An Assessment of Genetic Counselors’ Opinions on How Non-Invasive Prenatal Diagnosis May Impact Genetic Counseling Services

Master’s Thesis

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By
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ABSTRACT

An Assessment of Genetic Counselors’ Opinions on How Non-Invasive Prenatal Diagnosis May Impact Genetic Counseling Services

A thesis presented to the Genetic Counseling Program

Graduate School of Arts and Sciences
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By
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Non-invasive prenatal diagnosis (NIPD) is a promising prenatal diagnostic technology that is currently being developed. The premise behind it is that fetal DNA can be detected in maternal blood plasma and potentially enable women to pursue reliable and timely prenatal diagnosis, while eliminating the risk of miscarriage associated with current methods. The goal of this study was to determine how genetic counselors believe the integration of NIPD would impact the field of genetic counseling. We recruited prenatal genetic counselors from the National Society of Genetic Counselors listserv for participation in an anonymous, online survey. A total of 206 counselors completed the survey, which consisted of 25 multiple-choice and 4 open-ended response questions. The questions were designed to ascertain the counselors’ opinions regarding NIPD, as well as elucidate how the technology might affect patient decision-making, the role of genetic counselors, and other aspects of prenatal genetic counseling services. Our results showed that 87.4% of counselors believed NIPD would
be an important asset to prenatal care. The majority of counselors foresaw NIPD being clinically available within five years, and anticipated that it would be offered to all women in addition to the current prenatal tests. Only a very small percentage (6.8%) predicted NIPD would become a replacement diagnostic technology. Although the majority of counselors anticipated that their time spent counseling and educating patients would not change, they acknowledged that introducing NIPD would have ethical implications, including challenging the process of obtaining proper informed consent. Because of this concern, respondents recommended that all women be offered genetic counseling services before any prenatal testing. Our findings suggest that the introduction of NIPD will require increased attention to patient understanding, as well as the development of educational tools to help prepare patients and providers for the clinical, ethical, and logistical issues that will inevitably arise.
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Introduction

Background:

Testing for birth defects and inherited diseases during pregnancy first became possible in the late 1960’s with the development of lab techniques that were able to grow fetal cells found in amniotic fluid. A procedure known as amniocentesis, allowed access to the cells by removing a sample of amniotic fluid from the uterus. Since the cells contained the genetic blueprint of the developing fetus, this advance allowed chromosome abnormalities, such as Down syndrome, and certain biochemical disorders, to be detected during the second trimester of a woman’s pregnancy. Another method of obtaining the fetal cells, chorionic villus sampling (CVS), was later developed to avoid the medical and psychological complications that can accompany the later diagnosis offered by amniocentesis. This has been used as a first-trimester prenatal diagnostic technique for over thirteen years. (Roberts, 2007)

Today, amniocentesis and CVS are typically indicated in cases where the mother is of advanced maternal age (over 35), there is a family history of an inherited condition that can be detected prenatally, structural defects are noted by ultrasound, or there are abnormal prenatal screening results for various chromosomal and inherited conditions. (Roberts, 2007) By directly sampling the fetal genetic material, both tests are considered to be highly accurate in detecting fetal chromosomal abnormalities. CVS has a sensitivity estimated between 98.9% and 99.6% and a specificity of 99.8%, and
Amniocentesis has a 99.3% sensitivity and a 99.6% specificity, however these numbers can vary according to the specific lab test that is being performed on the sample collected. (Alounini, 2007) CVS has the advantage of being performed as early as the tenth to twelfth week of gestation, and there is a 1% risk for miscarriage. Amniocentesis, on the other hand, cannot be performed until the sixteenth to eighteenth week of gestation, but the risk for miscarriage is lowered to approximately .5%. (Alounini, 2007) Risk numbers range slightly depending on the hospital practice, and some are quoted as low as .2%.

It is because of these procedure-related risks, and how they weigh against the value of the information obtained, that many women opt out of having prenatal diagnostic testing. For some women, despite wanting the information or considering it valuable, they are simply not willing to risk miscarriage. If a woman chooses not to have diagnostic testing, the most knowledge she can gain is through combining ultrasound findings with maternal serum screening. Fetal ultrasounds image the fetus to measure its development and search for potential problems. Maternal serum screening is a maternal blood test that measures biochemical markers associated with fetal abnormalities and provides a risk assessment. Miscarriage is not associated with either of these screening methods, however they are not diagnostic tests. This is clear with the detection of Down syndrome, for example, where fetal ultrasound and maternal serum screening combined has only a 90% detection rate, with a 5% false positive rate. (Alouini, 2007) This often places women in a stressful position where they need to make a very difficult decision: know with risk, or not know at all.
Evolving Technology:

In 1997 a research group headed by Y.M Lo were the first to report the existence of free fetal DNA (fFDNA) in the maternal circulation. (Lo, 1997) The work stemmed from a previous study where tumor DNA was detected in the plasma and serum of cancer patients. To determine if the fFDNA found in the plasma and serum could potentially be used for prenatal molecular diagnosis, the authors did a similar search for fetal DNA in pregnant women, and they discovered that fetal DNA did indeed circulate in maternal plasma. (Lo, 1997, Stroun, 1998) In fact, fFDNA compromises 3% of total free DNA in the maternal circulation, and increases as pregnancy progresses. (Lo, 1998) These findings had significant implications for the possibility of non-invasive prenatal diagnosis (NIPD).

The next step was to determine whether aneuploidies, such as Trisomy 21 (Down syndrome), were associated with quantitative variations of circulating fetal DNA in maternal plasma. Using real-time PCR analysis of maternal plasma, researchers discovered that the concentration of fetal DNA in the maternal circulation is higher in Trisomy 21 pregnancies than in euploid pregnancies. (Lo, 1999) They realized how valuable this information would be in assessing chromosomal abnormalities of a fetus, and therefore making a diagnosis, and from that point the concept of non-invasive prenatal diagnosis grew.

It was speculated that NIPD would be able to give women the best of both worlds: diagnostic accuracy with no risk of miscarriage. With a simple blood test, diagnosis could be given with high certainty during the first trimester of pregnancy, sometimes as early as the seventh week of gestation. This is significantly earlier than what can be
achieved using traditional methods, which provide diagnosis after the tenth to twentieth week of gestation. Although not yet widely used in clinic, it is currently possible to determine fetal sex, establish Rh genotype of the fetus, and diagnose genetic disorders, aneuploidies, or carrier status for paternally inherited mutations. In addition, the sensitivity of this technique produces highly accurate results. One recent study reported 90% sensitivity and 96% specificity for the detection of Down syndrome using NIPD (Chiu, 2009).

Nevertheless, there are considerable technological strides that have to be made regarding the efficacy of NIPD before it can be used routinely in prenatal practice. Despite many attempts to isolate the fetal cells in sufficient quantities from the maternal blood to make a fetal diagnosis, fetal cells constitute only a tiny proportion of the total maternal blood cell population. There seems to be sufficient ffDNA in the blood plasma to determine fetal RhD genotype and fetal sex, but not to detect an aneuploidy. Current research is aiming to increase the proportion of fetal to maternal DNA, and both chemical and size separation approaches are being explored. (Chiu, 2009) To date, there have not been any large-scale studies evaluating this new approach, and much work remains to be done before this could be a practical technology.

*Potential Effect on Prenatal Genetic Counseling:*

It is important to try to understand how NIPD may affect the field of genetic counseling so that health professionals can anticipate necessary changes and ensure smooth integration into practice. The first step to achieving this is understanding how patients perceive the risk associated with testing and how they make their decisions
regarding prenatal testing. Reports suggest that there are generally two categories of women when it comes to how they assess risk of prenatal testing: those who choose diagnosis because they need certainty and reassurance, have high anxiety, or are possibly more likely to terminate, and those women who chose against testing because they are more worried about the risks or consequences of the test rather than of their baby being affected. (Kobelka, 2009) Although many other factors (i.e. education, family values, religion, life experience, family pressure, culture, and financial constraints) can also play a role in a decision of this magnitude, it seems NIPD could be especially helpful for the group of women who opt against testing because of their fear of miscarriage. Since women can be hesitant to pose even the slightest risk to the fetus, diagnostic testing is sometimes rejected on this premise. This can result in fetal abnormalities going undetected until late in the pregnancy, or post-natally, both of which tend to result in consequences beyond those that may arise following earlier diagnosis. Non-invasive prenatal diagnosis could simplify the decision making process and offer women a more appealing prenatal testing option and prevent unnecessary procedure related losses. Not only can earlier detection expand a woman’s choices with regard to termination, but it could help families who choose to continue the pregnancy as well. Earlier knowledge of a fetal anomaly would allow more time for preparation, education, and acceptance of the condition. It would also allow time to alert pediatric specialists and put a medical treatment plan in place.

