PATIENT SURVEY ON PRENATAL TESTING FOR FETAL GENETIC CONDITIONS AND TRAITS

By

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ABSTRACT OF THE THESIS

Patient Survey on Prenatal Testing for Fetal Genetic Conditions and Traits

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Our aim was to assess patient opinions on prenatal genetic testing to determine which health risks, physical traits, and genetic conditions patients are interested in learning about their unborn child. We analyzed factors such as religion, education, and familiarity with disability to assess whether these influence patient preferences on fetal testing and termination of pregnancy due to a diagnosis. We categorized conditions as benign, mild, moderate and severe. We found that patients were highly motivated to learn about a range of fetal conditions including benign, mild, moderate, and severe conditions via non-invasive testing. However, they were generally only interested in follow up diagnostic fetal testing for severe fetal indications. We found that patients who did not indicate a religious affiliation were 7.5 times more likely to consider/pursue termination due to a fetal indication than those individuals with a religious affiliation. A patient's level of education and familiarity with disability were not significant factors in determining preferences for prenatal testing and termination for fetal indications. For adult onset conditions, patients were highly motivated for fetal screening using non-invasive technology, but were less inclined to pursue follow up diagnostic testing and significantly less likely to pursue termination, if a fetus was confirmed to be at risk. This raises an ethnical consideration on whether prospective parents have the right to have this

information for adult onset conditions. Our data shows some interesting insight into the type of information prospective parents may be interested in learning about their unborn child.

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Introduction

Several studies have evaluated patient and parental attitudes towards Down syndrome and trisomy screening during pregnancy (1, 2). However, limited data is available regarding general patient perspectives on assessing fetal risk for genetic diseases or non-health related traits. Historically, Down syndrome and other trisomies have been the main focus of prenatal genetic testing. However, these are more prevalent in high-risk patient populations; particularly women of advanced maternal age. With rapidly evolving technology, prenatal screening and diagnostic testing has evolved beyond the common aneuploidies. Patients will continue to have increased opportunities to learn genetic information regarding their fetus (3).

Previous studies have evaluated parental perspective in targeted populations, already impacted by one specific condition, such as thalassemias, cystic fibrosis, pediatric deafness, Treacher Collins syndrome, Muenke syndrome and sickle cell anemia (4,5,6,7,8,9). The limitations of these studies are that these families have already been impacted by the genetic condition and the focus is limited to one specific disease. No study has yet been undertaken to query the general population regarding their views on genetic testing for a diverse group of fetal diseases and fetal non-health related traits.

This study assesses patient opinions on prenatal testing for various health and non-heath related characteristics, and compares whether patients would utilize noninvasive or invasive methodologies to learn information regarding their fetus. Currently in the United States, cell free DNA screening (cfDNA) in maternal serum is being routinely

used as a screening tool for Down syndrome, trisomy 18, trisomy 13, and the common sex chromosome aneuploidies. Recently, cfDNA screens have been developed to also include select microdeletions and some panels even include all chromosome assessment (10). Cell free DNA screening for single gene disorders is also available in the United States on a limited basis (11,12,13). The application of cell free DNA for diagnostic purposes is currently being utilized for achondroplasia and thanatophoric dysplasia in the UK National Health Service (NHS) approved in 2012 (14). Additionally NIPD is now in clinical practice in the UK NHS for cystic fibrosis, spinal muscular atrophy, and Duchenne muscular dystrophy (12, 15, 16,17). NIPD is also being done for various monogenic disorders for known mutations in the United States (12). The application of this technology will continue to advance and diversify. Therefore, it is important to study patient preferences regarding fetal testing and evaluating the testing modalities and interventions these patients would consider.

With rapidly evolving advances in genetic testing, it is now possible to test prospective parents for hundreds of conditions to assess their carrier status and determine if their future offspring are at risk for a recessive disorder (18,19). At the same time it as become commonplace for patients to access to direct-to-consumer tests to learn about certain physical traits such as freckles, hair/eye color, and lactose intolerance (20). Moving forward it would not be surprising if patients were to seek this information about their unborn child. Often technological advances outpace the ethical and clinical considerations and professional guidelines outlining implementation. As part of understanding the impact of novel technology, it is important to study patient preferences and how they would use this information during their pregnancies.

We surveyed patients to determine when they were most likely to pursue an amniocentesis following a positive screening result and under what circumstances they would pursue a termination of pregnancy for a fetal diagnosis. In this study we determine if patients are interested in learning whether their unborn child is at risk for certain physical traits and genetic conditions and what factors may motivate them towards wanting genetic testing. There is very limited data exploring patient opinions on possible future uses of NIPT, and diagnostic testing. The information gained may help shape the type of testing available to expectant parents in the future.

Materials and Methods

Sample and Procedures

An anonymous survey was distributed to all patient and their partners (if present) who came for prenatal or pre-pregnancy genetic counseling. All patient were 18 years of age or older. This study was conducted at a single site, Perinatal Genetics at Rutgers, Robert Wood Johnson Medical School in New Brunswick, NJ. The surveys were distributed from October to December 2019. Instructions for survey completion were provided on the survey. This study was approved by the Rutgers IRB. Documentation of consent was waived for this study; however, the subjects were consented with a long-form consent attached to the front of each survey. Completed surveys were placed directly by the patients in a secure designated box and collected at the end of the day. Conditions were categorized based on cognitive impact, age of onset, quality of life, and available treatment/management.

Instrumentation

The investigator-created survey consisted of a 19-item questionnaire divided in to 5 sections. Sections were: demographics and background (13 questions), Non-invasive testing preferences “maternal blood test” (1 question assessing 24 different conditions/traits), invasive testing preferences “amniocentesis” (1 question assessing 24 different conditions/traits), termination preferences (1 question assessing 24 different conditions/traits), and targeted questions (3 questions). The first part of the survey contains demographic information, excluding personal identifiers, and assesses the participants’ familiarity with genetic diseases and genetic counseling. The second part of

the survey assesses their opinions towards certain genetic tests for a variety of traits and conditions. The majority of questions evaluated level of agreement using a 5-point Likert scale. Since all survey questions were voluntary, a fluctuation in question specific response rate was possible. The entire survey is attached and labeled as patient opinion study survey in the appendix.

Data Analysis

For two-by-two contingency tables, analyses were conducted using a Fischer exact test with statistical significance set at 0.05 level. For variables that were yes or no answers, a chi square goodness of fit test was conducted and with significant significance set at a 0.05 level.

Results

In total, 71 patients completed the survey, resulting in a 28.4% response rate based on the 250 paper surveys that were distributed. Participants were 97% female and 55% Caucasian. The youngest participant was 18 and the eldest was 66, with a mean age of 32. The majority (70%) of respondents were pregnant. Almost half of respondents (49%) did not have children, and 51% had at least one child. The majority (85%) had an education level of college or higher, with only 15% having completed some high school or graduated from high school. Eighty-three percent (83%) indicated they associated with a religion, with the most single common religion identified as Roman Catholic (28%). Seventeen percent identified as non-religious. The majority of respondents (70%) selected English as their primary language. However the remaining 30% indicated a wide variety of primary languages including: Spanish, Arabic, Ashanti, Chinese, Gujarati, Japanese, Russian, Tagalog, Telugu, Urdu, and Vietnamese. Twenty percent of respondents reported a personal or family history of disability or genetic condition, and were considered to have some familiarity with disability. The demographic and targeted questions results are reflected in Table 1 and Figure 1.

