

**FACTORS INFLUENCING DECISION-MAKING  
IN PRENATAL SCREENING FOR DOWN SYNDROME**

by

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## **Abstract**

**Objectives:** This paper aims to determine what factors pregnant women and their partners use to determine whether to undergo prenatal screening for Down syndrome, and what further information they need to make informed decisions.

**Methods:** Medical and social science databases were used to identify articles related to uptake of prenatal screening for Down syndrome and decision-making.

**Results:** The majority of studies were qualitative survey or interview studies. Factors that influenced decisions of whether to undergo prenatal screening included preexisting risk, anxiety, ability for action, personal values, disability experiences, demographic characteristics, family and friends, medical providers, trust the medical establishment, and norms around routine care.

**Conclusions:** As prenatal screening improves in effectiveness and becomes a part of routine prenatal care, decision-making factors must be considered when providing information to ensure informed decision-making. Policy discussions should include multiple stakeholders, including women and their partners, medical professionals, genetic counselors, families affected by disability, and people with Down syndrome. Policies and practices must ultimately support both the reproductive rights of women and adequate, nonstigmatizing services for children.

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## Introduction

### Down syndrome

Down syndrome, also known as trisomy 21, is a chromosomal abnormality in which there is an aneuploidy, or extra copy, of chromosome 21.<sup>1</sup> It is the most common aneuploidy in humans, and is the most common genetic cause of mental retardation.<sup>2</sup> Down syndrome can also cause a number of other conditions requiring treatment, including cardiac defects, duodenal atresia, thyroid problems, hearing loss, increased risk of leukemia, and seizures.<sup>3</sup>

Down syndrome affects about a quarter million families in the United States.<sup>4</sup> Approximately 5000 children are born each year in the US with Down syndrome, and the incidence of Down syndrome is estimated to be 1 in every 700 live births.<sup>4</sup> Investigators pooled population-based data from the National Birth Defects Prevention Network for all states that used active case-finding surveillance. For 1999-2001, prevalence estimates of Down syndrome were 13.65 per 10,000 live births when adjusted for maternal age and 12.78 per 10,000 live births when adjusted for race and ethnicity.<sup>5</sup> Using the same methods, when updated with data from 2004-2006, prevalence estimates were 14.47 per 10,000 and 13.56 per 10,000, respectively.<sup>6</sup> Compared with non-Hispanic

<b>Table 1: Down syndrome risk by maternal age.</b>		
<b>Maternal Age</b>	<b>Midtrimester</b>	<b>Term</b>
35	1/250	1/384
36	1/192	1/303
37	1/149	1/227
38	1/115	1/175
39	1/89	1/137
40	1/69	1/106
41	1/53	1/81
42	1/41	1/64
43	1/31	1/50
44	1/25	1/38
45	1/19	1/30

whites, Hispanics have been found to have a higher birth prevalence of Down syndrome (OR 1.12, 95% CI 1.03-1.21); non-Hispanic blacks have been found to have a lower birth prevalence of Down syndrome (OR 0.77, 95% CI 0.69-0.87) than non-Hispanic whites.

The prevalence of Down syndrome increases with maternal age (Table 1). Prevalence has increased in recent years due in part to the increasing number of women of

advanced maternal age (AMA) giving birth. Within the literature, AMA is considered to be age 35

years or older. In 1980, the birth prevalence for Down syndrome was 1 in 960, approximately 5% of pregnant women were AMA, and 24% of babies with Down syndrome were born to AMA mothers. By 2002, the birth prevalence of Down syndrome without prenatal intervention was 1 in 629, almost 14% of pregnant women were AMA, and 51% of Down syndrome babies were born to AMA women.<sup>7</sup>

Caring for a child with Down syndrome can be costly to the family of the child and society. Children with Down syndrome may need a number of intervention services such as medical treatment and special education. Additional monetary costs of raising a child with Down syndrome have been estimated at \$762,748 (in 2006 dollars)<sup>8</sup> and \$228,400 (in 2003 dollars).<sup>9</sup>

## **Problem Statement**

General practice guidelines from the American College of Obstetricians and Gynecologists, the American College of Medical Genetics, and the Institute for Clinical Systems Improvement state that all pregnant women should be offered prenatal genetic screening for the detection of Down syndrome and other anomalies.<sup>10-12</sup> Screening tests have become widely available in the United States and their use is becoming standard practice in prenatal care. Although voluntary, some pregnant women and their partners may find making a decision about whether to undergo screening a difficult one, while others may have no trouble. This paper seeks to address both the science of testing procedures and the decision making processes regarding prenatal genetic screening for Down syndrome by assessing the following questions:

- How sensitive and specific are prenatal screening tests for detecting Down syndrome?
- What proportion of pregnant women accept or decline screening tests for Down syndrome?
- What do pregnant women and their partners decide to do when faced with a positive screening or diagnostic test result?

- What factors do pregnant women and their partners consider when deciding whether to undergo screening and diagnostic tests?
- How do pregnant women and their partners interact with health care professionals to assist in decision-making regarding prenatal genetic screening and diagnosis?
- What further information do women and their partners need in order to make informed decisions about prenatal screening and diagnostic testing?

### **Prenatal screening and diagnostic testing for Down syndrome**

Prenatal diagnosis of Down syndrome, through the use of amniocentesis and karyotype analysis was first proposed in the 1970s and has become regularly offered for AMA pregnant women and other women of higher risk due to family history or a previous fetus with aneuploidy.

With the availability of less invasive screening tests, and the regular usage of invasive diagnostic tests, prenatal genetic screening for Down syndrome is being more widely offered to pregnant women, regardless of age or risk status. The ACOG issued recommendations in 2007 that maternal age should no longer be used as a criterion for offering prenatal screening or diagnostic tests.<sup>10</sup> The ACGM similarly stated that amniocentesis and CVS should be offered to all pregnant women, not only those over 35 years of age.<sup>11</sup> Although risk for having a Down syndrome fetus increases with age, and is particularly high for those older than age 35, women of younger ages are still at risk, and as many as 80% of all babies born with Down syndrome are to mothers younger than 35 years of age.<sup>4</sup>

A number of genetic screening and diagnostic options are now available and are described below. Second trimester screening tests are described first, as these were the first available, and first trimester tests are an adaptation of them.

## Second Trimester Screening Tests

### Triple Test

The second-trimester triple test screens for three markers in maternal serum: alphafetoprotein (AFP), unconjugated estriol (uE3), and human chorionic gonadotropin (hCG), which can be intact or the free  $\beta$  subunit. In fetuses that potentially have Down syndrome, AFP and uE3 are often found to be lower than average, while hCG is found to be elevated.<sup>1</sup> The triple screen is conducted during 15 and 20 weeks' gestation, and the detection rate is

Table 2: Prenatal screening tests for Down syndrome and detection rates.		
Strategy	Analytes	Detection Rate (%) (based on a 5% false positive screen rate)
<i>First-trimester screen</i>	NT, PAPP-A, hCG or free beta-hCG	79-87
<i>Nuchal Translucency</i>	NT	64-70
<i>Triple Test</i>	MSAFP, hCG or free beta, uE3	60-69
<i>Quadruple (Quad) test</i>	MSAFP, hCG or free beta, uE3, inh	67-81
<i>Integrated sequential screen</i>	First-trimester screen and Quad test – results withheld until Quad test completed	94-96
<i>Stepwise sequential screen</i>	First trimester screen and quad test -1% offered diagnostic test after first trimester screen -99% proceed to Quad test, results withheld until Quad test complete	90-95
<i>Contingent sequential screen</i>	First trimester screen and Quad test -1% offered diagnostic test after first-trimester screen -15% proceed to Quad test, results withheld until Quad test completed -84% have no additional test after first-trimester screen	88-94
NT: Nuchal translucency; PAPP-A: Plasma protein-A; hCG: Human chorionic gonadotropin; free beta-hCG: Free beta-human chorionic gonadotropin; MSAFP: Maternal serum alphafetoprotein; uE3: Unconjugated estriol; inh: Inhibin A.		

approximately 60-69%.<sup>1</sup> (See Table 2 for a description of each test and associated detection rates adapted from Williams Obstetrics, 23<sup>rd</sup> edition, 2010<sup>1</sup>).