By altering how patients view diagnostic testing, NIPD may provide the opportunity for reliable, timely, and safe prenatal diagnosis. In addition to eliminating the risk of miscarriage, it is speculated that NIPD would lead to many advantages and
improvements to the field, such as allowing for greater uptake of testing, definitive diagnoses earlier in pregnancy, safer terminations of affected pregnancies, reduction of parental anxiety, and decreased medical costs. (Benn, 2009)

**Ethical Issues Surrounding NIPD:**

It is essential to realize that there are significant ethical issues that are associated with NIPD. One major concern deals with ensuring that women retain their right to informed consent for testing. (Van Den Heuvel, 2008) The worry is that with the risk of miscarriage removed, health care providers may fail to adequately inform the patients of the remaining implications of test outcomes, including learning prior to birth that they are pregnant with a child affected with a genetic disease, and thus patients may be faced with serious decisions that they were not prepared for. Information obtained may lead to difficult decisions and serious outcomes, and so this testing should not be thought of as just another simple blood test, similar to how some view maternal serum screening currently. Increasing terminations of pregnancies, options for regulation, and non-medical uses such as sex selection, are also raised as potential ethical concerns. (Van Den Heuvel, 2008) Efforts may need to be made to educate patients and ensure that they have fully contemplated all of the potential implications of opting for or against non-invasive prenatal diagnosis.

**Study Purpose:**

If NIPD is on the cusp of entering clinical practice, health professionals need to be aware of everything it will entail. With regard to the clinical implementation of NIPD three scenarios are possible: it might be added to or replace current prenatal screening
tests, it might be interposed between screening and the traditional amniocentesis or CVS testing, or it might replace those invasive tests altogether. This largely depends on its sensitivity and specificity. Ideally, however, the third option of NIPD eventually being diagnostic on its own would be the ultimate goal. Despite all of the potential benefits that NIPD offers, it is also important to recognize that its introduction can be viewed as a challenge to providers. Integrating the technology into a clinical setting may require the medical system to change how patients are counseled and how cases are managed.

Although various authors have speculated about the potential benefits, limitations, and ethical issues surrounding the clinical introduction of NIPD (Benn, 2009, Newson, 2008, Schmitz, 2009, Smith, 2006, Van Den Heuvel, 2008), nothing has been documented that expresses the opinions of genetic counselors regarding the use of this technology in their clinical practice. Since genetic counselors are intimately involved in the delivery of high risk prenatal genetic testing and counseling, their views on how NIPD could be integrated into their practices are extremely valuable. The goal of this study is to determine what way genetic counselors believe NIPD may affect the field of genetic counseling, gain insights about pertinent issues, and identify potential challenges to the delivery of prenatal diagnostic services. This advanced knowledge will hopefully allow a smoother transition of this technology into clinical services, and will ultimately result in better patient care.
Methods

This was a cross-sectional quantitative study of genetic counseling professionals using a self-administered online survey. A qualitative analysis was carried out on open-ended survey questions. We received a status of exempt on February 5, 2010 from the Brandeis Institutional Review Board (IRB).

Study Sample:

Individuals who subscribed to the National Society of Genetic Counselors’ (NSGC) general listserv between February 8, 2010 and March 8, 2010 had access to our research study. Inclusion criteria to take part in the study included that the participants were currently providing prenatal diagnostic genetic counseling services, and were either board certified or board eligible by the American Board of Genetic Counseling (ABGC). We did not exclude based on demographic characteristics such as age, gender, or geographic location.

Data Collection Process:

The data collection tool was an anonymous survey (Appendix C). It was administered online, using surveymonkey.com, an online survey tool. Recruitment of participants was done through the National Society of Genetic Counselors (NSGC), a professional organization for genetic counselors. A committee member, who was also a member of NSGC, posted a recruitment notice (Appendix B) on February 8, 2010 to the
listserv. The notice invited members to participate in the study and included a link to the survey. Our study did not require us to obtain informed consent, as there was little risk to the participants. Nevertheless, we provided the contact information of both the principle investigator and the thesis committee chair and instructed participants to contact us if they had any questions or concerns regarding the study. Two reminders were also posted, the first on February 22, 2010 and the second on March 1, 2010. In total, the survey was available for four weeks.

Survey Instrument:

The survey included a brief background and description of NIPD, quoting the specificity and sensitivity rates that are currently in the literature. Participants were first asked if they were currently a practicing prenatal genetic counselor. If the answer was “No”, they were then directed to the “Thank you” page at the end, as they did not meet inclusion criteria. The first section of the survey consisted of four mandatory demographic questions on geographic location, year of graduation, and years of experience both as a genetic counselor and providing prenatal diagnostic services. Following this, there was a section consisting of twenty-five multiple-choice questions (likert scale, multi-answer, and forced choice) on non-invasive prenatal diagnosis. The survey also included four open-ended questions in the last section, which allowed us to do qualitative data collection. The objective was to elucidate what genetic counselors considered the appropriate uses for non-invasive prenatal diagnosis would be, and what the pros and cons of implementing the technology into prenatal care would be. Additionally, the goal was to reveal how the genetic counselors believed it would affect
the role of the genetic counselor, the use of current prenatal testing options, termination rates, patient choices, and informed consent.

**Data Analysis:**

The data was analyzed using Statistical Package for the Social Sciences (SPSS) software. We eliminated any participants that were not currently practicing as prenatal genetic counselors. The first step of data analysis was a univariate descriptive analysis of the sample characteristics such as mean age, years in practice, and geographic location. That was followed by a bivariate comparison of the sample to the population that we reached out to on the listserv to determine the generalizability to the study population. A univariate analysis of each survey question provided an overall description of the responses. Bivariate analyses, using independent T-tests and chi square testing were used to compare responses by the respondents’ years of prenatal counseling experience, years since graduation, and familiarity with the technology. Open-ended questions were qualitatively analyzed using an inductive approach to identify themes in opinions about the technology that had not been previously identified. We reviewed the open responses and identified emergent themes. We then analyzed the frequencies of codes across all four of these questions and for each individual question.
Results

We organized the data we collected into the following categories: 1) Demographics (including geographic region, year of graduation, and years of experience), 2) technology implementation, 3) patient decision-making, 4) potential changes to prenatal genetic counseling, and 5) the role of the genetic counselor.

Demographics:

A total of 206 genetic counselors completed the survey. We excluded 9 respondents from analysis because they were not currently practicing as prenatal genetic counselors. Table 1 shows the counselors’ geographic locations, year of graduation from their genetic counseling programs, total years of experience as genetic counselors, and total years experience delivery prenatal diagnostic services. The majority of respondents were from the Northeast (72 total), and the remainder of the population was well dispersed across the country (31 from the Southeast, 46 from the Midwest, 23 from the Northwest, and 34 from the Southwest). The year that the counselors graduated from their genetic counseling programs ranged from 1977 to 2009, with the most common year being 2008 (26 respondents). We found that years of total genetic counseling experience and years of experience delivering prenatal diagnostic services did not vary significantly. Regarding years of total experience as a genetic counselor, the responses ranged from less than one year to thirty years. As expected from the median year of graduation (2004), the median years of experience was 5 years. The average was 6.99 years.
Similarly, when looking at the total years delivering prenatal diagnostic services, we found that the responses also ranged from less than one year to thirty years. The mean here was slightly less at 6.57 years, with the most common response being one year.

