

5-2021

## Genetic Testing in Pregnancies with Ultrasound Anomalies: Exploration of Factors that Influence Uptake

Lukas D. Kruidenier

Follow this and additional works at: [https://digitalcommons.library.tmc.edu/utgsbs\\_dissertations](https://digitalcommons.library.tmc.edu/utgsbs_dissertations)



Part of the [Bioethics and Medical Ethics Commons](#), [Health Communication Commons](#), and the [Obstetrics and Gynecology Commons](#)

---

### Recommended Citation

Kruidenier, Lukas D., "Genetic Testing in Pregnancies with Ultrasound Anomalies: Exploration of Factors that Influence Uptake" (2021). *The University of Texas MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences Dissertations and Theses (Open Access)*. 1098.  
[https://digitalcommons.library.tmc.edu/utgsbs\\_dissertations/1098](https://digitalcommons.library.tmc.edu/utgsbs_dissertations/1098)

This Thesis (MS) is brought to you for free and open access by the The University of Texas MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences at DigitalCommons@TMC. It has been accepted for inclusion in The University of Texas MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences Dissertations and Theses (Open Access) by an authorized administrator of DigitalCommons@TMC. For more information, please contact [digitalcommons@library.tmc.edu](mailto:digitalcommons@library.tmc.edu).


Genetic testing in pregnancies with ultrasound anomalies: Exploration of factors that  
influence uptake


by

*Lukas Daniel Kruidenier, BA*

APPROVED:

DocuSigned by:  
  
C10672EF115A430...  
Blair Stevens, MS, CGC  
Advisory Professor

DocuSigned by:  
  
6D32F456B171400...  
Han-Yang Chen, PhD

DocuSigned by:  
  
DB2E20E8C91F412...  
Meagan Choates, MS, CGC

DocuSigned by:  
  
4D9554A323C8477...  
Anthony Johnson, DO

DocuSigned by:  
  
EF8FA427B6424FA...  
Claire Singletary, MS, CGC

APPROVED:

\_\_\_\_\_  
Dean, The University of Texas  
MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences

Genetic testing in pregnancies with ultrasound anomalies: Exploration of factors that  
influence uptake

A

Thesis

Presented to the Faculty of

The University of Texas

MD Anderson Cancer Center UTHealth

Graduate School of Biomedical Sciences

in Partial Fulfillment

of the Requirements

for the Degree of

Master of Science

by

Lukas Daniel Kruidenier, BA  
Houston, Texas

May, 2021

# Genetic testing in pregnancies with ultrasound anomalies: Exploration of factors that influence uptake

Lukas Daniel Kruidenier, BA

Advisory Professor: Blair Stevens, MS, CGC

Prenatal genetic diagnostic and screening tests have been rapidly evolving over the past decade with the introduction and expansion of cell free DNA screening (cfDNA) and the use of chromosomal microarray (CMA) as a first-line test for evaluation of fetal anomalies. Understanding patient motivations for or against expanded genetic testing options is paramount, therefore this study aimed to ascertain the patient perspective. Ninety-nine patients with an ultrasound anomaly participated in an anonymous research survey assessing coping strategies, factors influencing the genetic testing decision, and demographic variables. After multivariable analysis, the desire for directive counseling regarding testing was correlated with increased uptake of diagnostic tests (RR 1.52, 95% CI 1.02-2.27). Conversely, higher perceived procedure-related risk reduced uptake of diagnostic testing (RR 0.24, 95% CI 0.10-0.56). Mitigating the risk of genetic testing through expanded cfDNA options will likely further shift how patients evaluate genetic testing decisions in the future. Simultaneously, this raises concerns about the potential for routinization of genetic screening which can hinder informed consent and personalized care. The majority of patients (95%) had some form of genetic testing, despite over 20% not expressing desire for prenatal knowledge of a genetic condition, and 36% not feeling it would impact the medical management of the pregnancy. Mistrust of the medical team was significantly correlated with screening and diagnostic decisions, but the relative degree of effect could not be ascertained. More individuals with high school education or less (23% versus 5% with at least some college education) stated that they would not want the prenatal team to know if there was a genetic condition, whereas race/ethnicity was not significant. Therefore, it appeared that mistrust tracked in our cohort with lower educational attainment

rather than race/ethnicity. This study shows that even with new testing options, the procedure-related risk of diagnostic testing remains a powerful influence on the uptake of genetic testing. Mitigating the perceived risk of genetic testing will likely increase the complexity of the decision-making process for patients and the need for clinicians to provide patient centered counseling to facilitate these decisions.