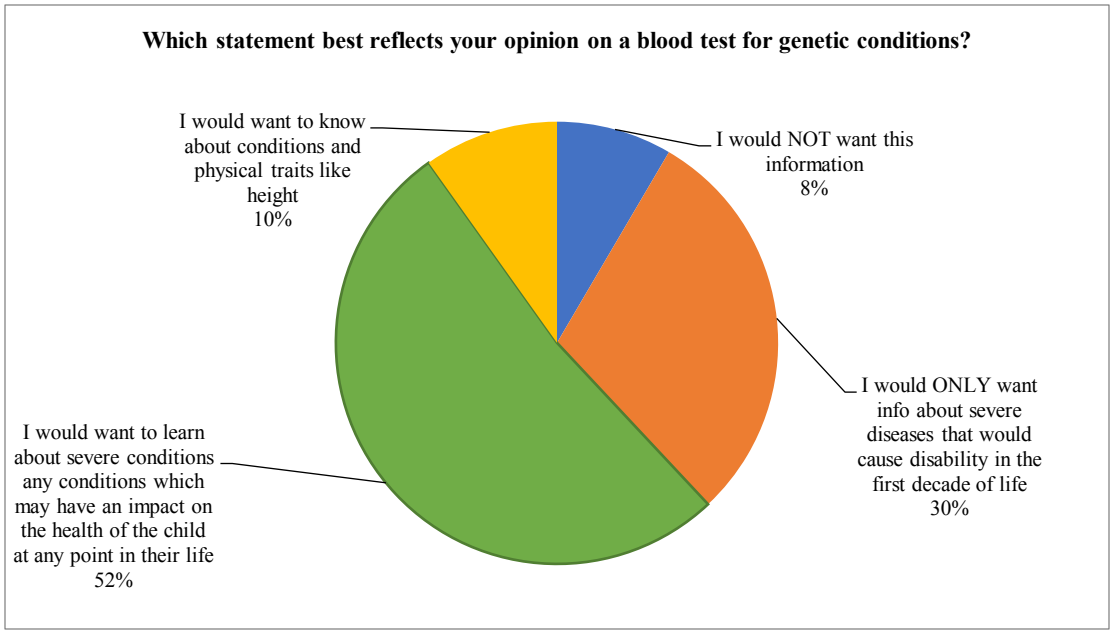
Table 1. Responder demographics and targeted questions

Gender	Responses (n)	Percentage
Female	69	97%
Male	2	3%
Age	Responses (n)	Percentage
18 to 34	38	56%
35 to 66	30	44%
Education Level	Responses (n)	Percentage
Some High school/High school	11	15%
College	32	45%
Graduate/Professional	28	40%
Race	Responses (n)	Percentage
Asian	12	17%
Black	7	10%
Caucasian	39	55
Other	12	17%
Did not answer	1	1%
Ethnicity		
Hispanic	14	19%
Non-Hispanic	56	80%
Did not answer	1	1%
Income		
<$30,000	12	17%
$30-60K	13	18%
$60-100K	16	23%
100-200K	19	27%
>200K	9	13%
Did not answer	2	2%
Religion		
Buddhist	2	3%
Christian	17	24%
Hindu	3	4%
Jewish	8	11%
Muslim	3	4%
Roman Catholic	20	28%
Other	6	8%
None	12	17%
Number of Children		
No children	35	50%
One child	19	27%
Two children	11	15%
Three + children	6	8%

Table 1. Responder demographics and targeted questions (cont.)

Which statement best reflects your opinion on a blood test for genetic conditions? *Imagine there was a blood test that you and your partner could have which would tell you whether your unborn child/children would be at risk for hundreds of genetic traits/conditions. Please answer the below questions, as it pertains to this type of blood test.*	Responses (n)	Percentage
I would NOT want this information	6	8%
I would ONLY want info about severe diseases that would cause disability in the first decade of life	21	30%
I would want to learn about severe conditions any conditions which may have an impact on the health of the child at any point in their life	37	52%
I would want to know about conditions and physical traits like height	7	10%
Timeframe *The best time for this type of testing is?*	Responses (n)	Percentage
Never	4	6%
Before marriage	5	7%
Preconception	37	52%
Once a pregnancy	25	35%
Perception of High Risk *If you had a blood test during your pregnancy, which showed a high risk for the fetus to have a disability, such as Down syndrome, at, what number do you start to classify high risk?*	Responses (n)	Percentage
0.5% (1 in 200)	12	6%
1% (1 in 100)	12	6%
5% (1 in 20)	14	21%
10% (1 in 10)	13	19%
25% (1 in 4)	5	7%
50% (1 in 2)	11	16%

Figure 1. Imagine there was a blood test that you and your partner could have which could tell you whether your unborn child/children would be at risk for hundreds of genetic traits/conditions. Respondents were asked which statement best reflects their opinion on a blood test for genetic conditions.



Non- Invasive testing preferences classified by severity of condition

We found that respondents were significantly more likely to pursue non-invasive testing. The majority 67/71 (94%) of respondents would likely/definitely pursue non-invasive testing for at least one or more condition (Table 2) (Figure 2). With increasing severity of the conditions, the uptake rates for noninvasive testing increased.

Table 2. Non-invasive testing preferences

Non-Invasive Testing	Counts	Percentages
Yes	67	94%
No	4	6%
Total	71	100%

Chi Goodness of fit test P value less then 0.001

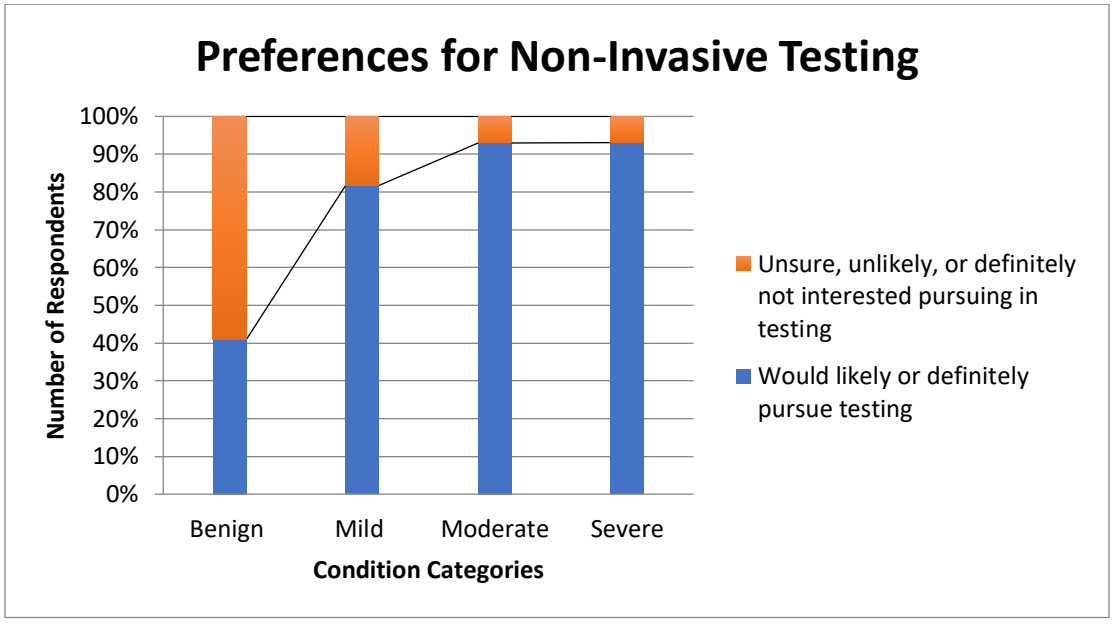


Figure 2. Non-invasive testing preferences categorized by condition/ trait severity

