<sup>176</sup>.

The results with respect to decisional conflict are varied. One may intuitively expect higher decisional conflict in women who are undecided about testing and less decisional conflict in women who are decided about amniocentesis compared to those who were undecided before consultation.<sup>171</sup> In the study by Bekker et al, decisional conflict seemed to lessen over time with decision analysis<sup>176</sup>. In the study by van den Berg<sup>169</sup>, decisional conflict seemed to be less when the woman made a more informed choice. In the most recent study by Kuppermann et al<sup>171</sup>, there was no difference in decisional conflict between the women exposed to the decision tool and the control group followed with usual care.

#### Attitudes and anxiety

The majority of women use US to visualize and to be reassured of the normalcy of the fetus. A positive finding on the NT was associated with a higher rate of amniocentesis<sup>165</sup>. Indecisiveness about testing was not related to knowledge level but to women's reluctance to face the dilemmas linked to a positive screening result. Rowe did not find a correlation between women's attitude to testing and knowledge level<sup>163</sup>, but attitude to selective termination, perception of test efficacy and positive subjective norm to testing were associated with a higher intention to test.<sup>177</sup> In couples and women who refuse testing, the reasons given were that the screening tests had unfavourable characteristics and were unnecessary.<sup>178</sup> Side effects related to invasive procedures including screening inaccuracy or insufficiency and anxiety were also quoted for refusal.<sup>178</sup> The other reasons for refusing testing included acceptance for 'deviance' and recognition that health care is a complex experience.<sup>175</sup>

There is evidence in these quantitative studies that parents have to justify their refusal to the health care professionals. In some studies, it was noted that quality of life conceptions and attitudes towards testing can change with time. Parents are uncomfortable facing the moral conflicts associated with testing, causing them to adopt an attitude of leaving things to fate. In the study by Tercyak<sup>39</sup>, the attitude towards abortion was the single most important factor to determining the decision to undergo amniocentesis. In the study by Kaiser,<sup>175</sup> despite reassuring NT screening, an adjusted risk and a decrease in the risk perception, women still had a high amniocentesis uptake rate. Weinans<sup>165</sup>

also found that the ultrasound was a factor that led women to invasive testing. In the study by Brajenovic<sup>172</sup>, women's indecisiveness for amniocentesis was lower in the women who had received consultation and there was a higher uptake of amniocentesis after consultation.

Rowe<sup>163</sup> found that the level of anxiety was correlated with depression at each time point during the pregnancy and, in the short term, there was no difference between women who were informed compared to those uninformed. In van den Berg and Tercyak<sup>39,169</sup> studies, the level of anxiety was related to the uncertainty of test results and influenced by the perception of risk severity of DS and perception of degree of non-acceptance of DS syndrome in society. However, these remain weak predictors of the intention to test.<sup>177</sup>

The most recent randomized controlled trial by Kuppermann is the only study that had as a primary outcome measure testing frequency. It demonstrated that the decision aid use was associated with an overall decrease in testing and a decrease in invasive testing in the context in which financial considerations for women were absent<sup>171</sup>.

#### Informed decision-making

van den Berg et al<sup>169</sup> evaluated the concept of informed decision-making with the MMIC score, a measure which incorporates information about knowledge, attitudes and behavior. A decision was value consistent when, for example, a positive attitude score involved accepting testing. To determine if a decision was informed the knowledge scores were integrated with value consistency so that an informed decision was based on good knowledge and value consistent and, alternatively, uninformed decisions were either based on poor knowledge and/or value inconsistent. Only 51% of women made informed choices about amniocentesis, less so in the test acceptors than in the decliners on the basis of less deliberation in the former group. In the study, although informed choice was scored as relatively high, it was still lower than value consistent decisions<sup>169</sup>. Informed choice was associated with less decisional conflict in test acceptors with more decision satisfaction, but not less anxiety<sup>169</sup>.

#### Decision-making and the use of decision aids

The quantitative studies corroborate key findings from the qualitative studies. Women experience shock and incredulity at the announcement of an abnormal screening result for fetal anomaly at what is presumed to be a routine test for conforming normality and at not having the necessary

information about the screening nature of ultrasound. Many do not know that a decision about diagnostic testing is required if screening results are positive.

What the quantitative studies show is that knowledge scores related to the nature and reason for testing are increased after an intervention such as the use of a consultation, education program or/and decision aids. However, gaps in knowledge exist such as recognizing test accuracy or the potential adverse findings such as the necessity to consider invasive diagnostic procedure if the screening test result is positive or the possibility of detection of other fetal malformations or genetic conditions.

Knowledge level does not appear to be related to indecision. Rather, indecision is linked to the hesitation of having to make a decision about whether to undergo amniocentesis or to terminate a pregnancy in the context of a positive screening result. Decisional conflict scores appear to be lower in those women who are already decided from the outset for an invasive procedure. In some women, decisional conflict is decreased after the use of an intervention with the rates of testing increased in the women who were undecided prior to the consultation. Yet, in different contexts, women over 35 years were less likely to participate in invasive testing compared to women in the control groups.

The attitudes towards testing seemed to be influenced by a number of complex factors. The mere “seeing” of one’s baby increased the chances of invasive testing, while in other contexts the perception of testing efficacy and the positive subjective norm of testing desirability were influential factors in the decision for women to undergo testing. The effects of contexts and policies seem to have an influence on the acceptance of testing. For example, in the Netherlands and in California, women over 35 years are more likely in favor of invasive testing and, in Sweden, 82% of women had already decided on invasive testing before the test offer. In a culturally pro-testing setting, intention for invasive testing increased in undecided women following an intervention, but not in women who were already decided about their intentions prior to the intervention. In contexts where testing is conceived as opt-in, many women do not opt for testing. In some contexts, the study intervention, which included the PT tool was associated with less willingness to undergo any testing. The attitude of women towards DS may orient to invasive testing and termination, but this was not consistent with all women or across contexts.

In many studies, women of different risk category experienced anxiety with regards to prenatal testing. In one context, pregnancy was found to be associated with a state of anxiety throughout and

it did not appear to be modified when the woman considered having made an informed choice. Ultrasound screening seems to be related with a greater amount of anxiety than with the MSM, but seems to be reduced once the NT adjusted individual risk is explained. This anxiety seems to be related to the perceived severity of the DS diagnosis and the perceived subjective norm (acceptance or not of a child with DS), although this is a weak predictor of the testing choice. Anxiety is in part also related to risk perception, which in all studies was found to be higher than the actual risk. Women who perceived the highest risk of carrying a DS affected foetus were those who experienced the most anxiety. However, actual or perceived risk did not appear to be the factor that influenced the decision to undergo amniocentesis. Rather, the perceived efficacy of the test and the attitude toward abortion were the most important contributors to the decision for amniocentesis.

#### Methodological issues highlighted by the quantitative studies review

The studies we reviewed suggest that women consider screening as a formality to confirm the normality of the fetus and assent rather than consent to decision-making. As underscored by van den Berg<sup>177</sup>, the reception and conceptualization of the test is influenced by the “expert” view and a technological imperative. This is the only study that addressed the issue of informed choice and the process of informed decision-making. These authors developed and tested a model adapted from expected utility, expectancy value and protection motivation theory of planned behavior. Informed choice was associated with more satisfaction with the decision and less decisional conflict, but not less anxiety. The authors differentiate between a value consistent decision and an informed decision. They suggest that the MMIC score is not sufficient and recommend an analysis of the procedure for making an informed decision.<sup>177</sup>

They also identify that attitude towards termination and subjective norm played a central role in the decision to undergo screening. Perceived risk and perceived severity of DS appeared to be determinants of anxiety, but anxiety was only weakly predictive of intention to test. The finding that a positive subjective norm influences the acceptance of testing is of importance in the context of “autonomous” decision-making. The results from this study differ from other studies with regards to the high level of knowledge and value consistent decisions. This study examined decision-making in women in the low risk category in the Netherlands at a time when the policy was to offer testing to women only in the ‘high risk’ category. Thus, women made more deliberate decisions outside the context of routinization of tests. These participants also had the benefit of written information in the

form of a booklet and consultation with a midwife or gynecologist as the counseling was standardized for the study. Overall, one third of the women did not make informed decisions. In a little more than half of these, the reasons were for value inconsistency. It is not known why some women accepted testing while having a negative attitude or vice versa, i.e., declined testing while having a positive attitude. Informed choice was associated with better psychological outcomes. The authors highlight that a measure should be developed to assess how women use and perceive knowledge.

Understanding the latter could perhaps shed light as to why in some studies informed decisions are associated with less decision satisfaction and higher anxiety, contrary to the findings of the van den Berg study.

A number of studies showed an increased uptake of amniocentesis by women after consultation, which could be explained by an informed decision-making process. An alternative explanation could lie with the attitudes adopted by women or with the fact that amniocentesis is performed to allay the anxiety that persists in women despite the consultation.

Interesting findings from the studies of Kupperman et al would need further investigation. In the 2009 study<sup>171</sup>, women over 35 years of age who underwent the PT tool intervention and who were more inclined to use amniocentesis prior to the decision aid were less likely to undergo testing. Those less inclined to testing had higher rates of invasive testing after the tool, when compared to the control group. This could suggest that the tool improved the understanding of screening and diagnostic procedures or rendered 'risk' more comprehensible or acceptable. It could have had the effect of reassuring the undecided women about the amniocentesis and to reassure differently the decided women. This interpretation seems to be in keeping with the subsequent study<sup>172</sup> where not only were women less likely to use invasive diagnosis, but also any testing altogether.

### **A comparison of the results from the meta-ethnography and the narrative summary**

The two reviews contribute to a better understanding of the experiences of women and couples undergoing prenatal testing. They reveal similarities that consolidate the themes common to both and differences that are consistent with their respective strengths and weakness. Both reviews found a lack of informed decision-making, but the quantitative studies quantified the knowledge gaps that were present in the different settings. The concept of values was shown to be problematic in both reviews. In the quantitative studies, "values" were interpreted as preferences with discussions limited



to options: that is, to do or not an amniocentesis, to terminate or not an affected fetus. The concept of values was limited in some of the qualitative studies, but others clarified how participants understood values as an integration and contextualization of knowledge that takes moral judgments into account. When participants are not properly informed about the basic reasons for testing, the disorders tested and their clinical presentations, the effects are to further limit this particular understanding of values.

Quantitative studies reported on measures of anxiety. An important critique of these studies is the absence of a valid measure of anxiety, plus the fact that baseline anxiety level of the participant is often unknown. Furthermore, anxiety can be impacted by many variables, including the degree of emotional and structural support, and the level of resilience of the pregnant woman or couple facing a decision. None of the quantitative studies discussed the impact of these limitations on the results and their clinical relevance. The quantitative studies revealed, nonetheless, that women experienced anxiety that persisted throughout the testing procedure and was attenuated in some by obtaining an individual adjusted risk estimate or after amniocentesis.

The meta-ethnography showed that anxiety was an important theme for women who receive screening results, refuse screening or have to decide whether they will undergo a diagnostic procedure or termination of pregnancy. It also identified persistence of the anxiety states throughout the pregnancy, one that extends beyond the testing experience or even actual pregnancy and alters future family plans. The meta-ethnography thus enabled a richer understanding of the impacts of anxiety.

Both reviews identified risk perception by women as being much higher than actual risk. The qualitative studies showed that the level of risk tolerance is much lower than the medically accepted "low risk" category. Some quantitative studies found that the anxiety related to prenatal testing was in part influenced by risk perception and in both reviews anxiety was not only related to the risk of having a child with DS, but also the risk of miscarriage induced with amniocentesis. The quantitative review identified that anxiety and uncertainty of test results were not related to the testing decision. The qualitative studies described indeed the state of apprehension and moral conflict with the decision regarding termination of a pregnancy in which the fetus has a malformation. Women realized that the decision is ultimately theirs, but at the same time they view it as an unwanted burden.

This may be partly explained by the perceived subjective norm of the desirability of testing and the positive attitude towards termination, which were factors identified in both reviews and were associated with a greater intention for invasive testing in the quantitative studies.

The contribution of the quantitative review comes predominantly from its emphasis on the measurement of informed consent. van den Berg's study<sup>178</sup>, which used decision theory models and specifically detailed scored measures is unique and important for improving the conceptualization of a measure of informed consent.

In contrast, the richness of the qualitative studies was to uncover the overall experiences of women and couples in prenatal diagnosis. These studies pinpoint a different approach to biomedicine, an understanding of nature, and a different world view in those couples who chose not to undergo testing. In these experiences, the bias by health care professionals towards testing becomes obvious as parents had to justify their decision not to test and subsequently felt isolated in their choice. Some of the most insightful articles discussed the different forms of experiential knowledge and how such knowledge along with concepts of disability interplay with biomedical knowledge, thereby affecting a decision for amniocentesis. The concepts of experiential knowledge along with 'perceived norm' for testing that stemmed from the qualitative studies could be explored as potential contributors to the processes and measures of the value consistent and informed decision-making concepts.

### **The Prenatal Testing (PT) Tool: A quality criteria analysis**

In order to consider the usefulness and limitations of decision aids in prenatal testing, we chose to analyze more specifically a tool that was recently assessed by Kuppermann et al<sup>171</sup> within a randomized clinical trial. Following a multifaceted approach to prenatal testing, the tool was "designed to promote preference based decision-making." The primary outcome of the trial was invasive test use by pregnant women and the secondary outcomes included testing strategy undergone, knowledge about testing, understanding of risk, decisional conflict and regret.

We applied the original version of the IPDAS quality criteria (Appendix 2) to analyze the decision aid. The reader can find in Appendix 5 the values clarification tool provided by Kuppermann et al<sup>171</sup> to the participants. It also includes how the authors scored the knowledge level of the participants. The PT tool is an interactive computer program with audio, video and text for which a reference was not

available and thus could not be fully analyzed. Nonetheless, a critique of the tool is still possible using the information provided in the methodology of the article.

In reference to the original IPDAS framework,<sup>113</sup> criteria in the first domain includes those related to the systematic development of the tool. The criteria cover the issue of field testing and the validity of using such a tool, ensuring that both patient and practitioner view the tool as appropriate for the decision required. Kuppermann and colleagues do state that the tool was field tested with women, but it was impossible with the information given to identify other criteria that might have been met in the first domain.

In the second domain, with regards to options given in the tool, all of the criteria appear to have been fulfilled. However, the positive and negative outcomes and the chance of occurrence can be presented with bias depending on how the information is formulated and the style of communication adopted. The question related to the detection and treatment of disease, which would not have caused problems if the screening had not been done, seems of crucial importance in prenatal diagnosis. More specifically, decision-making in the era of expanding knowledge of genetic testing in which variants of unknown significance and benign variants will be increasingly detected, this criterion will require an ethical analysis on its own.

Criteria in the third domain, and especially the one regarding the presentation of probabilities, is very crucial for interpreting risk and its perception. It was impossible to comment on the correctness of the medical information nor on the potential biases in the role of values, preferences and descriptions of the medical conditions presented in the video. Such biases could be present in the number of options given, the risk figures, but also in the strategies for testing. The measurement of recall of information gives no indication on whether the patient understands the meaning of probability statements at the aggregate level and their relevance to individual decision-making.

The criterion “placing the chance of what might happen in the context of other situations (such as developing other diseases, or dying from common occurrences)” could help the women better situate their inappropriate high risk perception into context and decrease it to a level more in keeping with the actual risk. This would be beneficial and necessary based on the findings presented above. In a few of the quantitative studies reviewed, the NT risk-adjusted and age-adjusted figures were associated with decreased anxiety. Presumably the NT risk-adjusted and age-adjusted figures were provided, but contextualization of risk was not commented.

In the fourth domain of “values”, the criteria 4.1 and 4.2 require the decision aid to provide descriptions for each option in order to help patients imagine the various physical, emotional and social effects and think about the positive and negative effects of each option that matter most to them. In the case of prenatal testing, this could be referring to the various procedures such as option for screening, amniocentesis or no procedure. However, it is also possible that it could be referring to the various options of having or not having a child with a genetic or fetal malformation. This would need clarification.

As it stands now, the values clarification tool (see Appendix 5) adopts an attitude based on the format of the questions that could bias decision-making and does not address the value of the option of ‘no testing’ fairly. Furthermore, possibilities of positive and negative experiential outcomes in cases of the presence or absence of a condition are not explicated. The tool does suggest a strategy for testing for the individual participant based on the responses given to the values clarification and individual NT/age adjusted risks. However, it does neither identify whether the participant understands the suggested strategy, nor does it allow the participant to document whether she has made a decision that is consistent with the values clarification exercises. Moreover, the women are not encouraged to discuss with significant others. The authors’ intention is to use the hospital chart to identify whether the patient has enacted the suggested strategy using the PT tool.

The fifth domain deals with the use of patient stories for decision-making. It does not appear to have been used in the PT tool, but there is no strong favor for their use in the literature. However, future consideration of using patient stories should be accorded as it is known that pregnant women known to be at risk or to carry foetus affected with DS appreciate meeting people living with the condition before deciding whether to terminate a pregnancy<sup>15</sup>.

As per the sixth domain criterion “guiding/deliberation and communication,” the goals and use of decision aids are still contested among different stakeholders. It is interesting to note that the option in the list of “working with a training coach to help patients prepare to talk about the decision with a practitioner” was rated highest amongst the patient group. This criterion was not met in this study. Criterion 6.1 seems to have been fulfilled with the PT tool given the sequence of presentation of the information and the ability to verify one’s choices in different formats.

Criteria in the seventh domain refer to disclosing conflicts of interest and those in domain eight with web based tools. The former was not discussed and the latter did not seem applicable for this tool.

The fulfillment of criteria for the domain nine could not be commented since the information was not available. It is not clear why the criteria in this domain are not included with domain two, which pertains to balancing the presentation of options.

Plain language should be used in decision aids. The authors of the PT tool did not identify the reading level, the formula for its derivation or the professional standards that guided its development, but the tool did fulfill three of the other four criteria for the tenth domain.

Criteria ensuring scientific integrity such as 'quality of the scientific research', 'the steps used for acquiring the evidence' and the 'use of evidence from groups of patients similar to those that will eventually use the aid' should be ascertained. The importance of these criteria was divergent among different stakeholders and they were not addressed in the methodology of the article.

As for domain twelve, entitled establishing effectiveness, the criteria enumerated seem in part redundant with the previous domains, but are non-specific as to how to evaluate the stated goal. For each, it is stated that "there is evidence," but for none of the sub-criteria is it stated how this evidence is to be evaluated or obtained. The last criteria — 'there is evidence that the patient decision aid improves the match between the features that matter most to the informed patient and the option that is chosen' — is the foremost objective of decision aids. Kuppermann and colleagues found that the participants who used the PT tool obtained a high concordance between the suggested testing strategy and the prenatal testing performed. However, one may wonder whether this concordance reflects a match with the patient's true values or preferences and whether the aid increases patient involvement in decision-making and patient ownership of their decisions.

In summary, Kuppermann et al.<sup>172</sup> tried to ensure a complete evaluation of the process of decision-making for prenatal testing with knowledge and values clarification questionnaires in addition to the PT tool, which was seemingly appropriately adapted to the context. The authors discuss the many facets of the improved video/audio PT tool, which may fulfill additional IPDAS criteria compared to their previous prenatal testing tool<sup>171</sup>. The goal was to ensure that a preference-based informed consent was obtained by the participants using the PT tool. When reviewing the information available in the article, many of the IPDAS quality criteria were fulfilled, but the tool fell short in fulfilling all of the criteria.