## Table of Contents

Approval Page	i
Title Page	ii
Abstract	iii
Table of Contents	v
List of Illustrations	vii
List of Tables	viii
Abbreviations	ix
Introduction	1
Methods	2
Results	4
<hr/>	
Study Participation and Analysis Groups	4
Demographics and Diagnostic Testing Decision	5
Factors Influencing the Diagnostic Testing Decision	8
Demographics and Facilitated Testing Decision	11
Factors Influencing the Fetal Center Facilitated Testing Decision	13
Multivariable Models	16
Non-significant Correlates	19
Fetal Intervention	19
Discussion	19
<hr/>	
Risk of Diagnostic Testing	19
Value of Knowledge and the Influence of Pregnancy Management	21

Limitations of Screening	22
The Effect of the Medical Team	22
Strengths and Limitations	23
Future Directions	24
Conclusion	24
Appendix	25
<hr/>	
Appendix A – Four-Point Likert Tables	25
Appendix B – Coping Strategy Results	31
Bibliography	32
Vita	37

## **List of Illustrations**

*Figure 1* – Participation, Analyses, and Testing Decision

**5**



## **List of Tables**

<i>Table 1</i> – Demographic Information and Diagnostic Testing Decision	<b>6</b>
<i>Table 2a</i> – Diagnostic Testing and Decision-Making Factors	<b>8</b>
<i>Table 2b</i> – Diagnostic Testing and Decision-Making Factors	<b>9</b>
<i>Table 3</i> – Demographic Information and Facilitated Testing Decision	<b>11</b>
<i>Table 4a</i> – Facilitated Testing Decision and Decision-Making Factors	<b>13</b>
<i>Table 4b</i> – Facilitated Testing Decision and Decision-Making Factors	<b>14</b>
<i>Table 5</i> – Multivariable Analysis of Diagnostic Testing Decision	<b>16</b>
<i>Table 6</i> – Multivariable Analysis of Facilitated Testing Decision	<b>17</b>
<i>Table 7a</i> – Diagnostic Testing and Decision-Making Factors (4-point Likert)	<b>25</b>
<i>Table 7b</i> – Diagnostic Testing and Decision-Making Factors (4-point Likert)	<b>26</b>
<i>Table 7c</i> – Diagnostic Testing and Decision-Making Factors (4-point Likert)	<b>27</b>
<i>Table 8a</i> – Facilitated Testing Decision and Decision-Making Factors (4-point Likert)	<b>28</b>
<i>Table 8b</i> – Facilitated Testing Decision and Decision-Making Factors (4-point Likert)	<b>29</b>
<i>Table 8c</i> – Facilitated Testing Decision and Decision-Making Factors (4-point Likert)	<b>30</b>
<i>Table 9</i> – Coping Strategy Indicator and Testing Decision	<b>31</b>

## Abbreviations

<b>cfDNA</b>	cell free DNA
<b>CI</b>	confidence interval
<b>CMA</b>	chromosomal microarray
<b>FTD</b>	facilitated testing decision; represents any genetic testing (screening or diagnostic) decision provided after counseling at the fetal center
<b>RR</b>	risk ratio
<b>M</b>	mean
<b>MSS</b>	maternal serum screen
<b>SD</b>	standard deviation
<b>ES</b>	exome sequencing

## Introduction

Many studies have been performed examining the factors that influence genetic diagnostic and screening test utilization in the prenatal setting. The decision to undergo clinical genetic testing can be complex and should not be solely viewed from the lens of seeking medical knowledge. Factors such as the seriousness of the indication, perceived susceptibility to a genetic condition, anticipated benefit [1], attitudes towards elective abortion [2,3], and perceived risk of the test itself [2-6] have been shown to impact decision-making.

Acknowledging how the field of prenatal testing has evolved in recent years is critical in understanding genetic testing decisions. Since its introduction in the United States in 2011, cell-free DNA testing (cfDNA) has decreased invasive testing (particularly amniocentesis) [7-11] and maternal serum screening utilization [7,9,11]. Additionally, there have been examples of changes in the nature of referrals for genetic counseling and diagnostic testing [9, 10]. For instance, there are more referrals for carrier screening, ultrasound anomalies, and significant family history with a relative decrease in the number of referrals for advanced maternal age and abnormal maternal serum screens [10]. Now cfDNA stands as the recommended screening modality for all pregnant women [12]. While current recommendations for cell-free DNA screening only encompass trisomy 21, 18, 13 and certain sex chromosome abnormalities, the capability of cfDNA reaches far beyond detection of viable aneuploidies. Cell-free DNA screening is clinically available for select microdeletion syndromes, genome wide deletions and duplications as well as select monogenic disorders. Additionally, genetic testing advances have expanded routine diagnostic testing beyond karyotype alone. Chromosomal microarray is recommended as a first line diagnostic test in the presence of a fetal anomaly [13] and exome sequencing is poised to become the next step in the presence of fetal anomalies [14-16].

The utilization of genetic testing in pregnancies with fetal anomalies is of particular interest, as these pregnancies are at higher risk to have an underlying genetic condition. Studies have shown that uptake of genetic testing is higher when an ultrasound abnormality is detected [17-19] and the yield of testing is higher in these pregnancies [16, 20-22]. However, little has been elucidated about how patients'

make testing decisions in the context of an ultrasound anomaly. Due to the complexities of the decision-making process, it is unclear what factors weigh most heavily on this decision.

It is also unclear how the mitigation of obstacles to testing such as cost and risk may impact testing uptake. Decision making may shift towards the ultimate question of whether a patient finds value in a prenatal diagnosis. Clinicians need the insight to tailor pre-test counseling using a patient centered framework to elicit the underlying motivations. These motivations may not be as tangible as eliminating risk and reducing cost.

