

5-2016

## Patient Perception of Negative Non-Invasive Prenatal Testing Results

Ann Theresa Wittman

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PATIENT PERCEPTION OF NEGATIVE NON-INVASIVE PRENATAL TESTING

RESULTS

by

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PATIENT PERCEPTION OF NEGATIVE NON-INVASIVE PRENATAL TESTING

RESULTS

A

THESIS

Presented to the faculty of

The University of Texas

Health Science Center at Houston

and

The University of Texas

MD Anderson Cancer Center

Graduate School of Biomedical Sciences

In Partial Fulfillment

Of the Requirements

for the Degree of

MASTER OF SCIENCE

by

Ann Theresa Wittman, BS

Houston, Texas

May 2016

## ACKNOWLEDGEMENTS

This project reflects the collaboration and effort of many talented individuals. I have been incredibly lucky to have such a wonderfully supportive chair, Claire Singletary, without whom I would not have been able to complete this project. Thank you for all the countless hours of guidance and encouragement you have provided during this process and for being my mentor and friend during the past two years; your insight and patience is truly unparalleled. Additionally, I would like to thank my committee members: Dr. Syed Hashmi, Blair Stevens, Salma Nassef and Dr. Hector Mendez Figueroa for their invaluable support and contributions which have resulted in a final project that I am very proud of.

I cannot express enough gratitude to the University of Texas Genetic Counseling Program: Claire Singletary, Jennifer Czerwinski, Sarah Noblin, Telisha Green and numerous other supervisors, with whom I have had the pleasure of completing my genetic counseling training. I can't imagine a more supportive and enriching environment in which to complete a graduate program.

I am fortunate to have such great support from my family and friends. I would especially like to thank my husband for his endless encouragement and love during my graduate school journey. My parents deserve a huge thank-you for all of the love and support they have always given me. Additionally, I would like to acknowledge Kimberly Bruce, David Saldana and Abigail Ayangade for their unwavering friendship and understanding during my graduate school endeavors. I am also endlessly grateful for the encouragement of and could not have gotten through graduate school without my wonderful classmates: Torry Breen, Katie Chan, Christina Falugi, Meagan Giles, Jessica Ross, Ginger Tsai and Victoria Wagner.

# PATIENT PERCEPTION OF NEGATIVE NON-INVASIVE PRENATAL TESTING

## RESULTS

Ann Theresa Wittman, BS

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### Abstract

Non-invasive prenatal testing (NIPT) uses cell-free fetal DNA to assess for fetal aneuploidy during pregnancy. NIPT has higher detection rates and positive predictive values than previous methods; however, NIPT is not diagnostic. Studies suggest patients may underestimate the limitations of prenatal screening. Therefore, we conducted a prospective cross-sectional study of ninety-four women from genetic counseling clinics in Houston, Texas to assess patient understanding of the residual risk for aneuploidy after receiving a negative NIPT. The majority of participants (66%) understood the residual risk for Down syndrome following negative NIPT; however, 34% of participants indicated that negative NIPT completely eliminated the risk. Individuals with at least four years of college education were more likely to understand that NIPT does not eliminate the chance of trisomy 13/18 ( $p=0.012$ ) and sex chromosome abnormality ( $p=0.039$ ), and were more likely to understand which conditions NIPT tests for ( $p=0.021$ ), compared to women with less formal education. These data demonstrate that despite the recent implementation of NIPT into obstetric practice, the majority of women are aware of its limitations after genetic counseling. However, clinicians may need to consider alternative ways to communicate the limitations of NIPT to those women with less formal education to ensure understanding.

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## Introduction

Chromosomal aneuploidy is estimated to occur in 1/160 live births, the vast majority consisting of trisomy 21, trisomy 18, trisomy 13, and sex chromosome conditions (Driscoll et al., 2009). Before the advent of recent prenatal testing options, women seeking information about aneuploidy in their pregnancy generally had two options: invasive diagnostic testing that confers a risk for miscarriage or non-invasive screening, which generally had false positive rates of 5% or more and positive predictive values between 1 and 10% (Wapner, 2003; BJOG, 2005).

In November 2011, Non-Invasive Prenatal Testing (NIPT), or prenatal cell free fetal DNA screening, became clinically available for use in high-risk populations. NIPT was validated in a high-risk population in multiple studies, all of which have shown similar accuracies for aneuploidy detection (Palomaki, 2011, 2012; Bianchi, 2012; Gil, 2013). The most recent meta analysis by Gil et al. in 2015 analyzed data from 37 relevant studies and determined that NIPT detection rates for the most common aneuploidies are approximately 99.2% for trisomy 21, 96.3% for trisomy 18, 91% for trisomy 13 and 90-93% for sex chromosome aneuploidy. While the detection rates and positive predictive values (PPVs) for NIPT are increased in comparison to other methods of prenatal screening, NIPT is not a diagnostic test, and a negative NIPT result does not guarantee a pregnancy is unaffected (Neufeld-Kaiser et al. 2015). NIPT laboratories' marketing efforts and website content often focus on the detection rate rather than positive predictive value or residual risk (Mercer et al. 2014). It is unclear whether the general patient population understands this distinction, which may have implications for downstream uptake of invasive testing and emotional preparation at birth (Tiller, 2015; Hall, 2000). Therefore, we conducted a prospective cohort study to

assess patient understanding of the residual risk for trisomy 21, trisomy 18, trisomy 13 and sex chromosome aneuploidy after receiving a negative NIPT result.