The criteria listed have undoubtedly a value for researchers, yet, it is difficult to see which of these criteria are the most important for participants' decision-making and to which end. In the clinical

context, the use of a PT tool that would fulfill all of the IPDAS criteria might be impractical and it is not clear which criteria would be most relevant. Nonetheless, Kuppermann and colleagues did confirm with a patient chart review that the choices made by the majority (75%) of the participants were concordant with the strategy proposed by the tool. This finding does not solve in and of itself the question of the quality of the decision-making.

The authors were able to demonstrate a statistically significant difference in knowledge level and lower use of prenatal invasive testing in the group of women who had been randomized to the intervention group. Possible reasons for such a finding were introduced previously. The use of a PT tool in such a study is provocative since it begs the question as to whether the primary outcome of decision aids should be health outcomes, the coherence of the decision with the participants' own values or the quality of the decision-making process. Hence, the revised IPDASiv4 criteria still appear to be a challenge for decision aid developers.

Although those who developed the IPDAS criteria state that the fulfillment of all 28 criteria is not necessary, they are relevant to decision-making as they stem from the initial framework of 2006<sup>113</sup>. It is not known which of these criteria are crucial for participants, in different context and with different time lines and objectives. A recent review called into question the validity of some of the IPDASi v4 criteria in 30 decision aids and offered a critique for improvements<sup>114</sup>. The limitations and biases of the expert based modified Delphi approach that supported the IPDAS development need to be reminded. The validity and feasibility of the criteria are also important issues that need further exploration. Given the limitations discussed above and as evidenced by the critique of a PT tool, the quality of prenatal testing decision aids<sup>115</sup> and their role in decision-making should be called into question. The value of the format, content, context and timing of use of such aids, as perceived by those affected by the decision, need to be elucidated.

## **Discussion**

Relying on a meta-ethnographic approach to the synthesis of qualitative studies, one aim of this thesis was to develop a richer understanding of the experiences of women and couples undergoing prenatal diagnosis. It provides insight into the various psychosocial and cultural factors that influence these experiences, thereby complementing the HTA qualitative and quantitative data presented by Green et al<sup>57</sup>. As we further discuss below, our conceptual framework clarifies the different steps where possible interventions and policy initiatives could be implemented to improve these experiences. The narrative summary of the quantitative studies focused on the relevant processes of decision-making; it confirmed many of the qualitative themes, but also underscored the limitations of informed decision-making in prenatal diagnosis. Using the IPDAS quality criteria, our analysis of a published decision aid for prenatal diagnosis showed that many questions can be raised regarding the value of such tools in the 'real world' of clinical practice. The objectives of the tools, their underlying theory as well as the tools themselves remain value-laden.

### **The implications of the conceptual framework**

By exploring the phenomenological issues of women undergoing prenatal screening and diagnosis —a practice that has been in existence for several decades—, our findings uncovered many concerning issues that should lead women and health care providers to improve the overall experience of women and couples. The factors that intervene along the process can be broken into macro, meso and micro-levels. These factors have implications with regards to public education, governmental policy, organization of care, evaluation of prenatal screening programs and the patient-physician dyad. Although these factors are discussed below at one level, they often have impacts at multiple levels.

### **Macro-level factors**

#### Context, roles and culture

It is important to underscore that our findings showed many similarities in the experiences of women and couples, even though the studies we reviewed had been conducted in different countries, with different policies and organisational models. For example, in the Netherlands and Scandinavian countries, prenatal diagnosis counseling is performed predominantly by midwives, whereas it is performed by physicians in many other countries. The role and contexts in which professionals

provide information for informed consent vary greatly. While some women were able to obtain counseling and results of testing the same day as the testing procedure was performed, others required several visits prior to testing. For Vassy et al<sup>84</sup>, such differences in organization have an impact on the experience of women. In the UK and USA, inclusive prenatal screening programs have existed longer than in the Netherlands. Social norms and attitudes of women regarding the use of prenatal testing in these countries were seen as more liberalized when compared to the Netherlands where universal screening became available in 2007 and women's attitudes tended to be more conservative.<sup>84</sup> The studies also differed by the type of technology that was used. Over time, a given preponderant technology evolved with its particular advantages and disadvantages compared to others and this may have modified attitudes towards screening and diagnosis in different contexts. Such differences need to be acknowledged when seeking to adjust policies, procedures and processes for diagnosis and informed consent according to the goals of the local context.

This thesis contributes to current understanding of the gendered experiences of prenatal diagnosis identified at least in the western cultures. There are many similarities in the types of experience between men and women, highlighting the timing and context of their respective experiences. Socially accepted norms and roles have an impact on men's and women's grieving processes. The feeling of exclusion, lack of support or respect experienced by men evidences the presence of socially anchored roles that are subconsciously present in the form of a gendered ideology in health care. This affects relations between the couple and the professional, and within the couple itself. This will have to be addressed in prenatal screening programs. Based on the shared decision-making model, as presented by Charles et al<sup>93</sup>, professionals will have to provide space for the male partner, a role that needs to be agreed upon with the woman. Professionals will also have to define how to continue to support men and women throughout their ultimate decisions. Furthermore, the differences in these roles need to be explicitly discussed within couples in order to limit the degree of suffering that each partner experiences.

In this thesis, culture —as defined by the authors— appeared to have an impact on the decision to undergo amniocentesis or termination of pregnancy for a foetal anomaly. In Taiwan<sup>179</sup>, women did not experience testing as a choice, but trusted modern technology and professionals. Yet, they experienced at the same time powerlessness when facing health care professionals. In the Hebrew culture, a group of middle class educated women of Ashkenazi ancestry were in favor of testing because of the prevailing concepts and attitude of genetic anxiety and 'good motherhood'<sup>150</sup>. In



contrast, another group of Israeli women showed a poor understanding of testing procedures, invoked the law against abortion and tended to refuse testing.<sup>150</sup> In other studies, Muslim women were reported as neither seeing disability as a problem, nor a reason to terminate a pregnancy<sup>145</sup> and Latina women refused testing by invoking faith in God.<sup>153</sup> The diverse cultures and the prevailing beliefs and attitudes within a society needs to be affirmed and recognized since they broadly influence public understanding of prenatal programs, their goals, benefits and the decision-making process. Culture also influences the relationship between the physician and the woman or couple and may interfere with the process of informed consent. This was evidenced by the work of Ahmed et al. and Vassy et al<sup>84,134</sup>.

What is extremely relevant to distinguish and important for health care providers and all of society in which prenatal diagnosis programs exist is to recognize the attitudes adopted by the women and the many dilemmas facing them when it comes to the issue of choice. The 'choice' is related to various phenomenological experiences, which have been presented in the introduction and results section. McCoyd<sup>180</sup> identified important dilemmas with termination of pregnancies. In the USA, neither the 'pro-life' nor 'pro-choice' camps truly accept women who have to make a decision regarding a possible termination of their pregnancy. The pro-choice camp cannot accept the expression of love that a woman feels for her potential "baby" and the pro-life camp cannot tolerate the woman's willingness to terminate the pregnancy. There are no support groups or advocacy groups to embrace this sort of "choice" they must make.

The subsequent dilemma that the woman has to face is that of identity. Does one become the mother of a disabled child or a bereaved mother? Pregnant women who terminate a pregnancy for foetal anomaly are not identified as mothers. Furthermore, in the American culture, "good mothers" cannot have "bad" babies. Hence, women are caught between having a stigmatized medical procedure without recognition of being a mother or being a "bad mother." For McCoyd<sup>180</sup>, one has to recognize the importance and severity of the stress that women undergo in prenatal diagnosis, why there may be long term effects and thus the importance of addressing the social and psychological factors related to prenatal screening programs and, more specifically, to termination of pregnancy. Coping with grief and the adjustments to termination of pregnancy have been addressed in several works by Korenromp et al<sup>181-184</sup>. These authors estimated that psychological consequences such as depression or post-traumatic stress were still present in about half of the women at four months and present in

20% of women one year after the decision. Doubt, low self-efficacy, gestational age, being religious and the partner support were factors that contributed to such long-term psychological effects.

Additional ethical issues have been extensively studied by qualitative analyses of Garcia et al<sup>153</sup>. These included autonomous choice and moral dilemmas such as “worth of life with disability”, “parental rights and responsibilities”, “moral status of the fetus” and “abortion”. The authors analyzed their results according to whether the women were acceptors or decliners of diagnostic testing; although both groups of women were generally in agreement, both had mixed feelings. Both groups of women reported that disability could have a positive influence on the family. But, those who accepted were concerned about the burden, thinking that they would be unable to give enough attention to all family members, whereas decliners felt they had the capacity to deal with the difficulties of having a handicapped child. In both groups, termination was morally problematic and not accepted unconditionally. The parents viewed quality of life of the family members as colliding with the right to life of the fetus. Some parents also mentioned the ultimate risk of eugenics with the expansion of testing. These findings thus highlight how cultural values may conflict with the personal decision-making of parents.

Although the above reported study was undertaken in the Netherlands, it would seem reasonable to believe that a large proportion of women and couples identify with these dilemmas in much the same way in other countries. Till now these issues have not been addressed in prenatal diagnosis programs. It behooves agencies and governments as well as the society at large to address issues of inequities unless one is willing to accept double standards. Policies need to be adjusted to accept individuals with differences. It seems contradictory and hypocritical that countries that pride themselves on human rights records and advocate for equality for all, promote what many women themselves consider a eugenic mentality when it comes to prenatal diagnosis. If governments are going to give funding to develop technologies that pose serious threats to the existence of certain kinds of human being, it is incumbent on them to provide equal funding to promote an informed decision-making process.

Based on the conceptual framework we developed, moral space needs to be created within institutions, communities, ethnic and cultural groups for sharing views and establishing dialogue. Health care providers of different specialties, ethicists, health care researchers along with parents should be able and supported to discuss openly the values, goals and moral dilemmas that pervade

prenatal diagnosis. At a micro-level, such discussions may include significant others, in consultation with an expert if required.

### **Meso-level factors**

Basic uncertainties, 'values', risk and organization

In this thesis, several factors that pose major limitations to an informed decision-making process were identified. These include basic uncertainties with prenatal diagnosis, differences in the way 'values' and 'knowledge' are understood by women, couples and health care providers and the acceptance and interpretation of risk by women. Women and couples are uncertain about the benefits of genetic testing in general and about the quality and quantity of information they need to receive and may benefit from.<sup>141</sup> These uncertainties interfere with the informed consent process.

In our opinion, the major hindrance to the informed consent process lies in the various interpretations of the meaning of 'values'. For many women, values are the expressions of moral views or ideas about how life should be lived. Knowledge, on the other hand, results from the process of obtaining information, which entails subsequent prioritization and interpretation of factual information through the woman's own experience and that of others. It is important for women to "think through" the personal implications of the testing.<sup>120</sup> Concepts of values and knowledge are conceived by quantitative researchers and experts in decision aids as preferences and factual retention respectively. These differences need to be clarified by those developing and using decision aids if further work in shared decision-making and the use of decision aids is to have pertinence.

The meta-ethnography identified in an objective way that all risk levels were considered intolerable and cause for anxiety. Health care providers' concept of low risk had no valence for decision-making for the women. Henceforth, the concept of risk, its understanding and explanation in prenatal diagnosis would merit further research. Risks have been studied in economics, psychology and neurosciences and perhaps concepts derived from these domains may aid in the clarification of the ways that risks should be presented and discussed. However, the concept of risk should not discount the prevailing societal attitude that Lippmann described where 'being pregnant is to be at an increased risk state'.

More specifically, the notion that risk estimates for screening procedures will be irrelevant in the very near future because the NIPT technique will be conceived and used as a diagnostic procedure neither

obviates the need to explain probabilities and statistics related to a prognosis, nor alters the vast number of genetic variants of unknown significance. The latter requires acceptance of uncertainty, which is difficult in the Western context given our propensity to 'control' our health. Probabilities are known to be difficult concepts to understand. As such, it would seem necessary to be able to contextualize this information for parents to better understand. Within this perspective, the development of a decision aid tool for understanding risk alone might be beneficial.

Further meso-level considerations with regards to organization of prenatal testing services and practice need to be underscored. They include the degree of medicalization of a condition within an institution, the accessibility and ease of use of the health service and the variability in the level of expertise available. These factors may influence the adoption of a screening program policy and the type of information that is transmitted to the women, thereby affecting informed consent. Obviously, whether the program is publicly or privately funded and the extent of genetic testing and knowledge available will influence the medical culture, which will impact on decisions for certain screening tests. Furthermore, the setting in which the woman is consulting could differ, even within the same cultural environment, leading to a different decision-making process. For example, the process and influence on decision-making would be different with a family physician as opposed to a geneticist since both physicians would hold knowledge and biases with regards to testing that could influence the decision aid and type of communication. The geneticist could have a tendency to focus on the biomedical knowledge underlying testing at the expense of evaluating the women's attitudes and baseline values. The family physician may not be able to counsel with regards to the ultimate goals and have limited knowledge on the reliability of the tests, their advantages and risks and on the emotional burden caused by various test results.

### **Micro-level factors**

#### Narratives

Both reviews highlighted attitudes that affect decisions with regards to invasive testing and termination of pregnancy. The levels of anxiety, decisional conflict and risk perception are influenced by the use of decision aids, but it is not clear whether these modifications lead to better decision-making. Embodied knowledge was a key concept identified in the review of the qualitative studies that could explain the complexity of informed decision-making, including how it seems unpredictable.

A sense of agency could be at play. Through an analysis of the narratives of 26 pregnant women from predominantly Hispanic and African American low income communities, Hurst identified that they felt having the responsibility to positively influence the course of their pregnancies and their children's lives, even when they accepted aspects of heritability that were genetic and beyond their control.<sup>185</sup> These 'narratives of resistance' run counter to the dominant medicalized narratives in prenatal care. Women told complex stories, embodied and imbedded in their culture that have implications for narrative medicine.<sup>185</sup> Professionals should "listen to the narratives, grasp and honor their meanings and be moved to act on the patient's behalf. Only attentive listening and understanding can solidify the relationship and improve the quality of care given and received".<sup>185</sup> This would be the expected norm in the shared decision-making model of patient care, but it is not what women currently experience in prenatal testing.

#### Challenges in the current use of decision aids and areas for improvement

Decisions surrounding both prenatal testing and the use of decision aids are imbued with values. Values relate to the willingness of both patient and physician to interact according to the 'accepted' normative model of shared decision-making. Values also refer to broader theoretical assumptions such as utility theory being a valid approach to construct decision aids. Both health care providers and patients have to be aware of the inherent biases of limiting choices in these aids and of the values clarification exercises, realizing that they may be indirectly influenced by culture and political biases. Similarly, Boivin et al. found that the presence of values, interests and power relationships are embedded in the contexts, content and evaluation of decision technologies<sup>186</sup>.

An in-depth analysis of the values underlying screening health conditions, risk perception and various understandings of risk estimate should be encouraged. Improvements in these areas may promote a better understanding of the prenatal experience as a whole, a preferable outcome than the actual degree of information acquisition. Many contend that a decrease in decisional conflict with the use of decisional aids should be sought, but this is questioned by others<sup>105</sup>. There needs to be an improved measure for evaluating anxiety, which at this point is not discriminating enough for decision aids in the prenatal diagnosis context. Recently, factors found to be determinant for the use of decision aids in prenatal testing included subjective health literacy, attitudes, moral and descriptive norms and anticipated regret. The beliefs that are important for the intent to use decision aids included reassurance, facilitation with partner, knowing advantages and disadvantages of testing.<sup>187,188</sup>

What this thesis added to current knowledge is the importance of considering the development of decision aids directed more specifically to men given their limited participation in the in prenatal diagnosis process. This may help improve communication between health care professionals and men and with their partner. This may lessen the burden that women feel in the decision-making.

Decision aids that rely on the clarification of values should specifically address ethical issues surrounding prenatal testing including the concepts of autonomy, handicap and justice in health care. Women and couples should be able to situate their decision in the broader context of community and values that fall beyond health care per se. In addition, the experiential knowledge of women, either their own or that of significant others, regarding handicap or disabilities are not taken into consideration in the use of decision aids. This blind spot may explain the incongruence one finds between value preferences and the decision being made. Within this perspective, the revised IPDAS qualification and certification criteria may not reduce the tension as they appear onerous to use. The relatively limited criteria only address the issue of improving the overall knowledge base and not the most important reasons for which aids were developed, that is ensuring value consistency.

The limitations of decision aids and value clarifications exercises that seem to be the most worrying lie in the impression by women and couples that their use is time limited, that revision of decisions is not possible and that consultation with others is neither required nor desirable. These limitations run against the paradigm of shared decision-making and patient-centred care. They are also contrary to significant findings in decision research, which suggests that the appropriate response to decision-making is:

to suspend the selection of an initially favored option, as an early preference may be based on irrelevant attributes and a decision made before receiving all relevant information. The values clarification methods should remind patients of their full array of values and cue values that are relevant to the decision<sup>189</sup>.

Indeed, decision aids should encourage patients to take more time before committing to a final preference.<sup>189</sup> Given the nature and complexity of the decisions to be made, these tools may be best considered useful when they are presented at various stages of the prenatal experience and adjusted for literacy level and social context as recommended by Kuppermann et al<sup>171</sup>.

## **Strengths and limitations of this study**

The limitations of this thesis are numerous. First, the results are the fruit of a combination of two bibliographic search strategies and two sets of selection criteria that were adapted either to qualitative or quantitative research. Despite this complexity, only the author of the thesis screened and reviewed the abstracts, titles and articles. This leads to potential bias in the final selection of the studies and in the interpretation and analysis of their findings. Second, the analysis of the prenatal diagnosis decision aid suffers from a similar limitation since an evaluation with an inter-judge agreement would have been more solid. Third, the original sources we reviewed sometimes suffered from a lack of details. This applies to the articles that reported on the development and use of decision aids and wherein the tools were not always completely presented or lacked appropriate references. Hence, the observation that the majority of the tools did not fulfill all the certifying IPDASi v4 criteria may be partly attributable to the way information about the tools was reported. This is why our critique also examined the usefulness and limits of such criteria.

Among the strengths of the thesis one may highlight the methodological approach which consisted of a mixed method review that relied on a meta-ethnography of qualitative studies and a systematic review of quantitative studies. Within the field of HTA, such syntheses are gaining recognition since they can inform policy and practice in a more complete way. The meta-ethnography provided an enriched explanatory understanding of the experiences of women, couples and men. The review of quantitative studies was key in elucidating themes that are measurable and around which hypotheses may be tested. Second, this mixed review was complemented by a critical analysis of a specific decision tool using the IPDAS criteria, showing how both the review and the critique are relevant for developing solutions to improve the informed consent process. Third, the experiences of women and couples undergoing prenatal testing identified in this thesis were examined from a constructivist and critical theory epistemology. Such an interpretative synthesis can lead to theoretically and socially significant improvements in concepts and practice in prenatal diagnosis. Such improvements can tap on an interdisciplinary analysis of bioethical and social scientific dimensions including, feminist theory, decision theory and communication theory.

### Areas for further research

Current limitations in the quality of the decision aids as revealed by the IPDAS criteria and their questionable usefulness in clinical practice requires more research. The still unresolved contested

goals of decision aids and practical factors such as implementation, organization and dedication by professionals for the use of the tools may be at play. An important obstacle to decision aid use is also noteworthy; physicians need to be convinced that it is in their interest to increase patient participation in decision-making.<sup>190</sup> A recent study examining health care providers' attitudes upholds this observation. Factors that increased the likelihood of use of a decision aid included a positive appraisal of the tool, availability of the tool in the office, a colleague's approval, time available and finding it a relevant source of information<sup>191</sup>.