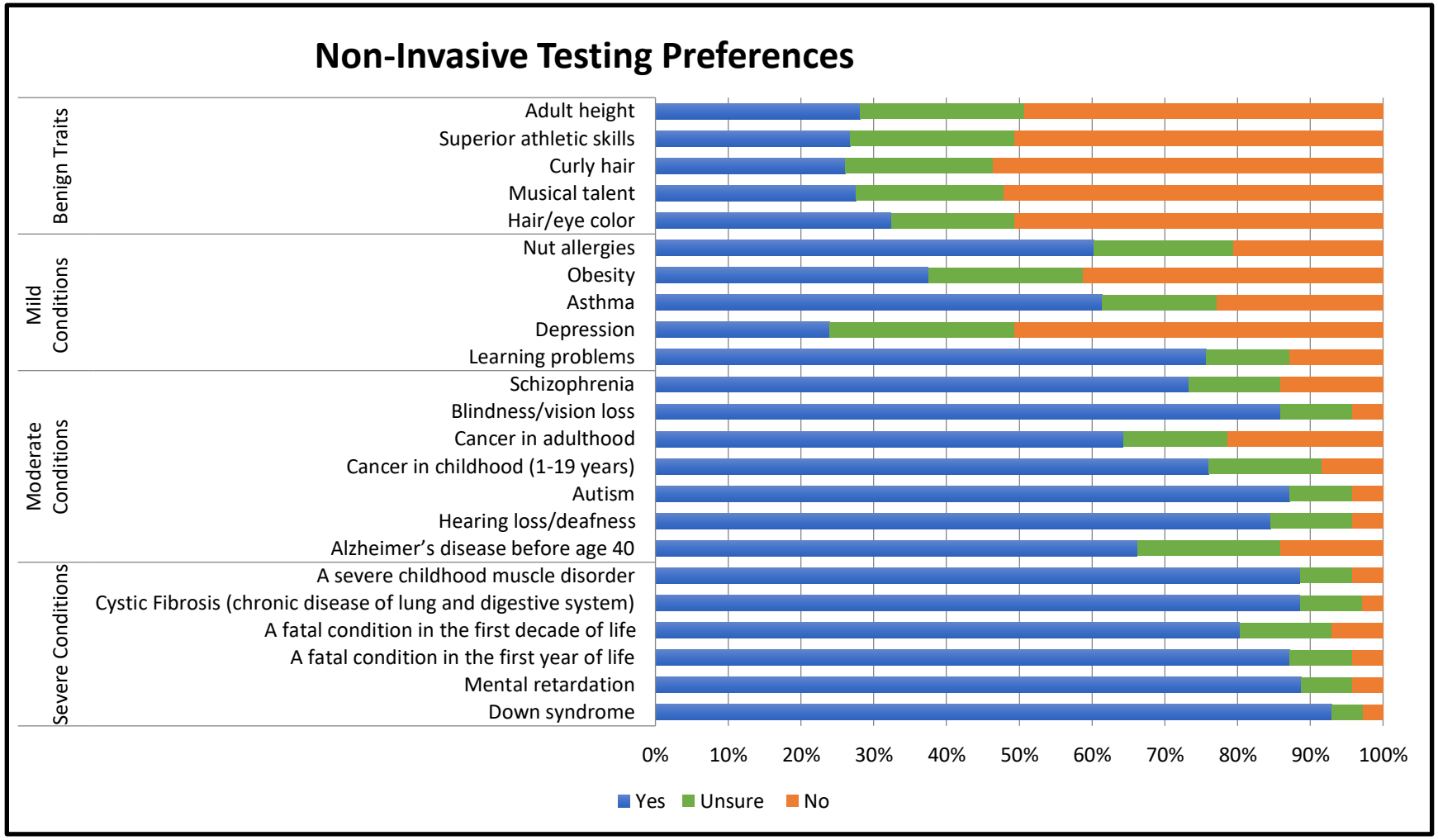


Figure 3. Responses when patients were asked if they would consider non-invasive testing for various conditions/traits

Under the benign condition category that included; Hair/eye color, superior athletic skills, musical talent, curly hair, and height, 29/71 (40%) of respondents would likely/definitely pursue non-invasive testing for at least one or more benign condition. Forty-two or 60% of respondents were unsure, unlikely, or definitely not interested in pursuing non-invasive testing for all of the benign conditions listed. The trait that most patients were interested in learning the fetal status was hair and eye color (Figure 3).

Under the mild condition category that included; asthma, nut allergy, depression, obesity, and learning problems, 58/71 (82%) respondents would likely/definitely pursue non-invasive testing for at least one or more mild condition (Table 3). We found that respondents were significantly more likely to pursue non-invasive testing for mild conditions (Figure 3).

Table 3. Non-Invasive Testing for Mild Conditions

Non-invasive Testing preferences for Mild conditions	Counts	Percentages
Yes	58	82%
No	13	18%
Total	71	100%

Chi Goodness of fit P value is less then 0.001

Under the moderate condition category which included; hearing loss, Alzheimer's < 40, cancer adulthood, schizophrenia, autism, cancer childhood, and blindness/vision loss 66/71 (92.9%) of respondents would likely/definitely pursue non-invasive testing for at least one or more of the moderate conditions (Figure 3).

Under the severe condition category which included; Down syndrome, mental retardation, fatal condition first decade of life, cystic fibrosis, muscle condition presenting in childhood, and a fatal condition in infancy, 67/71 (94.3%) of respondents would likely/definitely pursue non-invasive testing for at least one or more severe conditions (Figure 3).

Invasive testing preferences classified by severity of condition

We surveyed respondents on their willingness to pursue fetal diagnostic testing due to a positive screening result for various conditions/traits. The majority 56/71 (78.9%) of respondents would likely/definitely pursue amniocentesis for at least one or more severe condition (Table 4) (Figure 4).

Table 4. Overall Invasive Testing Preferences for Severe Conditions

Invasive Testing	Counts	Percentages
Yes	56	78%
No	15	22%
Total	71	100%

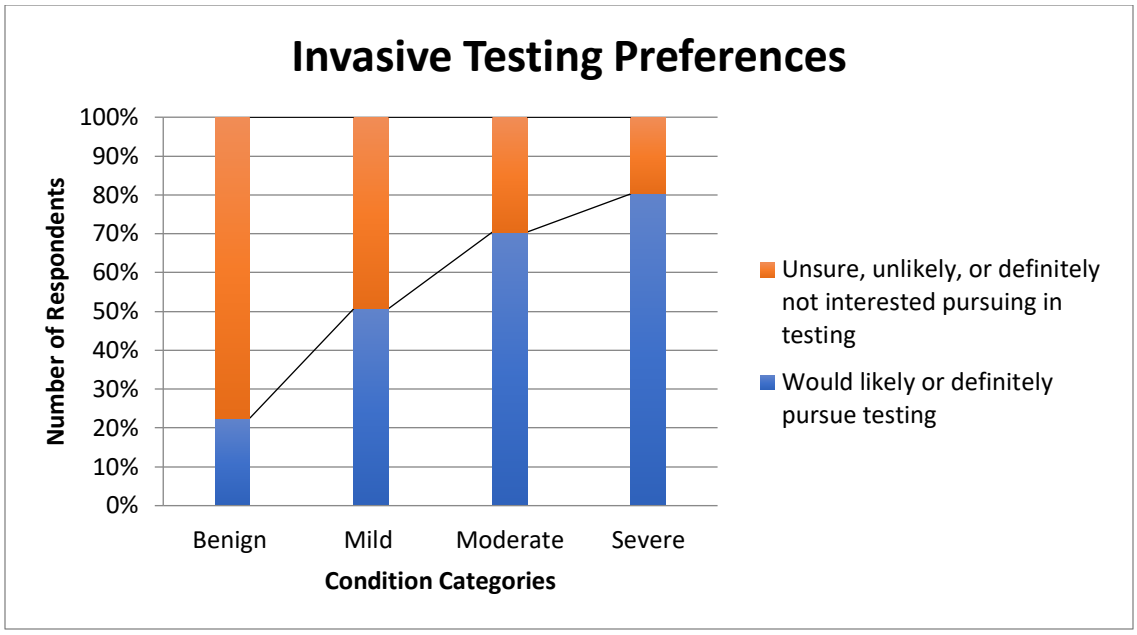


Figure 4. Invasive testing preferences categorized by severity of condition/trait