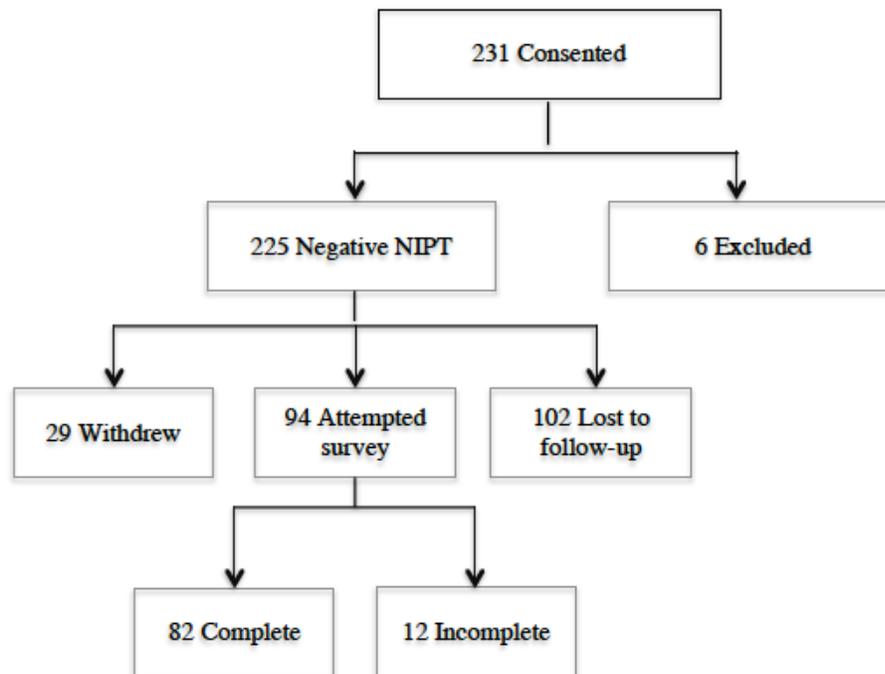
### **Methods**

From August 1, 2015 through January 29, 2016, women who were at least 18 years old, English or Spanish speaking, and had been consented for NIPT during their genetic counseling appointment were invited to participate in the study. Participating centers were staffed by University of Texas Health and Baylor College of Medicine prenatal genetic counselors in the Houston, Texas area and approved by the Institutional Review Boards: the University of Texas Health and Memorial Hermann Hospital (HSC-MS-15-0444), Baylor College of Medicine and affiliated Texas Children's Hospital (H-37683) and the Harris Health System (15-09-1193). Those patients willing to take part signed a consent form agreeing to be contacted after their NIPT results were available (Appendix A), and only those with a negative result were contacted to participate. The survey consisted of a section designed to assess patient understanding of the limitations of NIPT, a section to assess worry level for various conditions, a section regarding subsequent testing, and a section with demographic information (Appendix B). An online survey tool, Redcap, was used to securely administer the survey via email and collect the data. Those participants unable to complete the survey via email were called and given the survey over the telephone. Data from telephone calls were manually added to the Redcap data set. Data were analyzed using STATA, (v.14.1, College Station TX). Comparison of data between groups was evaluated using Chi-square analysis, Fisher exact test, Wilcoxon signed-rank test or Mann Whitney test where appropriate. Statistical significance was assumed at a Type I error rate of 5%.

## Results

A total of 231 women agreed to participate in the study and be contacted for the survey. Six women were excluded either due to a positive NIPT result (n=3) or failure to follow-through with the blood draw (n=3). Two hundred twenty-five women were contacted after their negative NIPT result and asked to participate in the survey either through email or phone call. Twenty-nine women (13%) declined to participate after being contacted and 102 women (45%) were never successfully contacted, leaving a total of 94 participants (42%) from the original 225 consented. Twelve (13%) of the surveys were incomplete, the majority of which were missing the last several questions of the survey (Figure 1).

**Figure 1: Survey Completion Flow Diagram**



The majority of participants (59%, n=55) were referred to genetic counseling due to advanced maternal age and most identified as non-Hispanic White (36%, n=34) or Hispanic

(29%, n=27). The majority of participants (64%, n=60) reported having at least a four-year college degree (Table 1).

**Table 1: Participant Demographics (n=94)**

<b>Participant Demographics</b>		
	<b>n</b>	<b>%</b>
<b>Ethnicity</b>		
Non Hispanic White	34	36
Hispanic	27	29
Afr. American	16	17
Asian	11	12
Other	5	5
No Answer	1	1
<b>Household Income</b>		
Less than \$25,000	10	11
\$25,000 to \$49,999	15	16
\$50,000 to \$74,999	16	17
\$75,000 to \$99,999	15	16
\$100,000 to \$149,999	20	21
\$150,000 or more	12	13
Do not wish to answer	6	6
<b>Education</b>		
Some high school	1	1
High school/GED	11	12
Some college	22	23
4-year degree	32	34
Graduate degree	28	30
<b>Marital Status</b>		
Married/living with partner	84	89
Unmarried	9	11
Do not wish to answer	1	1
<b>Age</b>		
21-29 years	15	16
30-34 years	15	16
35-39 years	54	57
40-43 years	10	11
<b>Indication</b>		
Advanced Maternal Age	55	59
Positive Serum Screen	11	12