Further research into ways to determine which types of decision aid to use and in which clinical context (test, treatment, characteristics of the disease, etc.) would be helpful.<sup>101</sup> Furthermore, it might be useful for patient decision aid developers to be provided with resources that help them to understand what aspects of health care context and patient experiences might be biasing the patient's judgments and what techniques enable to 'de-bias' them and why.<sup>105</sup> For example, it would be important to know whether the utility elicitation technique does challenge patients' prior beliefs or, to the contrary, facilitate a confirmation of existing preferences. Certain diagrams or tables may enable patients to create a more accurate mental representation of the decision context and assimilate information that is already 'out there' with their own values. Hence, studies that integrate decision theory and health research outcomes are needed. Examining the quality and quantity of information that can be shared as well as the methods for conveying such information effectively requires multiple expertise (linguistics or communication experts, decision theorists, health care researchers, clinicians, patient groups) as recommended by Bekker et al<sup>105</sup> and Durand et al<sup>114</sup>.

The validity of concordance between the patient values and the options chosen remains somewhat problematic. Which values are to be considered in an analysis of congruence between values and decision-making in the context of prenatal testing and care? When and how should this congruence be measured? How does the use of a decision aid and shared decision approach affect this congruence? How does one determine whether this is the "best" goal of decision aids? These are fundamental questions requiring research that involves the patients, an aspect that remains belittled by collaborators of the IPDAS criteria.

An ideal study design through which to investigate the experiences of women using decision aids in prenatal diagnosis would be to combine quantitative and qualitative data on the same group of participants. A randomized trial with one or several interventions compared to the standard care



could evaluate the outcomes of the tools as well as patient-related measures such as quality of life in the short and long term. Its embedded qualitative component could investigate the perceived value of the decision tool and the experiences of decision-making by women, men and couples.

Practice implications: A paradigm shift for decision-making and care

The previous sections suggested individual, institutional and societal factors that could be modified to improve the experiences of women and couples undergoing prenatal testing and underscored key conceptual and practical issues with decision aids. Although some may altogether object to the use of decision aids given their limitations and normative a priori, we believe there are possible solutions to mitigate their shortcomings. The use of decision aids should result in a decision that is informed and consistent with patient values. Patients are experts for considering values and various options should be presented to those who are faced with a preference-sensitive decision. However, normative issues are not unsolvable.

Decision aids should not be conceptualized as a substitute to the interaction with a health care provider; rather, the patient-provider dyad should remain a locus where exchanges are participatory and supportive of an informed and autonomous decision-making process, i.e., a standard of practice. For Kuppermann et al<sup>171</sup>, decision aids “should provide scientific information for the health of the women and the fetus, on the risks and benefits of all options in an unbiased and non-directive way and assist the women in clarifying their personal values in outcomes and adverse events.”

Nonetheless, the results of this thesis suggest that the provision of unbiased non-directive scientific information in the context of prenatal care is neither possible, nor wished for by women or couples and fall short of fulfilling the expectations of shared decision-making.

The validity of the concept of informed choice in shared decision-making, understood by many in Western countries as comprising autonomous decision-making and an attitude of non-directiveness for an experience of quality care in prenatal diagnosis, is put into doubt. It could be argued that informed decision-making takes place in the context of an informational model of patient care<sup>75</sup>. This model presumes that, for informed decision-making to take place, women seek (or should seek) information outside of the exchanges that occur between clinicians and women.

There is a growing body of literature describing how patients use the internet, friends and family and other sources of information to inform their health decisions but little

theorizing about the ways women seek, retrieve, and use information when trying to make a decision about participation in prenatal diagnosis<sup>75</sup>.

The work of Vanstone, who draws on women's own reports, suggests that decision-making is an iterative process that involves interaction with physicians, but also getting information from popular books and from the sharing of experiences with friends and family members. Health care providers seeking to support women in their informed decision-making should thus help them to obtain relevant and credible sources<sup>75</sup>. Our findings are concordant with those of Vanstone who found that information and knowledge are contextualized considering each woman's circumstances, perception of risk and understandings of motherhood, disability and family. Vanstone suggests that acknowledging this process may change the way we currently understand the role of physicians in informed decision-making in prenatal screening and diagnosis.<sup>75</sup>

This thesis' implications for professionals who provide prenatal care are to lay bare some of the key reasons why their goals in the presently conceived model of patient-centred care need to be reconsidered. Should the physician continue to fulfill the role of a provider of facts and non-directive bystander? Should the physician give up the responsibility of a knowledge provider to become a pure technologist? What is the significance for the quality of health care and the patient-physician relationship of these varying goals and roles? Do health care providers not hold the duty to contextualize and guide the patient in such a complex process exactly because they know (or are supposed to know) the limits and usefulness of the technology better than anyone else? Including benefits and burdens that go beyond the biomedical issues? The attitudes adopted by the radiologists in the study by Schwennsen and Koch<sup>102</sup> are an example of non-directive care. They tried to contextualize information for the women and adopt attitudes that were meant to help decision making and limit suffering experienced by women. Yet, it could be argued that their approach did not result in truly informed decision-making even if it was considered good care by the women. In any case, before undertaking the process of informed decision-making both the physician and the woman have to have an idea of how involved each wants to be in the decision-making process. Physicians in particular have to recognize that informed decision-making is an evolving process and women need time and discussion with others before arriving at a decision.

Another consideration that will impact decision-making in this domain is the growing complexity of the genetic information that is accumulating and the limited human resources available for

interpretation and counseling. Some have questioned whether individual informed consent can continue<sup>15,56</sup> and whether different categories of informed consent procedures should be created. One option would be to refute the concept of informed decision-making in the context of patient-centred care in favor of an alternative that would include informing women in an indirect impersonal way. This could occur with the development of online educational resources, which could be accessed prior to consultation. Then, electronic information could be used in the office at the time of consultation and counseling provided by non-physicians or non-specialized counselors. Perhaps in this context decision aids could be conceived to have a limited role, that is of encouraging patient participation rather than ensuring an informed, good decision.

Evidence that such tendencies are already present is confirmed by a recent study in which Hui and Hyett<sup>192</sup> have developed a “model” or algorithm for integrating NIPT in prenatal screening programs. Here the concept of care is limited to obtaining the most efficient results with the least amount of risk or burden to the patient and health care system. Those interested in policy or management may argue that this is the most that can be expected from an already overburdened health care system whose role is primarily to cure and prevent disease and not deal with the psychosocial and cultural impact of illness. However, the findings presented throughout this thesis offer a strong counter-argument to this vision: the extent to which prenatal diagnosis has become largely imposed on women despite its short- and long-term deleterious effects calls for more responsible care.

Paradigm shift: Towards relational autonomy

The concept of relational autonomy is premised on the shared conviction that persons are socially embedded and their identities formed within the context of social relationships. Individual autonomy and moral agency are thus understood through the intersubjective and social dimensions of selfhood<sup>193</sup>. Contrary to the concept of agent autonomy, relational autonomy recognizes decisions draw on emotional and rational reasoning. In relational autonomy, deciders can rely on significant others for advice or defer decision-making to others.

The role of the health care provider is thus expanded to engage emotional experience of the decision-maker and offer guidance in decision-making<sup>194</sup>. The importance and role of emotion is acknowledged and the influence of others on patient decision-making is expected<sup>194</sup>. Adopting this concept in prenatal testing would, of course, mean a paradigm shift, one that recognizes formally the importance of the others in decision-making. Such a paradigm shift is congruent with the results of

this thesis and the literature. It could better recognize the importance and meaning of concepts such as parenthood and fatherhood and question the concept of 'patient' from a parental perspective. It would also give further reasons to improve research and practice around decision aids.

According to Elwyn and collaborators,<sup>194</sup> the guiding principles of shared decision-making are based on the concepts of self-determination and relational autonomy. The latter emphasizes that individuals are not totally free self-governing agents since their decisions are embedded in, and affected by interpersonal relationships and mutual dependencies. If these premises are accepted, they allow for an extended concept of informed consent, one that goes beyond a simple act of knowledge transfer in view of honoring informed preferences. For Ells and colleagues,<sup>195</sup> explicitly adopting an attitude of relational autonomy as an integral aspect of patient-centred care can narrow the theory-practice gap. According to Elwyn et al,<sup>191</sup> this needs to be based on the core skills of building rapport and structuring clinical consultations. A concept of care that adopts a more transparent and encompassing approach was introduced by Elwyn et al<sup>196</sup>. This model draws on empathic and respectful communication as a fundamental basis to good patient deliberation. Clinicians thus need to be curious about and respectful of patient's informed preferences.

What this model adds to patient-centred care is that it formalizes the elicitation and integration of patient preferences, which is one component in the use of decision aids. The perspective taken in this model is that a patient does not have a single set of clear preferences. The patient in the clinic has preferences that may differ from those of the patient embedded in a social unit. Recognition of the latter is the first step in obtaining informed consent that is compatible with the shared decision-making model. It is also the basis of a health care provider-patient relationship that endorses relational autonomy.

Overall, to improve the experiences of women and couples in prenatal diagnosis there will be a need for additional education and resources for primary health care providers, obstetricians, midwives and geneticist and health researchers. Otherwise, the continued expansion of genetic testing will impose tremendous societal challenges.

## **Conclusion**

The aims of this thesis were to identify the lived experiences of prenatal testing in the western perspective, consider the concept of informed consent and its present actualization and identify ways that decision aids may improve the care experience in prenatal diagnosis. The study approach stemmed from constructivist and critical theory and the methodology relied on a mixed synthesis of qualitative and quantitative studies, complemented with the critical appraisal of a prenatal testing decision aid using IPDAS criteria. Our findings have practical implications to advance further knowledge, research and change in clinical practice in the concrete everyday encounter and organization of delivery of prenatal diagnosis.

Informed consent is crucial in clinical practice and research in genetic diseases and malformations. The practice of prenatal testing raises ethical queries as do the application of the various technologies that have emerged in this field. Variations in their use can have repercussions on the very essence of the meaning given to human existence and, as such, they demand the utmost respect when using them. The concept of informed consent that has been examined in the context of the shared decision-making model is supposed to protect the very essence of the meaning of “respect” for person, which ultimately allows the exercise of autonomy. However, because of the complexities of genetic knowledge, the decision-maker has to be supported for autonomy to be realized. The goal of decision aids is to support the patient in making a decision that is value congruent with the possible options for treatment or diagnosis in situations where the value for one is not clearly superior to the other.

To our knowledge, this is the first meta-ethnography that provides a conceptual framework of the experiences of prenatal diagnosis by women and couples. The narrative summary of quantitative studies identified themes complementary to those of the qualitative review, but proved particularly relevant for identifying the factors necessary for informed consent and the way decision aids may affect this process. In theory, informed consent fits neatly within a shared decision-making model where value congruence is emphasized. Nonetheless, the literature shows that the norms of ‘autonomous decision-making’ and ‘non-directive counseling’ were experienced as problematic by women and couples.

Although the key aim of the IPDAS criteria is to ensure congruence between the choice made and personal values as well as quality unbiased decisions, few decision aids fulfill these objectives. They

improve knowledge scores, but do not affect risk perception or anxiety levels. There is little evidence that decision aids improve informed decision-making. The limited availability and usefulness of decision aids in prenatal diagnosis does not allow sufficient information to be extracted as to the value of these tools in an improved patient care model. This thesis did, nevertheless, uncover areas for further clarification and research where both the theoretical and practical aspects of decision aid in prenatal diagnosis were found lacking. The results suggest that a paradigm shift around the concept of relational autonomy would greatly benefit patient-centred prenatal care.

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**Table I. Characteristics of qualitative studies included in the review**

Author	Country	Participants	Data collection	Methods	Main experiences
Santalahti et al.1998 Social Science and Medicine	Finland	45 index screen positive for AFP and HCG) and 46 control women	Semi structured interviews at 31 wks gestation	Thematic analysis	Experiences of women during the screening process and their role in decision-making
Browner et al, 1999 American Journal of Public Health	California, USA	147 mexican origin women and 120 hispanic partners	Semi structured interviews- conjoint in 49% after the decision was made for amniocentesis	Content analysis	Considerations women found pivotal in deciding to undergo amniocentesis, to account for their decisions and how their conflict was resolved.
Carroll et al, 2000 Canadian Family Physician	Ontario Canada	60 pariticipants	6 Focus groups from various communities	Thematic analysis	Explore ideas, feelings, experiences of women who had undergone MSS
Redlinger-Grosse et al 2002 American Journal of Med Genetics	Maryland USA	20 couples and 4 women with prenatal diagnosis of holoprosencephaly	In depth interviews with parents who choose to continue with the pregnancy	Thematic analysis	Describing parent’s experiences while making the decision and their needs from family friends and health care professionals
Williams et al. 2005 Social Science and Medicine	UK	15 women.	28 semi- structured interviews. Pre post, screening and post natal longitudinal perspective	Thematic analysis	Experiences of women 1rst trimester screening
Heyman et al. 2006 (SSM)	London,UK	27 women, different stages of pregnancy	Interviews pre, post screening/ diagnostic testing	Framework/ thematic analysis	Meaning to the offer screening & entry into high risk status of women undergoing prenatal maternal screening for chromosomal

Author	Country	Participants	Data collection	Methods	Main experiences
Locock et al, 2006 Social Science and Medicine	Oxford, UK	N=41 33 women, 6 couples, 2 male partners (half had anomalies)	In-depth narrative interviews during pregnancy up to two years after birth or termination	Thematic analysis modified grounded theory approach	anomalies Explores how men experience fetal screening and diagnosis
Remennick 2006 Sociology of Health and Illness	Israel	27 women who chose elective serum testing for genetic mutations and 23 women who chose not to be tested were their controls	Women were interviewed pre- and post testing (n=25) once the results were known n= 21 were already pregnant and 6 were planning	Thematic and narrative analysis	Women's perspectives on the key social influences of the growing range and prevalence of prenatal genetic testing
Chiang et al, 2007 Journal of clinical nursing	Taiwan China	27 women with a positive result of maternal serum screening	Semi structured interviews	Grounded theory	Women's own perceptions of 'maternal self ' in context of a positive screening result
Garcia et al, 2008 Social Science and Medicine	Netherlands	59 women a sub sample of a quantitative study offered NTS or MSS	Semi-structured interviews exploring moral status of foetus, abortion, rights and disabilities and life worth living	Two steps inductive thematic analysis	Explore the impact of personal ethical beliefs in decision-making for prenatal testing
McCoyd 2008, Qualitative Health Research	New Jersey USA	30 women who were no longer pregnant at the time of the interviews	30 women who were no longer pregnant at the time of the interviews	Exploratory study via phenomenological narrative and using grounded theory and reflexive analysis	Factors weighted in by women in the decision-making in the context of foetal anomalies where the pregnancy was wanted and would have continued if there was no anomaly
Carolan et al. 2009,	Canada	10 women at high risk	20 interviews/ 2 in-depth	Thematic analysis/	Experiences based on uncertain

Author	Country	Participants	Data collection	Methods	Main experiences
Midwifery		pregnancy clinic, tertiary care hospital, 2 or 3 trimester	interviews over 6 to 8 months. Inclusion criteria, detection of soft marker in normal pregnancy	grounded theory	ultrasound findings and referral to tertiary center for at risk
Kelly 2009, Sociology of Health and Illness	USA	40 interviews of parents attending a genetic clinic with one child afflicted with a genetic condition	In depth interviews with parents of children being evaluated or followed by a genetics outreach clinic	Thematic analysis Ethnographic study	Elicit parent narratives by engaging temporal, experiential and attitudinal responses
Hawthorne and Ahern 2009, Applied Nursing Health	Australia	20 women, 11-12 weeks gestation before ultrasound	Semi-structured interviews	Hermeneutic	Experiences of women contemplating NT
Gottfredsdottir et al, 2009, Midwifery	Iceland	10 couples, low risk for fetal anomalies, 7-11 weeks and 20-24 weeks, male and female, community health centers	Semi-structured 40 interviews, separate mother and father	Framework analysis/ grounded theory	Influences on prospective parents' decisions regarding NT, screening in early pregnancy, differences in views of benefits and implications of screening b/w men and women
Gottfredsdottir et al. 2009, Social Science and Medicine	Reykjavik	10 couples interviews at 7-12 and 12-24 weeks, low risk, 4 primary care centres	40 semi-structured interviews	Thematic/ framework, Nvivo software	Exploration of decision-making on a prospective basis for DS that refuse screening
Ahman et al, 2010 Patient Education & Counseling	Sweden, Uppsala	11 women, 25-30 weeks pregnancy and 7-13 weeks after discovery of soft marker, Academic Hospital	Semi-structured interviews	Thematic analysis	Investigating women's' expectations of routine ultrasound and factors for amniocentesis decision

<b>Author</b>	<b>Country</b>	<b>Participants</b>	<b>Data collection</b>	<b>Methods</b>	<b>Main experiences</b>
Durand et al, 2010 Health Expectations	UK	17 health professionals and 17 pregnant women	Semi structured interview with women offered amniocentesis	2-step thematic analysis, descriptive phenomenology	Clarify and categorize pregnant women's information and decision support needs for amniocentesis
Markens et al, 2010 Sociology of Health & Illness	USA	147 women, Mexican ethnicity	Semi-structured interviews after decision for amniocentesis	Grounded theory	Explore how women draw on various knowledge sources, specifically for amniocentesis testing
France et al, 2011 Health Expectations	UK	24 women and 4 partners	26 full interviews	Framework analysis	Describe experiences of disability in women and couples in context of fetal anomalies on diagnosis
France et al. 2011 Social Science and Medicine	UK	36 women and 9 men, 8 couples interviewed together	37 interviews for 55 pregnancies/ diagnostic testing for fetal abnormalities	Framework analysis	Source and context of types of knowledge used by women for pre-natal testing decision
Garcia et al. 2011, J Med Ethics	Netherlands	59 women sub sample offered either NT or MSM	Interviews 1 week after test offer received and prior to testing performed	Qualitative substudy of a RCT of NT and MST vs no offer  2 step induction, Nvivo software	Investigate the meaning of ethical consideration in decision-making for prenatal testing. Meanings of appeals to nature by participants and the impact of their considerations on decision-making.
Ahman et al, 2012 Midwifery	Upsala Sweden	17 expectant fathers	Semi structured in depth interviews 6-12 wks after US discovery of soft tissue marker	Naturalistic inquiry	Explore men's expectations of routine ultrasound and experiences when soft markers are discovered

<b>Author</b>	<b>Country</b>	<b>Participants</b>	<b>Data collection</b>	<b>Methods</b>	<b>Main experiences</b>
Aune and Moller 2012 Midwifery	Norway	20 interviews with 10 pregnant women pre- and post testing results uncomplicated pregnancy	Semi structured interviews, women accepted offer of first trimester screening	Grounded theory	Women's experience of early ultrasound for risk assessment for chromosomal anomalies and perception of those risks
Hickerton et al 2012 American Journal of Medical Genetics Part A	Victoria Australia	9 participants with a child afflicted or high reproductive risk of genetic condition prenatally who continued pregnancy after diagnosis or refused prenatal testing	Semi structured interviews each parent in a couple interviewed separately  Purposive sampling	Grounded theory	Explore experiences and attitudes of parents continuing a pregnancy in which a genetic condition was or could have been detected prenatally
Pivetti et al, 2012 Prenat Diagn	Italy	n=20 pregnant women and new mothers	5 focus groups discussion guide developed and informational session given	Content and thematic analysis	Explore underlying values and beliefs for women's reasoning for prenatal genetic test uptake
Barr and Skirton 2013 Nursing and Health Sciences	Plymouth, UK	n=22 pregnant women and or partners and n=22 HCP	4 focus groups of each	Thematic analysis	Explore views of parents and HCP regarding informed decision-making for antenatal screening
Dheensa et al 2015 Midwifery	UK	12 men	Semi structured interviews cross sectional	Grounded Theory	Explore what men want from antenatal screening and midwives in pregnancy anomalies or not
Gitsels-van der Wal, Midwifery 2015	Netherlands	Women between 20-36 years of age of various education levels and parity of Moroccan descent	Interviews between 21-32 weeks gestational age	Grounded theory	Themes important to Islamic women. Particularly differences with motherhood, religious and handicap issues that are primary