### ***Quad Test***

The quadruple marker test (“Quad test”) is similar to the triple test, but with slightly better detection rates than the triple test. It includes the same three markers, but adds a fourth, Inhibin A.<sup>2</sup> The detection rate for the quad test is approximately 67-81%.<sup>1</sup>

### ***First Trimester Screening Tests***

#### ***First Trimester Combined Screen***

The first trimester combined screen, or “first screen”, uses both serum markers and ultrasonography to detect Down syndrome. Free  $\beta$  hCG is elevated, and plasma protein-A (PAPP-A) is found to be low in potential cases of Down syndrome.<sup>2</sup> Nuchal translucency (NT) thickness is the measure of subcutaneous fluid at the back of the fetal neck, and is associated with Down syndrome as well. The first trimester combined screen tests free  $\beta$  hCG and PAPP-A in maternal serum and an NT measurement all taken between 11 and 14 weeks’ gestation.<sup>2</sup> The first trimester combined screen has a detection rate of approximately 79-87%.<sup>1</sup>

### ***Combined Screening Tests***

There are several methods of combining first and second trimester tests, with various levels of detection and varying positive and negative considerations.

#### ***Integrated Sequential Screening (sometimes referred to as Full Integrated Screen)***

Integrated sequential screening is a two-stage test that measures the serum markers used in the first screen and the quad screen and a Nuchal Translucency ultrasound to detect risk of Down syndrome.<sup>2,13</sup> First and second trimester measurements are collected between 11 and 14 weeks’ gestation and then again between 15 and 20 weeks. The full integrated screen has the highest



detection rate (94-96%)<sup>1</sup>, but women receive no results until the second trimester after both samples have been collected and used to create an individualized risk assessment.<sup>2</sup>

### ***Serum Integrated Screen***

Serum integrated screening is a two stage test very similar to the full integrated screen, but does not use an NT ultrasound in addition to serum samples. This testing protocol may be more appropriate for low resource settings that are not able to do NT ultrasound. Blood is collected during the same windows, and results are provided in the same manner.

### ***Stepwise Sequential Screen***

Sequential integrated screening is also a two stage protocol and is similar to the integrated sequential screen, but instead of waiting until after the second trimester screening component to provide results, an interim risk is developed.<sup>2</sup> Approximately 1% of women are offered a diagnostic test after a positive first trimester screen, while 99% proceed to the quad test, where results are withheld until completion of the test.<sup>1</sup> The detection rate is 90-95% for the stepwise sequential screen.<sup>1</sup>

### ***Contingent Sequential Screen***

Similar to the integrated sequential screen and stepwise sequential screen, this is an integrated test that combines the first screen and quad screen tests, but only conducts second trimester tests if the interim risk from the first trimester test is sufficiently high (eg,  $\geq 1$  in 25 or  $\geq 1$  in 50).<sup>2</sup> With this test, women are divided into three risk groups: high, moderate, and low. Approximately 1% are high risk and are offered diagnostic testing after the first-trimester screen, 15% are moderate risk and proceed to the quad test, where results are withheld until the quad test is completed, and 84% are low risk and have no additional test after the first trimester screen.<sup>1</sup> Detection rates are lower than those of the other sequential screening methods, at 88-94%.<sup>1</sup>

All of these tests incorporate maternal age when creating a risk estimate.

### ***Diagnostic Testing***

In addition to screening tests, diagnostic tests are available for genetic karyotyping. While screening tests provide results in terms of a risk level, diagnostic tests can almost definitively (about 99%) tell a person whether fetal genetic abnormalities exist, yet little about the severity or prognosis of the condition. These diagnostic tests are more invasive, in that they require removing amniotic fluid or cells from the abdomen, and carry a slight risk of miscarriage, which is why health professionals generally suggest less invasive screening tests before prenatal diagnostic tests.

### ***Amniocentesis***

Amniocentesis is usually performed at 15 to 20 weeks' gestation, and is when a needle is inserted into the amniotic sac while avoiding the placenta, umbilical cord, and fetus to extract approximately 20ml of amniotic fluid for fetal karyotyping. Complications are rare but include vaginal spotting or amniotic fluid leakage in 1-2% and chorioamnionitis in less than 0.1%. Earlier studies reported a fetal loss rate of 0.5-1%, but ACOG has concluded that the procedure-related loss rate is closer to 1 in 300 to 500. Early amniocentesis has a greater likelihood of post-procedural complications, especially clubfoot.<sup>1</sup>

### ***Chorionic Villus Sampling***

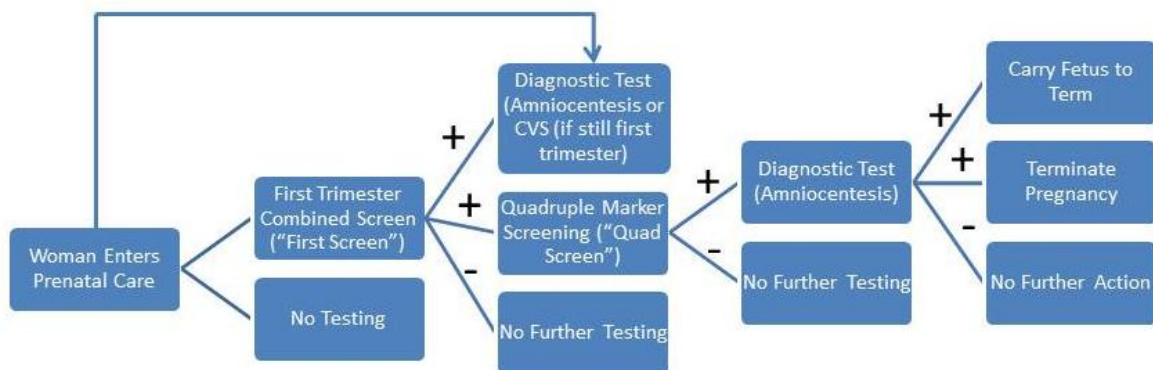
Chorionic villus sampling (CVS) is a biopsy of the chorionic villi (or placental tissue), and can be performed earlier than amniocentesis, at 10 to 13 weeks' gestation. Complications of CVS are similar to those of amniocentesis. Early CVS (around 7 weeks' gestation) can increase the incidence of limb-reductive defects.<sup>1</sup>

### Future Directions in Testing

There is potential for a new, non-invasive diagnostic test for Down syndrome to be widely available within the next few years. Investigators have recently identified cell-free DNA and RNA in maternal serum that are from fetal tissue.<sup>2</sup> Sequencing these fetal nucleic acids in maternal serum may provide a way to detect fetal aneuploidies such as Down syndrome through a test that is not invasive and could not potentially harm the fetus. This diagnostic testing method is already being validated in clinical trials. In a recent study, the new blood test was tested on 753 pregnant women at high risk for fetal trisomy 21 who had undergone definitive diagnosis (either amniocentesis or CVS). They found that trisomy 21 fetuses were detected at 100% sensitivity and 97.9 specificity, which is very close to current diagnostic testing practices.<sup>14</sup>

Figure 1 shows a decision tree with scenarios that a person might undergo when deciding whether or not to screen for Down syndrome.

Figure 1: Decision tree of scenarios for screening for Down syndrome.



## **Critical Review of Selected Literature and Interpretation of Findings**

The online databases, PubMed, PsycInfo, and Google Scholar, were used to search for publications with the search terms Down syndrome, trisomy 21, aneuploidy, prenatal screening, decision-making, effectiveness, uptake, and practice guidelines that would most appropriately answer the questions put forth in this paper. For particularly relevant publications, references lists also provided a source of additional articles for review. Articles were not restricted to the United States. Most study participants were pregnant or recently postpartum women, but studies containing information from partners or health care professionals were not excluded. Articles were restricted to the years 2000 to 2011, unless they were pivotal articles that provided a necessary foundation for the more current research.