<table>
<thead>
<tr>
<th>Table 1. Demographics of study population (n=197)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic:</td>
</tr>
<tr>
<td>Geographic region:</td>
</tr>
<tr>
<td>Northeast</td>
</tr>
<tr>
<td>Southeast</td>
</tr>
<tr>
<td>Midwest</td>
</tr>
<tr>
<td>Northwest</td>
</tr>
<tr>
<td>Southwest</td>
</tr>
<tr>
<td>Mean (range):</td>
</tr>
<tr>
<td>Graduation Year</td>
</tr>
<tr>
<td>Years Experience as GC (total)</td>
</tr>
<tr>
<td>Years Experience as GC (prenatal services)</td>
</tr>
</tbody>
</table>

The National Society of Genetic Counselors Professional Status Survey, which provides a detailed profile of the current NSGC membership, supports that our respondents accurately represented the members of NSGC. It reported that the majority of genetic counselors who subscribe to the NSGC have less than 10 years experience, are from the Northeast and Midwest, and have graduated between 2000 and 2005. The majority of our study participants fall within these ranges.

*Technology Implementation:*

To gain an understanding of their prior knowledge of NIPD, we first asked respondents what context, if any, NIPD was discussed at their workplace. Approximately 49% of participants had only heard of the technology through casual conversation among colleagues, and 14% of the participants had not discussed it at work at all. Many
participants reported that they had been involved in NIPD related studies (“Research” category), which accounted for approximately 10% of the total responses. Only a small number of participants (8%) had ever been involved in a discussion regarding incorporating the technology into their clinical practice.

Participants were then asked to speculate on various details of the clinical implementation of NIPD. They were asked to rate the statement, “NIPD could be an important asset to prenatal care” from strongly agree to strongly disagree, and explain their answer. We found that 87.4% agreed with this statement (59 respondents who strongly agreed, and 94 who agreed), and 3.4% disagreed with the statement (1 respondent who strongly disagreed, and 4 who disagreed). Of the 175 counselors who responded, 32 provided explanations for their answers. Seventeen people cited that they felt this technology would be beneficial because eliminating the risks that correspond with invasive testing would provide more options to their patients.

*Many families choose not to undergo diagnostic testing because of the risk of the procedures. This would allow families the benefit of diagnostic information, especially for those who are seeking information in order to be appropriately prepared for the birth, without the risk of current diagnostic procedures.*

Three people were concerned about labeling NIPD as “diagnostic” since the false negative rate may give patients a misleading sense of security. The remainder of the comments pertained to concerns about the accuracy of the technology at this point in time.

We then asked more specific questions to get a detailed representation of how the genetic counselors envisioned NIPD in a clinical setting. Figure 1 shows the genetic counselors’ opinions on when NIPD would be clinically implemented. Although very few respondents (3%) thought it would be ready in the next year, the majority (56%) felt
it would be clinically available within the next 5 years. The remaining 27% (n=47) were unwilling to provide a timeframe; 20 said they simply did not know, and 27 thought it depended strongly on how soon the quality of the test improves.

To assess if the counselors’ ages had any effect on how they viewed NIPD, we performed a t-test to see if there was a correlation between the respondents’ total years of experience as a genetic counselor and when they believed NIPD would be clinically implemented. Based on their years of experience, we found no difference in the timeframe in which the counselors thought the technology would be implemented, and so they were not significantly correlated.

We performed a separate chi-square analysis to see if there was a relationship between the geographic regions that the counselors practiced in and when they believed NIPD would be clinically implemented. We found that there was borderline significance (p = .052). Table 2 shows the crosstabulation of what geographic region the counselors
were from and what time frame they believed NIPD would be clinically implemented in. The majority of respondents from all regions believed it would happen in the next 5 years. Some respondents from the Northeast, Southeast, and Southwest (3.6%, 17.9%, and 7.4% respectively) believed that NIPD would never be clinically implemented, while no counselors in either the Midwest or Northwest felt this way.

Table 2.
When do you foresee NIPD being implemented into your clinical practice?
In which geographic region do you practice prenatal genetic counseling?
Crosstabulation

<table>
<thead>
<tr>
<th>When do you foresee NIPD being implemented into your clinical practice?</th>
<th>In which geographic region do you practice?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Northeast</td>
</tr>
<tr>
<td>Within next year</td>
<td>Count</td>
</tr>
<tr>
<td></td>
<td>Expected Count</td>
</tr>
<tr>
<td></td>
<td>Region</td>
</tr>
<tr>
<td>Next 5 years</td>
<td>Count</td>
</tr>
<tr>
<td></td>
<td>Expected Count</td>
</tr>
<tr>
<td></td>
<td>Region</td>
</tr>
<tr>
<td>Never</td>
<td>Count</td>
</tr>
<tr>
<td></td>
<td>Expected Count</td>
</tr>
<tr>
<td></td>
<td>Region</td>
</tr>
<tr>
<td>More than 5 years</td>
<td>Count</td>
</tr>
<tr>
<td></td>
<td>Expected Count</td>
</tr>
<tr>
<td></td>
<td>Region</td>
</tr>
<tr>
<td>Unsure</td>
<td>Count</td>
</tr>
<tr>
<td></td>
<td>Expected Count</td>
</tr>
<tr>
<td></td>
<td>Region</td>
</tr>
<tr>
<td>Total</td>
<td>Count</td>
</tr>
<tr>
<td></td>
<td>Expected Count</td>
</tr>
<tr>
<td></td>
<td>Region</td>
</tr>
</tbody>
</table>

Next, counselors were asked to rank their agreement with the statement, “NIPD will become routine prenatal care within the next 3-5 years, similar to current screening methods”. Although a large number of respondents had previously agreed that NIPD
would be clinically implemented within the next five years, the results from this question showed that not as many agreed with it becoming routine care in that same time frame. Approximately 51% of genetic counselors either strongly agreed or agreed with the statement, and the remaining 49% either disagreed or strongly disagreed with it.

We asked participants how they foresaw NIPD being used in clinical practice. As Figure 2 shows, the majority of the genetic counselors (63%) believed that NIPD would be offered to patients in addition to all of the prenatal testing options that are currently available. Following that, approximately 23% thought that NIPD would replace screening only. Only 2% thought it would replace diagnostic testing, and 7% thought it would replace all of the current prenatal testing options. We created a new “Unsure” category since five respondents stated that they could not answer the question based on the accuracy of the technology at this time.

![Figure 2. How GCs foresee NIPD being used in clinical practice](image)
After speculating about the timing and placement of NIPD into clinical practice, we then asked participants to consider which women NIPD should be offered to. Approximately 79% of genetic counselors believed that all women should be offered this test. This number includes those that responded in the “Other” category stating that NIPD should be offered to all women who were interested or who qualified. From there, the numbers drop significantly and between 15-18% of genetic counselors believed that only women of advanced maternal age, with a positive screening result, or who were high risk for another reason should be offered the test. Figure 3 shows the results of this question, however the percentages on the graph do not add to 100% because respondents had the opportunity to choose more than one answer.

![Figure 3. GCs Opinions Of Who NIPD Should Be Offered To](image)

**Patient Decision Making:**

Our main goal in asking the next few questions was to determine how eliminating the risks associated with invasive prenatal testing might affect patient decision-making with regard to prenatal testing. We first asked participants what they found to be the
most common reason their patients currently decide against having diagnostic testing. Approximately 65% answered that the reason was the risk of miscarriage associated with the test. A later question supported this finding when approximately 99% of participants acknowledged that the risk of miscarriage affects the patient’s decision-making with regard to prenatal diagnostic testing. Fifty four percent of them strongly agreed with that statement and 44.8% agreed. The majority of participants (96%) also agreed that NIPD would alter patient decision-making with regard to prenatal testing in some way. The participants were then asked what they believed the most common reason their patients would decide against having diagnostic testing if NIPD were offered in a clinical setting. As expected, the response percent for the risk of miscarriage went down to 1.7%. Approximately 45% of genetic counselors also believed that if NIPD were used in a clinical setting, patients would view diagnostic testing as safe enough that they would consider having it. Another 41.5% believed patients would be unsure about diagnostic testing but interested hearing more information, and only 4.1% thought patients would consider it unsafe enough that they would not have it. Figure 4 shows the results of this question.
We considered that diagnostic testing and its implications may be viewed differently in different parts of the country. To investigate this, we performed correlation analysis on the region that the counselors practiced in and how they predicted their patients would view diagnostic testing if NIPD were an option. The test revealed no significant correlation, perhaps because there were not enough responses.