Ultrasound Abnormality	11	12
Low Risk	9	10
Two or More Indications	8	9

### **Patient Perception of Residual Risk Post- Negative NIPT Results**

Participants were asked about their residual risk for Down syndrome, trisomy 13/18, sex chromosome aneuploidy, and any other genetic syndromes after a negative NIPT result. The majority of participants indicated their risk was decreased but not eliminated. Sixty-one percent (n=57) of women indicated their risk to have a baby with Down syndrome was much lower, 55% (n=52) indicated that their risk was much lower for trisomy 13/18 and 49% (n=46) said that their risk to have a baby with a sex chromosome aneuploidy was much lower. A proportion of women also indicated that there was no residual risk after a negative NIPT. Specifically, 34-39% of participants indicated there was no longer a chance for their baby to have Down syndrome, trisomy 13/18 or a sex chromosome aneuploidy after receiving a negative NIPT result. Additionally, participants were asked to indicate their risk to have a baby with a genetic condition other than Down syndrome, trisomy 13/18 or sex chromosome aneuploidy after receiving a negative NIPT result. Thirteen percent (n=12) correctly answered that their risk was not lower than before, 29% (n=27) indicated that there was no longer any chance for their baby to have any genetic problem, 49% (n=46) answered that it was much lower than before and 9% (n=8) responded that it was somewhat lower than before. Women with less than a four-year college education were significantly more likely to incorrectly respond that there was no longer a risk for their baby to have trisomy 13/18 ( $p=0.012$ ) or a sex chromosome abnormality ( $p=0.039$ ). Participants with less than a four-year education also appeared to be more likely to indicate that there was no longer a chance for their baby to have Down syndrome; however, this did not reach significance ( $p=0.086$ ).

Other demographic factors did not show a significant influence on patient perception of negative NIPT results (Table 2).

**Table 2: Patient Perception of Risk Post Negative NIPT (n=94)**

<b>Perception of Residual Risk Post Negative NIPT</b>				
	Down Syndrome (%)	T13/T18 (%)	Sex Chromosome Aneuploidy, (%)	Any Other Genetic Condition, (%)
Not lower than before	0	1	5	13
Somewhat lower than before	5	10	7	10
Much lower than before	61	55	49	49
No longer a chance	34	34	39	29
<b>Influence of Demographic Factors on Risk Perception Post Negative NIPT</b>				
	Down Syndrome	T13/T18	Sex Chromosome Aneuploidy	Any Other Genetic Condition
Ethnicity	$p=0.440$	$p=0.119$	$p=0.177$	$p=0.130$
Income	$p=0.588$	$p=0.540$	$p=0.166$	$p=0.752$
Education	$p=0.086$	$p=0.012$	$p=0.039$	$p=0.159$
Age	$p=0.649$	$p=0.550$	$p=0.486$	$p=0.885$
Indication	$p=0.238$	$p=0.082$	$p=0.324$	$p=0.700$

**Most Important and Least Important Reasons for Pursuing NIPT**

Participants were asked to share the most important and least important reasons for pursuing NIPT on a scale of one to six, with one being the most important and six being the least important. There was no significant difference between demographics and how participants ranked their reasons for pursuing NIPT (ethnicity  $p = 0.586$ , income  $p = 0.747$ , education  $p = 0.212$ , age  $p = 0.373$ , indication  $p = 0.123$ ), (Table 3).

**Table 3: Most and Least Important Reasons For Pursuing NIPT (presented as percentages, n=85)**

	Level of Importance <sup>a</sup>						Trendlines
	1	2	3	4	5	6	
Gender	6	19	13	29	13	19	
Down Syndrome	42	13	7	8	9	15	
Other Aneuploidy	8	39	11	8	20	13	
Avoid Amnio	1	7	31	33	20	7	
Make Dr. Happy	26	12	5	2	14	38	
Relieve Anxiety	9	9	33	18	22	7	

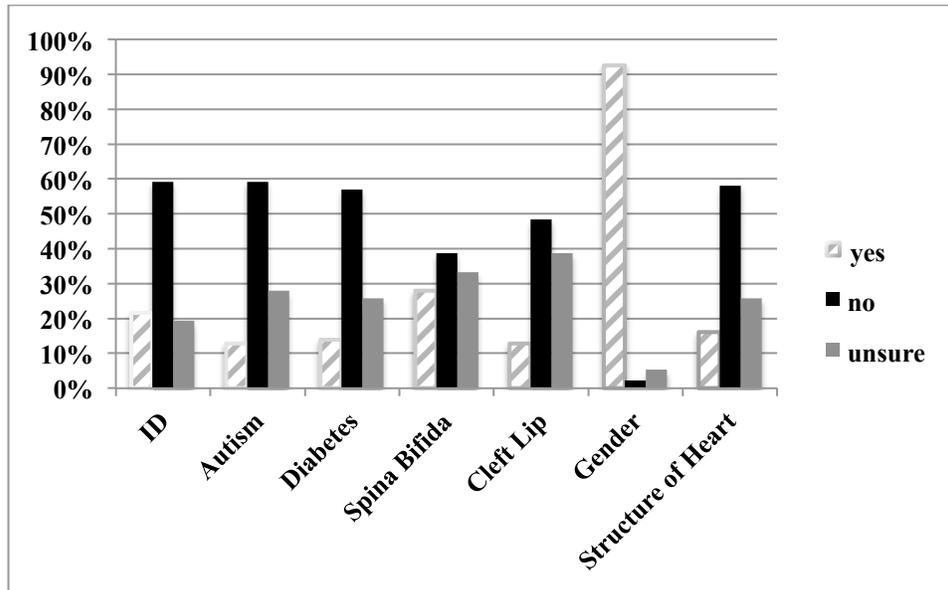
<sup>a</sup> Level of Importance: 1 (most important) to 6 (least important)