### ***Effectiveness of Prenatal Screening***

Four large clinical trials in the United States and United Kingdom have evaluated the sensitivity and specificity of various types of screening tests for Down syndrome. These include the Blood, Ultrasound, Nuchal (BUN) study of 8,216 high-risk women and 61 cases of Down syndrome<sup>15</sup>; the One-stop Clinic to Assess Risk (OSCAR) studied 15,030 pregnancies and 82 cases of Down syndrome<sup>16</sup>; the Serum, Urine, Ultrasound Study (SURUSS) with 47,053 pregnancies and 101 Down syndrome cases<sup>17</sup>; and the First and Second Trimester Evaluation of Risk (FASTER) study with 33,557 pregnancies and 84 Down syndrome cases.<sup>18</sup>

Since these initial studies of detection rates, several other studies have been conducted using these data. Some evaluate the cost-effectiveness of various testing strategies, some aim to

determine the most appropriate cut-off values for risk, and others sought to determine if results are replicable in the smaller, clinical setting.

For first trimester combined screening alone, with fixed false positive rates of 5%, the BUN, OSCAR, SURUSS, and FASTER studies had detection rates of 79%, 90%, 86% and 85%, respectively. The four studies together average to approximately 85%.<sup>2</sup> If the goal of improving screening is to reduce false positive rates instead of increasing detection rates, and a detection rate of 85% is fixed, the full integrated test has significantly lower false positive rates than the first or second trimester screening tests alone or the first and second trimester serum integrated test.<sup>2</sup> For the SURUSS and the FASTER studies, the triple test has false positive rates of 9.3% and 13.6%, quad test 6.2% and 7.3%, first trimester combined test 6.0% and 4.8%, and the full integrated test 1.3% and 0.8%.<sup>2</sup>

Other studies modeling effectiveness of these tests showed similar results. In addition to measuring the number of fetuses with Down syndrome detected as an outcome measure, studies often also used cost to the individual and society of testing or raising a child with Down syndrome and pregnancy loss due to either CVS or amniocentesis. All validation and cost effectiveness studies found integrated screening, either sequential or contingent, to have the highest detection rates while being the most cost effective, having the lowest false positive rates, having the fewest number of procedure related euploid miscarriages and unnecessary terminations. Sensitivity of integrated, sequential, and contingent screening ranged from 85% to 96% with false positive rates of 5% or lower.<sup>8,19-22</sup>

Screening test sensitivity and outcomes have been evaluated in clinical settings. At the New York Weill-Cornell Medical Center, all patients who presented from January 2003 through September 2004 with singleton pregnancies and underwent first-trimester combined screening were included. Chromosomal status was determined by prenatal karyotype analysis, cytogenic studies on tissue, or phenotypic evaluation after delivery. Of the 4883 patients that underwent first

trimester aneuploidy screening, there were 22 fetuses diagnosed with trisomy 21. The detection rates for a 5% false positive rate and a 1% false positive rate were 90.9% and 77.3%, respectively.<sup>23</sup>

With regards to forgoing screening tests and using old guidelines to offer diagnostic testing to women over 35 years of age, using data from the SURUSS, Gekas et al. recommend that scheduling amniocentesis for women  $\geq 35$  years of age without a prior screening result is not cost effective and may produce approximately 7 times the number of procedure related losses than contingent screening.<sup>20</sup>

Problems acknowledged in the studies that affect effectiveness, particularly for integrated screening, were time of entry into prenatal care and non-compliance with additional procedures. Approximately one-third of pregnant women seek prenatal care after the first trimester,<sup>20</sup> which makes them ineligible for integrated screening. Non-compliance with completing the second-step of integrated screening has been as high as 25%.<sup>3</sup>

### ***Screening and Diagnostic Testing Uptake***

Uptake of prenatal screening for Down syndrome is quite variable depending on age, year, location, and number of people investigated, but seems to range between about 50% and 90%. Diagnostic testing is more dependent on risk level and result of a positive screening test. An Australian study that linked screening results with the state birth registry and birth defects registry aimed to map screening pathways and determine uptake of prenatal diagnostic testing. Of the 126,305 births, 65,692 (52%) had a prenatal test for Down syndrome, most being screening tests. Of the 3,349 with an increased screen result, 2,390 (71.4%) proceeded with a diagnostic test. 2.5% of women with a low risk result also opted to undergo diagnostic testing.<sup>24</sup> In the United States, screening uptake appears to be somewhat higher, with about 70% of women in the United States have maternal serum screening and/or ultrasound screening to detect risks for common birth

defects during pregnancy.<sup>25,26</sup> In another study in San Francisco, California, where providers are required by state law to offer prenatal screening for Down syndrome, most women younger than 35 years had prenatal testing (84.8%). 80.4% started with screening and 4.4% went straight to invasive testing. Approximately the same proportion of women 35 and older underwent testing (88.2%), but many more (53.5%) started out with invasive testing.<sup>27</sup> In another study, among women who had already undergone prenatal screening for trisomy 21, 77.6% of women who received an estimated risk of 1:300 or more underwent invasive diagnostic testing; of women who received an estimated risk of less than 1:300 had invasive diagnostic testing.<sup>28</sup>

A randomized controlled trial was conducted in the Netherlands with three groups: those being offered nuchal translucency measurement, a second trimester serum test, and a control group. Researchers had to get special Ministry of Health permission because offering prenatal screening for Down syndrome is not permitted routinely in the country. Of women offered screening, 53% accepted the NT measurement and 38% accepted the maternal serum test.<sup>29</sup>

### ***Factors Influencing Choice to Undergo Screening and Diagnostic Testing***

A review of the literature on decision-making around the topic of prenatal screening for Down syndrome revealed several general themes of what motivates pregnant women and their partners to decide to undergo screening or not. Interestingly, some of the motivating factors that deterred some people from screening encouraged others to undergo screening, and often these differed by risk-status. Most of the studies were smaller, qualitative studies consisting of interviews, surveys, or focus groups. This section will highlight the overarching themes of decision-making influences discussed in the literature.

## ***Risk and Anxiety***

Most of the studies indicated that risk and anxiety are in some way related to how pregnant women perceive prenatal screening and diagnostic testing. These risks include individual risk of having a fetal Down syndrome diagnosis as well as risks associated with the tests themselves, such as false positives, missed diagnoses, or in the case of diagnostic testing, iatrogenic miscarriage. Associated with both individual and testing-related risks are anxiety and stress, both that screening tests would cause more anxiety and that they may relieve much anxiety.

Because increased age is a risk factor for having a fetus with Down syndrome, it is not surprising that many studies found age to be associated with greater screening and diagnostic testing uptake. Van den Berg and colleagues found that an increased risk of having a child with Down syndrome was one of the top three reasons women chose to undergo screening (15% of test accepters).<sup>29</sup> A relative risk level in which a woman is comparing her risk result to that of another person with her characteristics, as opposed to an absolute risk level may also play a role in decision to test, particularly for diagnostic testing. In an Australian uptake study, women whose screening results revealed an increased risk from their *a priori* risk were more likely to have a prenatal diagnostic test than those who had an increased risk result but the numerical risk decreased from the *a priori* risk (75.9% vs. 59.7%).<sup>24</sup> However, a qualitative study among parents of children with Down syndrome by Kelly et al. revealed that of the approximately one-third of participants that had a subsequent pregnancy after the child with Down syndrome, most (three-quarters) did not undergo prenatal genetic screening.<sup>30</sup> The large rate of declining testing among this high-risk group may indicate that increased risk is not always a decision factor, and may be mediated by personal experience with disability.