Potential Changes to Prenatal Genetic Counseling:

We asked respondents about specific changes they thought could potentially occur if NIPD were to be clinically implemented. They were asked to speculate on how NIPD might alter patient anxiety levels, the uptake of diagnostic testing, detection of fetal abnormalities, termination numbers, and the number of test induced miscarriages. Table 3 summarizes the results of these questions.
Table 3. NIPD Compared to Current Testing Options

<table>
<thead>
<tr>
<th>Question:</th>
<th>Answer Choices:</th>
<th>Percentage:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Increase</td>
<td>14.7%</td>
</tr>
<tr>
<td>Patient Anxiety</td>
<td>Remain the same</td>
<td>58.2%</td>
</tr>
<tr>
<td></td>
<td>Decrease</td>
<td>27.1%</td>
</tr>
<tr>
<td>Uptake of diagnostic testing</td>
<td>Increase</td>
<td>52.6%</td>
</tr>
<tr>
<td></td>
<td>Remain the same</td>
<td>20.5%</td>
</tr>
<tr>
<td></td>
<td>Decrease</td>
<td>26.9%</td>
</tr>
<tr>
<td>Detection of fetal abnormalities</td>
<td>Sooner</td>
<td>41.8%</td>
</tr>
<tr>
<td></td>
<td>Same time</td>
<td>57.6%</td>
</tr>
<tr>
<td></td>
<td>Later</td>
<td>.6%</td>
</tr>
<tr>
<td>Number of terminations</td>
<td>Increase</td>
<td>30.0%</td>
</tr>
<tr>
<td></td>
<td>Remain the same</td>
<td>68.8%</td>
</tr>
<tr>
<td></td>
<td>Decrease</td>
<td>1.2%</td>
</tr>
<tr>
<td>Number of test induced miscarriages</td>
<td>Increase</td>
<td>3.5%</td>
</tr>
<tr>
<td></td>
<td>Remain the same</td>
<td>36.8%</td>
</tr>
<tr>
<td></td>
<td>Decrease</td>
<td>59.6%</td>
</tr>
</tbody>
</table>

Again looking to investigate if the region that the counselors’ practiced in had any effect on how they believed the uptake of diagnostic testing would change, we performed chi-square analysis. No significant relationship was found. We also considered whether the counselors’ total years of experience had any effect on how they believed the uptake of diagnostic testing would change. A chi-square analysis was performed and again, there was no significant correlation here.

Role of the Genetic Counselor:

Once we gained perspective on how NIPD might be clinically implemented and what the new technology might mean to prenatal genetic counseling services, we then wanted to explore how it might change the role of the genetic counselor. We were interested in learning if the counselor would need to spend more time counseling and educating patients and also wanted to address the greatly discussed issue of maintaining
informed consent. Figure 5 shows genetic counselors' opinions on the amount of time it will take to counsel and educate patient regarding NIPD as compared to how much they spend doing the same for current prenatal tests. The results indicated that for both counseling and educating the majority (60.1% and 54.9% respectively) believed it would take the same amount of time.

The next group of questions dealt with how the counselors felt clinically implementing NIPD may impinge on the patients right to informed consent. We asked participants if they believed health care providers would have to work harder to ensure that women retain their right to informed consent. Approximately 45% strongly agreed, 39% agreed, and 16% disagreed. When asked if they believed that health care providers would adequately inform the patients of the remaining implications of testing, including having a child affected with a genetic disorder or the option of termination, 68% of genetic counselors responded that they thought it would be the same as with current
testing options. Approximately 24% felt it would be less than with current testing options, and only 7% thought it would occur more often. The majority (89.5%) of respondents thought that genetic counselors would have to work more closely with obstetricians to ensure informed consent with NIPD. Regarding the general role of the genetic counselor, approximately 70% of respondents thought it was likely to expand if NIPD was used in a clinical setting. Fifty five percent of respondents thought that with the availability of NIPD, the demand for pretest counseling would increase, and following that logic 62.2% also believed that with NIPD in place patients should be seeing a genetic counselor before any testing (including screening) is performed.

Open-Ended Responses:

The last section of the survey consisted of four open-ended questions that were designed to elicit more in-depth information regarding genetic counselors opinions on NIPD. We coded each response to fall into specific themes, however many responses qualified for more than one theme, so value totals equal to more than the number of actual responses.

The first question, as shown in Table 4, was broken into three parts and asked participants to describe how they foresaw their counseling practice changing if NIPD were to be offered at their workplace. The first part dealt with the organization of their practice. Seventy-seven counselors responded and their answers were coded into five themes: there will be no significant change, they will have to see more patients and make scheduling changes, they will see patients earlier in pregnancy and have to do more pretest counseling, their work load will increase as they will have to spend more time
counseling and ensuring proper informed consent, and they were unsure of how things would change. The most common theme was that nothing will change, however many counselors did also feel that the time in pregnancy that patients are seen and the total number of patients would be affected.

"I don’t think I would need to change much about how I organize my counseling sessions, although referrals would need to change so patients can be seen earlier."

The second part asked about changes to the respondents’ counseling techniques. There were 78 responses; we noted five unique themes: there will be no significant change, there will be more information to discuss with patients, the timing of the sessions will change, the number and type of patients will change, and more personal education will be needed. As seen in the quotes below, the two most common themes were that there will be a lot more information to discuss with patients, and that the timing of sessions will be altered.

"Techniques would not necessarily change, but information discussed during each session would expand to include this information as an option for all women, regardless of indication."

"I will have to spend more time educating a patient regarding the benefits/limitations of testing and will not have the time to counsel them or work with them on a psychosocial level."

The last part of question one in the open-ended section was answered by 53 participants and pertained to changes in any other aspect of their practice. There was a large variety in the answers given and so for this section we categorized the responses into seven themes: the focus of the sessions will change, a need for more education to providers, change in the types of patients or reasons for referral, change to the dynamic of services, better patient care, no change, and a change in revenue.
The second question in the open-ended response section asked the genetic counselors to explain what they believed the differences may be in how cases would be managed if NIPD were an option, compared to what they currently do. Fifty-nine participants responded to this question and their answers were categorized into five themes. Sixteen of the counselors thought they would have to spend more time with each patient and that their work load would increase.

*All patients will need much more extensive education and counseling about NIPD and it’s implications than they get now with serum screening; this will need to be as early in the pregnancy as is reasonable, say at the first prenatal visit, before other tests are done, so the patient has time to process and consider her options.*
Ten respondents believed that with NIPD patients would be better prepared and receive better prenatal care overall. The next largest group (7 respondents) were those who thought there would be a difference in the types of referrals and patients they would receive if NIPD were an option. Five participants thought NIPD would change how patients view testing, and another five were worried that there would be less utilization of genetic counselors.

More of my patients who currently decline invasive testing are likely to take up the non-invasive test, however those patients that currently elect invasive testing I think would elect invasive testing even if NIPD was available.

Since the most common theme among the responses to this question dealt with the counselors having to do more work to accommodate NIPD being offered to patients, we considered whether there was a correlation between the respondents who felt that way and the ones who had previously answered that they believed all women should be offered NIPD. It seemed reasonable to think that if someone believed NIPD would be offered to every pregnant woman, that they would then consider the amount of extra work that would entail. A chi-square analysis was performed, and it was found that there was actually no significant correlation.

The next question asked the participants what their concerns were when facing the possibility that NIPD may become clinically available in the next year or so. A total of 89 participants responded. We found five major themes: lack of education and knowledge on the part of the health care providers, problems ensuring proper informed consent, the test not being accurate enough, there will be a greater burden on genetic counselors, and the cost of the technology. The breakdown of responses can be seen in Figure 6. The most common response given by counselors was that they were concerned
that there may be a problem ensuring women give a proper informed consent prior to
testing.

[My concern is] “that OB’s will NOT ADEQUATELY counsel their patients before this test, and that I will
end up seeing many women who would NOT have done this test if they actually knew what it was. Trust me,
I see women all the time who had NO IDEA that they got maternal serum screening and now they are very
upset that the risk is positive. Imagine the same situation but instead of saying, ‘Your screening result is
high’, you have to say, ‘Your baby has Trisomy 18’.”

Feeling that the technology was not yet accurate enough was the second most
common theme among counselors. This accounted for both the lack of accuracy with the
testing and the fact that it cannot pick up the full range of abnormalities that invasive
testing can.