This study aimed to examine and broaden our knowledge of potential decision-making factors related to genetic testing in pregnancies with fetal anomalies. We aimed to both validate previously identified factors, but also consider other potential psychosocial aspects of the decision-making process in the light of new testing options. We examined the coping strategies of patients, patient's perceptions of the care team, and social factors to determine if there were any specific facets to consider during pre-test counseling. This information may help clinicians better understand patients' decision making and provide better care during a vulnerable period in their pregnancy.

## **Methods**

This was a cross-sectional, single site study performed at a tertiary maternal-fetal medicine center at Children's Memorial Hermann Hospital in Houston, Texas from July 2020 to February 2021. IRB approval for the study protocol was obtained through the University of Texas Health Science Center Review Board (HSC-GEN-19-0479).

Participants in the study had to be 18 years or older, English or Spanish speaking, and referred to genetic counseling for a fetal anomaly. After the patient consented to the study, the genetic counselor recorded demographic information including maternal age, gestational age, genetic testing history, obstetric history, and a brief explanation of the reason for referral in a study log. No protected health information was documented by the counselor and the medical record was not accessed for the purposes of the study after the appointment.

Prior to genetic counseling, the patient was provided the Coping Strategy Indicator [23]. This is a validated, 33-question, Likert-scale tool that assesses three strategies of coping: problem-solving, social support seeking, and avoidance in the context of typical behaviors in previous stressful situations. Responses are categorized based on the provided scale which corresponds to the likelihood that an individual would utilize each coping strategy. The survey was offered prior to meeting the medical team to minimize the direct influence of the consultation on the reporting of typical coping strategies.

After the genetic consultation was completed and the testing decision was made, patients were asked to complete a second survey, coded to the first survey response and study log, designed to assess for various factors that may have influenced the genetic testing decision. These factors broadly focused on concern for the indication, perceived utility and risk of the testing, the influence of the medical team, social decision making, and the influence of a belief system. Patients reported these factors via a 20 question four-point Likert scale. Additional demographic information such as educational attainment, belief system, and marital status was provided by the patient. This measure was not validated. Patients who participated in the study were offered entry into a drawing where the identifying information was separate from their survey responses.

Demographics, coping strategy, and decision-making factors were correlated with the patient's genetic testing decision. In the analysis of the factors influencing the testing decision, the Likert items (strongly agree, agree, disagree, strongly disagree) were reduced to binary results (agree, disagree). Concern was reduced (none, minimal, some, a great deal) to low and high concern. Experience with disability or special needs was reduced (none, minimal, some, a great deal) to less and more experience. The genetic testing decision was examined through two lenses: whether they accepted diagnostic testing at any point and whether they elected any new testing (screening or diagnostic) after counseling at the fetal center. The latter group is referred to as 'Facilitated Testing Decisions' (FTD). Screening decisions could include those who had maternal serum screening (MSS) and elected cfDNA, repeat cfDNA for various reasons including low fetal fraction, additional cfDNA analysis for microdeletions and duplications not previously examined, or carrier screening. Patients who were seeking fetal intervention

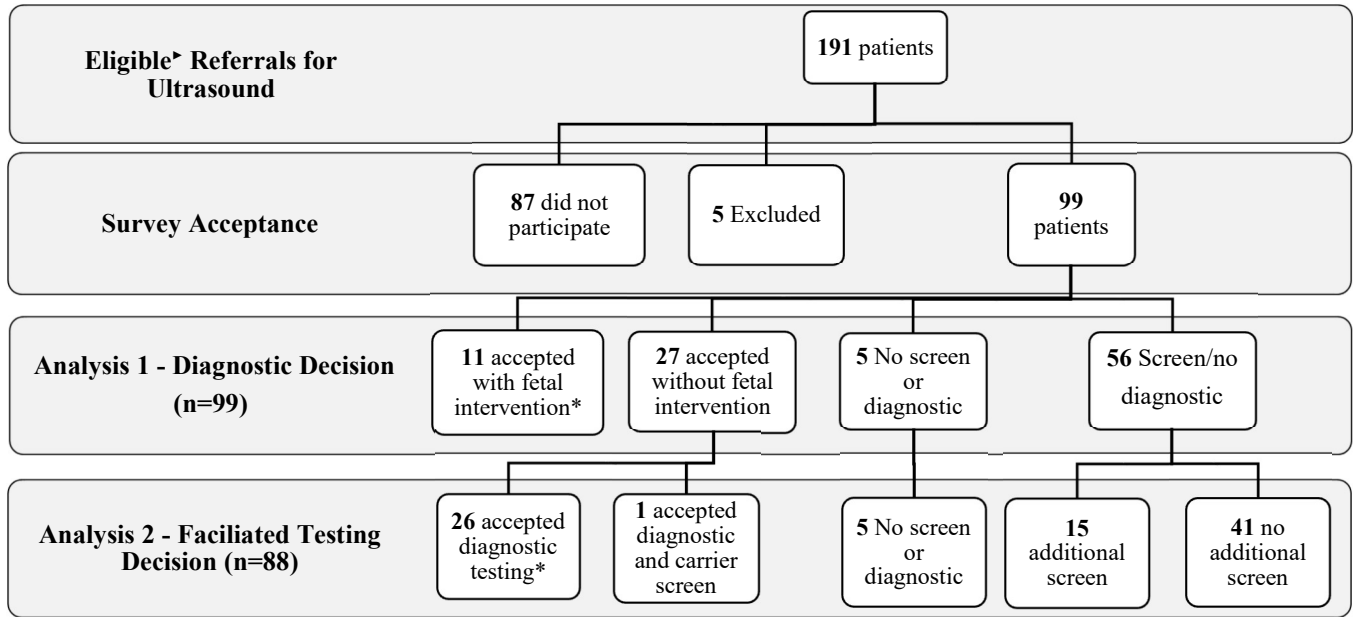
(e.g. in utero repair for a neural tube defect) were excluded from the FTD analysis as diagnostic testing is required for these patients which could confound the results. Pearson  $\chi^2$  or Fisher's exact tests were used for categorical analyses. Multivariable Poisson regression models with robust error variance were utilized to evaluate the association between factors and the outcomes. Crude and adjusted risk ratios (RRs) were reported with 95% confidence intervals (CI). Two-sided student's T-tests were used for evaluation of age-related variables.  $\chi^2$  goodness of fit was utilized to evaluate if the study sample was racially representative of the population surrounding Harris County. Significance was assumed at  $p < 0.05$ . Analysis was performed utilizing STATA (v.13.1, College Station, TX) and Jamovi (v.1.6) statistical software.