### Patient Perception of Conditions Tested by NIPT

Participants were asked to indicate whether NIPT could test for the following: intellectual disability, autism, diabetes, spina bifida, cleft lip, gender and structure of the heart. The vast majority of participants (92%, n=86) were able to correctly identify that NIPT can test for gender. When looking at the remaining six items from this question, a participant had to indicate that NIPT did not test for the item in order to be scored as correct. Cleft lip, structure of heart and spina bifida were considered structural abnormalities, while intellectual disability, autism and diabetes were considered non-structural. Those with less formal education were significantly less likely to recognize what NIPT could not test for and had lower scores overall ( $p= 0.021$ ). Fourteen percent (5/36) of women with less formal education correctly answered all of the questions in comparison to thirty-seven percent (22/60) of those women with at least four years of college. Overall, the participants were more likely to believe that NIPT could test for structural abnormalities (cleft lip, spina bifida and structure of heart) versus non-structural abnormalities (intellectual disability, autism and diabetes) ( $p < 0.0005$ ) and women with less than a four-year degree were even more likely

than those with higher education to believe that that NIPT could test for both structural abnormalities ( $p= 0.024$ ) and non-structural abnormalities ( $p= 0.010$ ), (Figure 2).

**Figure 2: Patient Perception of Conditions Tested by NIPT (n=93)**



### Worry Levels Before and After Negative NIPT

Participants were asked to rank their worry level about having a child with Down syndrome, trisomy 13/18 and sex chromosome abnormality pre-testing via NIPT on a scale of one to five with one being unconcerned and five being very concerned. Similarly, women were asked what their level of concern was to have a baby with any genetic condition after a negative NIPT result. There was a significant decline when comparing the general level of worry before NIPT to each of the worry levels for Down syndrome ( $p<0.0001$ ), trisomy13/18 ( $p<0.0001$ ), sex chromosome aneuploidy ( $p<0.0001$ ) and any other genetic condition after a negative NIPT result ( $p<0.0001$ ). Despite the fact that NIPT cannot reduce risk for all genetic conditions, the majority of participants ( $n=67$ , 70%) reported a decrease in worry to have a baby with any genetic disorder (Table 4).

**Table 4: Worry Levels Before and After Negative NIPT (%), n=94**

	Worry Level*					Trendlines					Significance (p-value)
	1	2	3	4	5						
General Worry Before NIPT	10	13	27	20	31	—	—	—	—	—	—
Worry about DS (after NIPT)	62	19	9	3	7	■	■	■	■	■	<0.0001
Worry about T18/T13 (after NIPT)	65	14	12	4	5	■	■	■	■	■	<0.0001
Worry about SCA (after NIPT)	66	13	14	3	4	■	■	■	■	■	<0.0001
Worry about any syndrome (after NIPT)	50	23	12	6	9	■	■	■	■	■	<0.0001

\* Worry Level: 1 (least worried) to 5 (most worried)

## Discussion

This study aimed to assess patient perception of the residual risk for Down syndrome, aneuploidy other than Down syndrome, birth defects, and other genetic conditions, after a negative non-invasive prenatal test. To our knowledge this is the first study to examine patient understanding of the limitations of NIPT. Our data demonstrate that despite the relatively recent implementation of NIPT into obstetric practice, the majority of women who receive genetic counseling by genetic counselors are aware of its limitations. Overall, most participants were able to recognize that NIPT is a screening test and that it significantly reduces risk for those conditions it tests for, but does not eliminate the risk entirely. Of note for practitioners, patient comprehension of NIPT's screening ability increased significantly with education level. Therefore, practitioners may need to spend additional time discussing the implications of a screening test with patients who have less formal education.

Similarly, many women correctly recognized that NIPT does not test for non-structural abnormalities such as autism, intellectual disability and diabetes or structural abnormalities such as heart defects, cleft lip and spina bifida. Interestingly, participants were more likely to incorrectly respond that NIPT could evaluate for structural abnormalities compared to the non-structural abnormalities. It is unclear why patient comprehension

differed between these groups. Heart defects and cleft lip are often associated with aneuploidy, therefore women may have falsely assumed that a negative NIPT reduced the risk for non-aneuploidy associated heart defects and clefting. In addition, many women at our participating centers had an ultrasound following their genetic counseling appointment. Thus, they may have confused reassurance for structural conditions from the ultrasound with reassurance from NIPT. Furthermore, blood may be drawn to assess alpha fetal protein (AFP) levels and spina bifida risk at the same time as blood is drawn for NIPT, thus women may have falsely believed these tests are one in the same. Additional studies may wish to delve into the underlying reasons behind this misunderstanding.