**Table II. Themes derived from the qualitative studies**

<i>Themes</i>	<i>Second order constructs</i>	<i>First order constructs</i>
<b>Attitudes</b>		
<b>Uninformed screening</b>	She felt strongly she should opt for the screening as it was part of routine screening and it would confirm, reassure her that her baby was healthy	I haven't thought it through...doctor felt it was a self-evident act...I just thought this is something you do when you are pregnant (Gottfredsdotirr et al 2009)
No option	Half of the women said they considered participation to be routine, a self-evident act, 'natural'	It was self evident to participate. I was too busy to think'what then if there would be something in the result? (Santalahti 1998)
	Participants emphasized that these genetic tests are not like other tests and cannot be added to routine blood work	When you are offering tests.... please don't don't just pass it off like it's....just a blood test checking if you're iron deficient...This is serious you know (Carolan et al, 2009)
Seeking reassurance	Two thirds of the women conceptualized the pregnancy as an essentially abnormal process...emphasis on exclusion rather than healthy baby	I am more interested in knowing that the baby does not have anything wrong with it (Hawthorne and Ahern, 2009)
	His use of words of safety and risk...his motives referring to managing and controlling the process	Everything you can explore in advance is positive... it reduces uncertainty and increases your certainty (Gottsfredstorrir et al, 2009)
Knowledge lack about screening	Women regretted their screening decisions and blamed it on lack of information pre-screening test	For me that was a terrible rollercoaster...Don't have the blood test if you don't know the rest of the consequences (F, 35 declined amniocentesis) (Durand 2012)
	The focus for parents was not on screening but rather on the scan performing a social function	The midwife should sit down with me...they are not doing this scan for you to see your baby...so you can have a picture for your purse...they are doing it to see if he is developing properly (Barr and Skirton, 2013)
Unpreparedness	Several of the women felt important for the couples to have a discussion about the choice in advance...if not result in important decisions in state of emotional imbalance	No I can't make decisions...would like others to make decisions for me...looking forward to ultrasound result but I do worry about the choices afterward...no matter what the risk we

<i>Themes</i>	<i>Second order constructs</i>	<i>First order constructs</i>
<b>Vs. Decline screening</b>		have to make a choice (Aune and Moller, 2012)
Realistic expectations and changed life path	<p>One has to be realistic about the condition of these children and their life should not be glorified</p> <p>Many parents before the diagnosis envisage a particular life path for their child... after ...received diagnosis this path changed requiring parents to make sense of and reassess their view of the future</p>	<p>It is demanding to raise a child with Down's syndrome. I know quite a few teenagers. Their development stops...and they will perhaps always be like 12 year old children (Gottfredsdottir et al, 2009)</p> <p>and suddenly there is that loss that all is not going to happen in the way that you expected it to...that was your mental path for your child and suddenly you've not got that path...you can't see where you are going and you know you are never going to get on that path ever again...It's broadened my perspective and a whole new world (Hickerton et al, 201)</p>
Tolerance for diversity	Parents at the same time felt that variability and complexity in ability and health should be maintained in society	For me it is not necessary to know...People have been born with various kinds of anomalies but lived happy lives (Gottfredsdottir et al, 2009)
Unreliable test	Many participants indicated that their decision to decline screening was influenced by the fact that NT was a probability test...information was insufficient for them and did not give them accurate answers	This feeling of uncertainty after the NT screening. You know nothing. It is not possible to provide any accurate answers after the NT screening. I would not like to proceed with this screening...and end up with that possibility and have to live with that uncertainty throughout the pregnancy (Gottfredsdottir 2009)
Uncertainty and apprehension to testing	<p>From the outset...had reservations to test...while those that went ahead with testing spoke about a possible influence of health professionals on the decision to test</p> <p>Reasons for being apprehensive about screening and testing included the risk of miscarriage, lack of knowledge of the condition or considering it a moral dilemma</p>	<p>There was no problem for having the amnio but I just didn't know if I would need it" perhaps because of your age we should...that's why I went ahead...I was going through the ultrasound anyway and it's the same place same person so... (Hickerton et al, 2012)</p> <p>We were then faced with not only the dilemma of raising a child with a terminal disability but also the moral decisions of "OK we'll do the</p>

<i>Themes</i>	<i>Second order constructs</i>	<i>First order constructs</i>
	as Steve discussed	testing and then what do we do after that? Do we terminate or do we continue on? So there's another sort of moral decision that never would normally have entered our minds (Hickerton et al, 2012)
<b>Reaction to positive screening result</b>		
Uncertainty to screening result	It was apparent that many women had tried to think through the possibility of a high-risk result and what they may do	I panic because where do you draw the line...whatever it's got wrong with it you still love... but that's why the test would be hard for me because I wouldn't be straight away oh if there is something wrong I won't have it (Williams et al, 2005)
Time pressure and anxiety	Factors mentioned by women that weaken prerequisite for informed consent	I was asked if I had anything to ask...I wanted more information but no questions came to my mind in that situation(Santhalathi,  I trusted the specialists and felt that my fate was in their hands whatever happened (Santalahti et al, 1998)
Info giving gaps and overload	Screening was confused with amniocentesis  Although needing information many parents felt overwhelmed and had difficulty prioritizing the information  Translated material not available or easily accessible	...like the Down test. The first thing I would think is you know is a huge needle going straight through your stomach (Barr and Skirton, 2013,)  You get so much information put to you...I should have asked more questions (Barr and Skirton 2013)  They decided to roll it out in English...the translations haven't followed (Barr and Skirton,2013)
Make sense/ Incongruent messages	Others were disbelieving and wondered how such significance could have been missed  Participants described efforts to reassure them but most women felt a mismatch between information received and follow up	...but why would you just find out in this scan and not on the other scan (Carolan et al, 2009  She (doctor) said it would probably disappear ...not to worry..like she was telling me it was so common.. you're high risk now but that's ok.



<i>Themes</i>	<i>Second order constructs</i>	<i>First order constructs</i>
	action required.	Why am I high risk if there is nothing to worry about? (Carolan et al, 2009)
Men as “bystanders”	Two women reported that their husbands were not offered a chair becoming literally ‘bystanders’ while the woman had the scan	...And my husband stood sort of in the corner of the room and I think he could see the screen but I mean there wasn’t really any facility for him to sit near me...or you know be able to- it was almost like he was, it was irrelevant he was there (Locock et al, 2006)
Frustration and thoughts about consequences	Period of uncertainty caused frustration Immediately upon realizing scan anomaly men thought about possible consequences for their family by having a disabled child	it was terribly frustrating to know that the marker had some kind of significance and later you get to talk to the doctor...all this make you create a bigger thing out of it (Ahman et al, 2012)  What efforts will be needed, what will happen to my job...secure the financial side of it. That’s something that is stuck in us men, I think (Ahman et al, 2012)
Facts to gain control	Men confused at not having facts, anxious not to draw wrong conclusions before they could decide how to deal with the situation  Perception of high risk of something wrong changes after additional info and time to reflect on what these figures really mean	...when things happen, then I start to consider it. It’s unnecessary to go around thinking and planning like that for things that aren’t real that haven’t happened. (Ahman et al, 2012)  It felt as if they built a bigger picture of a greater risk than you actually had to worry about (Ahman et al, 2012)
Men perceived need to support partners	One man explained how because of his partner’s strong reaction...leading role during the consultation by asking questions and listening carefully	I was mainly focusing on my partner...trying to explain to her the thing she did not understand...from what the doctor said...Because she reacted the way she did...my, I was the one who took the dominant role then (Ahman et al, 2012)
Men advocates	These women asked men to advocate for them. Upon trying these men continued to feel excluded by HCP but persisted with	I made sure I am in the discussions without being pushy and without being overbearing. I don’t want to come across as that but it’s not,

<i>Themes</i>	<i>Second order constructs</i>	<i>First order constructs</i>
	communication nonetheless...felt that their persistence could be regarded by midwives as dominance or coerciveness	it's a case of wanting to show that(wife) and I are in this together (Dheensa,et al, 2015)
<b>Perceived professional attitudes</b>		
Non-supportive	Health care professionals' actions and words were not supportive	Having your doctor that you've had for 10 years...say this pregnancy is not going right. Let's just start all over.... You're like oh so we are just done?... that was the most puzzling part to me (Redlinger-Grosse, et al, 2002)
Limited concern	Parents felts HCP more concerned for the safety of the mother than the safety of the foetus	He said: I've got one patient I can do anything for and that's you and the best thing we can do is get you unpregnant as quick as possible (Redlinger-Grosse et al, 2002)
Isolation in decision-making	Informants felt the decisions should be made by a woman even though it was definitely an advantage that the couple come to an agreement  For other parents this isolation came from a change in the way they were treated after decision to continue pregnancy...purposeful as a result of liability concerns by professionals	To tell you the truth, I think it was fear. I think that the people there put a fear into you. I was so afraid, I thought better to end this...not knowing is terrifying (Redlinger-Grosse et al, 2002)  You got a very liability conscious set of recommendations: what we need to do is go ahead and you can have an abortion and we'll take care of it which to me becomes a doctor practicing law rather than medicine (Redlinger-Grosse et al, 2002)
Supportive positive experiences	Health professionals played an important role in making parent's experiences positive	...they presented the information very sensitively and I so appreciate that. I look back on that day and think, they handled it well. They saw who we were as people first rather than diagnosis (Hickerton et al, 2012)
<b>Coping with moral conflict</b>		

<i>Themes</i>	<i>Second order constructs</i>	<i>First order constructs</i>
Responsible/ good mother	<p>It was during the time of contemplating the scan that these women thought about the sort of mother they would be</p> <p>Motherhood begins in utero... assuming role of enlightened and caring mother and responsibility means first and foremost preventing suffering of the child...</p> <p>Motherhood begins with becoming pregnant and is the lens with which decision-making process was made...Motherhood, termination and disability were inseparably linked</p>	<p>I need to be aware of my responsibilities...like risk for things like Down's and Listeria.... talk to people and see what they have done...to me that's what being a mother is all about these days (Hawthorne and Ahern, 2009)</p> <p>Look if anything is wrong...I will never stop blaming myself...our society is rather cruel towards deformed..so my credo is I'd rather be safe than sorry (Remnick et al, 2006)</p> <p>Sure you've got to consider the parents as well as the disabled baby itself. I mean going to the hospital all the time can't be much fun. But then on the other hand you've got to be pleased that you were blessed with the gift of motherhood at all (Gitsels van den Wal 2015)</p>
Stigmatizing	<p>Stigma perceived with the at risk foetus was related to interpersonal experience connecting the individual and to social relationships and social meaning of having a child with Down syndrome</p>	<p>It is though you have added to your name card the line 'I have a Down syndrome baby'. Even if the foetus is normal I will still feel like the label has stuck... (Chiang, 2007)</p> <p>If my mother in law finds out about this she might comment that I am an unfit wife for her son (Chiang 2007 3)</p>
Reserving emotional attachment	<p>The recognition of such potential difficulties in relation to the ultrasounds scans is not new</p>	<p>And she just said...just concentrate on the screen, but I just looked away...because I didn't want to get attached to this thing that was moving (Williams et al, 2005)</p>
Anxiety/ Immobility	<p>For some women, there was growing tension on the days before examination with physical and mental discomfort...describe how they try to maintain a distance from the foetus</p>	<p>I don't know if I can bear to deal with it yet... I haven't been quite looking forward to it nor had so many thoughts about this pregnancy yet. No I have it on hold until I found out some things here (Aune and Moller, 2012)</p>
Guilty feelings	<p>The feeling of guilt expressed included thoughts of termination of pregnancy due to</p>	<p>And who am I to decide... Accepting early ultrasound gave me a bit of a bad conscience because you do it to identify something which</p>

<i>Themes</i>	<i>Second order constructs</i>	<i>First order constructs</i>
	<p>chromosomal defect</p> <p>Clara thought that if she refused the procedure she might offend her physician that had ordered the test in hope of understanding the reason for previous miscarriages</p> <p>Fear of being perceived as ignorant by the health care professional</p> <p>Guilty feelings for not 'being a saint'</p>	<p>can lead in turn to the termination of pregnancy...I turn it over now and then in my mind, the respect for life (Aune and Moller, 2012)</p> <p>I didn't want her to think that I did not have faith in her... (Browner et al, 1999)</p> <p>It seems to me that if I had refused the test, they would have said 'Oh this woman is ignorant, she knows nothing' (Browner et al, 1999)</p> <p>I have guilt for not being the type of person that parents this particular type of special need. There is a lot about this chromosome deletion that resembles a mental illness and I grew up with a sister who is schizoaffective...If I were a different kind of person I could have parented this child...but here I am with my own tremendous limitations (McCoyd 2008)</p>
Social ostracism/ pressure/ avoidance reaction	A number of women wrestle with the political and social implications of their decision-making. Ricki worked with a disability rights self help organization and feared telling one of her close friends that she had worked with that her foetus had spina bifida	I have a good friend that uses a wheelchair and has cerebral palsy...I had great trepidation telling her... I just hoped she would not see our decision as a denial of who she was. What if she saw this as: we don't think that people with disabilities have a life preserving (McCoyd,2008)
<b>Decision-making</b>		
Unwanted burden of decision-making	<p>Social pressure in accepting the offer of the risk assessment came from friends, their partner and family</p> <p>It was also expressed that social developments in society have led to difficulties in bringing up a severely disabled baby</p> <p>Fear of retribution and blame for the wrong</p>	<p>It's the woman who has the final decision...Most likely that's the way it should be, but then I will be held responsible because this could have been decided differently (Aune and Moller, 2012)</p> <p>I plan to conceal this until I have had the amniocentesis. Because I think it's actually me who is going to have the principal liability...but you are influenced yes.. the less they know the easier it is for me. That's why I don't say</p>

<i>Themes</i>	<i>Second order constructs</i>	<i>First order constructs</i>
	decision	anything (Aune and Moller, 2012)
		If it came (born with birth defects) and I had not done the tests I would think well I did not do everything they told me...now I have to pay (McCoyd, 2008)
Understand risk	Participants described that a low risk for them was a level of risk that allowed them to comfortably discount Down's...feeling had little to do with the actual statistical probability...low risk is not the medically ascribed risk of 1:300	I like to think that I will get the chance down to almost 1:3000 (Hawthorne and Ahern, 2009)
	Risk of miscarriage is a justification against amniocentesis	Because when you do amniocentesis, there is a risk of miscarriage (Pivetti et al, 2012)
	There is a risk of harming the foetus related to the anxiety of undergoing amniocentesis	Anxiety damages you...if the baby has no problems, that way you make the baby sick...all the anxiety you have...I can see it, I'm anxious and she (the baby) gets crazy (Pivetti et al, 2012)
<b>Experiential knowledge</b>		
Own	Mercedes' explanation of how she knew her baby was fine	My baby I felt it moving since I was four months pregnant, a lot sooner than with my daughter and this one moves a lot (Markens et al, 2010)
	Lack of trust with previous experiences of 'horror stories'	At that time the ultrasound scanner technician was not good enough, he should of seen the situation because the baby girl missed the chest...she only had a little skin (Pivetti et al, 2012)
	Women accepting amniocentesis were more likely to accept abortion (75) but also associated with a skepticism of their own experiential knowledge	You just hope that the baby is fine. But I don't think I can feel it, like "Oh I know it's ok" (Markens et al, 2010)
Familial	Monica like many women who declined (amniocentesis) use experiential sources from both her and her family's reproductive history	If someone in my family had had tests and I would have seen that the baby was born healthy then I would have said yes (to the tests) (Markens et al, 2010)

<b>Themes</b>	<b>Second order constructs</b>	<b>First order constructs</b>
Disability	<p>Others said that having a disabled child was not the life they envisaged for themselves or their family. Vanessa felt that a disabled child would be a “burden”</p> <p>The women were aware of disabled life but nonetheless they were not interested in the possibility of termination of a pregnancy in case of an anomaly</p>	<p>I’m very sure that I couldn’t bring up a disabled child, I don’t want to bring up a disabled child.</p> <p>I’ve got friends with disabled children and I can see what a very very difficult life they have (France et al, 2011)</p> <p>For me a child has a right to live no matter what condition...You have to accept what God gives you (Gitsels-van der Wal, 2015)</p>
<b>Biomedical knowledge</b>	<p>Many of the women who decline amniocentesis distrust doctors and medicine in general and have more trust in experiential knowledge</p> <p>Lack of trust in physician’s abilities to counsel well is an explanation against amniocentesis</p> <p>Those who accepted amniocentesis...and would not abort... decision viewed in the context of faith in doctors and medicine</p>	<p>I’m not a doctor but I know what I feel. I take what they tell me and I weigh it. Nowadays more doctors exaggerate. What is to guarantee that the doctor knows? (Markens et al, 2010)</p> <p>I would say that in this case the gynecologist is not good...there are so many unprepared people around! (Pivetti et al, 2012)</p> <p>I think as soon as she gets pregnant she should go to the doctor and get test</p> <p>They are doctors for a reason, they have studied and that is why they can tell us if the baby is fine or not (Markens et al, 2010)</p>
<b>Inherent morality of nature</b>		
Passive acceptance	<p>Participant opined meaning in everything that happens. In group nature not ought be changed nor totally controlled (acceptor of testing)</p> <p>Many parents stated that part of acceptance of their decision involved valuing their decision to have children</p>	<p>You should sometimes accept that certain things are meant to be and you should deal with them. It sounds quite philosophical but you just cannot avoid all difficulties. I strongly believe you have a certain destiny and things happen with a purpose and you should learn from them (Garcia et al, 2011)</p> <p>Basically, we decided together that you don’t determine your baby’s worth by the way they look like or what they have or don’t have. You</p>

<i>Themes</i>	<i>Second order constructs</i>	<i>First order constructs</i>
<b>Imagined futures</b>		decide to have children then you decide to have children (Hickerton et al, 2012)
Quality of life/pain	<p>Feelings of anticipated guilt especially couple with the hope of having a normal baby influenced their choice to continue the pregnancy</p> <p>Participants concerned about the boundaries between 'desirable' and 'undesirable' characteristics especially those with Down's and acceptor of testing and against abortion</p> <p>For their part acceptors defined the test offer as a possibility to control nature and to interfere in the outcomes of pregnancy in order to guarantee a good life for themselves and their children</p> <p>Apply prior experiential knowledge of more common disabilities to anticipate what their baby's life might be like.</p> <p>Marie...felt they understood what it would be like for their child to live the condition (SC). They knew how painful it could be.</p> <p>Another aspect of the baby's potential life was the likelihood that he or she would encounter prejudice because of his or her disability</p>	<p>...my own selfish reason not to do it, the guilt on me. I don't think I can live with myself if we said we can't handle this anymore, lets induce and then she is healthy and she dies because it is too early (Hickerton et al, 2012)</p> <p>It is impossible to judge the quality of life of the child. A disabled child can have a good life. We find it burdened but nobody knows if the child is happy. Down's syndrome has many gradations. This makes it more difficult to know what is acceptable and unacceptable (Garcia et al, 2011)</p> <p>I think that when you talk about these cases, of having no life expectancy, for example then I think that if nature does not do its job then you should decide for yourself (Garcia et al, 2011)</p> <p>I read a few stories of people's experiences with Patau syndrome...I just thought there is no quality here...And plus I suppose my experience of looking after some children at work that I've seen that are so poorly that it's terrible and you just think "not for my child" (France et al, 2011)</p> <p>I'd been through so many pains and my idea is that I don't want to bring someone into the world and have so much pain (France et al, 2011)</p> <p>He would regularly say to her "why am I different? Why are people so horrible to me?... because children are cruel. And therefore he had a horrible time I think (France et al, 2011)</p>
<b>Long term</b>		