## **Results**

### *Study Participation and Analysis Groups*

One hundred-four patients out of an estimated 191 eligible patients participated in the study during the specified timeframe (54.4%), (Figure 1).

**Figure 1 – Participation, Analyses, and Testing Decision**



\*An eligible referral for ultrasound is considered an ultrasound finding with a known association with a genetic etiology

\*Twenty-two had genetic screening prior to terminal diagnostic testing decision (n=4 fetal intervention patients; n=18 patients who did not consider fetal intervention)

Eighty-seven eligible patients did not participate, either due to time constraints prohibiting administration of the survey or because patients declined participation. Five surveys were excluded based on indication or irregularities with the survey. The remaining 99 patient responses were used in the analysis. Ten surveys (9.9%) were from Spanish-speaking patients. Evidence of previous screening (cfDNA, carrier screening, or maternal serum screening) was noted for 78 (78.8%) patients. Five (5.1%) individuals had declined all diagnostic and screening tests before and after the fetal center consult.

#### *Demographics and Diagnostic Testing Decision*

Demographic characteristics of study participants and their association with diagnostic testing uptake are described in Table 1. This cohort was believed to be representative of the known racial demographics for Harris County, Texas based on 2019 census data[24] and  $\chi^2$  goodness of fit testing (df=4, p=0.81).

Educational attainment ( $p=0.034$ ), insurance status ( $p=0.030$ ), and trimester ( $p=0.039$ ) were all significantly correlated with the diagnostic testing decision. Specifically, those with higher education, private insurance, and in the first and second trimester of pregnancy were more likely to undergo diagnostic testing based on relative proportions.



**Table 1 – Demographic Information and Diagnostic Testing Decision**

Variable	Total (n=99)	% Total	Diagnostic Decision				p-value
			Yes (n=38)	% of Yes	No (n=61)	% of No	
<b>Maternal Age (Mean<sup>†</sup>/SD<sup>‡</sup>)</b>	28.1 <sup>†</sup>	6.2 <sup>‡</sup>	29.6 <sup>†</sup>	6.4 <sup>‡</sup>	27.1 <sup>†</sup>	6.0 <sup>‡</sup>	0.053
<b>Race/Ethnicity</b>							0.27
<i>White, Non-Hispanic</i>	27	27.3	14	36.8	13	21.3	
<i>Black/African American</i>	22	22.2	9	23.7	13	21.3	
<i>Hispanic</i>	40	40.4	11	28.9	29	47.5	
<i>Other</i>	9	9.1	4	10.5	5	8.2	
<i>Unknown</i>	1	1.0	0	0.0	1	1.6	
<b>Education</b>							0.034
<i>Less than high school</i>	10	10.1	3	7.9	7	11.5	
<i>High school graduate</i>	28	28.3	5	13.2	23	37.7	
<i>Some college</i>	29	29.3	13	34.2	15	24.6	
<i>College graduate or above</i>	32	32.3	16	42.1	16	26.2	
<i>Unknown</i>	1	1.0	1	2.6	0	0.0	
<b>Marital Status</b>							0.067
<i>Married/partner</i>	70	70.7	30	78.9	40	65.6	
<i>Not married</i>	28	28.3	7	18.4	21	34.4	
<i>Unknown</i>	1	1.0	1	2.6	0	0.0	
<b>Insurance Status</b>							0.030
<i>Public</i>	53	53.5	15	39.5	38	62.3	
<i>Private</i>	45	45.5	23	60.5	22	36.1	
<i>Uninsured/Self-Pay</i>	1	1.0	0	0.0	1	1.6	
<b>Trimester</b>							0.039
<i>First (≤13 weeks)</i>	3	3.0	3	7.9	0	0.0	
<i>Second (14-26 weeks)</i>	63	63.6	28	73.7	35	57.4	
<i>Third (≥27 weeks)</i>	33	33.3	7	18.4	26	42.6	
<b>Gravidity</b>							0.96
<i>Primigravida</i>	31	31.3	12	31.6	19	31.1	
<i>Multigravida</i>	68	68.7	26	68.4	42	68.9	
<b>Parity</b>							0.93
<i>Nulliparous</i>	46	46.5	17	44.7	29	47.5	
<i>Uniparous</i>	29	29.3	11	28.9	18	29.5	
<i>Multiparous</i>	24	24.2	10	26.3	14	23.0	
<b>Previous Genetic Counseling</b>							0.68
<i>Yes</i>	34	34.3	14	36.8	20	32.8	
<i>No</i>	65	65.7	24	63.2	41	67.2	
<b>Religious</b>							0.40
<i>Yes</i>	80	80.8	29	76.3	51	83.6	
<i>No</i>	8	8.1	5	13.2	3	4.9	
<i>Unknown</i>	11	11.1	4	10.5	7	11.5	