This study also demonstrated that negative NIPT results significantly decreased worry levels of patients regarding having a baby with Down syndrome ( $p < 0.00001$ ), trisomy 13/18 ( $p < 0.00001$ ), and sex chromosome aneuploidy ( $p < 0.00001$ ). This asserts the clinical utility of non-invasive prenatal testing to provide appropriate reassurance for women who experience anxiety regarding their risk to have a baby with aneuploidy. However, this study also showed that women who undergo non-invasive prenatal testing are also more likely to experience a false decrease in worry levels for conditions not screened by NIPT, suggesting that negative NIPT results may provide patients with false reassurance in addition to appropriate reassurance for aneuploidy. It is unclear whether or not this is due to lack of understanding related to NIPT or general unfamiliarity with other genetic conditions.

Although the majority of women are likely to understand the limitations of non-invasive prenatal testing after genetic counseling, it is clear that education level plays a role in comprehension. Women who had less than a four-year college education were more likely to believe that their non-invasive prenatal testing could eliminate their risk to have a child

with aneuploidy. Similarly, women with more education were more likely to understand what conditions were included in NIPT. These data are consistent with previous studies examining the role of education on patient literacy and perception of prenatal screening tests. A study by Wong et al. in 2012 demonstrated that women with less formal education were more likely to perceive second trimester ultrasound as more sensitive and diagnostic in comparison to those women with a higher level of education. Moreover, past studies regarding patient understanding of prenatal maternal serum screening demonstrated that low health literacy and comprehension of the limitations are associated with less years of formal education (Goel, 1996; Cho, 2007). Women with low health literacy may also have difficulty with numeracy, confounding their interpretation of the sensitivity, specificity and predictive values of prenatal screening methods. In 2004 Gates et al. examined the role of numeracy on patient understanding and concluded that women with lower levels of literacy and numeracy have the most difficulty in accurately interpreting information about risk. The effect of education and health literacy on patient understanding of prenatal screening is an important consideration, as approximately 40% of women 25 years and older in the United States do not have any formal education beyond high school (US Census Data 2014).

An additional issue that may confuse patients is the manner in which the 99% detection rate for NIPT is often highlighted by the media and laboratory testing materials rather than focusing on the individual patient's PPV and NPV. Without sufficient background knowledge, women may get the impression that the PPV and detection rates are both 99%. A study by Mercer et al. in 2014 examined the impact of the availability and use of the Internet for gathering information about non-invasive prenatal testing. Their study showed a lack of comprehensiveness and quality of information regarding non-invasive

prenatal testing obtained through Internet sources. Moreover, many of the websites either failed to mention or downplayed information about the limitations and disadvantages of NIPT while simultaneously promoting the accuracy of the test without mentioning the importance of negative and positive predictive value calculations. It is no wonder that women who research NIPT on the Internet may not appreciate the residual risk for aneuploidy, especially women without advanced formal education.

### **Conclusions and future directions**

This study demonstrates that NIPT invokes similar issues as previous prenatal screening modalities and that providers should be cognizant of the tendency for women with less formal education to overinflate the power of screening to decrease or eliminate their risk for a baby with a genetic condition. The incorporation of non-invasive prenatal testing into obstetric practice has proved both exciting and overwhelming. Although it is clear that this new screening option can provide tremendous benefits to women worried about having a baby with a common aneuploidy, proper pretest genetic counseling is essential to ensure that patients are informed of the limitations and potential results from NIPT. There appear to be numerous barriers to complete patient comprehension of non-invasive prenatal testing, including the low numeracy and health literacy of many members of the general population and the potentially misleading portrayal of the limitations of NIPT on the Internet. Genetic counselors and obstetricians must prioritize communicating information regarding NIPT accurately and clearly, so that women considering it as a screening option may be adequately informed. When possible, attention should be paid to a patient's education level and information should be tailored accordingly. The development of patient friendly decision aids

that clearly state the limitations of screening and what a negative test means may assist in residual risk communication, informed consent, and decision making (Vlemmix et al. 2013).

As this was a pilot study with a limited number of participants, more research is needed to examine patient perception of the limitations of non-invasive prenatal testing and how this may vary based on patient demographic and geographic factors. Additionally, future studies may wish to examine whether the implementation of targeted educational materials and decision aids augment patient understanding of NIPT, especially as the testing platforms are expanded to cover more chromosomal abnormalities. Furthermore, research should be done to assess patient perception of positive NIPT results and whether or not women who screen positive accurately understand the implications and limitations of the results.

### **Limitations**

This study was limited by the small sample size. The majority of women were referred either due to advanced maternal age or positive serum screen. Therefore, we cannot confidently extrapolate to the low risk population. In addition, 64% of participants had at least a 4-year college degree. Given the association of education level with understanding, a larger sample size might have allowed for parsing out sub-groups from women who had less than a four year degree into those with some college, those with a high school diploma, and those without a high school diploma to further stratify the finding. Additionally, the survey used was carefully developed to evaluate the aims of this study; however, this assessment tool has not been validated in other studies. Finally, this research was limited to the greater Houston, Texas area, thus these results may not be generalizable to other geographical regions.