Consideration of risk, particularly due to advanced maternal age should not be taken as an indicator on its own. Because age has been used as a factor in determining standard of care



practices to offer amniocentesis for decades, it is difficult to determine whether it is the individual risk level itself or the medical and societal expectation of genetic testing for older women that is the determining factor. For example, Farrell et al. found that despite the updated ACOG recommendations and evidence that all women are at risk for fetal aneuploidy, patients discussed advanced maternal age as the primary indication for testing and felt that younger women would not need to undergo aneuploidy screening.<sup>31</sup>

While increased individual risk was frequently a main reason women chose to accept testing, these were often balanced by risks that could arise from the tests themselves. Feelings were generally mixed about whether women felt comfortable with the low-risk nature of screening and diagnostic tests, or felt they could cause more harm than good. Van den Berg et al. found that another primary reason for accepting testing was the “favorable characteristics of the screening test” (18% of accepters gave this reason).<sup>29</sup> On the other hand, as a part of this same study, they found that among those people declining prenatal screening, 42% listed “unfavorable characteristics of the screening test” as a reason and 32% named adverse characteristics of the invasive tests as a reason.<sup>29</sup>

Women considered immediate risks, but also thought in terms of downstream risks that might occur. Markens et al. found that most women declining screening tests did so due to the risks that the tests may ultimately confer, such as amniocentesis, miscarriage, and abortion.<sup>32</sup> For women considering whether or not to undergo amniocentesis, risk of miscarriage was an even greater consideration. In a study of women’s acceptance of diagnostic testing. Among the 5 of 11 women who chose not to opt for amniocentesis, 3 said their concern for miscarriage was an important factor.<sup>33</sup> In particular, problems with fertility may increase this fear. If women had previously had difficulty maintaining pregnancies, they were less likely to accept testing, particularly amniocentesis.<sup>34</sup>

Since no screening test is perfect, and the purpose is to be a first line of detection, one must find a balance between the risk of not detecting a case of Down syndrome, and the risk of causing unnecessary worry and medical intervention due to a false positive. Mulvey et al. surveyed 120 Australian pregnant women entering prenatal care and interested in prenatal screening to determine whether they would prefer a screening test with a higher detection rate or a lower false positive rate. A majority (n=80) preferred a lower false positive rate, with the reason being minimizing risk of miscarriage if a diagnostic test were indicated. More women in the older age group (37 years and older), however, chose the test with the higher detection rate (64% of them). Those choosing a higher false positive rate stated they would prefer to miscarry rather than miss a diagnosis of Down syndrome.<sup>35</sup>

Although patients recognize the physical risks associated with screening and testing, Farrell et al. found that many were much more concerned about the emotional sequelae associated with screening.<sup>31</sup> Some women wanted to undergo testing to ease anxiety that there is something wrong. In a small, interview study, one woman felt that the screening test was not an invasive procedure, and thus, not a harmful procedure to her, and could confirm that everything was going well.<sup>36</sup> In another study of knowledge about prenatal testing, researchers found that several women accepted testing because they wanted to be sure everything was okay in their first pregnancy, but had more of an intuition and felt there was less necessity for testing in their second pregnancy.<sup>34</sup>

Stress and emotional attachment to the fetus were common themes discussed in interview studies. One woman, who declined screening said, "Everyone with any kind of feeling would feel stressed if they found out that something might be wrong, especially because the whole pregnancy thing is a very unknown to a lot of women, especially if it's your first time around. You don't know what to expect; you don't know what's going on in your body, and to be kind of wary of something else being wrong adds undue stress to that whole adjustment period to your life."<sup>34</sup> Several women

in another study also thought making a decision for diagnostic testing or termination would be even more difficult after screening with an ultrasound. One woman changed her mind through the process of screening. "It became a bit different when I saw the little baby with hands and feet and fingers and toes.... There was no point for me to risk anything by amniocentesis, because I had already made a decision...I would have accepted the amniocentesis if I hadn't gotten the early ultrasound." <sup>37</sup>

### ***Ability to Take Action***

In the van den Berg study, researchers found that the primary reason for accepting prenatal screening was to gain knowledge about the health of the fetus (50% of accepters).<sup>29</sup> Prenatal screening provides the opportunity to undergo diagnostic testing to determine whether a fetus has Down syndrome or not. This knowledge can give parents the opportunity to terminate the pregnancy or to be better prepared for raising a child with a disability. While the tests cannot generally give information about the severity of the condition, they can often help couples take steps to be better prepared.

In general, women who were more likely to terminate a pregnancy of an affected fetus were more likely to test (OR 2.94,  $p=0.002$ ).<sup>27</sup> Conversely, when physicians were asked for the primary reasons they think women might decline screening, 63% of respondents suggested that it was because they would not terminate a pregnancy due to Down syndrome.<sup>38</sup> However, in their analysis of fetuses with a congenital malformation, Peller and colleagues found that while prenatal screening in the 88 fetuses with Down syndrome (ultrasonography, amniocentesis, CVS) increased significantly from 16.7% in 1974 to 91.7% in 1999, the termination rates fluctuated and did not increase within that same time period.<sup>39</sup> This may possibly indicate that couples feel that there is value in knowing the status of a fetus even when termination is not part of the consideration for testing. Among some of the more nuanced reasons people gave for wanting to know in advance was worry that the child

would end up with no one to care for her/him because the parents were old.<sup>37</sup> or concern about how having a disabled child might affect another child in the family.<sup>34</sup>

### ***Personal Values***

Personal values were also provided as potential factors in deciding whether or not to undergo prenatal screening. These values included beliefs about religion, ethics, abortion, and quality of life. People with strong religious beliefs were less likely to undergo prenatal screening for Down syndrome. In the Netherlands, where prenatal genetic screening is not offered routinely, 53% of women who were offered the screening accepted the NT measurement and 38% accepted the maternal serum test. Test uptake was only 21% among women who reported being more actively religious.<sup>29</sup>

In semistructured interviews, Etchegary et al. found that many women suggested feelings that the option to end a pregnancy because of an anomaly should not lie in human hands. One woman said, "I find human life should be valued no matter how it is, you know? God has chosen you to have children, and He's decided what kind of children you should have...so, you know, if He decides to send you a child that's not quite as healthy as we'd want, well gee, life's not perfect, you know?"<sup>34</sup> Another of the participants said, "Well, I think when it comes to any type of genetic testing, I would always go back to the medical ethical book.... What is ethical? What are we trying to create? We have science and technology available to us, what are we going to use that for? Is the goal here to create an Aryan race, you know?...So that has to be considered too." <sup>29,34</sup>

Other women declined screening because they were generally opposed to abortion. In the study conducted by van den Berg et al., 15% of participants that declined screening stated a reason for doing so was "being against abortion".<sup>29</sup>

Others were not opposed to abortion, but thought that quality of life should guide their decision. In Iceland, a study by Gottfredsdottir et al. found that most participants who declined

screening did so because they felt that Down syndrome was not severe enough to terminate a pregnancy. It should be noted, however, that disability law in Iceland reflects the country's commitment to providing comprehensive services to allow disabled people to live independently.<sup>36</sup> This was evident, as all the participants (n=20) had a positive attitude toward Down syndrome. Eight of the participants emphasized that all parents want a healthy child, but felt that diversity in ability and health should be maintained in society.<sup>36</sup> One man commented that, "people have been born with various kinds of anomalies but lived a happy life."<sup>36</sup> Quality of life from an unborn person's perspective, however, is difficult to assess. In another interview study, one woman described how she would feel unable to choose, were she to become pregnant again. "See, I sit on both sides of the fence almost, you know. I don't know what decision I would make if I was pregnant again and I knew the exact same thing was going to happen...and maybe that's why I haven't wanted another kid because I don't want to have to make that decision, because it would be very hard, you know. Because I see people with Down's syndrome and things like that that have a very full and very meaningful lives. And I would hate to prevent something like that. But yet, making someone go through – or knowing someone was going to go through what (her child) has gone through, with all of his medical problems, would be hard to think that I may – that I willingly made that decision knowing that I was going to put him through that... It's a question, I don't know... That people would abort children just for having one little flaw. Or trying to make the perfect baby. None of us are perfect. I don't know, it just kind of bothers me. It's kind of like messing with things that we have no right messing with."<sup>30</sup>

### ***Experiences with Disability***

Personal experiences with disabilities, or knowing about the experiences of family or friends with disabled children had a strong influence on decision to undergo testing. Typically, greater knowledge about experiences with Down syndrome was associated with people choosing to

undergo screening, while a lack of embodied knowledge about personal or familial illness tended to be associated with declining testing.<sup>34</sup> In one study, of 79 women who had experiential knowledge of congenital anomalies in their own families, 76% accepted screening. They were more likely to accept prenatal screening than those without personal experience (63% accepted,  $p=0.017$ ).<sup>40</sup> It is likely that experiences with disability were more often associated with testing uptake because they both gave people the knowledge that they would definitely want to terminate a pregnancy or would definitely want to be prepared to raise a child with Down syndrome. One who accepted screening and later terminated a pregnancy diagnosed with Down syndrome noted, "...Having a best friend with a Down syndrome child, discussing it with her, what are the impacts on your life and what did you give to your other child as a life,...it was easy to decide that we didn't want to go that way. We preferred to go through the abortion."<sup>34</sup>