The severe limitations [are] in how much information it can tell us (not full karyotype) and the potential for
still having to consider an invasive procedure. Also, I think it paints a very skewed picture that the only
thing to be concerned with is Down syndrome (which can be detected with NIPD) and that the other “stuff”
invasive testing detects is not nearly as “bad” as Down syndrome might be.

The last open-ended question asked if participants had any further comments to
make about the possible use of NIPD. There were 41 total responses for which six
themes were identified. Fifteen counselors believed that NIPD was not yet accurate enough, and that it couldn’t yet be considered “diagnostic”. Eight counselors believed it would have an affect of patient decision-making, however only one person believed it would change pregnancy outcomes.

…I think it will also force people to more closely examine their own feelings about having a child with disabilities than they have to right now; I think some people hide behind the risk of diagnostic procedures as the reason to decline, instead of examining their feelings about having a child diagnosed with Down syndrome.

Four participants thought that NIPD was an overall good option for women, and five fell into the theme of NIPD changing the role of the genetic counselor or the dynamic of prenatal services.

NIPD could potentially ruin or substantially hurt perinatology practices financially as probably there will be less patient referrals as well as the cost for amniocentesis & CVS will probably be [more] than the NIPD.

Seven of the counselors thought that prenatal care providers would have to make a bigger effort to allow for a smooth transition.

GCs need to be proactive about the message that is sent out to make it clear that counseling is a necessary and integral part of NIPD. So, we need to be out in front and guiding the message as the professionals to go to when in doubt.
Discussion

This study demonstrates that we were able to characterize the prenatal counselors’ attitudes and beliefs about the integration of NIPD into their practices. The quote below demonstrates the overall attitude counselors had toward NIPD and nicely exemplifies our findings.

*My patient population is already confused about all of the different testing options...first trimester screen, quad/AFP screen, sequential screen, carrier screening, etc. They are skeptical about blood tests and false positives. They fear risks associated with diagnostic testing and are afraid of needles. They say they wouldn’t terminate anyway. So, NIPD seems to me like it is going to be a huge hurdle to get patients to understand and proceed with testing. I fear the informed consent will be similar to screening and then patient population is not going to know how to handle the diagnostic results. I think in the long run there is benefit and promise to NIPD, but is scary to think about the first few years using NIPD. But, isn’t that what most counselors feared when first trimester screening came out and then modified sequential?...*

Patient Decision-Making:

Knowing and understanding how patients perceive risk and make their decisions regarding prenatal testing is extremely important in evaluating how NIPD may affect the field of genetic counseling. It is obvious that the risk of miscarriage involved in invasive prenatal diagnostic techniques greatly affects a patient’s decisions, and our study confirmed that point when 99% of counselors agreed with the given statement, “The risk of miscarriage associated with diagnostic testing affects the patient’s decision to have the test”. Based on the clinical experiences of the counselors, the risk for miscarriage was the number one reason (65%) why patients currently decide against having diagnostic testing. When later asked to speculate what their patients’ main reason might be if NIPD were an option, the risk of miscarriage went down to being the least common response
(1.7%). This is not surprising since the majority of counselors felt that NIPD would alter patient decision-making. Furthermore, with the risk eliminated, over 50% of the counselors believed that patients would then consider diagnostic testing safe enough that they would have it. These findings illustrate that the risk of miscarriage strongly influences a patient’s choice about whether or not to have prenatal diagnostic testing, and clinically introducing NIPD could significantly alter those choices.

Another factor that has been shown to influence a patient’s decision about prenatal testing is their experience with their genetic counselor. (Elimian, 2005) Although the non-directive nature of genetic counseling may give a sense that the influence of the counselor would be minimal, since many patients do not fully understand their testing options, or are unaware of them completely, the way in which the genetic counselor delivers the information can indeed alter a patient’s views and acceptance of testing, especially if the patient is undecided. (Elimian, 2005)

Taking into consideration the respondents’ concern about miscarriage with current prenatal diagnostic procedures and the counselors’ attitudes toward the efficacy of the test, we may draw conclusions about how NIPD will be welcomed and eventually affect prenatal genetic counseling services.

_Counselors’ Views on NIPD:_

It is clear from the results of this study that practicing prenatal genetic counselors generally have a favorable attitude regarding the concept of NIPD since the vast majority of participants (87.4%) agreed that NIPD could be an important asset to prenatal care. Counselors felt that NIPD would be ideal for patients since it has the potential to provide
another prenatal testing option, while eliminating the risk of miscarriage that is associated with invasive tests. Without having to weigh the benefits against the risks, some counselors thought that NIPD would be simpler for patients to understand and therefore anxiety levels may decrease.

*If it could provide reliable diagnostic testing options without a risk, this could make diagnostic testing options more accessible to more individuals.*

Additionally, the majority of counselors surveyed felt that all women, regardless of age or indication, should be offered this new technology.

*Everyone should be offered prenatal testing and given the choice of how much information they have during the pregnancy.*

**Ethical Considerations:**

It is essential to realize that there are significant ethical issues that are associated with NIPD, and while participants in this study generally felt optimistic about what NIPD has to offer patients, the majority of them also expressed their concerns regarding the ethical issues that surround it, particularly with regards to how NIPD may compromise informed consent.

There is a well-accepted agreement among health professionals and policy makers that prenatal testing decisions should reflect informed choices by the patient. (Heuvel, 2008) If patients accept an amniocentesis, for example, they have to do so on the basis of informed choice, meaning that they can accept or refuse the test based on their own personal wishes and moral beliefs. The concern with NIPD is that since women who undergo this type of testing would no longer have to contemplate the risk to the fetus or themselves, it might become a one-step diagnostic procedure and eliminate the patient’s
opportunity to contemplate testing, and possibly refuse it.

*I would mostly worry about inadequate patient education and consent from providers who may not have the time and expertise to counsel about all testing options.*

If patients were not first seen by a genetic counselor, the burden would be placed on obstetricians and other prenatal care providers to discuss the pros and cons of the NIPD, similar to how screening is commonly offered to patients currently. It is likely because of this that the majority of respondents thought that patients should be seen by a genetic counselor before any testing, including screening, is performed. Many women who undergo prenatal screening are unaware that it may ultimately lead to having to decide whether to undergo invasive testing and perhaps pregnancy termination. Often times they are unaware that they have even had the test until it comes back positive and they are deemed to be at high risk and sent to see a genetic counselor.

*I am concerned about it being offered to patients in the same manner that screening is currently offered, and that is with little true education. I worry that regular OBs could see it as a yes/no kind of test without referring the patient on to someone who can spend the time to explain the implications (good or bad).*

The introduction of NIPD may also lead to prenatal testing becoming a routine procedure. As has already been discussed, service providers’ attitudes towards prenatal care does have the potential to affect patient decisions, and so the likelihood of NIPD becoming routinized may depend on health professionals’ attitudes towards the technology. The fear among counselors is that NIPD might be treated as just a “simple blood test”.

*[My concern is] that the burden of counseling and education will fall solely on OB providers, who already don't have enough time to discuss these issues with their patients; that patients will not understand the implications and feel that “it's just a blood test.”*
Although this approach is never favorable, it is a more dangerous mindset to have with regard to NIPD because women would receive a definitive diagnosis, as opposed to the risk estimate obtained through a screening test, immediately following the blood test. Clearly, it would not be appropriate for women to receive a diagnosis of Down syndrome, or any other disorder, without having any prior education and counseling about it. If NIPD became another facet of standard prenatal care, it may cease to be something about which a deliberate patient decision needs to be made, therefore inadvertently eroding the patient’s right to informed consent.

Another product of eliminating the risk of miscarriage associated with testing is that it could potentially remove the opportunity to discuss the other consequences of testing. This is yet another way that NIPD could limit women obtaining true informed consent. Woman may fail to adequately consider the remaining implications of test outcomes, including the discussion of the option of pregnancy termination if test results indicate an affected fetus. Current invasive tests are usually offered to prospective parents in such a way that encourages them to consider two adverse consequences associated with testing: first, the risk of fetal loss inherent in the procedure itself, and second, the possibility of detecting a fetus affected with an abnormality. The fear with NIPD is that by removing the first, adequate consideration of the outcome might be overlooked.