## References

1. Driscoll, D. A., M.D., & Gross, S., M.D. (2009). Prenatal screening for aneuploidy. *The New England Journal of Medicine*, 360(24), 2556-62. doi:<http://dx.doi.org/10.1056/NEJMcp0900134>
2. Wapner, R., Thom, E., Simpson, J.L., Pergament, E., Silver, R., Filkins, K., Platt, L., Mahoney, M., Johnson, A., Hogge, W.A., Wilson, R.D., Mohide, P., Hershey, D., Krantz, D., Zachary, J., Snijders, R., Greene, N., Sabbagha, R., MacGregor, S., Hill, L., Gagnon, A., Hallahan, T., Jackson, L. & First Trimester Maternal Serum Biochemistry and Fetal Nuchal Translucency Screening (BUN) Study Group. (2003) First-Trimester Screening for Trisomies 21 and 18. *The New England Journal of Medicine*, 349 (15),1405-1413. doi:10.1002/pd.3873
3. BJOG (2005). Positive predictive value again An International Journal of Obstetrics & Gynaecology, 106(9), vii-viii. doi:10.1111/j.1471-0528.1999.tb08421.x
4. Palomaki, G.E., Kloza, E.M., Lambert-Messerlian, G.M., Haddow, J.E., Neveux, L.M., Ehrich, M., van den Boom, D., Bombard, A.T., Deciu, C., Grody, W.W., Nelson, S.F. & Canick, J.A. I (2011). DNA sequencing of maternal plasma to detect Down syndrome: an international clinical validation study. *Genetics in Medicine*: 13(11), 913.
5. Palomaki, G.E., Deciu, C., Kloza, E.M., Lambert-Messerlian, G.M., Haddow, J.E., Neveux, L.M., Ehrich, M., van den Boom, D., Bombard, A.T., Grody, W.W., Nelson, S.F. & Canick, J.A. (2012). DNA sequencing of maternal plasma reliably identifies trisomy 18 and trisomy 13 as well as Down syndrome: an international collaborative study. *Genetics in Medicine* 14(3), 296-305. doi:10.1038/gim.2011.73
6. Bianchi, D.W., Platt, L.D., Goldberg, J.D., Abuhamad, A.Z., Sehnert, A.J., Rava, R.P. & MatErnal BLOod IS Source to Accurately diagnose fetal aneuploidy (MELISSA) Study Group (2012) Genome-wide fetal aneuploidy detection by maternal plasma DNA sequencing. *Genome-wide fetal aneuploidy detection by maternal plasma DNA sequencing. Obstetrics & Gynecology*, 119(5), 890-901. doi:10.1097/AOG.0b013e31824fb482
7. Gil MM, Quezada MS, Bregant B, Ferraro M, Nicolaidis KH. Implementation of maternal blood cell-free DNA testing in early screening for aneuploidies. *Ultrasound Obstet Gynecol* 2013;42:34–40 *Medicine*, 13, 129
8. Gil, M. M., Quezada, M. S., Revello, R., Akolekar, R., & Nicolaidis, K. H. (2015). Analysis of cell-free DNA in maternal blood in screening for fetal aneuploidies: Updated meta-analysis. *Ultrasound in Obstetrics & Gynecology*, 45(3), 249-266. doi:10.1002/uog.14791

9. Neufeld-Kaiser, W. A., Cheng, E. Y., & Liu, Y. J. (2015). Positive predictive value of non-invasive prenatal screening for fetal chromosome disorders using cell-free DNA in maternal serum: Independent clinical experience of a tertiary referral center. *BMC*
10. Mercer, M. B., Agatista, P. K., & Farrell, R. M. (2014). What patients are reading about noninvasive prenatal testing: An evaluation of internet content and implications for patient-centered care. *Prenatal Diagnosis*, 34(10), 986-993. doi:10.1002/pd.4410
11. Tiller, G. E., Kershberg, H. B., Goff, J., Coffeen, C., Liao, W., & Sehnert, A. J. (2015). Women's views and the impact of noninvasive prenatal testing on procedures in a managed care setting. *Prenatal Diagnosis*, 35(5), 428-433. doi:10.1002/pd.4495
12. Hall, S., Bobrow, M., & Marteau, T. M. (2000). Psychological consequences for parents of false negative results on prenatal screening for down's syndrome: Retrospective interview study. *BMJ: British Medical Journal*, 320(7232), 407-412. doi:10.1136/bmj.320.7232.407
13. Wong, A. E., Collingham, J. P., Koszut, S. P., & Grobman, W. A. (2012). Maternal factors associated with misperceptions of the second-trimester sonogram. *Prenatal Diagnosis*, 32(11), 1029-1034. doi:10.1002/pd.3950
14. Goel, V., Glazier, R., Holzapfel, S., Pugh, P., & Summers, A. (1996). Evaluating patient's knowledge of maternal serum screening. *Prenatal Diagnosis*, 16(5), 425-430. doi:10.1002/(SICI)1097-0223(199605)16:5<425::AID-PD874>3.0.CO;2-2
15. Cho, R. N., Plunkett, B. A., Wolf, M. S., Simon, C. E., & Grobman, W. A. (2007). Health literacy and patient understanding of screening tests for aneuploidy and neural tube defects. *Prenatal Diagnosis*, 27(5), 463-467. doi:10.1002/pd.1712
16. Gates, E. A. (2004). Communicating risk in prenatal genetic testing. *Journal of Midwifery and Women's Health*, 49(3), 220-227. doi:10.1016/j.jmwh.2004.02.014
17. U.S. Census Bureau. (2014) *Educational Attainment in the United States*. Retrieved March 14, 2016, from <http://www.census.gov/hhes/socdemo/education/data/cps/2014/tables.html>
18. Vlemmix, F., Warendorf, J., Rosman, A., Kok, M., Mol, B., Morris, J., & Nassar, N. (2013). Decision aids to improve informed decision-making in pregnancy care: A systematic review. *BJOG: An International Journal of Obstetrics & Gynaecology*, 120(3), 257-266. doi:10.1111/1471-0528.12060