p-values calculated using a  $\chi^2$  or Fisher's exact test except for age variable calculated with a two-tailed student's T-test (bolded significant at p<0.05)

### *Factors Influencing the Diagnostic Testing Decision*

A number of decision-making factors were significantly correlated with the diagnostic testing decision (Tables 2a, 2b). The four-point Likert-data is available in the tables under Appendix A.

**Table 2a - Diagnostic Testing and Decision-Making Factors**

	<b>Total (n=99)</b>	<b>Yes (n=38)</b>	<b>No (n=61)</b>	<b>% yes</b>	<b>p-value</b>
<b>Rate your level of concern for a genetic condition</b>					0.138
<i>Low Concern</i>	35	10	25	28.6	
<i>High Concern</i>	64	28	36	43.8	
<b>Describe your experience or amount of interaction with individuals with special needs, physical or intellectual disabilities or genetic conditions</b>					0.96
<i>Less Experience</i>	57	22	35	38.6	
<i>More Experience</i>	42	16	26	38.1	
<b>I feel that invasive testing (amniocentesis or CVS) is too risky to the pregnancy</b>					<b>&lt;0.001</b>
<i>Agree</i>	48	5	43	10.4	
<i>Disagree</i>	47	32	15	68.1	
<i>Unknown</i>	4	1	3	25.0	
<b>I have a fear of needles and/or invasive procedures</b>					0.116
<i>Agree</i>	49	15	34	30.6	
<i>Disagree</i>	50	23	27	46.0	
<b>I feel that genetic testing could explain what caused the ultrasound finding in my pregnancy</b>					<b>0.026</b>
<i>Agree</i>	76	34	42	44.7	
<i>Disagree</i>	23	4	19	17.4	
<b>I feel that I understood the genetic testing options and was able to make an informed choice</b>					0.295
<i>Agree</i>	95	38	57	40.0	
<i>Disagree</i>	4	0	4	0.0	
<b>If there was a genetic condition, I would like to know about it before delivery</b>					<b>&lt;0.001</b>
<i>Agree</i>	75	37	38	49.3	
<i>Disagree</i>	22	1	21	4.5	
<i>Unknown</i>	2	0	2	0.0	
<b>The opinion of my partner or family member is important in helping me decide whether to have genetic testing</b>					<b>0.008</b>
<i>Agree</i>	81	36	45	44.4	
<i>Disagree</i>	18	2	16	11.1	
<b>The opinion of a friend is important in helping me decide whether to have genetic testing</b>					0.711
<i>Agree</i>	19	8	11	42.1	
<i>Disagree</i>	80	30	50	37.5	
<b>My religious faith influenced my genetic testing decision</b>					0.933
<i>Agree</i>	23	9	14	39.1	
<i>Disagree</i>	76	29	47	38.2	

p-values calculated using a  $\chi^2$  or Fisher's exact test (bolded significant at  $p < 0.05$ )

'% yes' represents the proportion of individuals that accepted diagnostic testing grouped by response