### ***Demographic Characteristics***

While it seems likely that demographic characteristics would play a role in decision to undergo prenatal genetic screening, the studies reviewed indicate it is inconclusive as to whether they actually do. There is little evidence of differences in accepting or declining prenatal screening for Down syndrome by race or ethnicity. This may be due to the fact that few of the studies even addressed race and ethnicity at all. In the one study that directly investigated race and ethnicity, race or ethnicity was only a significant predictor of decision to test among women aged 35 years and older. African-American women had lower odds (OR 0.17, CI [0.06-0.45]) of undergoing prenatal testing.<sup>27</sup> The authors stated that their population may still be rather homogenous, for example, the Mexican Americans being rather acculturated to the United States.<sup>27</sup>

Socioeconomic status may or may not play a role in decision to accept or decline prenatal testing. Kupperman et al. found that women with higher incomes (OR 1.22,  $p=.017$ ) and education (OR 1.31,  $p=.016$ ) were more likely to undergo screening.<sup>27</sup> Van den Berg et al., however, found that

test uptake was lower for women who were highly educated versus those overall (42% vs 53%).<sup>29</sup> Women of higher socioeconomic status may value adverse events differently than those of lower SES. In a study of preferences around screening of pregnant women in Chicago, the mean composite utility score, or an economic measure of relative satisfaction, for the birth of a child with Down syndrome (.73) was not significantly different from the mean utility score for miscarriage (.76). However, women with college degrees, who were married, who were non-Christian, who had a family income of at least \$60,000 per year, and who desired prenatal diagnosis or termination of an affected fetus had composite utilities for Down syndrome that were significantly lower than that for miscarriage.<sup>41</sup>

Acceptance of prenatal screening for Down syndrome may also vary by geographic region. Among a national sample of ACOG physician survey respondents, physician estimates for screening acceptance were highest in the Northeast and West regions at 71.77% and 70.34%, respectively. Estimated screening acceptance rates were lowest in the South and Midwest, at 59.11% and 69.84%, respectively. These are rates for patients under 35 years of age; acceptance among patients 35 and older was higher in all regions.<sup>38</sup>

### ***Influences of Partners, Family, and Friends***

The opinions and experiences of others important in the life of the pregnant woman were important in choosing whether to undergo screening. Sometimes these decisions were made independently or in collaboration with the partner. Gottfredsdottir et al. explored the role of the partner in decision-making, and how perceptions and expectations about screening differed between women and men. The researchers independently interviewed both members of heterosexual couples expecting a child, and found that although the couples claimed the decision to accept screening was mutual, when men were asked how they talked about the decision and how they understood the screening, they claimed it was the woman's decision to undergo screening.

None of the men had sought information on their own initiative, and none had discussed screening or the pregnancy with anyone other than his partner.<sup>36</sup> Men also tended to view screening tests differently than women. Men's expectations related more to the technical effectiveness, while women's expectations were a wish for a healthy baby. Men tended to use words like "safety" and "risk".<sup>36</sup> In some cases, male partners provided support for women in making difficult decisions. In a Swedish interview study about prenatal screening and diagnostic testing, the male partner's role was most obvious during decision-making about amniocentesis. "My husband was really calm and like, 'there's always a risk.' He handled it well and did absolutely not think we should do the amniocentesis."<sup>33</sup> In a study of women aged 37 years and older in Victoria, Australia, 70% of women reported their partners strongly influenced their decision. There was no significant difference in the importance of the partner role in the testing group and the no testing group, with 79.8% of the women in the prenatal test group saying the partner had a strong influence on their decision, compared with 73.9% of women in the non-prenatal test group.<sup>42</sup>

Partners are not the only people who influence a woman's decision of whether or not to undergo prenatal screening. In Victoria, Australia in the prenatal test group, 22.0% were influenced by a friend and 21.4% by a parent. These percentages were 11.6% and 19.4%, respectively, for the no prenatal test group (Jacques, 2004).<sup>42</sup> Not only are decisions influenced by friends and family, but women are both passively receiving and actively seeking information from these groups. In Iceland, Stefansdottir et al. found that 40% of women received information from friends and 22% from relatives.<sup>40</sup> In particular, interview studies reveal that women sought information about others' personal experiences with prenatal screening. "I did have some hesitancy in terms of whether to do the procedure... so I consulted with, you know, relatives that were pregnant recently or were at the same age, and whether they had decided to go ahead with it or not."<sup>43</sup> In the study investigating women's empathetic knowledge about screening, Etchegary et al. found that women's empathetic



knowledge about screening and disability was acquired most often from friends' and family members' experiences with raising a child with a disability and/or with screening procedures.<sup>34</sup>

Among test accepters, vivid empathetic knowledge included using friends' experiences with disabled children to think about how their own life with a disabled child would be to either prepare for such a life or weigh the option to terminate the pregnancy. Among test decliners, vivid empathetic knowledge consisted of friends' experiences with false-positive test results and the resulting stress.<sup>34</sup>

Women are also consulting other sources for information about screening and testing and reaching out to peers through the use of information technology. Stefansdottir et al. found that 22% of women in their screening study turned to the media for information. This is the same proportion seeking information from relatives.<sup>40</sup> One of the respondents in an interview study revealed the following: "People have many questions. But they rather ask each other than the professionals. If you go to such Internet sites, they ask about the more horrible things. They should have consulted the GP a long time ago, right? People are a bit afraid of getting in touch with the health care system. Instead, it's easier to ask someone you don't know from the Internet." <sup>37</sup>

### ***Influences of Medical Care Providers***

Although partners, family, friends, and the internet are important influences in decision-making about prenatal testing for Down syndrome among pregnant women, medical care providers are still the primary source of information about screening. In the Icelandic study, 53% of women said they received information from obstetricians and 46% from maternity care staff.<sup>40</sup> Not only are maternity care providers presenting information to women and couples, they have an influence on the decisions people make, which vary between those receiving testing and those declining testing. Among women in the prenatal test group in the Victoria, Australia study, 76.0% were strongly influenced by a doctor, 25.1% by a nurse, and 42.3% by a genetic counselor.<sup>42</sup> For those in the no

prenatal test group, 44.7% were influenced by a doctor, 14.8% by a nurse, and 20.6% by a genetic counselor.<sup>42</sup> Overall, women who did not receive prenatal screening tests stated they were significantly less influenced by medical providers than those who did undergo screening.<sup>42</sup>

In the United States, screening tests for Down syndrome are generally being routinely offered to pregnant women as a component of prenatal care. ACOG fellows and junior fellows (n=517) throughout the US were surveyed about their practices. Although not generalizable to the entire population of health care providers of obstetric care, offering prenatal genetic screening for Down syndrome was ubiquitous among ACOG fellow survey respondents. Ninety-five percent of respondents offered Down syndrome screening to all pregnant patients. Ninety-two percent routinely offer amniocentesis for chromosome testing to patients at least 35 years of age, and 15% offer it to patients under 35.<sup>38</sup>

Physicians indicated that they provide a large amount of information and counseling to patients about prenatal Down syndrome screening themselves. In the ACOG survey, 85% of respondents counseled patients themselves before Down syndrome screening. Fifty-five percent provided written information. If a patient screens positive in a first or second trimester screening test, 86% of respondents referred the patient to a genetic counselor or genetics service while 55% counseled patients themselves. 5% indicated that no genetic counseling service was available within a 90 minute radius.<sup>38</sup> One could infer that this number may be higher in places where Certified Nurse Midwives are the primary providers of maternity care. Seventy-eight percent of OB-GYNs personally counseled patients before diagnostic testing, and only 32% referred the patient to a genetic counselor or genetics program for pretest counseling. If a pregnancy was diagnosed with Down syndrome, 55% of OB-GYNs counseled the patient themselves and 89% of Maternal and Fetal Medicine physicians counseled the patient themselves.<sup>38</sup>

Though most physicians providing obstetric care are providing information and counseling patients on prenatal screening and diagnostic testing for Down syndrome, they may not be the most qualified people to undertake this role. Investigators in the ACOG study also asked a series of basic knowledge questions to physicians about prenatal testing procedures, detection rates, and patient risk. The percentage of people giving correct responses ranged from 44% to 84% for specific questions among obstetrician-gynecologists and 43% to 94% among maternal and fetal medicine specialists. Despite a large proportion of physicians that answered the knowledge questions incorrectly, 98% of respondents said they were “somewhat qualified” or “well qualified” to counsel patients about Down syndrome screening and risk, 96% to counsel a patient at elevated risk of fetal Down syndrome, and 91% to counsel a patient with a positive screening test for Down syndrome.<sup>38</sup>