## Appendix A

### Patient consent form

#### INFORMED CONSENT FORM TO TAKE PART IN RESEARCH

Title: Patient perception of residual risk post negative NIPT results

Letter of Information

HSC-MS-15-0444

Primary Investigator: Claire Singletary

You are invited to take part in a research study called, “Patient perception of residual risk post negative NIPT results”, conducted by Claire Singletary of the University of Texas Health Science Center at Houston. For this research project, she will be called the Principal Investigator or PI.

The purpose of this study is to evaluate patient perception of their negative NIPT results. If you decide to take part in the study, the total time commitment is 15 minutes. You are invited to take part in this study because you have elected to proceed with non-invasive prenatal testing (NIPT). Women who choose to participate will be contacted after they receive their NIPT results. You can refuse to answer any questions asked or written on any forms. Participation in this study is voluntary. A decision not to take part in this study will not change the services you receive through the University of Texas Health Science Center at Houston.

If you agree to take part in this survey, you will agree to a 15 minute survey.

You may not receive any benefit from taking part in this study. The information you provide will help to determine patient understanding of non-invasive prenatal testing. There are no known risks to take part in this study. The only possible risk may be breach of confidentiality. This information collected in the survey responses will not contain identifying information and will be kept on a secure server. You have the alternative to choose to not take part in this study and can withdraw at any time.

There is no cost and you will not be paid to take part in this study. However, upon completion of the survey you can choose to be entered in a drawing to win a \$50 Target gift card. You will not be personally identified in any reports or publications that may result from this study. Any personal information about you that is gathered during this study will remain confidential to every extent of the law.

If you have any questions about this project please contact study coordinator Theresa Wittman or PI Claire Singletary at 713-500-5599.

If you would like to be contacted to participate after you receive your NIPT results, please provide the following information:

Name: \_\_\_\_\_

Email: \_\_\_\_\_

Signature: \_\_\_\_\_

Phone Number: \_\_\_\_\_

Date: \_\_\_\_\_

If you agree to take part in the study your agreement is completion of the survey.

This research project has been reviewed by the Committee for the Protection of Human Subjects (CPHS) of the University of Texas Health Science Center at Houston (HSC-MS-15-0444) For any questions about research subjects rights call CPHS at (713) 500-7943.

For genetic counselor use only:

Date: \_\_\_\_\_

Indication: AMA Positive FTS Screen Positive Quad Screen Ultrasound  
Abnormality Positive Family History

Other \_\_\_\_\_

Age: \_\_\_\_\_

G: \_\_\_\_\_ P: \_\_\_\_\_

## Appendix B

### Prenatal patient questionnaire

You were seen for genetic counseling during your current pregnancy and offered to participate in a survey about having a blood test called non-invasive prenatal testing, or NIPT. Thank you for agreeing to be contacted to discuss your feelings about NIPT.

This survey should take approximately 10 minutes to complete. Whether or not you choose to participate will not impact your care in any way. Your participation is greatly appreciated.

Please choose the best answer for each question:

1. How many years of education you have completed?
  - a. Never attended high school
  - b. Some high school
  - c. High school/GED
  - d. Some college or 2 year/associates degree
  - e. 4-year degree (BA, BS)
  - f. Graduate or Professional degree (MS, MBA, PhD, MD, JD)
  - g. Do not wish to answer
  
2. What is your marital status?
  - a. Married/living with partner
  - b. Unmarried, living with other adults
  - c. Unmarried, living without other adults
  - d. Do not wish to answer
  
3. With which race/ethnicity do you most identify?
  - a. White, non-Hispanic
  - b. Hispanic
  - c. African-American
  - d. Asian/Pacific Islander
  - e. Native American
  - f. Other: \_\_\_\_\_
  - g. Do not wish to answer
  
4. On a scale of 1 to 5, with 1 being unconcerned and 5 being very concerned, please rate what your level of concern was for your baby to have any health problem before you had non-invasive prenatal testing (NIPT)  
1    2    3    4    5
  
5. On a scale of 1 to 5, with 1 being unconcerned and 5 being very concerned, please rate what your level of concern was to have a baby with a health problem, before you had non-invasive prenatal testing (NIPT)

1 2 3 4 5

6. You had a negative NIPT test. What do you feel that your chances are to have a baby with Down syndrome after receiving this result? After receiving a negative NIPT result I feel my chances are...