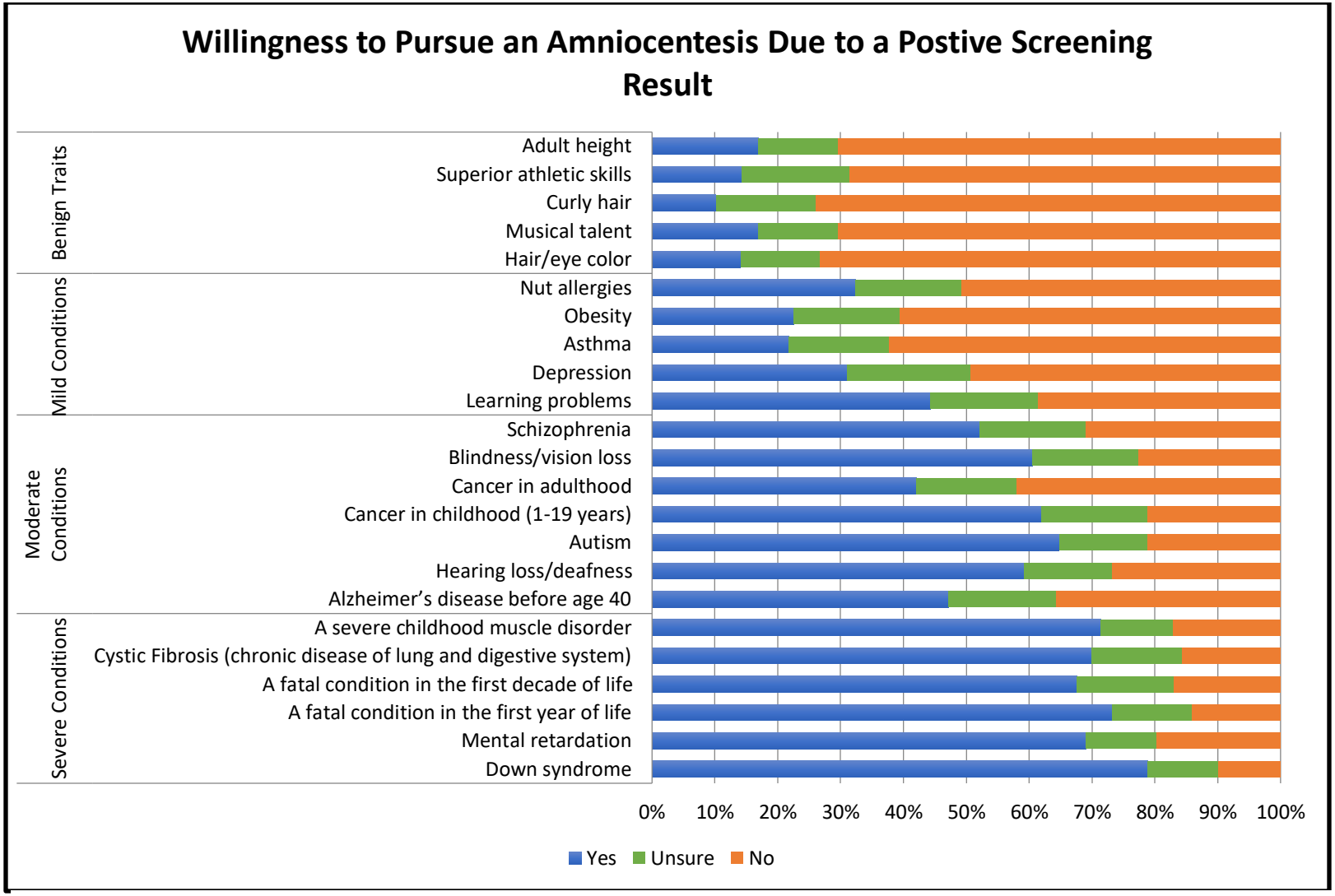


Figure 5. Responses when patients were asked if they would consider amniocentesis due to a high risk screening result

Under the benign condition category 16/71 (23%) of respondents would likely/definitely pursue amniocentesis for one or more condition. Fifty-five or (77%) of respondents were unsure, unlikely, or definitely not interested in pursuing non-invasive testing for all of the benign conditions listed. Respondents were significantly less likely to pursue invasive testing for benign conditions (Table 5) (Figure 5).

Table 5. Overall Invasive Testing Preferences

Invasive testing preferences for benign traits	Counts	Percentages
Yes	16	22%
No	55	78%
Total	71	100%

Chi Goodness of fit test P value is less then 0.001

Under the mild condition category 36/71 (51%) of respondents would likely/definitely pursue amniocentesis for one or more condition. Thirty-five (49%) of respondents were unsure, unlikely, or definitely not interested in pursuing non-invasive testing for all of the mild conditions listed. Respondents were not significantly more likely to pursue invasive testing for mild conditions as observed in the context of non-invasive testing for mild conditions (Figure 5).

Under the moderate condition category 50/71 (70%) of respondents would likely/definitely pursue amniocentesis for one or more condition. Twenty-one out of 71 (30%) of respondents were unsure, unlikely, or definitely not interested in pursuing non-invasive testing for all of the benign conditions listed (Figure 5).

Under the severe condition category 57/71 (80%) of respondents would likely/definitely pursue amniocentesis for one or more condition. Fifteen out of 71 (20%) of respondents were unsure, unlikely, or definitely not interested in pursuing non-invasive testing for all of the severe conditions listed (Figure 5).

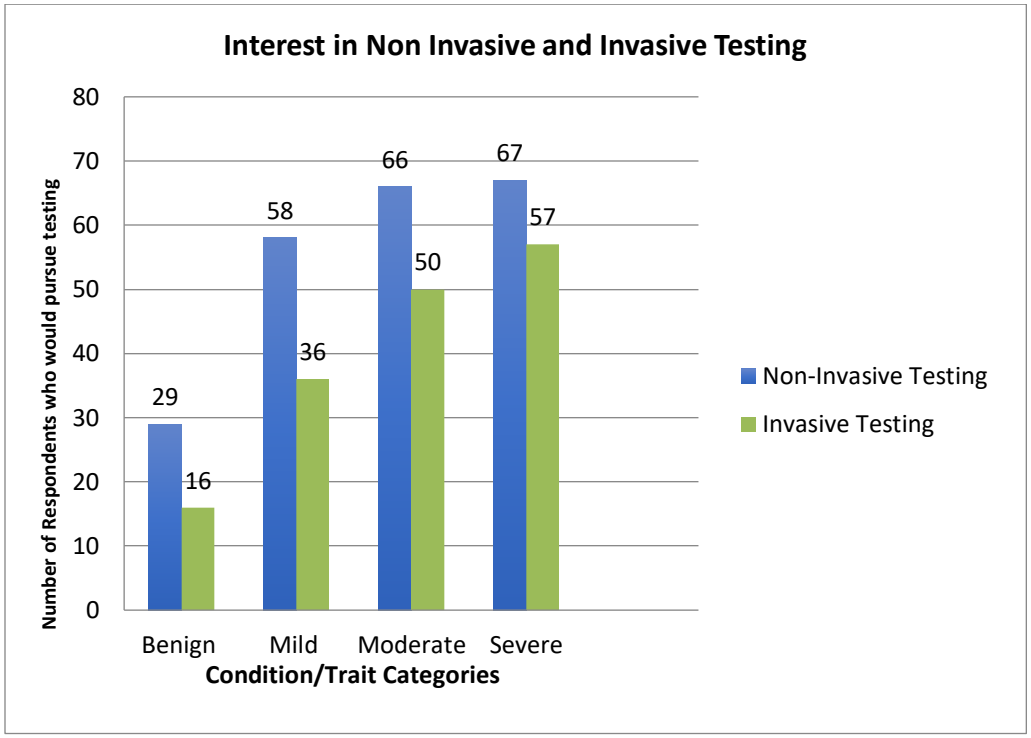


Figure 6. The number of respondents who would likely/definitely pursue non-invasive and invasive testing for various conditions/traits

Patients were significantly more likely to pursue testing for a range of fetal indication via non-invasive testing as compared to invasive testing. 29 respondents would likely/definitely pursue non-invasive testing for benign conditions/traits but only 16 would likely/definitely pursue invasive testing for benign conditions/traits. We evaluated the attrition, which we defined as the percentage of patients who would stop at noninvasive testing and not continue to diagnostic confirmatory testing. The attrition rate for benign conditions is 45% (*Figure*. 6).