#### ***Patient Understanding of Prenatal Screening Tests and Trust in the Medical Establishment***

Because women are using comparisons of risks (having a Down syndrome fetus, missing a diagnosis, iatrogenic miscarriage, potential anxiety, etc.) to evaluate whether or not to undergo screening, the understanding of *a priori* risk and the risk result from a test is important in decision-making. In the study conducted by Ahman et al., in which 11 women were interviewed, almost all of them were able to recount their risk ratios correctly, but several still had difficulties understanding the significance of these risks.<sup>33</sup> Aune et al. found that not all women had the same understanding of the calculated risk and used different methods of risk assessment to make decisions about screening. Some thought the proportion was informative enough and compared that with risk in younger women. Some compared the risk of miscarriage after amniocentesis with their given risk for a baby with a chromosomal anomaly to determine whether to undergo amniocentesis.<sup>37</sup> Some women expressed frustration with the way risk was presented. One woman stated in an interview, “I think risk scores can do more harm than good. Can’t you say more than that? Can’t you say more

than a score of 1/550, or you really shouldn't say anything. Because that information, I can't see which reasonable person could act on that." <sup>33</sup>

The method in which information is provided, both about the screening test and the test result could help reduce confusion among women. In a quasi-experimental qualitative study in Iceland, pregnant women in the first trimester of pregnancy (n=379) were divided into an intervention group (n=142) and a control group (n=237). Both received traditional care and information, but the intervention group also received an information booklet about prenatal screening and diagnosis. Women in the intervention group had significantly higher knowledge scores (4.8 vs 3.7,  $p < 0.0001$ ).<sup>40</sup> Although the goal is not necessarily to increase screening acceptance, they also found that women with higher knowledge scores were more likely to accept prenatal screening ( $p < 0.0001$ ).<sup>40</sup>

Framing the message about the risk is particularly important in understanding the test result and *a priori* risk. As Aune et al. note, it sounds very different to say you have a 1 in 20 risk of having a child with Down syndrome than you have a 19 of 20 chance that your child does not have Down syndrome.<sup>37</sup> In the Bekker analysis, people used a decision analysis tool to help aid decision-making about screening. More people in the decision analysis group perceived their screening risk to be a medium risk rather than high risk (Chi-3.8,  $p = 0.05$ ). However, the outcome measures of whether they underwent screening were not different between the group participating in the decision analysis consultation strategy and the control group.<sup>44</sup>

The timing and method which information is presented may also have an effect on understanding of prenatal screening tests, including what they measure, how they are performed, what a positive screening result is, and how one might proceed if she received a positive screening result. In most of the studies in which women were asked about the usefulness of the information received, women generally thought the information they received could be improved. Stefansdottir

et al. asked all women in their study how useful they found the information they received at maternity care clinics for the decision of whether or not to undergo prenatal screening. 63% found the information to be “very useful” or “quite useful.” 37% found the information either “not very useful” or did not complete the question. 57% thought the information was sufficient to make an informed decision, 11% thought it was not, and 28% were unsure.<sup>40</sup> In the Swedish ultrasound study using ultrasound screening to detect soft markers for Down syndrome, 7 of 11 women suggested that information about soft markers before the scan might have made it easier to understand what the findings meant.<sup>33</sup>

In some cases, women were given information about the screening tests without much explanation. In the Icelandic study, one woman explained that she felt that health care professionals needed to explain what prenatal screening entails instead of just saying, “this is an offer.”<sup>45</sup> Many felt that information provided by the health care center wasn’t sufficient enough for them to make decisions.<sup>45</sup> In the same study, 6 of 7 women who had their pregnancies confirmed at a private clinic stated that their obstetrician was in favor of screening and just presented them information about it. Two comments were, “He just handed the form for the screening to me before I left” and “He did not talk about it at all – just assumed that it was something for me.”<sup>36</sup>

The timing during which women received information also made using the information difficult for decision-making about screening. First trimester screening must be conducted soon after the very first prenatal visit, and often women do not even come in time for first trimester screening. Women generally come in for their first visit at 8 weeks or later. “You almost would have had to gone in [for the initial obstetric visit] knowing that it [Down syndrome screening] is an option.”<sup>31</sup> In addition, at the first visit, patients are already given a huge amount of information, “That first prenatal appointment is overwhelming. There is a lot of information presented to you and you don’t necessarily remember everything and you’re excited and you forget what questions

you do have.”<sup>31</sup> In the interview study by Aune et al., women thought that the information given before the screening exam was not good enough as is, and that “once you are there, it is too late.” They mentioned that even if women receive written material, it is they often do not read it.<sup>37</sup> In other cases, women may feel information is given too early to be relevant. In the Swedish ultrasound study, most of the women interviewed had received written information from their health care provider about the ultrasound, but many had not actually read it. They stated that the information was given so far in advance that it didn’t concern them.<sup>33</sup>

Unfortunately, it is difficult to determine how medical providers can improve the provision of information about risk and aid in the screening decision-making process. In a Cochran review on personalized risk communication (though not specific to Down syndrome screening), Edwards et al. conducted a comprehensive review of the influence of personalized risk communication interventions. They found little evidence that these interventions led to informed decision making. Of 22 studies included, there was weak evidence that personalized risk communication increases uptake of screening. Three studies showed a better and more accurate understanding among women of risk perception and three others showed increased knowledge.<sup>46</sup> Grant et al. suggest that a resource such as “Making Decisions About Prenatal Tests for Birth Defects,”<sup>47</sup> could be used as a starting point, prompting the woman to ask her provider questions about tests and herself questions about personal values.<sup>47</sup> Participants in another interview study felt that their health care providers needed to be upfront about the downstream options that may occur after the first screening test for aneuploidy. Many felt that their provider placed more emphasis on the specific screening tests than those other factors (such as whether they would terminate a pregnancy or not), which were the more important key decision-making factors.<sup>31</sup>

Regardless of how information was presented, trust in the medical establishment or in the screening tests themselves was influential in choosing whether or not to screen. In general, people

who were less trusting of the medical system and medical tests were less likely to choose screening. For some, decision to decline screening was rooted in a distrust of scientific probability.<sup>45</sup> There was a perception among some participants that NT screening was unreliable and that screening could never provide certainty.<sup>45</sup> In particular, 5 of 10 women referred to cases where they knew that healthy fetuses were lost from amniocentesis or cases where children with Down syndrome were born after a negative screening result.<sup>45</sup> Some women lacked overall trust in the medical system. Those who felt modern medicine interferes too much with pregnancy were less likely to undergo prenatal screening (OR .85,  $p=.036$ ).<sup>27</sup> However, declining a test did not necessarily indicate distrust in the medical system. Markens et al. found that most women who refused testing were not opposed to the medical establishment or the test itself, and many felt they may make a choice to accept the test in a different pregnancy or a different context.<sup>32</sup>

On the other hand, some people placed great trust in the medical system. In the Finnish interview study, a theme that emerged was that serum screening tests were not of a different nature than other tests during maternity care. For example, one woman made the statement, “When it was possible, I wanted to take advantage of it; it was like a blood-pressure test or other tests like that.” Women were highly trusting of the medical system and their health care provider. One woman said, “I have the principle that all the tests which are done are done for my and my baby’s best interests. It was self-evident to participate. I trust the Finnish maternity care system.”<sup>48</sup> It is important to remember that trust in the health care system is very contextual, both within countries and between countries.