- a. Not lower than before
- b. Somewhat lower than before
- c. Much lower than before
- d. There is no longer a chance that my baby will have Down syndrome

7. On a scale of 1 to 5, with 1 being unconcerned and 5 being very concerned, please select what your present level of concern is to have a baby with Down syndrome after a negative NIPT result

1 2 3 4 5

8. What are your chances to have a baby with trisomy 18 or trisomy 13 after receiving a negative NIPT result? After receiving a negative NIPT result I feel my chances are...

- a. Not lower than before
- b. Somewhat lower than before
- c. Much lower than before
- d. There is no longer a chance that my baby will have trisomy 13 or trisomy 18

9. On a scale of 1 to 5, with 1 being unconcerned and 5 being very concerned, please select what your present level of concern is to have a baby with a baby with trisomy 18 or trisomy 13 after receiving a negative NIPT result

1 2 3 4 5

10. What are your chances to have a baby with a sex chromosome condition such as Turner syndrome or Klinefelter syndrome after receiving a normal NIPT result?

After receiving a negative NIPT result I feel my chances are...

- a. Not lower than before
- b. Somewhat lower than before
- c. Much lower than before
- d. There is no longer a chance that my baby will have a sex chromosome condition

11. On a scale of 1 to 5, with 1 being unconcerned and 5 being very concerned, please select what your present level of concern is to have a baby with a sex chromosome condition after a negative NIPT result.

1 2 3 4 5

12. What are your chances to have a baby with a genetic condition other than Down syndrome, trisomy 18, trisomy 13 or a sex chromosome conditions after receiving a normal NIPT result? After receiving a negative NIPT result I feel my chances are...

- a. Not lower than before
- b. Somewhat lower than before

- c. Much lower than before
- d. There is no longer a chance that my baby will have any genetic condition other than other than Down syndrome, trisomy 18, trisomy 13 or a sex chromosome condition

13. Please select your level of worry about having a baby with a genetic condition other than Down syndrome, trisomy 18, trisomy 13 or sex chromosome condition

1 2 3 4 5

14. Please select whether NIPT is able to specifically test for any of the following:

a. Spina bifida	Yes	No	Don't know
b. Cleft lip	Yes	No	Don't know
c. Gender	Yes	No	Don't know
d. Structure of heart	Yes	No	Don't know
e. Intellectual disability	Yes	No	Don't know
f. Autism	Yes	No	Don't know
g. Diabetes	Yes	No	Don't know

15. Have you had your anatomy ultrasound (typically performed around 20 weeks of pregnancy)? Yes No

If yes, were any abnormalities found on your ultrasound?

If yes, please describe: \_\_\_\_\_

16. Did you have an amniocentesis procedure (needle test) or chorionic villus sampling (CVS) after receiving your negative NIPT results? Yes No

17. Are you planning to have an amniocentesis procedure (needle test) or chorionic villus sampling (CVS)? after receiving your negative NIPT results? Yes No

18. If yes, why did you or why will you have an amniocentesis or CVS? (check all that apply)

- Concerns from my NIPT
- Concerns on an ultrasound
- For piece of mind
- For greater accuracy
- To test for other conditions
- Other:

19. If you did not or will not have an amniocentesis (needle test) or chorionic villus sampling (CVS), why not? (check all that apply)

- NIPT results were reassuring enough
- My doctor/genetic counselor said I did not need it
- The risk of miscarriage
- I am not worried about other conditions NIPT did not test for
- I am not worried about Down syndrome, trisomy 18, trisomy 13 or sex chromosome conditions

- I do not like needles
- I will continue the pregnancy regardless of a genetic condition
- Other: \_\_\_\_\_

20. If your NIPT testing had come back abnormal, were you planning to have an amniocentesis or CVS?

Yes      No      Unsure

Why or Why Not?

21. How has having a negative NIPT test impacted your worry level about the pregnancy? (please check)

- I worry much less
- I worry a little less
- I worry about the same
- I worry a little more
- I worry a great deal more

22. Rank from most important (1) to least important (6) the reasons behind your decision to pursue NIPT?

- \_\_\_\_\_ To determine my baby's gender
- \_\_\_\_\_ To determine my baby's chance of having Down syndrome
- \_\_\_\_\_ To determine my baby's chance of having another chromosome condition, such as trisomy 18, trisomy 13, or a sex chromosome disorder
- \_\_\_\_\_ To avoid having amniocentesis or CVS
- \_\_\_\_\_ To make my doctor happy
- \_\_\_\_\_ To relieve anxiety

23. Please describe below any other reason not listed above that was important in your decision- to pursue NIPT

24. Please describe below any other comments or concerns you have regarding your non-invasive prenatal testing?

## Vita

Ann Theresa Wittman was born in Santa Fe, New Mexico, the daughter of Susan Lee Skelton and Donald Farrell Wittman. After graduating from Desert Academy High School in Santa Fe, NM, she enrolled at the University of New Mexico, during which she spent a semester abroad in Costa Rica. She received a degree of Bachelor of Science with majors in biology and Spanish and a minor in chemistry in December of 2011. After graduation Theresa moved to Houston and for the next two and a half years, she worked as a laboratory technician in a cancer research laboratory at Baylor College of Medicine. In August of 2014, she entered the Genetic Counseling program at The University of Texas Graduate School of Biomedical Sciences at Houston.

**Permanent address:**

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