For mild conditions, 50 respondents would likely/definitely pursue non-invasive testing and 36 would likely/definitely pursue invasive testing. The attrition rate for mild conditions was 55%. This was surprising because we would have expected the attrition rate to be highest for the benign trait category (*Figure*. 6).

For moderate conditions, 66 would likely/definitely pursue non-invasive testing, and 50 would likely/definitely pursue invasive testing. The attrition rate for moderate condition is 24% (*Figure*. 6).

For severe conditions, 67 respondents would likely/definitely pursue non-invasive testing and 57 would likely/definitely pursue invasive testing for severe condition. The attrition rate for severe conditions was the lowest at 15% (*Figure*. 6).

Termination preferences

Thirty-five percent (27/71) responded that they would not consider termination of pregnancy for any of the conditions listed. Sixty five percent (46/71) responded that they would consider termination for at least one or more fetal indication (*Figure 7*).

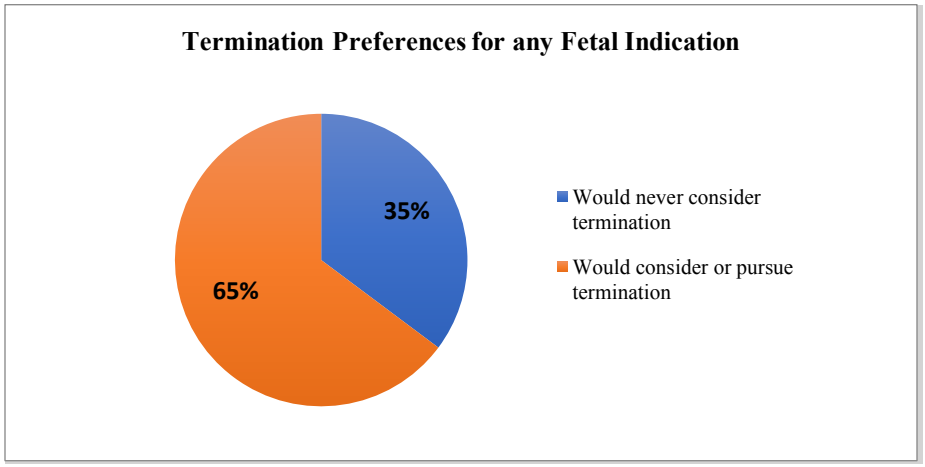


Figure 7. Summary of over all termination preferences for a fetal indication

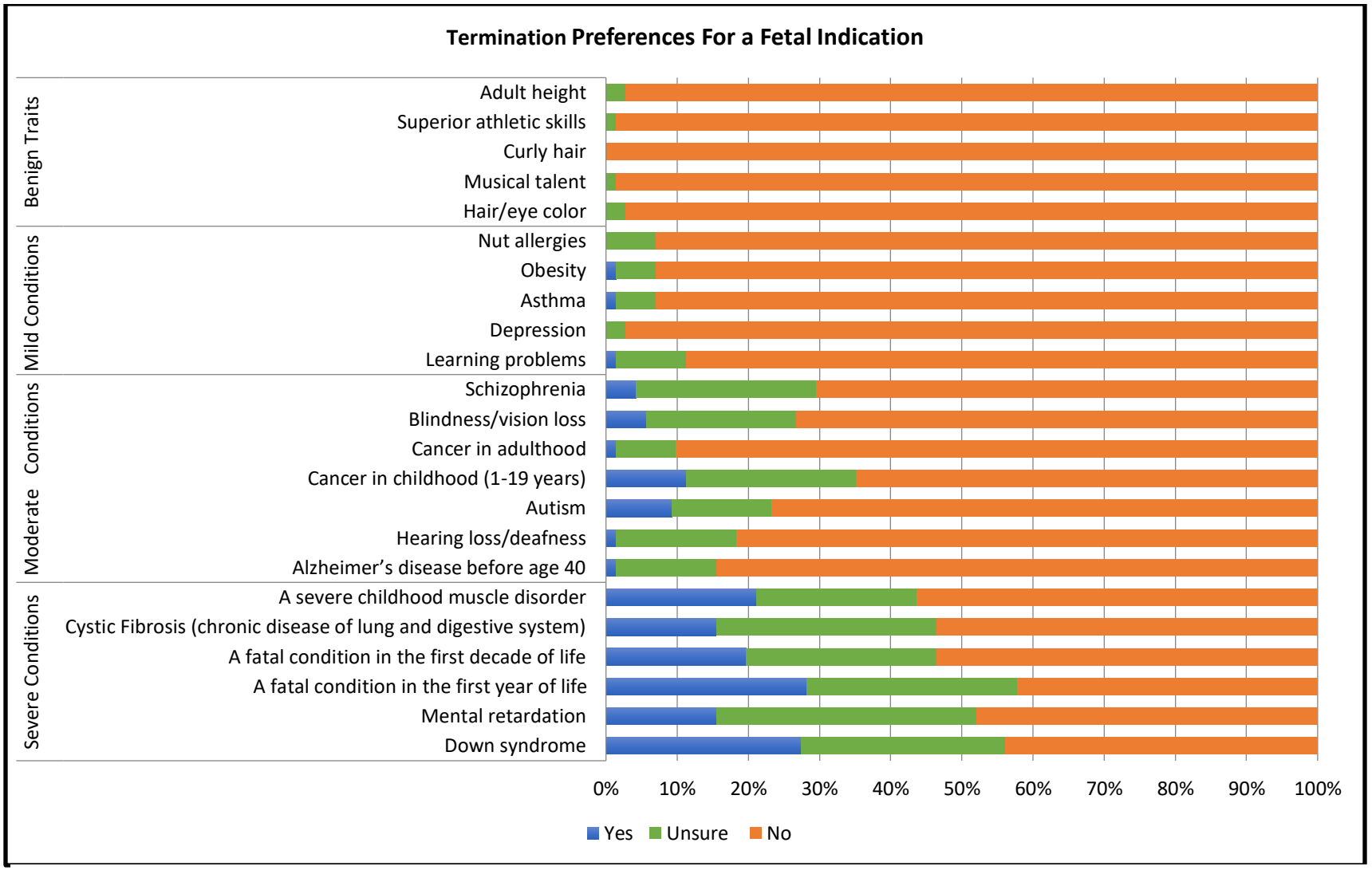


Figure 8. Responses when patients were asked if they would consider termination of pregnancy for the trait/condition state

A fatal condition in infancy had the highest number of individuals indicate that they would pursue termination, 20/71 (28%). The other most common conditions included Down syndrome, and a severe muscle condition in childhood, with 15/71 (21%) would pursue termination for each of these conditions. All of these conditions are categorized as severe and therefore these findings were expected. In regards to moderate conditions, cancer in childhood and autism had the highest number of individuals who would pursue termination under these circumstances (Figure 8). In regards to mild conditions 14/71 (20%) respondents would consider termination for a mild condition. The top two mild conditions which termination of pregnancy would be considered were learning problems and nut allergies. Only one respondent would pursue termination for one or more mild conditions. Fifty-seven out of 71 (80%) would never consider termination for the mild conditions listed. In regards to benign conditions, zero respondents would pursue termination. Five/71 (7%) of the 71 respondents would consider termination for one or more benign condition, including short stature, which may have been misinterpreted as achondroplasia. Sixty-six or (93%) of respondents would never consider termination for benign conditions (Figure 8).

Religion Affiliation and Termination Preferences

Fifty-nine (83%) of respondents indicated they associated with a religion (Table 6). However, this question failed to capture whether they considered themselves religious.