We found that nearly a quarter of the prenatal counselors do not think patients will be adequately informed. Fortunately this is not the majority, however it does show that testing implications are likely to be overlooked in many cases. Not surprisingly then, our study found that 83.8% of counselors speculated that health care providers will have to
work harder to ensure that women retain their right to informed consent.

*Potential Changes to Prenatal Genetic Counseling:*

The results of our study indicate that the introduction of NIPD will require improvements in pretest counseling, including making the detailed genetic counseling and consent process currently provided to women considering invasive testing available for every woman considering a NIPD. We found that the majority of counselors surveyed felt that with NIPD being offered, the demand for pretest counseling would increase because of the need to obtain proper informed consent and of the general increase in patient load. Monitoring will be required to ensure that women are making the best and most informed decisions.

If non-invasive prenatal diagnosis will soon be clinically available, health professionals need to be aware of everything it will entail. Regardless of whether NIPD is added to current testing options or replaces them, offering women an option for prenatal diagnosis so early in pregnancy with no risk for miscarriage will undoubtedly impact the delivery of prenatal genetic counseling services. One of the barriers that will be reduced by introducing this new technology is the uptake of diagnostic testing. As shown in our results, approximately 53% of counselors feel that NIPD will help increase the uptake of diagnostic testing. This is beneficial because it will potentially allow for definitive diagnoses earlier in pregnancy, a longer coping and decision-making period, safer terminations of affected pregnancies, reduction of patient anxiety regarding test-induced miscarriages, and reduction of medical costs.
Despite all of the potential benefits that NIPD offers, it is also important to recognize the potential challenges for providers. This study has allowed genetic counselors to express their concerns about the possible implications of NIPD with regard to their practice. If this new technology is offered to all women, genetic counselors will be seeing a much higher volume of patients. The sessions themselves may also be longer since counselors will have another testing options to discuss with their patients. This will require an adjustment in scheduling and appointment times, and there is concern that there are not enough genetic counselors to ensure that each patient is getting the proper time and care.

There will need to be more GCs on staff to handle the increase in patient volume (as more women will be offered these tests and will need counseling to obtain informed consent).

A few counselors suggested launching group counseling sessions to discuss NIPD with multiple patients at once and alleviate some of the workload. The majority of the participants in this study felt that when dealing with NIPD it would be best for patients to meet with a genetic counselor prior to having any testing. Because NIPD is offered so early in pregnancy, the demand for counselors will increase even further since they will be initially seeing patients earlier and there will be more follow-up involved if the pregnancy is affected. It is clear that implementing the technology into a clinical setting would require the medical system to change how patients are counseled and how cases are managed.

*Technology Implementation:*

With all the potential change in the delivery of care that the clinical availability of
NIPD may have, the question remains: How close are we to being able to offer patients the option of NIPD? The majority of they counselors that we surveyed did not feel that it would be clinically implemented in the near future. While a small group thought the test would be imminently available, the vast majority think it is still years away. There were concerns that as it stands, NIPD is not yet accurate enough to be labeled as a “diagnostic” test, and is instead more comparable to current screening methods.

*With a detection rate of 90%, it seems like another screening option rather than a diagnostic option. I’m not sure that it adds anything different than 1st trimester screening, which quotes a higher detection rate for DS through certain labs.*

NIPD is not able to detect the same broad range of abnormalities that the existing diagnostic testing does. Currently, first trimester detection of single gene disorders is limited by assay sensitivity and specificity due to the background maternal DNA. Because of the affect it may indeed have on prenatal care, NIPD must be introduced with caution, as it is too early in development to assume that it is fully diagnostic and precisely equivalent to chromosome analysis. Further development of techniques to enrich or separate the fetal component of the cell free mixture will broaden the scope and robustness of testing. (Norbury, 2008) Even then, though, it is questionable whether NIPD could ever be the only option offered to patients. With testing for Down syndrome, for example, NIPD targets the detection of a single-chromosome abnormality. This means that using NIPD as a complete replacement for current testing would allow other chromosomal abnormalities currently identified through amniocentesis to go undetected. (Benn, 2009) The results of this study showed that counselors were aware of the limitations of the technology since the majority did not think it could replace all current tests or that it could be considered a diagnostic test itself.
I think at first NIPD will be offered in addition, if it proves to hold up, it will likely replace screening. I think amniocentesis and CVS will always continue to play a role in testing offered.

It seems that until NIPD has been validated, and ongoing quality assurance of the testing demonstrates diagnostic accuracy, balancing the benefits of NIPD against the more comprehensive detection capabilities currently achieved by invasive testing would be required. For now, it seems that the best approach to introducing NIPD into clinical practice may be in addition to what is currently offered, and considered on a case-by-case basis.

Limitations and Future Directions:

This study only gained the perspectives of the genetic counselors that are members of the NSGC, and therefore cannot speak for all genetic counselors. One limitation of our study was the small sample size. This could have influenced why we were unable to find any correlation between demographical information and the respondents’ opinions on NIPD. Also, from that small population, counselors chose to participate in the study, which may have led to a selection-bias among the respondents. For example, counselors who have a greater interest in research and developing technologies may have been more inclined to participate. Another limitation to the study was that some of the questions were worded too vaguely and the respondents found it difficult to respond. For example, using the term, “health care providers” in question 19 was confusing since the counselors didn’t know whom exactly that was referring to. Many of the questions in the survey asked counselors to speculate on the technology and how it may impact the field. This proved harder for them than we anticipated since many did not feel comfortable enough with the available information to formulate and answer.
Standards of care and professional guidelines will be necessary for a smooth clinical implementation of NIPD. To establish these, large-scale objective clinical trials will need to be put in place. Once the test is proven valid, ongoing quality assurance of the testing will be needed to demonstrate its diagnostic accuracy. Also, to truly get an accurate portrayal of how NIPD is going to affect the field of genetic counseling, future research may wish to discuss the matter with OBs and other prenatal health care providers, as it will affect their work and practice, as well as their relationships with genetic counselors.
Conclusion

Participants in this study were asked to give their opinion on the new technology of non-invasive prenatal diagnosis, and speculate as to how its clinical introduction might affect the field of genetic counseling. Currently, screening tests are not at diagnostic standards and invasive tests, such as amniocentesis and CVS, come with severe risks. As compared with the present methods of prenatal diagnosis, then, NIPD has the advantage of high sensitivity with no risk for miscarriage. Our results indicated that most genetic counselors are optimistic about NIPD and believe it could have positive effects on the field, as it will offer women a more appealing prenatal testing option. In spite of this, there were also concerns among the counselors about how soon it will be clinically available to patients. Most counselors did not foresee NIPD being routinely used as a part of prenatal care for many years, largely due to the unperfected accuracy of the testing and the ethical implications involved. The results of this study are useful since even though it is evident that NIPD has potential benefits NIPD to offer, its introduction will undoubtedly present a challenge to prenatal health care providers. Genetic counselors generally agreed that their role will expand as patient volumes rise, women are seen earlier and are presented with more testing options, and obtaining informed consent becomes more complicated. The introduction of NIPD will require new approaches in genetic counseling, reassessments of the utility of related testing, and expansion of testing oversight, to ensure a smooth transition into clinical practice and the best patient care.


Hung, E.C et al., Detection of circulating fetal nucleic acids: a review of methods and


Sahin, N.H., et al., Congenital anomalies: parents’ anxiety and women’s concerns before prenatal testing and women’s opinions toward the risk factors, *Journal of Clinical Nursing* 17(6) (2008), pp 827-836


Van Den Heuvel, A., et al., Will the introduction of non-invasive prenatal diagnostic


Appendix A:

An Assessment of Genetic Counselors’ Opinions on how Non-Invasive Prenatal Diagnosis May Impact Genetic Counseling Services

STUDY PURPOSE: The goal of this study is to determine what genetic counselors believe the effect non-invasive prenatal diagnosis may have on the field of genetic counseling. Previous research has speculated about the potential benefits, limitations, and ethical issues surrounding the clinical introduction of non-invasive prenatal diagnosis, however nothing has been documented that shows the views and opinions of genetic counselors regarding the use of this technology in routine practice. Since genetic counselors are intimately involved in the delivery of high risk prenatal genetic testing and counseling, their views on how this technology could be integrated into prenatal diagnostic services and their practices, in particular, will be extremely valuable. This study will provide insights about pertinent issues and identify potential changes to the delivery of prenatal diagnostic services. Advanced knowledge will allow a smoother transition of this technology into clinical services, and will ultimately result in better patient care.