<i>Themes</i>	<i>Second order constructs</i>	<i>First order constructs</i>
Lingering concern	<p>Despite clean bill of health many mothers continued to have concerns about their baby's health</p> <p>Participants described how further to their pregnancy experiences they had altered their prior childbearing plans</p>	<p>With every little thing you think "oh my gosh is it his kidney...like teething.. if he is not himself how do I know if it his kidney playing up or if he has just a cold (Carolan et al, 2012)</p> <p>I suppose I understand now that things can go wrong...after this we realise that sometimes things can go wrong... you can't be sure of a perfect baby. Now I think we will have just one more child (Carolan et al, 2012)</p>
Internal coherence	<p>Husband confident testing not needed based on familial experience of six siblings normal despite both parents were carriers. Decision not to have testing</p> <p>In discussing her third and fourth pregnancies she explains the great stress of her son's illness on her... convinced she should test earlier in subsequent pregnancies</p>	<p>No one was thalassemia major. And there was good luck in my husband's family so I didn't get checked either. Then my mother in law became pregnant...son with thalassemia major... (France et al, 2011)</p> <p>Because it is hard. I have one affected child. There would be too much suffering for me (France et al, 2011)</p>
Choosing not to choose/ avoiding reproduction	<p>Dilemmas about choice about future reproduction with reference to societal attitudes about disabilities and pressures towards perfection and accountability in reproduction</p>	<p>See I sit on both sides of the fence...because I see people with Down's...that have meaningful lives... and I would hate to prevent something like that... but yet making someone go through what (her child) ...with all her medical problems... would be hard to think that I would put him through that (Kelly, 2009)</p>
Refusal of further testing in future pregnancies	<p>Many parents expressed a disjuncture between the biomedical view of genetic pathology and parents' life world experience of a different way of being that required them to develop a set of skills as a parent exposing the different ways of interpreting phenomenon of impairment by the parent and HCP</p>	<p>The doctor she wanted to do amniocentesis ...she said because you got two children with disabilities...I said why take a chance on an infection or something from that needle when I don't have to...I was totally against it (abortion) (Kelly, 2009)</p>



**Table III. Characteristics of the quantitative studies included in the review**

<i>Study</i>	<i>Goals</i>	<i>Participants</i>	<i>Context / location</i>	<i>Methodology</i>	<i>Results</i>	<i>Study quality</i>	<i>Bias / conflicts</i>
1985, Faden, Am J Public Health	Educational intervention in a MSAFP pilot screening program exploring knowledge of pregnant women	Women recruited from obstetrical practices participating in screening program; 131 physicians from 98 offices, only 51 actually sent specimens for AFP testing (from 32 offices). Recruitment for control group April-June 1980 and experimental group Jan1981-Jan1982	MSAFP pilot screening program Maryland USA Recruitment in 2 phases: Recruitment postcards four months prior to implementation of AFP screening program, these women served as pre-program control The experimental group were recruited after 5 months of implementation of program.	Quasi experimental design. The educational intervention in screening program was a consent pamphlet readable at a 10th grade level Control group n=50 were randomly selected (no offer of screening). Three randomly selected sub groups n=100 interviewed after AFP consent but before test performed (6-13 wks (all indicated they would have the test), =100 interviewed within one week of consenting to and having the AFP test but before the results 16-19 wks and n=100 interviewed after AFP	Knowledge level was higher on two tests but gaps in the knowledge base of women in the program. Women tended to interpret a negative test result too positively (Reassuring normality) One week after having consented 30% of women provide a completely incorrect response when asked to explain MSAFP to a friend and over 75% of these women provided incorrect response when asked to define NT but their recognition score was 16/20)	Fair as there was an explanation for how the score was obtained	Patient had to give their names and 13% for control and 22% experimental refused and those who did release their names, 10% controls and 19% experimental refused to be interviewed Interviews were by phone 45-50 minutes No examples of the test given. Respondents responses were not checked for reference to pamphlet

<i>Study</i>	<i>Goals</i>	<i>Participants</i>	<i>Context / location</i>	<i>Methodology</i>	<i>Results</i>	<i>Study quality</i>	<i>Bias / conflicts</i>
Tercyak, 2001 Patient Education and Counseling	Characterize the psychological status of pregnant women at increased risk for fetal genetic anomalies referred for genetic counseling and amniocentesis to determine which of the psychological factors would predict amniocentesis use	Women with higher risk pregnancies referred from urban clinics were evaluated for psychological measures prior to and following a single session of genetic counseling	During a six month period the women were recruited (n=129)	test was negative 22-24 wks. Counselor with a flip chart style notebook Counseled the women and provided an individual risk estimate State anxiety scale and coping measures were done prior to counseling and immediately after counseling Women filled a patient satisfaction survey, a comprehension questionnaire (including a post counseling rating of perceived risk) and a state anxiety measure. The waiting period for results of amniocentesis which was performed after the counseling was	The women had elevated perceptions of risk and moderate state anxiety despite adequate comprehension and satisfaction with the process and content of the consultations Logistic regression analysis shows that attitude towards abortion is the single best predictor of test uptake and more powerful than actual or perceived risk estimates Actual and perceived risks were not related to test uptake (after corrected for attitude to abortion) Women overestimated their risk 10 fold even after counseling Those women who perceive	High	Biases and limits stated related to measures used and generalizability of the study

<i>Study</i>	<i>Goals</i>	<i>Participants</i>	<i>Context / location</i>	<i>Methodology</i>	<i>Results</i>	<i>Study quality</i>	<i>Bias / conflicts</i>
				avg of 2 wks. Risk was presented as a ratio and a percentage. Comprehensive questionnaire modelled on the psychological impact of predictive testing; Coping: MBSS, State Anxiety:STAI	themselves to be at highest risk are those most prone to experience heightened distress before and after counseling		
Kohut, 2002, Journal of Genetic Counseling	Aims to interrogate women's understanding of prenatal ultrasound in terms of requirements for informed choice for the 18 wk ultrasound	Healthy uncomplicated pregnancy, Second trimester scan 18-20 <sup>th</sup> wk No previous high risk pregnancy n=117	Calgary, Alberta Canada radiology service with a large obstetrical ultrasound practice between March and Sept 1998	Descriptive study from a questionnaire of 8 questions	55% said received no info from HCP; 31% consider HCP not a very helpful source of info, yet 69% state HCP gave them info that facilitated understanding; 46% did not view US as screens for anomalies; 18.6% uncertain about safety; 26% uncertain about diagnostic capabilities 37% uncertain about limitations of testing	Poor	
2004, Bekker Prenatal diagnosis	The study was aimed to evaluate decision analysis as a	Women receiving a screen positive MSM result (1/250)	Leeds General Infirmary over a 15 month-period,	Randomize controlled trial design with two trial arms, routine vs routine	Equal number in the two groups underwent prenatal diagnosis.	Good	

<i>Study</i>	<i>Goals</i>	<i>Participants</i>	<i>Context / location</i>	<i>Methodology</i>	<i>Results</i>	<i>Study quality</i>	<i>Bias / conflicts</i>
	technique to facilitate women's decision-making about prenatal diagnosis for DS using measures of effective decision-making	n=117/132, 58 routine, 59 decision analysis	ethics approved in 1996	consultation structured by decision analysis. Those positive were invited to attend an additional information consultation. Non-participants received routine care. The same professional provided the consultation information for both those accepting and declining Interviews and questionnaires after consultation and when the test result was known	Informed decision-making was higher, perceived risk more realistic and decisional conflict over time lower in the decision analysis group. Decision analysis had no impact on knowledge or SEU scores, and was no more or no less directive, useful or anxiety provoking than the routine care		
2004, Kaiser, patient Education and Counselling	Psychological responses to prenatal NT counseling in women of advanced maternal age. Group counseling	Women were 35 yrs or older, between 11-14 wks gestation age electing to undergo NT responding to written self report questionnaires	Late maternal age urban clinic at a large Canadian teaching hospital between May and October 1999	Single group test-retest design with two sequential interventions which include a standardized educational group counselling Intervention and a post NT individual counseling	100% of those undergoing NT (who had reassuring results) participated in the study! Highly educated women are represented in the sample (age and clinic setting) Risk perception decreased	High	Questionable generalizability Questionable validity of the test as NT was likely viewed as an extra test and not as an

<i>Study</i>	<i>Goals</i>	<i>Participants</i>	<i>Context / location</i>	<i>Methodology</i>	<i>Results</i>	<i>Study quality</i>	<i>Bias / conflicts</i>
	and individualized risk counseling were the interventions	n=123		intervention in which women's NT adjusted risks were conveyed. Levels of knowledge, anxiety and decisional conflict were measured pre- and post each intervention. The information given was about the different characteristics of NT, MSM and ultrasound as well as amnio and CVS. Prior to being given the information participants completed self report questionnaires with measurements including attitudinal questionnaire, decisional conflict scale and STAI (Anxiety trait inventory). Analysis only included cases where data from all three measures at	significantly after receiving NT adjusted risks. Women overestimate their risk at each measurement Anxiety was decreased after reassuring NT adjusted risks were explained. Decisional conflict was less if patient had already decided about invasive testing than those not decided All experienced some decrease in decisional conflict and those that were undecided at outset experienced a decrease in decisional conflict all along uptake rates for invasive testing were different depending on the group. If NT and negative MSS only 8% had elective testing. If only NT 78% had invasive testing and 45% of those who had NT and		independent choice but women relied more on the MSM results

<i>Study</i>	<i>Goals</i>	<i>Participants</i>	<i>Context / location</i>	<i>Methodology</i>	<i>Results</i>	<i>Study quality</i>	<i>Bias / conflicts</i>
2004, Wienans, Prenatal Diagnosis	A comparison of the screen positive results of ultrasound and biochemical screening for DS: a pilot study	Women who had undergone CVS for screening abnormalities in which the results revealed absence of chromosomal abnormalities n=40, Questionnaires were sent when 20-32 wks pregnant.	University Hospital Groningen and Amsterdam Medical Centre or other hospitals in the region. During the study period MST in the first trimester was not available at the AMC and NT was not available at UHG	Pilot study Semi quantitative questionnaires Three parts to the questionnaires, one prior to screening, one before screening and one after the CVS.	each of the three testing times and where NT adjusted risks were lower than their age adjusted risks  positive MSM had invasive testing For those certain at the outset of decision for invasiveness, this did not change with time. for those uncertain, 50% tested  Reason for testing was reassurance of health of baby. 5/20 felt surprised and 2/20 insufficiently informed about the meaning of the test result. In the MSM group 10/20 suffered great anxiety and 2/20 felt insufficiently informed. In the NT group 18/20 had great anxiety. In the NT group seeing had been a reason to go to CVS 12/20 in the NT and 5/20 in the MSM group were still anxious after amniocentesis The majority would repeat the	Good	Bias consists in the fact that the questionnaires are filled out by patients and given back to the researchers  Median age for the MSM group was higher

<i>Study</i>	<i>Goals</i>	<i>Participants</i>	<i>Context / location</i>	<i>Methodology</i>	<i>Results</i>	<i>Study quality</i>	<i>Bias / conflicts</i>
2005, van den Berg, Genetic Medicine	Study aims to assess the level of informed decision-making that includes knowledge, deliberation and value consistency, and identify differences in measures between test acceptors and decliners	Women who were pregnant before 16 wks gestation were sent a letter and an informed consent form offered NT or MSM. n=1159	44 participating midwifery and gynecology practices from May 2001-May 2003	Questionnaires, Randomized control trial in 3 groups Intervention groups1consist of first trimester NT, Groups2 MSM second trimester for DS and triple test for neural tube Group3 control	experience n=835 had sufficient knowledge about prenatal screening, 82% made a value consistent decision to accept or decline, 68% made an informed decision. Informed choice was associated with more satisfaction with the decision, less decisional conflict but not associated with less anxiety One third of all choices were uninformed More value inconsistency in those over 35 years caused by test decliners with a positive attitude	Good	This study included low risk category only. Studies should focus on the high risk to see the impact of informed choice on decisional conflict, anxiety
Van den Berg, 2005, Patient Education and Counseling	Study aimed to assess the three elements of informed decision-making: knowledge, value consistency	Idem as Prenatal diagnosis N=4076 asked to participate n=2986 first,	Netherlands, where at this point no screening program at large but only for women 35 or more or otherwise	Randomized control trial of 3 groups with prenatal testing for DS and NT and control. Group 1 verbal explanation and informed home booklet	49% were. Informed (knowledge that was deliberated and value consistent). The test acceptors made less informed decisions based predominantly on lack	Good	Well recognized by the authors

<i>Study</i>	<i>Goals</i>	<i>Participants</i>	<i>Context / location</i>	<i>Methodology</i>	<i>Results</i>	<i>Study quality</i>	<i>Bias / conflicts</i>
	and deliberation It also investigated the differences in the level of informed decision-making between different choices (i.e accepting or declining testing	n=2277 second, 1968 n=1330 for the two intervention groups but neutral attitudes were excluded so in the end n=962	increased Patients from 44 participating midwifery and gynecology practices from different areas of the country May 2001-May 2003	NT; Group 2 verbal explanation and informed home booklet MSM and NT the NTdone in first and MSM in second trimesters. Three questionnaires, the first before the booklet, the second after they had read the booklet and decided for or against the screening but before the results and third after receiving the results. Women in the control group and those that refused screening got the second and third questionnaires at comparable time. There were 4 measures evaluated; knowledge, deliberation, test uptake and attitude. The variable value	of deliberation		



<i>Study</i>	<i>Goals</i>	<i>Participants</i>	<i>Context / location</i>	<i>Methodology</i>	<i>Results</i>	<i>Study quality</i>	<i>Bias / conflicts</i>
				consistency was constructed by combining test uptake and attitude categories and the variable informed decision-making was constructed from knowledge, deliberation and value consistency			
2005, van den Berg, Prenatal Diagnosis	Assess test uptake for NTS or MSM in a large unselected population of women at different times during pregnancy for screening offered in an unbiased way	Women before 16wks gestation asked permission to be sent a research info letter and informed consent Women were randomized. If first consult was after 10 wks randomized to MST or control  Booklets were pilot tested. n=4076 were asked,	44 participating midwifery and gynaecology practices from May2001-May2003 Dept. of Public and Occupational Health VU, University Medical Centre, Netherlands	Randomized controlled trial for three groups, NT, MSM and control. Women received postal questionnaires at three stages of their pregnancy; first at the time of receiving booklet, then after they had read the booklet and decided for or against and the third was after the test results were received.	Uptake of tests NT53% and MST 38%  Main reasons for accepting: "knowledge/curiosity (50%), favourable characteristic of screening test (18%), increased risk of a child with DS (15%).  Main reasons for declining were: unfavorable characteristic of screening test (42%), non applicable/non necessary (35%), anxiety/uncertainty (36%),	Good	Bias in the population studied compared to the general population as this group had higher education levels (19 vs 43% for pop gen and the study sample respectively)  An appendix of the questionnaire and of the original responses would have been

<i>Study</i>	<i>Goals</i>	<i>Participants</i>	<i>Context / location</i>	<i>Methodology</i>	<i>Results</i>	<i>Study quality</i>	<i>Bias / conflicts</i>
		n=2978 (73%) returned the first questionnaire, and of those n=2203 (74%) returned the second and n=1968 filled in third		The participants also received oral explanation which was standardized which covered the same topics as the information booklets as well as the counselling guides.  The 3 questionnaires collected patient characteristics, open ended questions in which participants had to give reasons for accepting or declining and the third questionnaire asked whether they had the screening test done or not.	adverse characteristic of invasive test (32%) and against abortion (15%)		appreciated
2008, van den Berg, Health Psychology	Understanding prenatal screening decision-making through testing a hypothesized decision	Pregnant women of less than 16wks gestational age dutch speaking,	44 midwifery and gynaecology practices in several areas of	Questionnaires to pregnant women offered screening for DS Women were given a booklet with the test offer which	Attitude toward termination, perceived test efficacy and subjective norm re desirability of having prenatal screening determined a woman's	Good	iatrogenic induced abortion is a variable that could influence decision-making was not

<i>Study</i>	<i>Goals</i>	<i>Participants</i>	<i>Context / location</i>	<i>Methodology</i>	<i>Results</i>	<i>Study quality</i>	<i>Bias / conflicts</i>
	model Path analysis and split sample validation	informed consent  n=4076 approached n=2986 consented, n=2177 were offered a prenatal screening  n=1666 76% filled in the questionnaire	Netherlands.  Half were offered NT and the other half MSM between May2001-May 2003	covered: characteristics of DS, age related risks of DS, test procedure, possible test results and implications, procedure and risks of diagnostic testing and a decision support section in which advantages and disadvantages of prenatal testing was listed  Participants were asked to fill the questionnaire before the test was performed  Path coefficients for variables of screening behavior model.	attitude toward prenatal testing  Anxiety level was influenced by perceived risk, severity of having a DS child and subjective norm, but weak predictor of intention to test. Pregnant women with positive attitude for prenatal screening and perceived subjective norm in favour had a greater intention to test		included in the model Screening for all women was not a policy at the time of this study that had to await approval by ethics committee
Rowe, 2006, Australian and New Zealand Journal of	Assess informed choice to participate in second trimester MSM in pregnant women using MMIC	Pregnant women between 8 and 14 wks at first prenatal visit	Four public antenatal clinics representing different models of maternity care at a	Prospective longitudinal study with participants assessed three times during their pregnancy,	48% of the women had a good knowledge score; 87% had a positive attitude to screening; At assessment two 62.4% had had the MSM screen; 37%	Fair	

<i>Study</i>	<i>Goals</i>	<i>Participants</i>	<i>Context / location</i>	<i>Methodology</i>	<i>Results</i>	<i>Study quality</i>	<i>Bias / conflicts</i>
Obstetrics and Gynecology	and to compare anxiety level according to knowledge level.		tertiary referral centre in Melbourne between Jan 2003- Dec 2004		were informed and those that did participate were more than twice as likely make an informed choice than those that did not participate; No sig association b/w knowledge level and attitude; Higher knowledge scores were in older and more educated women; 31% did not know that risk of miscarriage with invasive procedure and 24% were misguided as to the possible consequences if DS was confirmed; Another 29% stated they did not know what the options would be, hence what decision they would have to confront. Only 62% knew that termination would be offered; There was a significant correlation between anxiety and depression at each time point. There was no difference		

<i>Study</i>	<i>Goals</i>	<i>Participants</i>	<i>Context / location</i>	<i>Methodology</i>	<i>Results</i>	<i>Study quality</i>	<i>Bias / conflicts</i>
2008, Brajenovic-Milic, Women's Health Issues	Sought to evaluate pregnant women's attitudes towards amniocentesis in the context of second trimester screening results in low risk pregnant women and the impact of knowledge and educational level on attitude toward amniocentesis	Pregnant women under 35 yrs with no personal or family history of DS were surveyed	Rijeka, Croatia, screening began in Jan 2004	Quantitative Women were randomized into two groups each n=150 Consultation with a specially trained midwife  One group was surveyed by questionnaire before consultation with specially trained midwives  The other group were surveyed after consultation	between those informed and uninformed with regards to psychological scores at any of the three assessments  Knowledge gained during a pre-screening consultation influenced pregnant women's attitudes toward further diagnostic investigation.  A smaller proportion of women were indecisive in the group surveyed after consultation; Significantly more women were prepared to accept amniocentesis in the group after the consultation than before  Knowledge scores were correlated to education level only in the pre-consult group Indecisiveness was not affected by poor knowledge but rather by difficulty in knowing how they will feel	Fair	Results could be biased as the women that were surveyed after the consultation were not the same as those that were surveyed before the consultation?