In order to determine how a person's religious affiliation or lack there of can influence their reproductive choices; a Fischer exact test was performed comparing the two groups.

Individuals without a religious affiliation were seven times more likely to consider/pursue termination for a fetal indication as compared to those without a religious affiliation. Ninety-two percent of the respondents that did not have a religious affiliation would consider/pursue termination. Respondents that indicated they had a religious affiliation were significantly less likely to pursue termination for a fetal indication.

Table 6. Termination of Pregnancy for Fetal Indication based on Religious Affiliation

		Religious Affiliation	No Religious Affiliation
		Yes	**No**
Would or would not consider termination for a fetal indication	**Yes**	**35 (59%)**	**11 (92%)**
	No	**24 (41%)**	**1 (8%)**

Fisher exact test p value is 0.046

Education Level and Termination Preferences for Fetal Indication

Forty-six individuals had an education level of some high school, high school, and college. Twenty-eight individuals had an education level of a masters or post doctorate. A chi square test was performed comparing the two groups, in different combinations. We found that the level of education did not significantly impact on patient decision-making. be significant (Tables 7, 8, & 9).

Table 7. Interest in Termination based on Graduate Level Education versus College and High School level Education

		Graduate Education	College and High School Education
		Yes	No
Would or would not consider termination	Yes	21 (75%)	25 (58%)
	No	7 (25%)	8 (42%)

Fisher exact test p value is 1.000

Table 8. Interest in Termination based on College Education compared to High School and Graduate level education

		College Education	Graduate level and High School Education
		Yes	No
Would consider or would not termination	Yes	18 (56%)	28 (72%)
	No	14 (44%)	11 (28%)

Fisher exact test p value is 0.215

Table 9. Interest in Termination based on College level education and higher compared to High School level education

		Graduate and College Education	High School Education
		Yes (n)	No (n)
Would or would not consider termination	Yes	39 (65%)	7 (64%)
	No	21 (35%)	4 (36%)

Fisher exact test p value is 1.000

Information Seekers

Fourteen respondents would likely/definitely consider non-invasive testing for every single condition and trait listed in the survey. This accounted for 20% of respondents. We classified these respondents as "information seekers". Sixty-four percent (9/14) of these respondents would likely/definitely pursue invasive testing (amniocentesis) rating a 4 or 5 in at least one or more condition category. Of these 6/14 (43%) went on to consider termination under certain circumstances. Most of these respondents would consider or pursue termination in the case the fetus was identified to have down syndrome or a fatal condition in the first year of life. Other indications that at least one or more of the respondents would consider termination for were cystic fibrosis, mental retardation, a severe muscle condition in childhood, early onset Alzheimer's, and childhood cancer.

Familiarity with Disability

14 respondents indicated they themselves have a disability or genetic condition; they have an affected child, or they have an affected relative with a disability/genetic condition. These respondents were considered to have some familiarity with a disability/genetic condition. They accounted for 19.7% of the total number of respondents. All (100%) were very likely to consider/pursue non-invasive testing. Twelve (85.7%) of respondents would very likely/definitely pursue invasive testing. Nine (64.2%) would consider termination for a fetal indication. However, our analysis showed that individuals with familiarity with disability were not statistically more likely to consider testing and termination of pregnancy for a fetal condition, as compared to those that did not indication familiarity (Table 10,11,12).

Table 10. Non-invasive testing preferences comparing individuals with and with out a familiarity of disability/genetic condition.

		Familiarity Disability	No personal/family history
		Yes	**No**
Would or would not consider non-invasive testing	**Yes**	**12/12 (100%)**	**55/59 (93%)**
	No	**0/12 (0%)**	**4/59 (7%)**

The Fischer exact test has a P value of 1.000

Table 11. Invasive testing preferences comparing individuals with and with out a familiarity of disability/genetic condition

		Familiarity Disability	No personal/family history
		Yes	**No**
Would or would not consider invasive testing	**Yes**	**10/12 (83%)**	**46/59 (78%)**
	No	**2/12 (17%)**	**13/59 (22%)**

The Fischer exact test has a P value of 1.000

Table 12. Termination preferences comparing individuals with and with out a familiarity of disability/genetic condition.

		Familiarity Disability	No personal/family history
		Yes	**No**
Would or would not consider termination for a fetal indication	**Yes**	**7/12 (58%)**	**39/59 (66%)**
	No	**5/12 (42%)**	**20/59 (34%)**

The Fischer exact test has a P value of 0.742

Adult onset conditions

Respondents were asked about their preference for noninvasive and invasive testing for several adult onset conditions including cancer in adulthood and early onset Alzheimer's defined as onset of 40 or younger: Forty-seven (66.1%) respondents stated they would likely or definitely pursue non-invasive testing. Thirty-three (46.4%) respondents would likely/definitely pursue invasive testing for early onset Alzheimer's. Eleven (15%) of respondents would consider/pursue termination (Figure 9). Respondents were significantly more likely to pursue non-invasive testing for Alzheimer's then not (Table 13). There was no significance observed when respondents were asked about testing for this using non-invasive testing. However respondents were significantly less likely to pursue termination for a fetal indication (Table 14).

Table 13. Non-invasive Screening for Early Onset Alzheimer's Disease

Non-Invasive testing preferences for Alzheimer disease < 40 years	Counts	Percentages
Yes	47	66%
No	24	34%
Total	71	100%

Chi Goodness of fit test P value was 0.006341

Table 14. Termination preferences for fetal indication of Alzheimer's Disease

Termination preferences for Alzheimer disease < 40 years	Counts	Percentages
Yes	11	66%
No	60	34%
Total	71	100%

Chi Goodness of fit test P value was less then 0.001

Adult Onset Cancer: Forty-five (63%) respondents would likely/definitely pursue non-invasive testing. In the context of invasive testing 29/71 (41%) would likely/definitely pursue invasive testing for adult onset cancer. Seven (10%) would consider or pursue termination (Figure 9). Respondents were significantly more likely to pursue non-invasive testing for adult onset cancer then not. There was no significance observed when respondents were asked about testing for this using non-invasive testing (Table 15). However respondents were significantly less likely to pursue termination (Table 16).

Table 15. Non-invasive screening for Adult Onset Cancer

Non-Invasive testing preferences for Adult onset cancer	Counts	Percentages
Yes	45	63%
No	25	37%
Total	71	100%

Chi Goodness of fit test P value was 0.0168

Table 16. Termination Preferences for a Fetal Indication of Adult Onset Cancer

Termination preferences for Adult onset cancer	Counts	Percentages
Yes	7	10%
No	64	90%
Total	71	100%