**Table 2b - Diagnostic Testing and Decision-Making Factors**

	<b>Total (n=99)</b>	<b>Yes (n=38)</b>	<b>No (n=61)</b>	<b>% yes</b>	<b>p-value</b>
<b>My belief in the spiritual influenced my genetic testing decision</b>					<b>0.882</b>
<i>Agree</i>	23	8	15	34.8	
<i>Disagree</i>	75	30	45	40.0	
<i>Unknown</i>	1	0	1	0.0	
<b>Genetic testing would conflict with my faith</b>					<b>0.125</b>
<i>Agree</i>	4	0	4	0.0	
<i>Disagree</i>	94	37	57	39.4	
<i>Unknown</i>	1	1	0	100.0	
<b>I believe that genetic testing is being offered in my best interest</b>					<b>0.020</b>
<i>Agree</i>	92	37	55	40.2	
<i>Disagree</i>	6	0	6	0.0	
<i>Unknown</i>	1	1	0	100.0	
<b>I would want my medical team to know if there was a genetic condition before delivery</b>					<b>0.012</b>
<i>Agree</i>	89	38	51	42.7	
<i>Disagree</i>	10	0	10	0.0	
<b>If there was a genetic condition, it would change the way I medically manage my pregnancy</b>					<b>0.012</b>
<i>Agree</i>	63	30	33	47.6	
<i>Disagree</i>	36	8	28	22.2	
<b>If there was a genetic condition, it would change the way I feel about my pregnancy</b>					<b>0.203</b>
<i>Agree</i>	28	13	15	46.4	
<i>Disagree</i>	70	24	46	34.3	
<i>Unknown</i>	1	1	0	100.0	
<b>I did not feel pressured to undergo genetic testing</b>					<b>1.00</b>
<i>Agree</i>	91	35	56	38.5	
<i>Disagree</i>	8	3	5	37.5	
<b>I feel that I had adequate input from the medical team in making a decision about genetic testing</b>					<b>1.00</b>
<i>Agree</i>	98	38	60	38.8	
<i>Disagree</i>	1	0	1	0.0	
<b>I feel that I had adequate input from family and friends in making a decision about genetic testing</b>					<b>0.659</b>
<i>Agree</i>	78	32	46	41.0	
<i>Disagree</i>	20	6	14	30.0	
<i>Unknown</i>	1	0	1	0.0	
<b>I would have liked the genetic counselor or doctor to tell me if I should get genetic testing or not</b>					<b>0.041</b>
<i>Agree</i>	42	21	21	50.0	
<i>Disagree</i>	57	17	40	29.8	

p-values calculated using a  $\chi^2$  or Fisher's exact test (bolded significant at  $p < 0.05$ )

'% yes' represents the proportion of individuals that accepted diagnostic testing grouped by response

Decision-making factors that were significantly correlated with diagnostic testing uptake included the affirmation that genetic testing could explain the ultrasound finding in the pregnancy ( $p=0.026$ ), knowing about a genetic condition would be helpful before delivery ( $p<.001$ ), the opinion of the partner or family member is important to the decision ( $p=0.0008$ ), testing was being offered in the patient's best interest ( $p=0.020$ ), they would want the medical team to know if there was a genetic condition during the pregnancy ( $p=0.012$ ), a genetic condition would change medical management of the pregnancy ( $p=0.012$ ) and they would have liked the medical team to be more directive about testing ( $p=0.041$ ). The only factor significantly associated with the decision to decline diagnostic testing was the belief that diagnostic testing was too risky to the pregnancy ( $p<0.001$ ).

#### *Demographics and Facilitated Testing Decision (FTD)*

After excluding patients who underwent diagnostic testing as an eligibility requirement for fetal intervention, demographics and testing decision were evaluated for the remaining 88 patients (Table 3).

**Table 3 – Demographic Information and Facilitated Testing Decision**

Variable	Total (n=88)	% Total	Facilitated Testing Decision				p-value
			Yes (n=42)	% of Yes	No (n=46)	% of No	
<b>Maternal Age (Mean<sup>†</sup>/SD<sup>‡</sup>)</b>	28.1 <sup>†</sup>	6.1 <sup>‡</sup>	29.5 <sup>†</sup>	6.0 <sup>‡</sup>	26.8 <sup>†</sup>	5.9 <sup>‡</sup>	<b>0.033</b>
<b>Race/Ethnicity</b>							0.29
<i>White, Non-Hispanic</i>	22	25.0	10	23.8	12	28.6	
<i>Black/African American</i>	21	23.9	14	33.3	7	16.7	
<i>Hispanic</i>	37	42.0	15	35.7	22	52.4	
<i>Other</i>	7	8.0	3	7.1	4	9.5	
<i>Unknown</i>	1	1.1	0	0.0	1	2.4	
<b>Education</b>							0.45
<i>Less than high school</i>	9	10.2	3	7.1	6	14.3	
<i>High school graduate</i>	24	27.3	9	21.4	15	35.7	
<i>Some college</i>	25	28.4	14	33.3	11	26.2	
<i>College graduate or above</i>	29	33.0	15	35.7	14	33.3	
<i>Unknown</i>	1	1.1	1	2.4	0	0.0	
<b>Marital Status</b>							0.90
<i>Married/partner</i>	60	68.2	28	66.7	32	76.2	
<i>Not married</i>	27	30.7	13	31.0	14	33.3	
<i>Unknown</i>	1	1.1	1	2.4	0	0.0	
<b>Insurance Status</b>							0.91
<i>Public</i>	49	55.7	23	54.8	26	61.9	
<i>Private</i>	38	43.2	19	45.2	19	45.2	
<i>Uninsured/Self-Pay</i>	1	1.1	0	0.0	1	2.4	
<b>Trimester</b>							0.15
<i>First (≤13 weeks)</i>	3	3.4	3	7.1	0	0.0	
<i>Second (14-26 weeks)</i>	56	63.6	30	71.4	26	61.9	
<i>Third (≥27 weeks)</i>	29	33.0	9	21.4	20	47.6	
<b>Gravidity</b>							0.51
<i>Primigravida</i>	26	29.5	11	26.2	15	35.7	
<i>Multigravida</i>	62	70.5	31	73.8	31	73.8	
<b>Parity</b>							0.56
<i>Nulliparous</i>	42	47.7	18	42.9	24	57.1	
<i>Uniparous</i>	25	28.4	12	28.6	13	31.0	
<i>Multiparous</i>	21	23.9	12	28.6	9	21.4	
<b>Previous Genetic Counseling</b>							0.76
<i>Yes</i>	30	34.1	15	35.7	15	35.7	
<i>No</i>	58	65.9	27	64.3	31	73.8	
<b>Religious</b>							0.60
<i>Yes</i>	72	81.8	34	81.0	38	90.5	
<i>No</i>	6	6.8	4	9.5	2	4.8	
<i>Unknown</i>	10	11.4	4	9.5	6	14.3	