### ***Changing Norms and Routine Practice of Prenatal Screening for Down Syndrome***

Norms around prenatal screening tests and prenatal diagnostic tests are changing; presentation of these options and their acceptance are increasing. In a study of women in the United States determined to have fetuses with malformations, although prevalence of

malformations stayed approximately the same, ranging from 1.35% to 2.43%, the rate of amniocentesis increased from 7% in 1974 and 1979 to 89% in 1994 and 1999. (Two year periods were aggregated because of small numbers). Prevalence of second or third trimester ultrasonography use increased from 19.8% for 1974 and 1979 to 95.3% in 1994 and 1999.<sup>39</sup>

As screening becomes more and more routine, people may be making less of an active choice to accept or decline screening. In Australia, 46% of women reported that first-trimester screening was presented to them as a routine test, 52% as an optional test, and 2% were unsure. Jacques et al. found that women were more likely to be categorized as making an informed choice pre-screening if they reported screening as optional rather than routine (RR 1.26, CI=1.01-1.57,  $p=0.03$ ).<sup>49</sup> In Finland, antenatal care is provided in free maternity care centers and women are offered serum screening free of charge as part of their routine antenatal care. Here, where cost is not an a consideration in deciding whether to undergo a screening test, Santalahti et al. conducted interviews with women who had received a positive screening result and matched controls who had not to determine what motivated them to undergo or decline prenatal screening.<sup>48</sup> Although screening was often presented as “voluntary” or “an option”, 49% of people undergoing serum screening felt it was a “self-evident act.” Only 27% of women described themselves as “actively deciding” about whether or not to have the screening test.<sup>48</sup> These sentiments seem to echo through many industrialized countries. In Iceland, one woman summarized these feelings in saying, “But I haven’t thought it through. However, the doctor felt it was somehow a self-evident act and because of that I just made the appointment for the screening. She said that I should do that and I didn’t think about it further. I just thought, well, this is just something you do when you are pregnant.”<sup>36</sup>

Prenatal screening tests are becoming part of routine maternity care not only because of health providers offering the tests and patients’ increasing demand for them, but are also being



mandated by public policies. Of note, in 1986, the state of California became the first state to mandate all pregnant women who begin prenatal care prior to 20 weeks' gestation be offered AFP screening for Down syndrome and neural tube defects through the California Prenatal Screening Program (<http://www.cdph.ca.gov/programs/pns/pages/default.aspx>). By 1996, 68% of all pregnancies in California were screened, and have continued to rise.<sup>32</sup>

On the other hand, in the Netherlands, Dutch law requires ministerial approval for screening for "serious disorders that can neither be treated nor prevented." This includes prenatal screening for congenital disorders, since the legislature does not consider termination to be treatment or prevention. Therefore, providers may not offer prenatal screening to pregnant women unless they request it. The exception is for women over 35 years of age.<sup>29,50</sup> With ministerial approval, 1159 women were offered the NTM or MST to evaluate level of knowledge, value consistency, informed choice, decisional conflict, satisfaction with decision, and anxiety using questionnaires.<sup>50</sup> Van den Berg et al. found that when screening for chromosomal abnormalities is not introduced as a routine offer, people make their decisions more consciously.<sup>50</sup>

The option to screen for Down syndrome is not only becoming more routine in most developed nations, but has also shifted from only being available in the second trimester to now being an option during the first trimester. Women have mixed feelings about whether first trimester screening is better than second trimester screening, and the timing of screening may influence decisions to undergo screening. Graff et al. found that the vast majority of women who opt for prenatal screening prefer for screening to be carried out in the first rather than second trimester.<sup>51</sup> Some felt that screening could be more of a private decision in the first trimester, when a pregnancy cannot be detected by others, and that people could feel reassured earlier. Others felt that an earlier test might cause them to worry for a longer time.<sup>31</sup> Interestingly, physical and emotional risks of termination were not a large consideration about earlier screening. None of the participants

suggested that earlier diagnosis would be associated with decreased procedure related risks of termination, nor the emotional sequelae that may be more significant in the first trimester than the second.<sup>31</sup>

The fetal loss rate (spontaneous abortion) is fairly high among fetuses affected with Down syndrome. Nearly 80% of fetuses with Down syndrome are lost before birth.<sup>52</sup> The fetal loss rate of trisomy 21 fetuses is approximately 30% after 12 weeks' gestation, and 20% after 16 weeks' gestation<sup>53</sup> and greater than that at earlier gestation. Because of the frequency with which fetuses with Down syndrome spontaneously abort, Down syndrome risk is highest at the time one would undergo CVS and lowest at full term.<sup>47</sup> Earlier screening may result in earlier termination of pregnancies affected that may have spontaneously aborted on their own. This may result in varying psychological effects for pregnant women, as a woman may view a miscarriage differently than a decision to terminate the pregnancy. While this is still a fairly new consideration with the onset of earlier screening, and thus has not really been explored in the literature, it is still an important consideration when assessing women's decision-making processes around prenatal screening and diagnostic testing for Down syndrome.

The availability of a non-invasive diagnostic test likely available in the next few years also has the potential to affect the routine nature of screening and testing for Down syndrome. Many times, women are hesitant to undergo screening because of the potential of being directed to undergo invasive diagnostic testing, and many women refuse diagnostic testing due to the risk of miscarriage. Eliminating that risk may increase the acceptability among women to undergo more diagnostic testing.

## Limitations

Individual studies had independent limitations, but there were some overarching limitations that were frequent among all of the studies. In addition, because of the variability of studies, it is somewhat hard to draw conclusions when comparing across them all. Several of the limitations of this literature review are described below:

- *Many studies did not explicitly state their methodology.* Although most of the studies did share their methods, in general it would have been helpful to know more details about questions that were asked and testing uptake.
- *General themes found from smaller, qualitative studies are not always applicable to other groups.* Because of the nature of decision-making, in that it is fairly individual and variable, most of the studies regarding testing and decision-making were small ( $n < 60$ ), qualitative studies. While these are extremely valuable in determining themes and understanding nuances, it is sometimes difficult to draw conclusions that can apply to larger groups of people.
- *Many of the studies were from countries outside of the United States.* This paper originally intended to focus on decision-making regarding prenatal screening for Down syndrome in the United States, but more than half of the studies were conducted in Europe, Australia, and New Zealand. While they can provide some applicable information about factors around decision-making, cultural relevance and local public policies are important to these decisions, and themes may not be applicable across regions because of the cultural context.
- *Most studies had fairly homogeneous populations.* Participants in most of the qualitative studies were white, middle-class women. In addition, many of the studies were interested in screening and diagnostic testing among women of advanced maternal age, limiting the population even more. Even the studies that aimed to look at differences in race and

- ethnicity and were conducted in fairly diverse locations (e.g., San Francisco, CA) still had fairly homogeneous populations, especially in terms of immigrant acculturation.
- *The studies that were reviewed included others involved in prenatal screening decisions, not just pregnant women themselves* (e.g. health care providers, partners). Although participants in most of the studies around decision-making were pregnant women, a few included partners and health care providers as well. This limits the ability to compare responses, but is important as partner and health care provider perspectives may be important in decision-making processes.
  - *Studies were conducted at various stages of pregnancy and after birth of a child.* Studies were conducted at variable times including before screening, after screening, and after the birth of a healthy baby. Some had several follow-up sessions throughout the pregnancy. The stage of pregnancy, whether or not a person has already decided to undergo testing, and diagnosis of Down syndrome may impose response and recall biases making it difficult to compare across studies.
  - *The level at which different procedures were routine practice was variable and differed with location.* In some cases providers can choose which tests to offer and in others policy may mandate what is permitted. Additionally, cost and availability of tests may differ. This may skew results by how actively a person is making a decision.
  - *The time during which each study was conducted affects testing availability.* Although most articles referenced are from 2000 to 2010, some pivotal articles from before that were included. Changes in types of testing available and its regular use varied with time, and may change opinions about willingness to undergo screening. In addition, many of the prevalence rates for Down syndrome and rates of sensitivity and specificity of tests are from earlier time periods.

- *Few studies looked prospectively from the approach of whether certain criteria led a person to accept or decline screening.* Most studies asked those who had either chosen to accept or decline screening what factors influenced them in that decision. This may be a more appropriate strategy for the multifaceted nature of these types of decisions, but makes it harder to find predictors.

## Policy Implications

The Bush Policy Model provides seven policy evaluative criteria with which to assess policy: autonomy, preference satisfaction, equity, stigma, effectiveness, efficiency, and political feasibility. These criteria provide a framework with which one can analyze the policy implications of prenatal screening and diagnostic testing for Down syndrome, while taking into consideration the decision-making influences of whether to undergo testing. These evaluative criteria are typically used to evaluate the strengths and weaknesses of specific policy options. Although they can be used to create a quantitative summary of the strength of certain policy options, in this paper, they were used as a lens with which to review the literature, and recommendations were developed with the intention of meeting as many of these criteria as possible. The criteria are described here.