Chi Goodness of fit test P value was less than 1.0

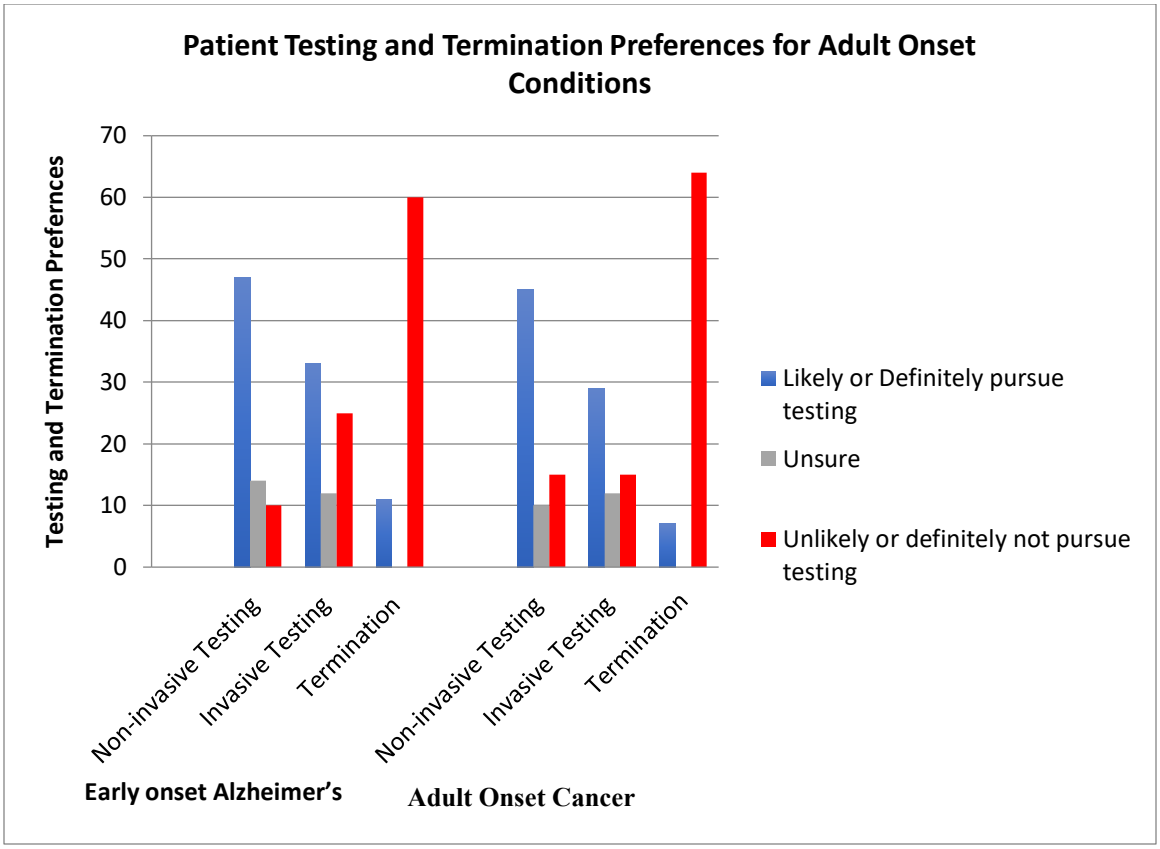


Figure 9. Genetic testing and termination preferences for a fetal indication of adult onset conditions

Discussion

We found that patients were highly motivated to learn about a range of fetal conditions including benign, mild, moderate, and severe conditions via non-invasive testing. This was supported by the responses received from the targeted question section. When respondents were asked, "Which statement best reflects your opinion on a blood test for genetic conditions?" the majority of respondents (52%) selected "I would want to learn about severe conditions any conditions which may have an impact on the health of the child at any point in their life". However, when faced with diagnostic testing, patients were primarily only motivated to pursue invasive testing for moderate and severe fetal indications. The majority of patients were interested in screening for mild conditions such as obesity and asthma via non-invasive testing. Of those respondents, more then half (55%) would not pursue fetal diagnostic testing for mild indications. This discordance between non-invasive and invasive testing was not observed when it came to moderate and severe fetal indications. This data supports that patients are motivated to use non-invasive technology to learn information about their unborn child for conditions having impact across the life span. However, they are less likely to pursue amniocentesis for diagnostic confirmation for health trait and mild conditions. The more severe the impact of the condition, the more likely patients are to pursue invasive diagnostic testing for confirmation.

Many respondents wanted to know this information for reasons unrelated to termination of pregnancy, highlighting the potential value respondents see with this information, aside from reproductive decision-making. Parents may be interested in this information for bonding and preparedness. These findings were consistent with a study conducted by

Bowman-Smart et al. 2019 that also demonstrated respondents indicated a higher interest in undergoing testing than undergoing termination due to a fetal indication for all conditions and traits (21).

The majority of respondents (60%) were not interested in non-invasive screening for benign traits such as musical talent and physical features. This was not surprising, as benign traits were not expected to be of utmost importance to prospective parents.

Twenty percent of respondents were interested in non-invasive screening for every benign, mild, moderate and severe condition prenatally. These respondents were defined as information seekers. Forty-three percent of information seekers went on to consider termination for moderate and severe fetal indications only. This supports the notion that patients are willing to screen for a range of fetal conditions via non-invasive testing, but generally only consider termination for more severe fetal indications.

Religious affiliation was found to have a significant impact on respondent's willingness to consider termination for a fetal condition. Those who did not identify a religious affiliation were 7.5 times more likely to consider/pursue termination as compared to those that did not identify a religious affiliation. However, our survey failed to actually capture whether those that identified with a religion affiliation considered themselves religious. Interestingly, for those that identified with a religious affiliation, it was close to a 50/50 split as to whether or not they would consider termination for a fetal indication. Our data shows that those not affiliated with a religion are more likely to

consider termination of pregnancy, but those with a religion affiliation are actually split evenly on how they would proceed when faced with a fetal diagnosis.

Based on our data, a patient's level of education was not found to be a significant factor in determining preferences for prenatal testing or termination due to a fetal indication.

A familiarity of disability also does not appear to impact a patient's preferences for fetal testing or termination for a fetal indication.

Our data supports that patients were highly motivated to screen for fetal risk of adult onset conditions via non-invasive means. This differed from a previous study by Bowman-Smart et al. 2019 that demonstrated a reduced interest in testing for adult onset conditions (21). Our respondents were less inclined to pursue invasive testing and significantly less likely to pursue termination for an adult onset condition. This poses the ethical concern as to whether prospective parents should have access to this type of information, if there is no known medical intervention to treat/prevent disease. Current guidelines state that if the medical benefits of a genetic testing will not be utilized until adulthood, genetic testing generally should be deferred unless testing will impact pregnancy management (ACOG Committee Opinion No. 410, 2019). This is to protect the autonomy of the unborn individual, and spare them emotional distress. If patients are interested in testing for reasons other than termination of an affected pregnancy, parents may be infringing on the rights of their unborn child to choose for themselves how and when a genetic status is disclosed. Currently the genetic information non-discriminatory

act protects individuals from discrimination by employers and health insurance companies. However, this law does not apply to long-term care, and life insurance. Additionally, the military can discriminate against individuals for genetic test results. Patients could potentially uncover a pre-existing condition in their fetus that could have negative implications for the future child. Currently prenatal screening/testing for adult onset conditions does not provide any clinical utility, unless the parents choose termination of pregnancy for a fetal diagnosis. However this could change in the future as advancements are made in gene therapy technologies.

Study Limitations

One of the limitations of this study is small sample size of 71 participants. A larger sample size may have yielded different results. The conditions/traits were categorized into four groups; benign, mild, moderate, and severe. It was challenging categorizing these conditions, as we would expect perceptions of the severity of each condition/trait to differ from person to person. While respondents were asked whether they themselves have a disability or genetic condition, an affected child, or relative with a disability/genetic condition, we did not ask respondents to specify what type of condition was present in their family. Additionally, we did not define disability or genetic condition. These respondents were considered to have some familiarity with a disability/genetic condition, however we were not able to assess their level of familiarity with disability/genetic condition. We asked about religious affiliation, but this may not correlate with how religious/devote individuals consider themselves. Some individuals

may identify with a religious but not necessarily practice the principles. The surveys were only available in English, which excluded patients from the study who were not proficient in English. Given that the majority of patients given the survey did not complete it, there may be a selection bias to our data. It is possible that patients who completed the survey are more likely to provide different answers than those that chose not to complete the survey. We do not have any data on patients who chose not to complete the survey including their reason for declining the survey.

Research and Recommendations

Future studies should further explore the reasons for which individuals would find screening for benign, mild, and adult onset conditions valuable. Additionally, future research should analyze motivations for fetal screening of adult onset conditions for reasons other than termination. We should assess the general prenatal patient population on their overall understanding of these conditions and the ethical and medical implications regarding screening/testing. Future research should include asking prenatal patients what conditions/traits they would wish to know about prenatally. We should also survey genetic counselors on opinions of the utility, ethical considerations, and level of comfort for counseling patients about this kind of testing.