STUDY SPONSOR: Brandeis University Genetic Counseling Program.

PRINCIPAL INVESTIGATOR’S QUALIFICATIONS TO DO THE RESEARCH: Kristen Maliszewski, the Principal Investigator, is a student in the Brandeis University Genetic Counseling Master’s Program and is conducting this research project as a requirement for the Master’s Thesis. The primary thesis faculty advisor is Barbara Lerner, M.S, CGC. She is a certified genetic counselor and a research specialist in the VA doing work in health sciences research. She is also currently getting her doctoral degree in health sciences research and is a PI on an AHRQ funded study about communication between patients and providers during the disclosure of genetic test results.

RESULTS OF PREVIOUS RELATED RESEARCH: The main premise behind non-invasive prenatal diagnosis is that with a simple blood test, free fetal DNA (fDNA) can be detected in maternal blood plasma, and used for prenatal diagnosis (Lo, 1997). Since fDNA has been reported to appear in maternal circulation as early as the seventh week of gestation, the test could enable women to obtain a diagnosis earlier than by using
traditional methods during the tenth to twentieth weeks of gestation. In addition, the sensitivity of this technique produces highly accurate results (Chiu, 2006). One recent study reported 90% sensitivity and 96% specificity for the non-invasive detection of Down syndrome using this technique (Chiu, 2009). To date, it has also been used to successfully detect paternally inherited alleles, sex-linked conditions, some single gene disorders, and other chromosomal abnormalities, although the exact detection rates have not all been determined (Lo, 2008). Perhaps its most appealing feature, however, is the fact that it is non-invasive, making it the first truly safe prenatal diagnostic technique for the detection of chromosomal abnormalities and many other inherited conditions.

Current diagnostic options offered to women, such as amniocentesis and chorionic villus sampling (CVS), come with some risk of miscarriage (Alouini, 2007). Since pregnant women and their doctors are hesitant to pose even a small risk to the fetus, diagnostic testing is rejected on this premise. This can result in fetal abnormalities going undetected until late in the pregnancy, or post-natally, both of which tend to result in consequences beyond those that may arise following earlier diagnosis. Non-invasive prenatal diagnosis could simplify the decision making process and offer women a way to test their pregnancies without fear of miscarriage. Such reasons have encouraged researchers to believe that analysis of ffDNA in maternal plasma will provide the opportunity for reliable, timely, and safe prenatal diagnosis, thereby changing the face of prenatal care. (Alberry, 2008) It will undoubtedly alter many aspects of prenatal diagnosis: affect the patient decision-making process, change the demand for screening, impact the rate of amniocentesis and CVS induced pregnancy losses, and elective termination rates.

In addition to the potential benefits associated with the clinical implementation of non-invasive prenatal diagnosis, the ethical issues that may arise have been considered as well. One major issue deals with ensuring that women retain their right to informed consent for testing. The concern is that with the risk of miscarriage removed, health care providers may fail to adequately inform the patients of the remaining implications of test outcomes, including having a child affected with a genetic disease or the option of termination. Information obtained may lead to difficult decisions and serious outcomes, and so this testing should not be thought of as just another simple blood test, similar to how some view serum screening currently. Efforts must be made to educate patients and ensure that they have fully contemplated all of the potential implications of opting for or against non-invasive prenatal diagnosis. Increasing terminations of pregnancies, options for regulation, and non-medical uses such as sex selection, are also raised as potential ethical concerns. (Heuvel, 2008)

Pregnant women’s anxiety for miscarriage may decrease with the option of non-invasive prenatal diagnosis, but because of the potential ethical issues discussed, it will be necessary to monitor the implementation and use of the technology, specifically with respect to genetic counseling services. Genetic counseling and education will still be required to ensure that women are making informed decisions. Because non-invasive prenatal diagnosis would likely lead to a greater uptake in prenatal diagnosis, and therefore greater demand for pretest counseling, new approaches to pretest genetic counseling may be needed. For example, group or phone-based counseling, or requiring that women read educational materials prior to counseling may be implemented more frequently than they are used now.
Through exploring the technology itself, and the potential ethical issues that surround it, the goal of this study will be to determine how genetic counselors believe non-invasive prenatal diagnosis will affect the field of genetic counseling. Identifying the benefits and any pertinent issues that may come up if this technology is clinically implemented, will allow any necessary changes to be made to the delivery of prenatal diagnostic services.

**SUBJECT CHARACTERISTICS:** The research subjects are clinical genetic counselors practicing in a prenatal setting who are members of the National Society of Genetic Counselors and subscribe to its listserv. A maximum of 400 subjects will be recruited for this study.

**SUBJECT INCLUSION/EXCLUSION CRITERIA:** The inclusion criteria are that subjects must be genetic counselors that are currently providing prenatal diagnostic genetic counseling services, and are either board certified or board eligible by the ABGC. They must be members of the National Society of Genetic Counselors (NSGC), the professional organization for genetic counselors, in order to access the survey. We will not exclude based on age, gender, geographic location, or other demographic characteristics.

**STUDY DESIGN:** This qualitative cross sectional study will anonymously survey clinical genetic counselors practicing in a prenatal setting through the use of an Internet-based survey.

**STUDY PROCEDURES**

**Recruitment procedures and materials:** The sample of eligible genetic counselors will be recruited from the subscribers to the listserv of the NSGC. A committee member, who is also a member of NSGC, will post a notice (See Appendix A) on the listserv inviting members to participate in the study. The post will include a link to the study. Two reminders will also be posted; the first will go up one week after the initial posting, and the second two weeks after that.

**Data Collection:** The data collection tool will be an anonymous survey (See Appendix B). This will be administered online, using surveymonkey.com, an online survey tool. In total, the survey will be available for approximately four weeks. The majority of the survey will be multiple-choice questions: demographic, likert scale, rank-ordered, true or false, and forced choice. It will also include a few open-ended questions at the end to allow for qualitative data collection. The objective of the survey will be to elucidate what
genetic counselors consider the appropriate uses for non-invasive prenatal diagnosis are, and what the pros vs. cons of implementing it into the field would be. In addition, our goal is to determine how genetic counselors believe it will affect the role of the genetic counselor, the use of screening, termination rates, patient choices, informed consent, and finances.

**Data Analysis:** The first step of data analysis will be a univariate descriptive analysis of the sample characteristics such as mean age, years in practice and geographic location. That will be followed by a bivariate comparison of the sample to the population that we reached out to on the listserv to determine the generalizability to the study population. A univariate analysis of each question will provide an overall description of the responses (i.e. mean, medium, variance, and range). If the response rate is adequate, we will carry out bivariate analyses comparing responses by years of prenatal counseling experience, years since graduation, and familiarity with the technology. SPSS, a statistical software package, will be used to conduct the quantitative analysis. Open-ended questions will be manually analyzed using an inductive approach to identify themes in opinions about the technology that had not been previously identified.

**ANTICIPATED RISKS AND BENEFITS TO PARTICIPATION IN THE STUDY:**
This study involves minimal risk to participants. Through the anonymous, online survey, we are asking the genetic counselors for their professional opinion about a new prenatal diagnostic technology. The survey does not deal with personal or harmful subject matter. However, it is possible that these questions may cause respondents some anxiety about how they may incorporate this technology into their practices.

**ADVERSE EVENTS:** I do not anticipate any major adverse reactions. However, if any individuals feel unforeseen distress they have they option to contact my primary committee head, Barbara Lerner, with any questions or concerns. This is an anonymous, voluntary, online survey, which can be stopped at any time.

**INFORMED CONSENT:** The study does not pose an excessive risk to responders. Most aspects of an informed consent document will be included in the recruitment notice and first page of the survey. Due to the anonymous nature of SurveyMonkey, the informed consent would be the only document that gives the principal investigator access to participant’s names. In addition, completing and submitting the survey implies consent to participate in the study. Therefore, I am requesting a waiver of informed consent.

**DOCUMENT STORAGE:**
Once data collection has ended, the anonymous data will be downloaded from SurveyMonkey and stored on the PI’s personal computer in a secured file. Only study personnel will have access to the data. The data will be deleted once the analysis and publications have been completed.