p-values calculated using a  $\chi^2$  or Fisher's exact test except for age variable calculated with a two-tailed student's T-test (bolded significant at p<0.05)

Of these patients, 42 (47.7%) elected to pursue some form of diagnostic or screening test. Diagnostic testing was elected in 27 (30.7%) cases, 18 of which had previous screening. Sixteen (18.2%) elected a screening test, 14 of which had previous screening. Forty-one (46.6%) had screening prior to the appointment and did not have further screening or diagnostic testing. The remaining five declined all testing, prior to and after their fetal center consultation.

Age was significantly correlated with increased screening/diagnostic testing uptake in the FTD group ( $p=.033$ ). Those who elected any new testing tended to be older compared to those who declined testing (Table 3). No other demographic factors were significantly correlated with testing decision.

#### *Factors Influencing the Fetal Center Facilitated Testing Decision*

A number of decision-making factors were also correlated diagnostic and screening decision within the FTD cohort (Table 4a, 4b). The four-point Likert-data is available in the tables under Appendix A.

**Table 4a - Facilitated Testing Decision and Decision-Making Factors**

	<b>Total (n=88)</b>	<b>Yes (n=42)</b>	<b>No (n=46)</b>	<b>% yes</b>	<b>p-value</b>
<b>Rate your level of concern for a genetic condition</b>					<b>&lt;0.001*</b>
<i>Low Concern</i>	28	6	22	21.4	
<i>High Concern</i>	60	36	24	60.0	
<b>Describe your experience or amount of interaction with individuals with special needs, physical or intellectual disabilities or genetic conditions</b>					0.723
<i>Less Experience</i>	52	24	28	46.2	
<i>More Experience</i>	36	18	18	50.0	
<b>I feel that invasive testing (amniocentesis or CVS) is too risky to the pregnancy</b>					<b>&lt;0.001</b>
<i>Agree</i>	45	13	32	28.9	
<i>Disagree</i>	39	28	11	71.8	
<i>Unknown</i>	4	1	3	25.0	
<b>I have a fear of needles and/or invasive procedures</b>					0.200
<i>Agree</i>	44	18	26	40.9	
<i>Disagree</i>	44	24	20	54.5	
<b>I feel that genetic testing could explain what caused the ultrasound finding in my pregnancy</b>					<b>&lt;0.001</b>
<i>Agree</i>	68	41	27	60.3	
<i>Disagree</i>	20	1	19	5.0	
<b>I feel that I understood the genetic testing options and was able to make an informed choice</b>					0.118
<i>Agree</i>	84	42	42	50.0	
<i>Disagree</i>	4	0	4	0.0	
<b>If there was a genetic condition, I would like to know about it before delivery</b>					<b>0.002</b>
<i>Agree</i>	64	37	27	57.8	
<i>Disagree</i>	22	4	18	18.2	
<i>Unknown</i>	2	1	1	50.0	
<b>The opinion of my partner or family member is important in helping me decide whether to have genetic testing</b>					0.092
<i>Agree</i>	71	37	34	52.1	
<i>Disagree</i>	17	5	12	29.4	
<b>The opinion of a friend is important in helping me decide whether to have genetic testing</b>					0.951
<i>Agree</i>	17	8	9	47.1	
<i>Disagree</i>	71	34	37	47.9	
<b>My religious faith influenced my genetic testing decision</b>					0.805
<i>Agree</i>	22	11	11	50.0	
<i>Disagree</i>	66	31	35	47.0	

p-values calculated with either  $\chi^2$ , Fisher's exact tests, or two-tailed Student's T-test (bolded p<0.05)

'% yes' represents the proportion of individuals that accepted diagnostic testing grouped by response