Conclusion

In summary, our data indicates that patients are motivated to screen for more conditions/traits and for a wider range of fetal conditions via non-invasive testing than via invasive testing. While non-invasive prenatal testing (NIPT) is a screening tool, it can provide information with little physical risk to the pregnancy. (23). Eventually NIPT may have the capability to screen for a variety of fetal conditions including those with a mild phenotype. This will have many benefits such as early interventions, emotional preparation, reassurance and the option to terminate due to a fetal condition. However international literature poses an ethical framework for prenatal screening that (NIPT) should only generate test outcomes that are relevant to reproductive decision-making, informed choice should be possible through adequate pre-test counseling, and the rights of future children should be respected (24). Our data indicates that patients would be willing to pursue NIPT for future applications that are not yet available. As individuals are interested in pursuing NIPT for a wide variety of conditions/traits, pre-test counseling is necessary to ensure patients understand the ramifications of screening. A role which, genetic counselors are expertly qualified to fulfill. Genetic counselors have extensive training in genetics and counseling, which facilitates increased patient understanding and informed decision-making. While NIPT may be viewed as a simple maternal blood test, the information it yields may be complex and has serious ethical and practical implications (25). We caution against the routinization of NIPT, as the general prenatal patient population likely do not fully appreciate the possible ethical and practical implications of such screening. There is concern that patients are seeking this information out of curiosity and not for the intended purpose of pregnancy management. Patients may

not discern the difference between the intended clinical utility of NIPT and wellness/trait testing offered by direct to consumer genetic testing companies. Health care providers have a duty to provide appropriate pre-test counseling to patients ensuring they understand the implications and limitations of non-invasive testing.

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Appendix

Patient Opinion Study Survey

RUTGERS
Robert Wood Johnson
Medical School

Thank you for filling out this survey to help us better understand patient opinions on prenatal genetic testing. The purpose of this study is to obtain information that helps us provide better care to you in the future. Please try to answer every question, but all items are optional and you may skip any question that you prefer not to answer.

Paper Survey

Study Title: Patient Opinions on Prenatal Genetic Testing

Gender: ↑Male ↑Female Your age: _____

Please indicate your race (circle all that apply):
↑American Indian ↑Asian ↑Black ↑Pacific Islander ↑White↑Other

Please indicate your ethnic background:
↑Hispanic ↑Non-Hispanic

Please indicate your religion:
Roman Catholic Christian Jewish Muslim Buddhist Hindu Other None

What your primary language spoken at home?
↑English ↑Spanish↑Other: _____

Please designate your family income range:
↑Less than $30,000/year ↑30,000-60,000/year ↑60,000-100,000/year
↑100,000-200,000/year ↑above 200,000/year

Your highest level of education:
↑Some High School ↑High school↑College ↑Master degree ↑Post-graduate (MD, PhD, JD, etc)

Are you pregnant or is your partner pregnant? Yes or No

Please circle how many children you have? 0 1 2 3+

Do you have a genetic condition or a disability? Yes or No

Have you had a child affected by a genetic condition or disability? Yes or No

Do you have a relative affected by a genetic condition or disability? Yes or No

If you have indicated that your or a family is affected by a genetic condition please indicate the degree of impact on the day to day functioning of the affected individual.
Mild Moderate Severe

Have you previously received genetic counseling or testing? Yes or No

This is a hypothetical exercise where we will ask you a set of questions geared towards understanding what genetic traits/conditions you would wish to know about in advance of your child being born. This information may be available through a simple blood test of the parents, carrying no risk to the pregnancy, or may require undergoing a procedure during pregnancy, such as the amniocentesis procedure. Amniocentesis is a test where a needle is inserted into the uterus to collect amniotic fluid during the pregnancy. This fluid may then be tested for specific genetic conditions or traits of the fetus. Amniocentesis is a generally safe test, but does carry a risk for miscarriage of about 0.5%.

If it was possible to do just a maternal blood test (no risk) during pregnancy to see if your unborn child has the below traits/conditions, how likely would you be to want to know this information. This blood test would not be 100% accurate, but would suggest a high chance of the condition. Please put an X in the box that most reflects your opinion.

	1 (would definitely not want to know)	2 (probably would not want to know)	3 (unsure)	4 (probably would want to know)	5 (would definitely want to know)
Down syndrome					
Hair/eye color					
Blindness/vision loss					
Superior athletic skills					
Hearing loss/deafness					
Learning problems					
Alzheimer's disease before age 40					
Autism					
Obesity					
Left or right handedness					
Mental retardation					
Asthma					
Cancer in adulthood					
A fatal condition in the first year of life					
Musical talent					
Cancer in childhood (1-19 years)					
Adult height					
Depression					
Schizophrenia					

A fatal condition in the first decade of life					
Nut allergies					
Cystic Fibrosis (chronic disease of lung and digestive system)					
A severe childhood muscle disorder					
Curly hair					

If you had a blood test that showed your unborn child would have a high chance for the below trait or genetic condition, how likely would you want to have the amniocentesis test during pregnancy to find out 100% if the fetus is actually affected? Remember, amniocentesis is generally safe, but does pose a 0.5% risk of miscarriage to the pregnancy.

	1 (would definitely not want to test)	2 (probably would not want to test)	3 (unsure)	4 (probably would want to test)	5 (would definitely want to test)
Down syndrome					
Hair/eye color					
Blindness/vision loss					
Superior athletic skills					
Hearing loss/deafness					
Learning problems					
Alzheimer's disease before age 40					
Autism					
Obesity					
Left or right handedness					
Mental retardation					
Asthma					
Cancer in adulthood					
A fatal condition in the first year of life					
Musical talent					
Cancer in childhood (1-19 years)					
Adult height					
Depression					
Schizophrenia					
A fatal condition in the first decade of life					
Nut allergies					
Cystic Fibrosis (Chronic disease					

of lung and digestive system)					
A severe childhood muscle disorder					
Curly hair					

If your unborn child was known to be affected by one of these conditions during pregnancy, how likely would you be to consider termination of pregnancy?

	0 (would never consider termination)	1 (may consider termination)	3 (would terminate an affected pregnancy)
Down syndrome			
Undesirable hair/eye color			
Cystic fibrosis (chronic disease or lung)			
Blindness/vision loss			
Poor athletic skills			
Hearing loss/deafness			
Learning problems			
Alzheimer's disease before age 40			
Autism			
Obesity			
Severe nut allergies			
Mental retardation			
Asthma			
Cancer in adulthood			
A fatal condition in the first year of life			
No musical abilities			
Cancer in childhood (1-19 years)			
Short stature			
Depression			
Schizophrenia			
A fatal condition in the first decade of life			
Severe childhood muscle disorder			
Curly Hair			

Imagine there was a blood test that you and your partner could have which would tell you whether your unborn child/children would be at risk for hundreds of genetic traits/conditions. Please answer the below questions, as it pertains to this type of blood test.

Which statement best reflects your opinion about such a test? (choose one)
___ I would not want this information
___ I would want only information about severe diseases that would cause disability in the first decade of life
___ I would want to learn about severe conditions and any conditions which may have an impact on the health of the child at any point in their life
___ I would want to know about severe conditions and any type of health condition and physical traits like height, eye color, etc.

The best time for this type of testing is: (choose one)
___ Never
___ Before getting married
___ Before getting pregnant
___ Once a pregnancy is identified

If you had a blood test during your pregnancy which showed a high risk for the fetus to have a disability, such as Down syndrome, at what number do you start to classify high risk? (choose one)
__ 0.5% (1 in 200)
__ 1% (1 in 100)
__ 5% (1 in 20)
__ 10% (1 in 10)
__ 25% (1 in 4)
__ 50% (1 in 2)

Thank you for your participation! If you have any questions about genetic testing after completing this survey, we encourage you to follow-up with our genetic counselor or maternal fetal medicine physician. Please place completed surveys or blank surveys if you choose not to participate in the sealed envelope and return to the lockbox at the front desk.