**COMPENSATION:** There will not be any compensation for research participants.

**PRIVACY/CONFIDENTIALITY:** The survey does not collect any personal or identifying documents from the participants. All participants will be anonymous.

**COSTS:** There will be no costs to study participants, apart from the time they invest to participate in the study.
Appendix B:

Are you a practicing prenatal genetic counselor?

Online Survey Respondents Needed for Research Study

The purpose of this study is to determine what potential effect genetic counselors believe that non-invasive prenatal diagnosis may have on the field of genetic counseling. Our goal is to uncover pertinent and potential issues and alert health care professionals to changes that will need to be made in the delivery of prenatal diagnostic services.

I am a graduate student seeking prenatal genetic counselors to participate in an online survey. Participation is voluntary and anonymous and will require approximately 15 minutes of your time.

If you are interested in completing the survey, please access the following website:

https://www.surveymonkey.com/s/MP2F9CJ

This survey and its results will comprise the foundation for a research thesis, a requirement for the completion of a Master’s of Science Degree in Genetic Counseling at Brandeis University. This study has been approved by the Brandeis University IRB.

If you have any questions or comments, please feel free to contact Kristen Maliszewski at ktmalisz@brandeis.edu or Barbara Lerner, MS, thesis committee chair at lerner@brandeis.edu

Thank you for your consideration!
Appendix C:

An Assessment of Genetic Counselors’ Opinions on how Non-Invasive Prenatal Diagnosis (NIPD) May Impact Genetic Counseling Services

Survey Questions

The main premise behind non-invasive prenatal diagnosis (NIPD) is that with a blood test, free fetal DNA (ffDNA) can be detected in maternal blood plasma as early as the seventh week of gestation, and possibly used for prenatal diagnosis. It is reported that the sensitivity of this technology is 90%, and the specificity is 96% for the detection of Down syndrome. To date it has also been used to detect paternally inherited alleles, sex-linked conditions, some single gene disorders, and other chromosomal abnormalities, although the exact detection rates have not all been determined.

Demographic Questions:

1. Do you currently practice as a prenatal genetic counselor?
   a. Yes
   b. No

2. In which geographic region do you practice prenatal genetic counseling?
   a. Northeast
   b. Southeast
   c. Midwest
   d. Northwest
   e. Southwest

3. What year did you graduate from your Genetic Counseling program?

4. How many total years experience do you have working as a genetic counselor?

5. How many total years experience do you have providing prenatal diagnostic services?
NIPD Questions:

1. How has the topic of NIPD been discussed with you at your workplace?
   a. In whether to incorporate the technology into your clinical practice
   b. As a part of a grounds lecture or journal club
   c. Casual discussion among colleagues
   d. Not at all
   e. Other (Specify____________)

2. When do you foresee NIPD being implemented into your clinical practice?
   a. In the next year
   b. In the next five years
   c. Never
   d. Other (Specify____________)

3. How do you foresee NIPD being used in clinical practice?
   a. In addition to all the current prenatal testing options currently available
   b. Replacing screening only
   c. Replacing current diagnostic testing only
   d. Replacing all the current prenatal testing options currently
   e. Not at all
   f. Other (Specify____________)

4. Once the technology has been validated, whom do you believe NIPD should be offered to? Check all that apply.
   __ All women
   __ Women who are of advanced maternal age
   __ Women with a positive screening result obtained via another technology
   __ Women considered high risk for other reasons (family history, ultrasound
      findings, etc)
   __ Other (Specify _________________)
5. NIPD could be an important asset to prenatal care
   a. Strongly agree
   b. Agree
   c. Not sure
   d. Disagree
   e. Strongly disagree
   Why: ______________________________________________________

6. From your experience, what is the most common reason that patients currently decide AGAINST having diagnostic testing?
   a. The risk of miscarriage
   b. Family pressure
   c. Anxiety about the test itself
   d. Do not feel the need to know
   e. Would not terminate regardless of the results
   f. Other __________

7. In your opinion, if NIPD is used in a clinical setting, therefore eliminating the risk for test related miscarriage, what would be the most common reason that patients decide AGAINST having diagnostic testing?
   a. The risk of miscarriage
   b. Family pressure
   c. Anxiety about the test itself
   d. Do not feel they need to know
   e. Would not terminate regardless of the results
   f. Other __________

8. If NIPD were used in a clinical setting, how do you then foresee patients viewing diagnostic testing?
   a. Safe enough that they would have it
b. Safe, but not worth having

c. Unsure and looking for more information

d. Unsure and don’t care to hear any information

e. Somewhat unsafe

f. Unsafe enough that they would not have it

9. The risk of miscarriage associated with diagnostic testing affects the patient’s decision to have the test.
   a. Strongly agree
   b. Agree
   c. Not sure
   d. Disagree
   e. Strongly disagree

10. NIPD will alter patient decision-making with regard to prenatal testing.
    a. Strongly agree
    b. Agree
    c. Not sure
    d. Disagree
    e. Strongly disagree

11. If NIPD is used in a clinical setting, the uptake of diagnostic testing will:
    a. Increase
    b. Remain the same
    c. Decrease
    d. Not sure

12. If NIPD is used in a clinical setting, on average fetal abnormalities will be detected:
    a. Sooner than with using current prenatal testing options
    b. Around the same time as with using current prenatal testing options
    c. Later than with using current prenatal testing options
d. Not sure

13. If NIPD is used in a clinical setting, the number of terminations can be expected to:
   a. Increase
   b. Remain the same
   c. Decrease
   d. Not sure

14. If NIPD is used in a clinical setting, the number of amniocentesis or CVS induced pregnancy losses will:
   a. Increase
   b. Remain the same
   c. Decrease
   d. Not sure

15. If NIPD is used in a clinical setting, patient anxiety with regard to prenatal testing will:
   a. Increase
   b. Remain the same
   c. Decrease
   d. Not sure

16. How do you expect the time it will take to COUNSEL patients about NIPD as compared to the time it takes to counsel about amniocentesis or CVS?
   a. Increase
   b. Decrease
   c. Remain the same

17. How do you expect the time it will take to EDUCATE patients about NIPD as compared to the time it takes to educate about amniocentesis or CVS?
   a. Increase
   b. Decrease
   c. Remain the same
18. If NIPD is used in a clinical setting, health care providers will adequately inform the patients of the remaining implications of testing, including having a child affected with a genetic disease or the option of termination.
   a. More often than with current testing options
   b. The same as with current testing options
   c. Less than with current testing options
   d. Other ________

19. If NIPD is used in a clinical setting, health care providers will have to work harder to ensure that women retain their right to informed consent for testing.
   a. Strongly agree
   b. Agree
   c. Not sure
   d. Disagree
   e. Strongly disagree

20. If NIPD is used in a clinical setting, the role of genetic counselors is likely to expand.
   a. Strongly agree
   b. Agree
   c. Not sure
   d. Disagree
   e. Strongly disagree

21. Implementing NIPD places the burden on genetic counselors to do more detailed counseling and patient education.
   a. Strongly agree
   b. Agree
   c. Not sure
   d. Disagree
   e. Strongly disagree

22. With the availability of NIPD do you anticipate the demand for pretest counseling to:
a. Increase
b. Decrease
c. Remain the same

23. NIPD will become routine prenatal care within the next 3-5 years, similar to current screening methods.
   a. Strongly agree
   b. Agree
c. Not sure
d. Disagree
e. Strongly disagree

24. If NIPD is used in a clinical setting, genetic counselors will have to work more closely with OBs to ensure informed consent.
   a. Strongly agree
   b. Agree
c. Not sure
d. Disagree
e. Strongly disagree

25. If NIPD is used in a clinical setting, when do you think it will be most practical for a pregnant woman to see a genetic counselor?
   a. Before any testing (including screening) is done
   b. After screening, but before diagnostic testing
c. After diagnostic testing
d. Both before and after any testing

Open ended questions:

26. How do you think you may have to change your counseling practice if NIPD is offered at your workplace with regards to:
   a. The organization of your practice
   b. Your counseling techniques
c. Other aspects of your practice
27. What are some differences in how cases will likely be managed if NIPD is an option?

28. What are your concerns about NIPD becoming clinically available in the next year or so?

29. Do you have any other comments to make about the possible use of NIPD?