<i>Study</i>	<i>Goals</i>	<i>Participants</i>	<i>Context / location</i>	<i>Methodology</i>	<i>Results</i>	<i>Study quality</i>	<i>Bias / conflicts</i>
2009, Seror and Ville,	To investigate pregnant women's attitudes to ultrasound and MSM and possibly invasive testing	Women who gave birth in a certain time period in the year were invited to fill a questionnaire n=400	Pilot study to assess combined screening of a maternity unit in a Paris district hospital between April-October 2005 i	Hierarchical cluster analysis on n=341 questionnaires	and what they will do if their screening result is positive  Many women were not aware of potential implications of screening or understand them. Half of the 301 women who did US and MSM did not foresee the need to make a decision about termination; One quarter do not understand the MSM results; One third did not anticipate invasive screening and these were associated with passive involvement in decision-making	Fair the methodology is not typical?	No ethics approval Justified by no effect on medical care, on decision-making, nor necessity for  No medical records were used and study collection was anonymous
2011, Dahl, Ultrasound Obstet Gynecol	Primary aim of study was to assess pregnant women's knowledge about first trimester combined screening and differences of knowledge and secondary outcomes	Women in first trimester part of a screening program n=6427 Risk assessment is based on maternal age, NT and MSM Invasive testing is	Three danish obstetric departments in university hospitals of the three largest Danish cities prenatal screening free of charge	Population based cross sectional questionnaire study including 15 multiple choice questions assessing different aspects of first trimester combined screening n=4095, 64% responder participants	Majority correctly identified the test concept and the main condition being screened for.  Few participants correctly recognized test accuracy and potential risk of adverse finding other than DS  Knowledge level was	High	Number and who participates in teaching sessions to the women is not clear

<i>Study</i>	<i>Goals</i>	<i>Participants</i>	<i>Context / location</i>	<i>Methodology</i>	<i>Results</i>	<i>Study quality</i>	<i>Bias / conflicts</i>
	were to identify relevant differences in knowledge levels in the subgroups (participants and non participants) informed in different ways about prenatal testing	with cut off at 1:300 based on the combined risk Information available on the web sites of the hospitals and one of the hospitals offers an extra individual information session	Sept 2007-march 2008 GPs were to deliver the basic information. Information sessions lasted 30 min and took place between gest age 9-11	and non-participants	positively associated with education and participation in the screening program		
2011, Dahl, Ultrasound Obstet Gynecol	To study the associations between pregnant women's knowledge of first trimester screening and decisional conflict, well being and worry	Idem	Idem	Idem Primary outcomes were measured using pre-existing validated scales i.e. The decisional conflict scale, the WHO Well Being Index and Cambridge Worry scale  n=4111	A higher level of knowledge was associated with less decisional conflict, higher levels of well being  Knowledge was not associated with worries either in general or more specifically with the foetus	Good	Potential overestimation of the clinical importance of the correlations between knowledge scores and other measures since not all potential confounders were included in the logistic regression

<i>Study</i>	<i>Goals</i>	<i>Participants</i>	<i>Context / location</i>	<i>Methodology</i>	<i>Results</i>	<i>Study quality</i>	<i>Bias / conflicts</i>
2013, Strauss	Evaluate women's knowledge about the individual risk of their fetus being affected by Down syndrome and their diagnostic preferences	Pregnant women with low risk ultrasound surveillance surveyed between 5-38 weeks gestation (med 21 weeks) n=246	Munich University Hospital prenatal clinic	Quantitative prospective cohort study using risk questionnaire n=246	Women overestimate their individual risk One fifth are not aware of aneuploidy risk  Finding independent of gestational age	Good	analysis
2009, Kuppermann, Obstet Gynecol	Use of a computerized interactive decision tool  Randomized trial with State health services educational booklet  English or Spanish speaking women 20wks or less	English/Spanish speaking women not yet undergone screening or diagnostic testing at 11 weeks gestation n=710	County hospital, community clinic, academic centres and medical centres of integrated health units in the San Francisco bay area	Randomized control trial of control which is a computerized version of AFP booklet offered by the obstetrician and the new tool designed by authors data analyzed according to age group	see Kuppermann 2014.  Women over 35 were more likely to be in favor of invasive testing from the outset and all women after the intervention, but less so In the PT tool group. significantly greater knowledge, risk awareness, intervention satisfaction, less decisional conflict, than control  Women in the PT group more than 35 yrs were less likely to be satisfied with health care providers prenatal counselling	Moderate	Only first trimester screening test described in the tool was NT; majority had college degrees and text heavy nature of the tool limits usefulness for lower literacy pop.  Observed statistically significant differences are clinically



<i>Study</i>	<i>Goals</i>	<i>Participants</i>	<i>Context / location</i>	<i>Methodology</i>	<i>Results</i>	<i>Study quality</i>	<i>Bias / conflicts</i>
2014, Kuppermann	Assess the use of prenatal testing and decision-making in the context of a decision support guide and elimination of financial barriers among pregnant women  Randomized control trial with usual practice	English/Spanish speaking women not yet undergone screening or diagnostic testing at 11 weeks gestation n=710	County hospital, community clinic, academic centres and medical centres of integrated health units in the San Francisco bay area with cost constraints removed	Quantitative randomized trial 2012-2013 comparing group using computerized interactive decision guide vs usual prenatal screening and follow up	The PT intervention group were less likely to use invasive testing, more likely to forego testing altogether,  PT had higher knowledge score and more likely to correctly estimate amniocentesis related miscarriage rate and estimated age adjusted chance of carrying a foetus with DS  No significant difference between groups for decisional conflict or regret	High	meaningful?

**Table IV. Summary of the thematic findings stemming from the quantitative studies**

<i>Study</i>	<i>Knowledge base</i>	<i>Informed decision-making</i>	<i>Attitudes</i>	<i>Risk Perception</i>	<i>Decisional conflict</i>	<i>Anxiety</i>
<i>Faden et al, 1985 Am J Public Health Maryland USA.</i>	Knowledge level was higher on two test but knowledge base gaps in the program group. One week after consenting 30% of women do not know to correctly explain AFP and 70% cannot define NT Yet recognition score was 16/20. It is obvious that informed consent is not necessarily associated with understanding			Women who screen negative for AFP are implicitly reassured that there foetus will be normal		
<i>Tercyak et al, 2001 Patient Education and Counseling Florida, USA</i>			78% agreed to testing Attitude towards abortion is the single most important predictor of amniocentesis uptake and more powerful than actual or perceived risk estimates	The women had elevated risk perception despite adequate comprehension and satisfaction with the content and process of genetic consultation. Post counseling the perceived risk of having a DS baby decreased although still high compared to actual		Women had a moderate state of anxiety despite adequate comprehension and satisfaction with the process and content of genetic consultation. Women who were more anxious before counseling remained more anxious after counseling. Pre-counseling anxiety was

			<p>risk Actual or perceived risks were not related to uptake of amniocentesis. Women perceive their risk 10 times higher than the actual risk and those women who perceive themselves to be at the highest risk experience more anxiety before and after consultation</p>		<p>independently associated with previous experience of prenatal diagnostic testing, increased perceived risk of birth anomaly and favorable attitude towards abortion</p>
<p><i>Kohut et al, 2002 Journal of Genetic Counseling Canada</i></p>	<p>Women's understanding of the role of US was still not clear. Almost half 46% did not view US as screens for anomalies, 26.5% did not know the diagnostic capabilities and 37% did not know the limitations of US and 19% were unsure about the safety of US</p>	<p>The majority of women do not feel that HCP provide information or support and for understanding the role of US in prenatal diagnosis</p>			
<p><i>Kaiser et al, 2004 Patient Education and</i></p>		<p>87% had a positive attitude to screening, A negative MSM following a NT was associated with a low rate (8%) of amniocentesis whereas</p>	<p>Risk was overestimated at each of the three evaluations, but decreased significantly after receiving NT adjusted risk</p>	<p>Decisional conflict was less in women who had already decided about invasive testing before the consultation. All experienced decrease</p>	<p>Anxiety was reduced once the NT reassuring adjusted risk was explained</p>

<p><i>Counseling</i> <i>Canada</i></p>		<p>NT was associated with a 78% rate of with amniocentesis. 45% had amniocentesis if MSS was positive. For women who were decisive for amniocentesis from the beginning this did not change with time but in those that were undecided, 50% went on to have amniocentesis.</p>		<p>in decisional conflict over time but those that were decided experienced a decrease only after the group counseling whereas those undecided continued to experience a decrease after the individual counsel session. Decisional conflict scores were higher in the undecided women.</p>	
<p><i>Bekker et al, 2004 Prenat Diagn</i> <i>UK</i></p>	<p>Evaluate the effect of decision analysis to decision-making using measure of effective decision-making. Informed decision-making was higher in this group</p>		<p>Decision analysis was associated with less perceived risk</p>	<p>Over time the decisional conflict was lower in the group of women using decisional analysis</p>	<p>Decisional analysis had no impact on anxiety</p>
<p><i>Weinans et al. 2004 Prenatal Diagnosis</i></p>		<p>The majority of women use US for reassurance and for visualizing the baby. NT with positive results was a reason to</p>			

<i>Netherlands</i>			do invasive testing		
<i>Van den Berg et al, 2005 Genetic Medicine Netherlands</i>	83% of women have sufficient knowledge of prenatal screening	In prenatal screening 68% make an informed decision and 82% made a value consistent decision to accept or decline screening.	Informed choice associated with greater satisfaction for decision	Decisional conflict was less with a more informed choice (applied only to test acceptors)	Informed choice was not associated with less anxiety
<i>Van den Berg et al 2005 Patient Education and Counseling Netherlands</i>	84% were sufficiently knowledgeable	75% of decisions were deliberate and 82% were value consistent  51% of participants made an informed choice for amniocentesis Test acceptors made less informed decisions as compared to test decliners. This difference was mainly due to less deliberation in this group.			

<p><i>Van den Berg M, et al 2005</i> <i>Prenatal Diagnosis</i> <i>Netherlands</i></p>			<p>The uptake for screening test NT was higher than for MSM; the major reason for uptake was 'knowledge and curiosity', and important reasons for not accepting testing were unfavorable characteristics of the test, test judged unnecessary and adverse effects of the invasive test</p>			<p>Anxiety/uncertainty was seen as a reason for non-acceptance of screening in 35%</p>
<p><i>Van den Berg et al 2008</i> <i>Health Psychology</i> <i>Netherlands</i></p>			<p>Attitude towards selective termination, perception of desirability to have testing and perceived test efficacy determined a woman's attitude to prenatal testing for DS. Positive attitude to testing and perceived positive subjective norm was associated with a higher intention to test.</p>			<p>Anxiety influenced by perceived risk, and perceived severity of having a DS child and perceived and by subjective norm of desirability but weak predictor of intention to test</p>
<p><i>Rowe et al</i></p>	<p>Only 48% had good knowledge of prenatal</p>	<p>Participating in a prenatal testing</p>	<p>87% had a positive attitude to screening. No</p>	<p>31% of women did not know there was a risk of</p>	<p>Correlation between anxiety and depression at each time</p>	

<p>2006 <i>Australian and New Zealand J Obstet Gynecol Australia</i></p>	<p>testing. Knowledge scores higher than average were associated with older women and with higher education. 29% of women did not know what options and decision they would have to face if screening result was positive including only 62% knew that termination was an option. 24% of women were misguided as to the possible consequences if DS confirmed</p>	<p>program was associate with higher likelihood of being 'informed' with twice the number of participants than those that were not informed</p>	<p>significant association between knowledge level and attitude toward screening</p>	<p>miscarriage with the amniocentesis</p>	<p>point but no difference between those women informed and non-informed (at least in the short term) and no difference to women of similar cohort (at the outset)</p>
<p><i>Brajenovic et al, 2008 Women's Health Issues Croatia</i></p>	<p>Women had greater total knowledge scores after consultation than before. Knowledge scores were correlated with education level only in the pre consultation score. Knowledge gained during a pre screening consultation influenced</p>	<p></p>	<p>A lesser number of women were undecided about amniocentesis in the consulted group and more women were prepared to accept amniocentesis after the consultation. Indecisiveness was not affected by knowledge level but with the moral dilemma of a positive</p>	<p></p>	<p></p>

	pregnant woman's attitudes toward further investigations		screening result
<i>Seror and Ville 2009 Prenatal Diagnosis Marseille, France</i>	A high number of women are not aware of the implications of screening or did not understand them. Half of the women who had US and MSS positive did not foresee the decision for pregnancy termination, 25% do not understand the results of US /MSS positive and 33% did not anticipate invasive diagnostic testing	52% were active vs 42 were in the passive mode of decision-making and 6% declined MSS.	Most women showed a preference for first trimester screening
<i>Dahl et al, 2011 Ultrasound Obstet Gynecol Denmark</i>	The majority identified the test concept and the condition screened for. Few participants correctly identified test accuracy and potential risk of adverse findings other than DS Knowledge level associated with higher education and participation in the		



	screening program				
<i>Dahl et al, 2011</i> <i>Ultrasound Obstet Gynecol</i> <i>Denmark</i>		With more knowledge there is a higher level of well being		A higher knowledge level was associated with less decisional conflict	A higher knowledge level did not affect worry in general or for the foetus
<i>Strauss et al 2013</i> <i>Arch Gynecol Obstet</i> <i>Munich Germany</i>	Investigated knowledge of use of US for DS. One fifth of women did not know that DS was being screened		67% of women over estimate their individual risk of DS with overall risk conceived as 1:33. and 23% underestimate by a factor of 2	Media, HCP and personal experience influence estimate	
<i>Kupperman et al 2009</i> <i>Obstet Gynecol</i> <i>California USA</i>	Significantly higher knowledge scores in the group with PT tool compared to control group	More women were satisfied with the PT intervention. Women over 35 years old with the PT tool were more likely to undergo invasive testing after the tool when previously they were less inclined to do so when compared to the control group	More likely to estimate amniocentesis related miscarriage rate and estimated age adjusted risk for DS	Less decisional conflict with the tool compared to controls	

<p><i>Kupperman 2014 et al,2014 California USA</i></p>	<p>Higher knowledge score in the PT group compared to controls</p>	<p>Women more inclined to undergo amniocentesis before the intervention were less inclined to do so compared to the women in the control group.</p> <p>The women that belonged to the intervention group were less likely to use invasive testing and more likely to forgo testing altogether. Women over 35 were less satisfied with HCP in the group PT, suggesting that the tool led to more sophisticated expectations from their HCP</p>	<p>Women in the PT group were more likely to correctly estimate the amniocentesis related miscarriage rate and estimated age adjusted risk of carrying a foetus with DS.</p>	<p>No significant difference in decisional conflict or decisional regret with PT tool</p>
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## **Appendix 1. Revised IPDASv4 criteria checklist**

Adapted from Durand et al, Patient Education and Counseling 98; 2015:462-468.

### **Qualifying (n = 6) and certification (n = 10) criteria**

#### **Category Code IPDASi item**

##### **Qualifying**

- Q1 Describes health condition or problem for which index decision is required
- Q2 Explicitly states decision under consideration (index decision)
- Q3 Describes the options available for the index decision
- Q4 Describes the positive features of each option
- Q5 Describes the negative features of each option
- Q6 Describes the features of options to help patients imagine the physical, social and/or psychological effects

##### **Certification**

- C1 Shows positive and negative features of options with equal detail
- C2 Provides information about the funding source used for development
- C3 Provides citations to the evidence selected
- C4 Provides a production or publication date
- C5 Provides information about update policy
- C6 Provides information about the level of uncertainty around outcome probabilities
- CT1 Describes what the test is designed to measure
- CT2 Describes next steps taken if test detects a condition/problem
- CT3 Describes next steps if no condition/problem detected
- CT4 Describes consequences of detection that would not have caused problems if the screen was not done

## Appendix 2. 2006 IPDAS criteria checklist

The Table below was adapted from the supplement to the following article: Elwyn G, O'Connor A, Stacey D, et al. Developing a quality criteria framework for patient decision aids: online international Delphi consensus process. *BMJ* 2006; 333:417.

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<i>Domain and quality criteria</i>	
<b>1</b>	<b>Using a systematic development process</b>
1.1	The patient decision aid has information about the credentials of the people who developed it.
1.2	Patients were asked what they need to prepare them to discuss a specific decision.
1.3	Practitioners were asked what they need to discuss a specific decision with patients.
1.4	Patients who were facing the decision field tested the decision aid.
1.5	Practitioners who counsel patients on the options field tested the decision aid.
1.6	Field testing showed that the decision aid was acceptable to patients.
1.7	Field testing showed that the decision aid was acceptable to practitioners.
1.8a	The decision aid was reviewed by outside experts [health professionals] who were not involved in its development or field testing
1.8b	The decision aid was reviewed by outside experts [patients who previously faced the decision] who were not involved in its development or field testing
<b>2</b>	<b>Providing information about options</b>
2.1	The patient decision aid describes the health condition related to the decision.
2.2	The patient decision aid lists the health care options.
2.3	The option of choosing none of the health care options [e.g. doing nothing] is included
2.4	The patient decision aid describes what happens in the natural course of a health condition if none of the health care options is chosen.
2.5	The patient decision aid has information about the procedures involved (e.g. what is done before, during, and after the health care option)
2.6	The patient decision aid has information about the positive features of the options (e.g. benefits, advantages)
2.7	The patient decision aid has information about the negative features of the options (e.g. harms, side effects, disadvantages)
2.8	The information about [outcomes] of options (positive and negative) includes the chances they [may] happen.

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- 2.9 The patient decision aid has information about what the test is supposed to measure.
  - 2.10 The patient decision aid has information about the chances of receiving a true positive, true negative, false positive and false negative test result.
  - 2.11 The patient decision aid describes possible next steps based on the test results.
  - 2.12 The patient decision aid has information about the chances of disease being found with and without screening.
  - 2.13 The patient decision aid has information about detection and treatment of disease that would never have caused problems if screening had not been done.

### **3 Presenting probabilities**

- 3.1 The patient decision aid presents probabilities using event rates in a defined group of patients for a specified time.
- 3.2 The patient decision aid compares probabilities of options using the same denominator.
- 3.3 The patient decision aid compares probabilities of options over the same period of time.
- 3.4 The patient decision aid describes the uncertainty around the probabilities (e.g. by giving a range or by using phrases such as 'our best guess is').
- 3.5 The patient decision aid uses visual diagrams to show the probabilities (e.g. faces, stick figures, or bar charts).
- 3.6 The patient decision aid uses the same scales in the diagrams comparing options.
- 3.7 The patient decision aid provides more than one way of explaining the probabilities (e.g. words, numbers, diagrams).
- 3.8 The patient decision aid allows patients to select a way of viewing the probabilities (e.g. words, numbers, diagrams).
- 3.9 The patient decision aid allows patients to see the probabilities of what might happen based on their own individual situation. (e.g. specific to their age or severity of their disease).
- 3.10 The patient decision aid places the chances of what might happen in the context of other situations (e.g. chances of developing other diseases, dying of other diseases, or dying from any cause).
- 3.11 The way the probabilities were calculated is described [in a reference section or accessible technical document]
- 3.12 If the chance of disease is provided by sub-groups [e.g., younger, middle-age, or older people], the tool that was used to estimate these risks is described [in a reference section or accessible technical document]
- 3.13 The patient decision aid presents probabilities using both positive and negative frames (e.g. showing both survival and death rates).