**Autonomy.** Particularly in the United States, autonomy over one's health decisions, reproductive choices, and parenting is highly valued. Although health decisions are generally advised by a doctor and often strongly encouraged in one direction, ultimately, it is the patient who makes the final decision. In the case of prenatal screening and diagnostic testing, it is the medical care provider that offers the test to the patient. Should prenatal screening be offered to all pregnant women or only those with a higher risk? Should diagnostic testing be offered to all pregnant women? How can truly informed decisions be made about prenatal screening, particularly as

prenatal screening tests become a part of routine practice? How should other people in the life of the pregnant woman, particularly the partner, be involved in the decision-making process?

***Preference Satisfaction.*** The ability to choose among various options based on competing criteria is also highly valued in the United States. In the case of prenatal screening, there are now several options of prenatal screening and diagnostic tests with varying levels of effectiveness, risk, timing, and cost. The best options should be provided so that people can choose what level and type of screening they are comfortable with.

***Equity.*** An important policy consideration is whether or not the policy is equitable to all people. In the case of prenatal screening and diagnostic testing for Down syndrome, do all people have equal access to services regardless of age, race or ethnicity, socioeconomic status, geographic location, sexual orientation, disability status, and previous knowledge about procedures? Does a policy like California's, mandating screening be offered to all people ensure equity?

***Stigma.*** Policies have the potential to increase or reduce stigma associated with certain groups or individuals. Stigmas around disability already exist and people with Down syndrome are not viewed by society in the same way as people without the disability. Will making Down syndrome screening a part of routine prenatal care increase stigma of those with disabilities? Is there potential to increase stigma against the mother because she either did not prevent her child from being born with Down syndrome or decided to terminate a pregnancy due to Down syndrome? Could screening lead to a reduction of disability services to those who need them?

***Effectiveness.*** As technology gets better, screening tests get more effective. When considering screening tests, one must determine which criteria are most important to effective testing. Women expressed desire for tests with high detection rates and low false positive rates. Improving effectiveness would aid in decision-making of whether or not to undergo testing. What is

the outcome indicator of interest? Is it the greatest number of Down syndrome cases detected? The greatest number of live births with Down syndrome averted?

**Efficiency.** In addition to being effective, efficiency is also important. Prenatal screening for Down syndrome can be costly, as can the associated tests that result from a positive result. What cost should society bear for prenatal screening and testing? Should cost-effectiveness that uses lifetime costs of disability services be considered when developing policies about screening for Down syndrome?

**Political Feasibility.** Because of varying viewpoints among divergent political parties, political feasibility is often one of the most difficult criteria to meet. With regards prenatal screening and diagnosis, is it most feasible to develop a public policy, or leave information and availability of screening to the individual? If public policies are created with which to provide or encourage screening, does society then have a responsibility to provide services for any outcome of a screening test, whether it be termination of an affected fetus, or bringing an affected child into the world? Is it politically feasible to publicly provide services beyond screening?

## Recommendations

In thinking about the themes brought up in the reviewed literature, policy evaluative criteria, and associated questions, I propose the following recommendations:

1. Prenatal screening for Down syndrome should be offered to all pregnant women. It is clear from the evidence and practice guidelines that although increasing age does increase risk of Down syndrome, it is difficult to say at what point that risk is “too high.” Screening should be recommended to both younger women and older women to avoid chorionic villus sampling and amniocentesis if possible (even though risk of miscarriage is low). Although

screening should be encouraged, women should be able to decide if they want to forgo screening and proceed with diagnostic testing.

2. Ensure that selecting screening is a conscientious decision, not just one “by default”.

Although prenatal screening tests are becoming more and more routine as a part of prenatal care, care providers should still present these tests as an important decision and encourage patients to think about what they would do and how they would feel in the case of getting a positive or negative result.

3. Information should be provided about both the testing procedure and the condition itself.

Often, information provided to patients about prenatal screening is primarily about the screening tests, such as the process and timeline in which the testing occurs. Less often are patients provided with information about the disease or condition that is being screened for (in this case, Trisomy 21). Provide information about the possible severity of disability and the possible care that might be required.

4. Information about Down syndrome should include consideration of the family experience of living with a family member with Down syndrome. Many women expressed concern about the way in which having a child with Down syndrome might affect their other child or children. While some families may find it difficult to adapt to the ongoing challenges associated with raising a child with Down syndrome, others are able to endure, survive, and even thrive.<sup>54</sup> Therefore, pregnant women and partners should be aware of the family experiences of others when making their decision of whether or not to undergo screening.

5. Providers should have a conversation to discuss the screening tests close to the time of screening/testing, preferably not only at the first prenatal visit. Many women discussed how the first prenatal visit is overwhelming with information and how screening was not discussed near the time of the procedure.



6. Health care providers should seek out educational opportunities about Down syndrome and prenatal screening. Since most physicians were doing at least some counseling themselves, they should be trained and qualified to do so, particularly if they're providing patients with information and decision-making assistance on a regular basis. More continuing education opportunities should be provided to maternity care providers.
7. Provide decision tools about screening and how one would further decide what to do with screening information. Ensure that patients understand this information, and offer a referral to a genetic counselor if they do not.
8. Providers should clearly outline what a "positive" screening result means. Ensure that patients are aware of the difference between screening and diagnostic testing. Determine some risk values with which to compare the risk, such as *a priori* risk level.
9. Include partners in information and decision-making counseling when possible. Include discussion of topics that are most important to male partners such as effectiveness of testing. Encourage partners to think about how their lives would change depending on what decision they made regarding screening and diagnosis.
10. Women and partners should be supported in whatever decision they choose to make. In the case of a positive diagnosis for Down syndrome, health care providers should help link families to support services, whether that be abortion support groups, disability support groups, etc.
11. There should be consistency and congruency among publicly funded programs and insurance providers. If a program or providers funds prenatal screening, it should also fund the steps that may result from a positive screening test, such as prenatal diagnosis and elective termination.

12. Be aware that women turn to other sources for information about prenatal screening, including the internet, friends, and family. Provide information about the most reputable sites for health information.
13. More research about decision-making factors related to prenatal screening in the United States is needed.

## Conclusions

As prenatal screening continues to evolve and improve in effectiveness and increasingly become a part of routine prenatal care, consideration for decision-making about these procedures must not be ignored. So often, the terms “informed consent” and “informed decision” are thrown around as an ideal goal, but what do these terms mean in the context of prenatal screening and testing for Down syndrome? It is also important to distinguish between satisfaction and informed decision. Green et al. sum it up well when they state, “Nearly all clinical guidelines for offering genetic tests stress autonomy in decision making, and most ethical guidelines emphasize informed consent for testing and the importance of having adequate social support during the testing process (e.g., World Health Organization, 1997). It has been pointed out that studies assessing the quality of decision making in pregnancy generally do not take into account that after the delivery of a healthy baby, most women are ‘satisfied customers,’ which is not necessarily the same as ‘having made informed decisions.’”<sup>55</sup> To fully aid informed decision-making, policies and practices must take into consideration the factors influencing women’s decisions of whether to undergo screening, including risk; emotional factors; ability to take action; personal values; experiences with disability; demographic characteristics; partners, family, and friends; medical care providers; and trust of the medical establishment.

When thinking about clinical practice and broader public policies, it is important to consider how to include groups outside of the medical profession. These include those most familiar with screening, diagnosis, and disability, such as genetic counselors, women who have been pregnant and faced the choice to undergo screening, and those who have been affected by Down syndrome either directly or indirectly. Families who have been affected by Down syndrome can share valuable information on the challenges associated with Down syndrome and ways to cope, as well as the joys and successes. In particular, figuring out how to include people with disabilities in policy-making processes is essential, as they have often been left out of the discussion, but many of the arguments for and against testing (such as quality of life), directly affect them.

Most importantly, women and their partners should understand that these screening tests are a choice, and on their own accord or with the help of others, should be able to make decisions that they understand and feel comfortable with.

In summary, deciding whether or not to undergo screening on an individual level, and determining practice and policy guidelines on a population level must balance two related but conflicting issues that are highly valued in the field of maternal and child health. Rayna Rapp has described these as: 1) to champion the reproductive rights of women, and 2) to support adequate, nonstigmatizing, integrative services for all children.<sup>56</sup>

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