### **4 Clarifying and expressing values**

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- 4.1 The patient decision aid describes the features of options to help patients imagine what it is like to experience their physical, emotional, and social effects.
- 4.2 The patient decision aid asks patients to think about which positive and negative features of the options matter most to them.
- 4.3 The patient decision aid suggests ways for patients to share [what matters most to them when] others are involved in the decision.
- 5 **Using patient stories**
- 5.1 The patient decision aid provides stories of other patients' experiences.
- 5.2 If stories are used in a patient decision aid, the stories represent a range of experiences (positive and negative).
- 5.3 If stories are used in a patient decision aid, the steps used to select these stories are described [in a reference section or accessible technical document].
- 5.4 If stories are used in a patient decision aid, the steps that experts used to review the information contained in these stories is included [in a reference section or accessible technical document]
- 5.5 If stories are used in a patient decision aid, a statement that the patients gave informed consent to include their stories is included. [in a reference section or accessible technical document]
- 6 **Guiding / coaching in deliberation and communication**
- 6.1 The patient decision aid provides a step-by-step way to make a decision.
- 6.2 The patient decision aid suggests ways to talk about the decision with a health practitioner.
- 6.3 The patient decision aid includes tools like worksheets or lists of questions to use when discussing options with a practitioner.
- 6.4 The patient decision aid offers the option of working with a trained 'coach' to help patients consider the options.
- 6.5 The patient decision aid offers the option of working with a trained 'coach' to help patients prepare to talk about the decision with a practitioner.
- 7 **Disclosing conflicts of interest**
- 7.1 The patient decision aid reports where the money came from to develop the decision aid
- 7.2 The patient decision aid reports where the money came from to copy and distribute the decision aid.
- 7.3 The patient decision aid reports whether the authors of the decision aid stand to gain or lose by the choices patients make after using a decision aid.
- 7.4 The patient decision aid reports whether the affiliations of the authors stand to gain or lose by the choices patients make after using a decision aid.
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7.5 If the patient decision aid includes stories of other patients' experiences, it reports if there was some financial or other reason why patients decided to share them.

## 8 **Delivering patient decision aids on the Internet**

8.1 If the patient decision aid is used on the Internet, it provides a step-by-step way to move through the web pages (screens) on the Internet.

8.2 If the patient decision aid is used on the Internet, it allows patients to search for key words in the decision aid.

8.3 If the patient decision aid is used on the Internet, it provides feedback on personal health information that is entered into the decision aid. [e.g. the chances you may get a complication]

8.4 If the patient decision aid is used on the Internet, the website provides security for personal health information entered into the decision aid.

8.5 If the patient decision aid is used on the Internet, it easy for patients to find their way back to the point they were at in the decision aid when they clicked on links to other web pages.

8.6 [If the patient decision aid is on the internet, it can also be printed as a single document (e.g., pdf document)]

## 9 **Balancing the presentation of options**

9.1 The patient decision aid makes it possible to compare the positive and negative features of the available options.

9.2 The patient decision aid shows the negative and positive features of options with equal detail (for example using similar fonts, order, display of statistical information).

9.3 Field testing showed that undecided patients felt the information was presented in a balanced way.

## 10 **Using plain language**

10.1 The patient decision aid describes the 'professional standards for plain language materials' that guided its development (e.g. Plain Language Association International)

10.2 The patient decision aid identifies the reading level at which it is written and the formula [method] used to determine the level.

10.3 The patient decision aid is written at a level that can be understood by at least half of the patients for whom it is intended.

10.4 The patient decision aid is written at a level no higher than grade 8 [or equivalent] according to a readability formula (e.g., SMOG or FRY).

10.5 The patient decision aid provides ways to help patients understand information other than reading (e.g. audio, video, or in-person discussion).

10.6 Field testing showed that the patient decision aid was understood by patients with limited reading skills.

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**11 Basing information on up-to-date scientific evidence**

- 11.1 The patient decision aid provides references to scientific evidence used.
- 11.2 The steps used to select the scientific evidence (e.g. finding, appraising, summarizing) is included [in a reference section or accessible technical document]
- 11.3 The patient decision aid reports the date when it was last updated.
- 11.4 The patient decision aid reports how often the information in the decision aid is updated.
- 11.5a The patient decision aid describes the quality of the scientific evidence (e.g. quality of research studies).
- 11.5b The patient decision aid describes the quality of the scientific evidence (e.g. quality of research studies) [including lack of evidence].
- 11.6 The patient decision aid uses evidence taken from studies on patients that are similar to the patients who would use the decision aid (e.g. age, gender).

**12 Establishing effectiveness**

- 12.1 There is evidence that the patient decision aid helps patients recognize that a decision needs to be made.
  - 12.2 There is evidence that the patient decision aid helps patients know about the available options.
  - 12.3 There is evidence that the patient decision aid helps patients know about different features of the options.
  - 12.4 There is evidence that the patient decision aid helps patients understand that values affect the decision.
  - 12.5 There is evidence that the patient decision aid helps patients be clear about which features of options matter most to them.
  - 12.6 There is evidence that the patient decision aid helps patients discuss values with their health practitioners.
  - 12.7 There is evidence that the patient decision aid helps patients become involved in decision-making in ways they prefer.
  - 12.8 There is evidence that the patient decision aid improves the match between the features that matter most to the informed patient and the option that is chosen.
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### Appendix 3. Search strategies for qualitative studies

#### PubMed

- 1- (Ethics[Mesh:NoExp] OR Bioethical Issues[mh] OR bioethics[mh] OR ethical review[mh] OR Morals[mh] OR informed consent[mh] OR decision-making[mh] OR ethics[Subheading] OR Ethic[tiab] OR ethics[tiab] OR ethical[tiab] OR bioethic[tiab] OR bioethics[tiab] OR bioethical[tiab] OR informed consent[tiab] OR informed consents[tiab] OR decision-making[tiab] OR decision-makings[tiab] OR Ethic[ot] OR ethics[ot] OR ethical[ot] OR bioethic[ot] OR bioethics[ot] OR bioethical[ot] OR informed consent[ot] OR informed consents[ot] OR decision-making[ot] OR decision-makings[ot])
- 2- (parents[mh] OR parental consent[mh] OR mother[tiab] OR mothers[tiab] OR father[tiab] or fathers[tiab] OR parents[tiab] OR parent[tiab] OR parental[tiab] OR paternity[tiab] OR paternal[tiab] OR women[tiab] OR maternal[tiab] OR mother[ot] OR mothers[ot] OR father[ot] or fathers[ot] OR parents[ot] OR parent[ot] OR parental[ot] OR paternity[ot] OR paternal[ot] OR women[ot] OR maternal[ot])
- 3- (Prenatal diagnosis[mh] OR prenatal diagnosis[tiab] OR prenatal diagnose[tiab] OR prenatal diagnoses[tiab] OR Prenatal diagnostic[tiab] OR prenatal diagnostics[tiab] OR prenatal screening[tiab] OR prenatal test[tiab] OR prenatal tests[tiab] OR prenatal testing[tiab] OR prenatal detection[tiab] OR intrauterine diagnostic[tiab] OR intrauterine diagnostics[tiab] OR intrauterine diagnosis[tiab] OR intrauterine diagnose[tiab] OR intrauterine diagnoses[tiab] OR intrauterine detection[tiab] OR antenatal diagnostic[tiab] OR antenatal diagnostics[tiab] OR antenatal diagnosis[tiab] OR antenatal diagnose[tiab] OR antenatal diagnoses[tiab] OR antenatal screening[tiab] OR antenatal testing[tiab] OR antenatal test[tiab] OR antenatal tests[tiab] OR antenatal detection[tiab] OR fetal diagnosis[tiab] OR fetal diagnose[tiab] OR fetal diagnoses[tiab] OR fetal screening[tiab] OR fetal testing[tiab] OR fetal test[tiab] OR fetal tests[tiab] OR foetal screening[tiab] OR foetal diagnosis[tiab] OR foetal diagnose[tiab] OR fetal diagnoses[tiab] OR amniocentes\*[tiab] OR Chorionic Villi [tiab] OR Chorionic Villus[tiab] OR Nuchal scan[tiab] OR nuchal translucency[tiab] OR nuchal fold[tiab] OR fetoscop\*[tiab] OR Amnioscop\*[tiab] OR Embryoscop\*[tiab] OR cervical length[tiab] OR prenatal diagnosis[ot] OR prenatal diagnose[ot] OR prenatal diagnoses[ot] OR Prenatal diagnostic[ot] OR prenatal screening[ot] OR prenatal test[ot] OR prenatal tests[ot] OR prenatal testing[ot] OR prenatal detection[ot] OR intrauterine diagnostic[ot] OR intrauterine diagnosis[ot] OR intrauterine diagnose[ot] OR intrauterine diagnoses[ot] OR intrauterine detection[ot] OR antenatal diagnostic[ot] OR antenatal diagnosis[ot] OR antenatal diagnose[ot] OR antenatal diagnoses[ot] OR antenatal screening[ot] OR antenatal testing[ot] OR antenatal test[ot] OR antenatal tests[ot] OR antenatal detection[ot] OR fetal diagnosis[ot] OR fetal diagnose[ot] OR fetal diagnoses[ot] OR fetal screening[ot] OR fetal testing[ot] OR fetal test[ot] OR fetal tests[ot] OR foetal screening[ot] OR foetal diagnosis[ot] OR foetal diagnose[ot] OR fetal diagnoses[ot] OR amniocentes\*[ot] OR Chorionic Villi[ot] OR Chorionic Villus[ot] OR Nuchal scan[ot] OR nuchal translucency[ot] OR nuchal fold[ot] OR fetoscop\*[ot] OR Amnioscop\*[ot] OR Embryoscop\*[ot] OR cervical length[ot])

- 4- (((Chromosome[tiab] OR chromosomes[tiab] OR chromosomal[tiab] OR cytogenetic[tiab] OR cytogenetics[tiab] OR cytogenetically[tiab] OR congenital[tiab] OR congenitally[tiab] OR fetal[tiab] OR foetal[tiab] OR fetus[tiab] OR foetus[tiab] OR genetic[tiab] OR genetics[tiab] OR genetically[tiab] OR birth[tiab])) AND (Anomaly[tiab] OR anomalies[tiab] OR anomalous[tiab] OR abnormality[tiab] OR abnormalities[tiab] OR abnormal[tiab] OR malformation[tiab] OR malformations[tiab] OR malformed[tiab] OR disorder[tiab] OR disorders[tiab] OR handicap\*[tiab] OR aberration[tiab] OR aberrations[tiab] OR defect[tiab] OR defects[tiab] OR deformity[tiab] OR deformities[tiab])) OR ((Chromosome[ot] OR chromosomes[ot] OR chromosomal[ot] OR cytogenetic[ot] OR cytogenetics[ot] OR cytogenetically[ot] OR congenital[ot] OR congenitally[ot] OR fetal[ot] OR foetal[ot] OR fetus[ot] OR foetus[ot] OR genetic[ot] OR genetics[ot] OR genetically[ot] OR birth[ot])) AND (Anomaly[ot] OR anomalies[ot] OR anomalous[ot] OR abnormality[ot] OR abnormalities[ot] OR abnormal[ot] OR malformation[ot] OR malformations[ot] OR malformed[ot] OR disorder[ot] OR disorders[ot] OR handicap\*[ot] OR aberration[ot] OR aberrations[ot] OR defect[ot] OR defects[ot] OR deformity[ot] OR deformities[ot]))))
- 5- (((ultrasonography[subheading] OR Magnetic Resonance Imaging[mh] OR ultrasonography[tiab] OR ultrasound\*[tiab] OR ultrasonic[tiab] OR imaging[tiab] OR MRI[tiab] OR magnetic resonance[tiab] OR echograph\*[tiab])) AND (fetus[mh] OR prenatal\*[tiab] OR antenatal\*[tiab] OR fetal[tiab] OR foetal[tiab] OR fetus\*[tiab] OR foetus[tiab] OR trimester[tiab] OR matern\*[tiab] OR pregnan\*[tiab])) OR ((ultrasonography[ot] OR ultrasound\*[ot] OR ultrasonic[ot] OR imaging[ot] OR MRI[ot] OR magnetic resonance[ot] OR echograph\*[ot])) AND (prenatal\*[ot] OR antenatal\*[ot] OR fetal[ot] OR foetal[ot] OR fetus\*[ot] OR foetus[ot] OR trimester[ot] OR matern\*[ot] OR pregnan\*[ot]))))
- 6- Chromosome Aberrations/diagnosis[mh] OR fetal diseases/diagnosis[mh] OR congenital abnormalities/diagnosis[mh] OR chromosomes disorders/diagnosis[mh] OR "Congenital, Hereditary, and Neonatal Diseases and Abnormalities/diagnosis"[Mesh] OR embryopath\*[tiab] OR embryopath\*[ot]
- 7- Questionnaire[mh] OR Qualitative Research[mh] OR focus groups[mh] OR interviews as topic[mh] OR interview[mh] OR narration[mh] OR Qualitative[tiab] OR focus group[tiab] OR focus groups[tiab] OR interview\*[tiab] OR questionnaire\*[tiab] OR experience\*[tiab] OR view[tiab] OR views[tiab] OR opinion[tiab] OR opinions[tiab] OR perspective\*[tiab] OR discussion\*[tiab] OR ethnograph\*[tiab] OR fieldwork[tiab] OR "field work"[tiab] OR "key informant"[tiab] OR Qualitative[ot] OR focus group[ot] OR focus groups[ot] OR interview\*[ot] OR questionnaire\*[ot] OR experience\*[ot] OR view[ot] OR views[ot] OR opinion[ot] OR opinions[ot] OR perspective\*[ot] OR discussion\*[ot] OR ethnograph\*[ot] OR fieldwork[ot] OR "field work"[ot] OR "key informant"[ot]
- 8- 3 OR 4 OR 5 OR 6
- 9- 1 AND 2 AND 7 AND 8
- 10- 9 NOT Case Reports [Publication Type]

#### Embase

- 1- Ethics/ OR Bioethics/ OR exp Medical ethics/ OR Morality/ OR exp Decision-making/ OR (ethic OR ethics OR ethical OR bioethic OR bioethics OR bioethical OR informed consent OR informed consents OR decision-making OR decision-makings).ti,ab,kw

- 2- Parent/ OR Father/ OR Mother/ OR Parental attitudes/ OR Parental behaviour/ OR Paternal behaviour/ OR Maternal behavior/ OR Parental consent/ OR (mother OR mothers OR father OR fathers OR parent OR parents OR parental OR paternity OR paternal OR women OR maternal).ti,ab,kw
- 3- Exp Prenatal diagnosis/ OR (prenatal diagnosis OR prenatal diagnose OR prenatal diagnoses OR Prenatal diagnostic OR prenatal diagnostics OR prenatal screening OR prenatal test OR prenatal tests OR prenatal testing OR prenatal detection OR intrauterine diagnostic OR intrauterine diagnostics OR intrauterine diagnosis OR intrauterine diagnose OR intrauterine diagnoses OR intrauterine detection OR antenatal diagnostic OR antenatal diagnostics OR antenatal diagnosis OR antenatal diagnose OR antenatal diagnoses OR antenatal screening OR antenatal testing OR antenatal test OR antenatal tests OR antenatal detection OR fetal diagnosis OR fetal diagnose OR fetal diagnoses OR fetal screening OR fetal testing OR fetal test OR fetal tests OR foetal screening OR foetal diagnosis OR foetal diagnose OR fetal diagnoses OR amniocentes\* OR Chorionic Villi OR Chorionic Villus OR Nuchal scan OR nuchal translucency OR nuchal fold OR fetoscop\* OR Amnioscop\* OR Embryoscop\* OR cervical length).ti,ab,kw
- 4- ((Chromosome OR chromosomes OR chromosomal OR cytogenetic OR cytogenetics OR cytogenetically OR congenital OR congenitally OR fetal OR foetal OR fetus OR foetus OR genetic OR genetics OR genetically OR birth) adj4 (Anomaly OR anomalies OR anomalous OR abnormality OR abnormalities OR abnormal OR malformation OR malformations OR malformed OR disorder OR disorders OR handicap\* OR aberration OR aberrations OR defect OR defects OR deformity OR deformities)).ti,ab,kw
- 5- (Ultrasound/ OR nuclear magnetic resonance imaging/ OR (ultrasound\* OR ultrasonic OR imaging OR MRI OR magnetic resonance OR echograph\*).ti,ab,kw) AND (prenatal\* OR antenatal\* OR fetal OR foetal OR fetus\* OR foetus OR trimester OR matern\* OR pregnan\*).ti,ab,kw
- 6- (exp congenital disorder/di OR exp genetic disorder/di OR fetus disease/di) OR embryopath\*.ti,ab,kw
- 7- Qualitative research/ OR narrative/ OR interview/ OR questionnaire/ OR (qualitative OR focus group OR focus groups OR interview\* OR questionnaire\* OR experience\* OR view OR views OR opinion OR opinions OR perspective\* OR discussion\* OR ethnograph\* OR fieldwork OR field work OR key informant).ti,ab,kw
- 8- 3 OR 4 OR 5 OR 6
- 9- 1 AND 2 AND 7 AND 8
- 10- 9 NOT case report/

**PsycINFO**

- 1- Ethics/ OR Bioethics/ OR Professional ethics/ OR Morality/ OR Informed consent/ OR Decision-making/ OR Choice behavior/ OR (ethic OR ethics OR ethical OR bioethic OR bioethics OR bioethical OR informed consent OR informed consents OR decision-making OR decision-makings).ti,ab,id
- 2- Exp parents/ OR Parental attitudes/ OR Parental involvement/ OR Parental expectations/ OR Parental investment/ OR Parental role/ OR (mother OR mothers OR father OR fathers OR parent OR parents OR parental OR paternity OR paternal OR women OR maternal).ti,ab,id

- 3- Prenatal diagnosis/ OR (prenatal diagnosis OR prenatal diagnose OR prenatal diagnoses OR Prenatal diagnostic OR prenatal diagnostics OR prenatal screening OR prenatal test OR prenatal tests OR prenatal testing OR prenatal detection OR intrauterine diagnostic OR intrauterine diagnostics OR intrauterine diagnosis OR intrauterine diagnose OR intrauterine diagnoses OR intrauterine detection OR antenatal diagnostic OR antenatal diagnostics OR antenatal diagnosis OR antenatal diagnose OR antenatal diagnoses OR antenatal screening OR antenatal testing OR antenatal test OR antenatal tests OR antenatal detection OR fetal diagnosis OR fetal diagnose OR fetal diagnoses OR fetal screening OR fetal testing OR fetal test OR fetal tests OR foetal screening OR foetal diagnosis OR foetal diagnose OR foetal diagnoses OR amniocentes\* OR Chorionic Villi OR Chorionic Villus OR Nuchal scan OR nuchal translucency OR nuchal fold OR fetoscop\* OR Amnioscop\* OR Embryoscop\* OR cervical length).ti,ab,id
- 4- ((Chromosome OR chromosomes OR chromosomal OR cytogenetic OR cytogenetics OR cytogenetically OR congenital OR congenitally OR fetal OR foetal OR fetus OR foetus OR genetic OR genetics OR genetically OR birth) adj4 (Anomaly OR anomalies OR anomalous OR abnormality OR abnormalities OR abnormal OR malformation OR malformations OR malformed OR disorder OR disorders OR handicap\* OR aberration OR aberrations OR defect OR defects OR deformity OR deformities)).ti,ab,id
- 5- (Ultrasound/ OR Magnetic Resonance Imaging/ OR (ultrasound\* OR ultrasonic OR imaging OR MRI OR magnetic resonance OR echograph\*).ti,ab,id) AND (prenatal\* OR antenatal\* OR fetal OR foetal OR fetus\* OR foetus OR trimester OR matern\* OR pregnan\*).ti,ab,id
- 6- ((exp congenital disorders/ OR exp genetic disorders/) AND (diagnosis/ OR medical diagnosis/)) OR embryopath\*.ti,ab,id
- 7- Qualitative research/ OR "Experiences (Events)"/ OR interviews/ OR interviewing/ OR interviewers/ OR (qualitative OR focus group OR focus groups OR interview\* OR questionnaire\* OR experience\* OR view OR views OR opinion OR opinions OR perspective OR perspectives OR discussion\* OR ethnograph\* OR fieldwork OR field work OR key informant).ti,ab,id
- 8- 3 OR 4 OR 5 OR 6
- 9- 1 AND 2 AND 7 AND 8
- 10- 9 NOT case report/

#### **EBM Reviews**

- 1- Ethics/ OR Bioethics/ OR exp Medical ethics/ OR Morality/ OR exp Decision-making/ OR (ethic OR ethics OR ethical OR bioethic OR bioethics OR bioethical OR informed consent OR informed consents OR decision-making OR decision-makings).ti,ab,kw
- 2- Parent/ OR Father/ OR Mother/ OR Parental attitudes/ OR Parental behaviour/ OR Paternal behaviour/ OR Maternal behavior/ OR Parental consent/ OR (mother OR mothers OR father OR fathers OR parent OR parents OR parental OR paternity OR paternal OR women OR maternal).ti,ab,kw
- 3- Exp Prenatal diagnosis/ OR (prenatal diagnosis OR prenatal diagnose OR prenatal diagnoses OR Prenatal diagnostic OR prenatal diagnostics OR prenatal screening OR prenatal test OR prenatal tests OR prenatal testing OR prenatal

detection OR intrauterine diagnostic OR intrauterine diagnostics OR intrauterine diagnosis OR intrauterine diagnose OR intrauterine diagnoses OR intrauterine detection OR antenatal diagnostic OR antenatal diagnostics OR antenatal diagnosis OR antenatal diagnose OR antenatal diagnoses OR antenatal screening OR antenatal testing OR antenatal test OR antenatal tests OR antenatal detection OR fetal diagnosis OR fetal diagnose OR fetal diagnoses OR fetal screening OR fetal testing OR fetal test OR fetal tests OR foetal screening OR foetal diagnosis OR foetal diagnose OR foetal diagnoses OR amniocentes\* OR Chorionic Villi OR Chorionic Villus OR Nuchal scan OR nuchal translucency OR nuchal fold OR fetoscop\* OR Amnioscop\* OR Embryoscop\* OR cervical length).ti,ab,kw

- 4- ((Chromosome OR chromosomes OR chromosomal OR cytogenetic OR cytogenetics OR cytogenetically OR congenital OR congenitally OR fetal OR foetal OR fetus OR foetus OR genetic OR genetics OR genetically OR birth) adj4 (Anomaly OR anomalies OR anomalous OR abnormality OR abnormalities OR abnormal OR malformation OR malformations OR malformed OR disorder OR disorders OR handicap\* OR aberration OR aberrations OR defect OR defects OR deformity OR deformities)).ti,ab,kw
- 5- (Ultrasound/ OR nuclear magnetic resonance imaging/ OR (ultrasound\* OR ultrasonic OR imaging OR MRI OR magnetic resonance OR echograph\*).ti,ab,kw) AND (prenatal\* OR antenatal\* OR fetal OR foetal OR fetus\* OR foetus OR trimester OR matern\* OR pregnan\*).ti,ab,kw
- 6- (exp congenital disorder/di OR exp genetic disorder/di OR fetus disease/di) OR embryopath\*.ti,ab,kw
- 7- Qualitative research/ OR narrative/ OR interview/ OR questionnaire/ OR (qualitative OR focus group OR focus groups OR interview\* OR questionnaire\* OR experience\* OR view OR views OR opinion OR opinions OR perspective\* OR discussion\* OR ethnograph\* OR fieldwork OR field work OR key informant).ti,ab,kw
- 8- 3 OR 4 OR 5 OR 6
- 9- 1 AND 2 AND 7 AND 8
- 10- 9 NOT case report/

#### **CINAHL**

- S1 (MH "ethics") OR (MH "Decision-making, Ethical") OR (MH "Morals+") OR (MH "Ethics, Medical") OR (MH "Ethics, Professional") OR (MH "Ethics, Nursing") OR (MH "Consent") OR (MH "Decision-making+") OR (MW ethical)
- S2 TI (Ethic OR ethics OR ethical OR bioethic OR bioethics OR bioethical OR consent OR informed consents OR decision-making OR decision-makings) OR AB (Ethic OR ethics OR ethical OR bioethic OR bioethics OR bioethical OR consent OR informed consents OR decision-making OR decision-makings)
- S3 (MH "Parents+") OR (MH "Parental Attitudes") OR (MH "Parental Behavior") OR (MH "Maternal Behavior") OR (MH "Paternal Behavior")
- S4 TI (parents OR parent OR mother OR mothers OR women\* OR maternal OR father OR fathers OR parental OR paternity OR paternal) OR AB (parents OR parent OR mother OR mothers OR women\* OR maternal OR father OR fathers OR parental OR paternity OR paternal)

- S5 (MH "Prenatal Diagnosis+") OR TI (prenatal diagnosis OR prenatal diagnose OR prenatal diagnoses OR Prenatal diagnostic OR prenatal diagnostics OR prenatal screening OR prenatal test OR prenatal tests OR prenatal testing OR prenatal detection OR intrauterine diagnostic OR intrauterine diagnostics OR intrauterine diagnosis OR intrauterine diagnose OR intrauterine diagnoses OR intrauterine detection OR antenatal diagnostic OR antenatal diagnostics OR antenatal diagnosis OR antenatal diagnose OR antenatal diagnoses OR antenatal screening OR antenatal testing OR antenatal test OR antenatal tests OR antenatal detection OR fetal diagnosis OR fetal diagnose OR fetal diagnoses OR fetal screening OR fetal testing OR fetal test OR fetal tests OR foetal screening OR foetal diagnosis OR foetal diagnose OR fetal diagnoses OR amniocentes\* OR Chorionic Villi OR Chorionic Villus OR Nuchal scan OR nuchal translucency OR nuchal fold OR fetoscop\* OR Amnioscop\* OR Embryoscop\* OR cervical length) OR AB (prenatal diagnosis OR prenatal diagnose OR prenatal diagnoses OR Prenatal diagnostic OR prenatal diagnostics OR prenatal screening OR prenatal test OR prenatal tests OR prenatal testing OR prenatal detection OR intrauterine diagnostic OR intrauterine diagnostics OR intrauterine diagnosis OR intrauterine diagnose OR intrauterine diagnoses OR intrauterine detection OR antenatal diagnostic OR antenatal diagnostics OR antenatal diagnosis OR antenatal diagnose OR antenatal diagnoses OR antenatal screening OR antenatal testing OR antenatal test OR antenatal tests OR antenatal detection OR fetal diagnosis OR fetal diagnose OR fetal diagnoses OR fetal screening OR fetal testing OR fetal test OR fetal tests OR foetal screening OR foetal diagnosis OR foetal diagnose OR fetal diagnoses OR amniocentes\* OR Chorionic Villi OR Chorionic Villus OR Nuchal scan OR nuchal translucency OR nuchal fold OR fetoscop\* OR Amnioscop\* OR Embryoscop\* OR cervical length)
- S6 TI ((Chromosome OR chromosomes OR chromosomal OR cytogenetic OR cytogenetics OR cytogenetically OR congenital OR congenitally OR fetal OR foetal OR fetus OR foetus OR genetic OR genetics OR genetically OR birth) N4 (Anomaly OR anomalies OR anomalous OR abnormality OR abnormalities OR abnormal OR malformation OR malformations OR malformed OR disorder OR disorders OR handicap\* OR aberration OR aberrations OR defect OR defects OR deformity OR deformities)) OR AB ((Chromosome OR chromosomes OR chromosomal OR cytogenetic OR cytogenetics OR cytogenetically OR congenital OR congenitally OR fetal OR foetal OR fetus OR foetus OR genetic OR genetics OR genetically) N4 (Anomaly OR anomalies OR anomalous OR abnormality OR abnormalities OR abnormal OR malformation OR malformations OR malformed OR disorder OR disorders OR handicap\* OR aberration OR aberrations OR defect OR defects OR deformity OR deformities))
- S7 ((MW ultrasonography) OR (MH "Magnetic Resonance Imaging")) AND ((MH "Fetal Diseases+") OR (MH Fetal abnormalities) OR (MH Fetus))
- S8 TI (ultrasonography OR ultrasound\* OR ultrasonic OR imaging OR MRI OR magnetic resonance OR echograph\*) N4 (prenatal\* OR antenatal\* OR fetal OR foetal OR fetus\* OR foetus OR trimester OR matern\* OR pregnan\*)
- S9 AB (ultrasonography OR ultrasound\* OR ultrasonic OR imaging OR MRI OR magnetic resonance OR echograph\*) N4 (prenatal\* OR antenatal\* OR fetal OR foetal OR fetus\* OR foetus OR trimester OR matern\* OR pregnan\*)
- S10 (MH "Chromosome Aberrations+/DI") OR (MH "Chromosome Disorders+/DI") OR (MH "Fetal Diseases+/DI") OR (MH "Hereditary Diseases+/DI") OR (MH "Congenital, Hereditary, and Neonatal Diseases and Abnormalities+/DI") OR (MH "Fetal Abnormalities")

- S11 TI (embryopath\*) OR AB (embryopath\*)
- S12 (MH "Qualitative Studies") OR (MH "Interviews+") OR (MH "Focus Groups") OR (MH "Questionnaires+") OR (MH narratives) OR TI (Qualitative OR focus group OR focus groups OR interview\* OR questionnaire\* OR experience\* OR view OR views OR opinion OR opinions OR perspective\*) OR AB (Qualitative OR focus group OR focus groups OR interview\* OR questionnaire\* OR experience\* OR view OR views OR opinion OR opinions OR perspective\* OR discussion\* OR ethnograph\* OR fieldwork OR field work OR key informant)
- S13 S1 OR S2 (ethics)
- S14 S3 OR S4 (Parents)
- S15 S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 (Prenatal diagnosis OR malformations)
- S16 S13 AND S14 AND S15
- S17 S16 NOT (MH "Case studies")

## Appendix 4. Search strategy for quantitative studies

1	Tools (libre)	(tool[TIAB] OR tools[TIAB] OR tooling*[TIAB] OR questionnaire*[TIAB] OR instrument*[TIAB] OR template*[TIAB] OR model[TIAB]) <b>OR</b> (tool[OT] OR tools[OT] OR tooling*[OT] OR questionnaire*[OT] OR instrument*[OT] OR template*[OT] OR model[OT])
2	Tools (contrôlé)	Health Impact Assessment [MH] OR Interviews as Topic[MH] OR Questionnaires[MH] OR Health Education[MH:NOEXP] OR Consumer Health Information[MH] OR Patient Education as Topic[MH]
3		#1 OR #2
4	Decision aids / informed consent (libre)	((ethic*[TIAB] OR bioethic*[ TIAB] OR bio ethic*[TIAB] OR decision-making*[TIAB] OR decision aid[TIAB] OR decision aids[TIAB] capacity building[TIAB] OR consent*[TIAB]) OR ((information*[TIAB] OR knowledge*[TIAB] OR fact[TIAB] OR facts[TIAB]) AND (translation[TIAB] OR transfer[TIAB] OR transmission[TIAB]))) <b>OR</b> ((ethic*[OT] OR bioethic*[ OT] OR bio ethic*[OT] OR decision-making*[OT] OR decision aid[OT] OR decision aids[OT] capacity building[OT] OR consent*[OT]) OR ((information*[OT] OR knowledge*[OT] OR fact[OT] OR facts[OT]) AND (translation[OT] OR transfer[OT] OR transmission[OT])))
5	Decision aids / informed consent (contrôlé)	Ethics[MH:NOEXP] OR Bioethics[MH] OR Bioethical Issues[MH] OR Morals[MH] OR Decision-making[MH] OR Capacity building[MH] OR Informed Consent[MH] OR Patient Acceptance of Health Care[MH]
6		#4 OR #5
7	Parents (libre)	(mother*[TIAB] OR matern*[TIAB] OR mom[TIAB] OR moms[TIAB] OR father*[TIAB] OR patern*[TIAB] OR dad[TIAB] OR dads[TIAB] OR parent*[TIAB] OR pregnan*[TIAB] OR childbear*[TIAB]) <b>OR</b> (mother*[OT] OR matern*[OT] OR mom[OT] OR moms[OT] OR father*[OT] OR patern*[OT] OR dad[OT] OR dads[OT] OR parent*[OT] OR pregnan*[OT] OR childbear*[OT])
8	Parents (contrôlé)	Parents[MH]



9		#7 OR #8
10	Parental consent (contrôlé)	Parental consent[MH]
11	Prenatal diagnosis (libre)	(((prenatal[TIAB] OR intrauterine[TIAB] OR antenatal*[TIAB] OR ante natal[TIAB] OR fetal*[TIAB] OR fetus*[TIAB] OR foetal*[TIAB] OR foetus[TIAB] OR embryo[TIAB] OR genetic*[TIAB])) AND (diagnos*[TIAB] OR screen*[TIAB] OR test[TIAB] OR tests[TIAB] OR testing[TIAB] OR detection*[TIAB] OR ultrasonography[TIAB] OR ultrasound*[TIAB] OR ultrasonic[TIAB] OR imaging[TIAB] OR MRI[TIAB] OR magnetic resonance[TIAB] OR echograph*[TIAB] OR ultrasonography[SH] OR magnetic Resonance Imaging[MH])) OR (amniocentes*[TIAB] OR amnioscop*[TIAB] OR OR embryocentes*[TIAB] OR embryoscop*[TIAB] OR embryopath*[TIAB] OR nuchal scan*[TIAB] OR nuchal translucency[TIAB] OR nuchal fold[TIAB] OR fetoscop*[TIAB])) OR (((prenatal[OT] OR intrauterine[OT] OR antenatal*[OT] OR ante natal[OT] OR fetal*[OT] OR fetus*[OT] OR foetal*[OT] OR foetus[OT] OR embryo[OT] OR genetic*[OT]) AND (diagnos*[OT] OR screen*[OT] OR test[OT] OR tests[OT] OR testing[OT] OR detection*[OT] OR ultrasonography[OT] OR ultrasound*[OT] OR ultrasonic[OT] OR imaging[OT] OR MRI[OT] OR magnetic resonance[OT] OR echograph*[OT] OR ultrasonography[SH] OR magnetic Resonance Imaging[MH])) OR (amniocentes*[OT] OR amnioscop*[OT] OR OR embryocentes*[OT] OR embryoscop*[OT] OR embryopath*[OT] OR nuchal scan*[OT] OR nuchal translucency[OT] OR nuchal fold[OT] OR fetoscop*[OT]))
12	Prenatal diagnosis (contrôlé)	Prenatal diagnosis[MH] OR fetal diseases/diagnosis[MH] OR Congenital abnormalities/diagnosis[MH] OR "Congenital, Hereditary, and Neonatal Diseases and Abnormalities/diagnosis"[MH] OR Chromosomes disorders/diagnosis[MH] OR Chromosome Aberrations/diagnosis[MH]
13		#11 OR #12
14		(#3 AND #6 AND #9 AND #13) OR (#3 AND #10 AND #13)
15		(#14 AND 1970:2016[DP] AND (english[LA] OR french[LA] OR italian[LA]))

## **Appendix 5. Values clarification exercise and knowledge questionnaire**

The questions below were extracted from “eAppendix 1” and “ eAppendix 2” of the following article :  
Kuppermann M, Pena S, Bishop JT, et al. Effect of enhanced information, values clarification, and removal of financial barriers on use of prenatal genetic testing: a randomized clinical trial. JAMA 2014; 312:1210-7.

### **Values Clarification Questions**

*Questions to help decide whether or not to have any testing (presented to all women):*

- How important to you is knowing whether or not your baby will be born with a birth defect such as Down syndrome?

1 =very important, 2=somewhat important, 3=I am not sure, 4=not very important, and 5=not important at all

- Would you choose to have a diagnostic test that would tell you for sure whether or not your fetus has Down syndrome, even if it could cause a miscarriage?

1=definitely, 2=probably, 3=I am not sure, 4=probably not, and 5=definitely not

- Which would be worse for you, having a child with Down syndrome or having a miscarriage caused by a prenatal test?

1=definitely worse to have a child with Down syndrome, 2=probably worse to have a child with Down syndrome, 3=I am not sure, 4=probably worse to have a miscarriage, and 5=definitely worse to have a miscarriage

*Questions to help choose between starting with screening or going straight to invasive testing (presented only to women who were considering having testing)*

- How important is it to you to avoid a false positive screening result?

1=very important, 2=somewhat important, 3=I am not sure, 4=not very important, and 5=not important at all

- How important to you is knowing for sure whether or not your fetus has Down syndrome?

1=very important, 2=somewhat important, 3=I am not sure, 4=depends on my risk, and 5=not important

- Would it help you to know your personal chance of having a baby with Down syndrome before deciding whether or not to have a diagnostic test (CVS or amniocentesis)?

1=definitely would help me, 2=probably would help me, 3=I am not sure, 4=probably would not help me, and 5=definitely would not help me.

*Questions to help decide which screening or diagnostic test to undergo (only presented to women who were considering having testing)*

- When would you prefer to receive results?

1=definitely during my 1st trimester, 2=probably during my 1st trimester, 3=it doesn't matter, 4=probably during my 2nd trimester, and 5=definitely during my 2nd trimester

- Would you be willing to go to another facility to have a nuchal translucency ultrasound?  
(presented only to women who preferred to start with screening)

1=definitely would not, 2=probably would not, 3=I am not sure, 4=probably would, 5=definitely would

### **Knowledge Questionnaire**

*Adapted from Maternal Serum Screening Knowledge Questionnaire. Response options for each item included "true," "false," and "not sure/don't know." The correct response to items 2, 8, 9, 10, 11, and 14 was "true"; the others were false. Scores range from 0 to 15, reflecting the number of correct responses.*

1. Amniocentesis involves taking blood from a pregnant woman's arm.
2. All people with Down syndrome have mental retardation
3. Women who have a "negative" or "low risk" result on a screening test can be sure that their baby will not have Down syndrome.
4. Amniocentesis is used to test for diabetes.
5. Nuchal translucency screening is a type of blood test.
6. Screening tests tell you for sure whether your fetus has Down syndrome.
7. Amniocentesis can tell you about the severity of mental disabilities that a baby with Down syndrome will have.
8. The chance of having a baby with Down syndrome increases with the age of the mother.
9. If a woman receives a "positive" or "increased risk" result on a screening test, further tests are needed to tell if anything is wrong.
10. Amniocentesis can cause a miscarriage.
11. Amniocentesis can tell you for sure whether or not your fetus has Down syndrome.
12. Down syndrome can be cured.
13. The Quad Marker Screening test only detects Down syndrome.
14. Amniocentesis is done later in pregnancy than chorionic villus sampling (CVS).
15. The Quad Marker screening test can cause a miscarriage.