**Table 4b - Facilitated Testing Decision and Decision-Making Factors**

	<b>Total (n=88)</b>	<b>Yes (n=42)</b>	<b>No (n=46)</b>	<b>% Yes</b>	<b>p-value</b>
<b>My belief in the spiritual influenced my genetic testing decision</b>					<b>0.601</b>
<i>Agree</i>	22	10	12	45.5	
<i>Disagree</i>	65	32	33	49.2	
<i>Unknown</i>	1	0	1	0.0	
<b>Genetic testing would conflict with faith</b>					<b>0.118</b>
<i>Agree</i>	4	0	4	0.0	
<i>Disagree</i>	83	41	42	49.4	
<i>Unknown</i>	1	1	0	100.0	
<b>I believe that genetic testing is being offered in my best interest</b>					<b>0.027</b>
<i>Agree</i>	81	41	40	50.6	
<i>Disagree</i>	6	0	6	0.0	
<i>Unknown</i>	1	1	0	100.0	
<b>I would want my medical team to know if there was a genetic condition before delivery</b>					<b>0.016</b>
<i>Agree</i>	78	41	37	52.6	
<i>Disagree</i>	10	1	9	10.0	
<b>If there was a genetic condition, it would change the way I medically manage my pregnancy</b>					<b>0.011</b>
<i>Agree</i>	55	32	23	58.2	
<i>Disagree</i>	33	10	23	30.3	
<b>If there was a genetic condition, it would change the way I feel about my pregnancy</b>					<b>0.649</b>
<i>Agree</i>	27	14	13	51.9	
<i>Disagree</i>	61	28	33	45.9	
<b>I did not feel pressured to undergo genetic testing</b>					<b>1.00</b>
<i>Agree</i>	81	39	42	48.1	
<i>Disagree</i>	7	3	4	42.9	
<b>I feel that I had adequate input from the medical team in making a decision about genetic testing</b>					<b>1.00</b>
<i>Agree</i>	87	42	45	48.3	
<i>Disagree</i>	1	0	1	0.0	
<b>I feel that I had adequate input from family and friends in making a decision about genetic testing</b>					<b>0.507</b>
<i>Agree</i>	70	32	38	45.7	
<i>Disagree</i>	17	9	8	52.9	
<i>Unknown</i>	1	1	0	100.0	
<b>I would have liked the genetic counselor or doctor to tell me if I should get genetic testing or not</b>					<b>0.152</b>
<i>Agree</i>	33	19	14	57.6	
<i>Disagree</i>	55	23	32	41.8	

p-values calculated with either  $\chi^2$ , Fisher's exact tests, or two-tailed Student's T-test (bolded p<0.05)  
 '% yes' represents the proportion of individuals that accepted diagnostic testing grouped by response

Patients with the FTD group were more likely to elect diagnostic testing if they believed: genetic testing could explain the ultrasound finding in the pregnancy ( $p<.001$ ), knowing about a genetic condition would be helpful before delivery ( $p=0.002$ ), testing was being offered in the patient's best interest ( $p=0.027$ ), they would want the medical team to know if there was a genetic condition during the pregnancy ( $p=0.016$ ), and testing would change medical management of the pregnancy ( $p=0.011$ ). The factors significantly related to the decision to decline any further testing (or no testing at all in the case of five patients) included the patient's belief that diagnostic testing was too risky to the pregnancy ( $p<0.001$ ), and that the patient's level of concern for a genetic condition was low ( $p<.001$ ).

#### *Multivariable Models*

Multivariable Poisson regression models with robust error variance were used to evaluate the association between factors and outcomes. Adjustments were made for all significant decision-making factors and demographic variables in both the diagnostic and FTD cohort (Table 5, 6).

**Table 5 – Multivariable Analysis of Diagnostic Testing Decision**

	p-value	Crude RR (95% CI)	Adj RR* (95% CI)
<b>Risk of invasive testing</b>	<b>&lt;0.001</b>		
<i>Agree</i>		<b>0.15 (0.06-0.36)</b>	<b>0.24(0.10-0.56)</b>
<i>Disagree</i>		1.00	1.00
<i>Unknown</i>		0.37 (0.07-2.05)	0.38(0.08-1.93)
<b>Genetic testing can explain finding</b>	<b>&lt;0.001</b>		
<i>Agree</i>		<b>2.57 (1.02-6.52)</b>	1.06(0.44-2.55)
<i>Disagree</i>		1.00	1.00
<b>Knowledge is useful at this time</b>	<b>0.002</b>		
<i>Agree</i>		<b>10.86 (1.56-75.48)</b>	5.84(0.91-37.31)
<i>Disagree</i>		1.00	1.00
<i>Unknown</i>		-	-
<b>Opinion of partner</b>	<b>0.008</b>		
<i>Agree</i>		<b>4.00 (1.05-15.21)</b>	2.22(0.81-6.03)
<i>Disagree</i>		1.00	1.00
<b>Change in medical management</b>	<b>0.012</b>		
<i>Agree</i>		<b>2.14 (1.10-4.18)</b>	1.47(0.81-2.70)
<i>Disagree</i>		1.00	1.00
<b>Directive</b>	<b>0.041</b>		
<i>Agree</i>		<b>1.68 (1.01-2.77)</b>	<b>1.52(1.02-2.27)</b>
<i>Disagree</i>		1.00	1.00
<b>Education</b>	<b>0.45</b>		
<i>Less than High School</i>		0.60 (0.22-1.65)	1.25(0.60-2.59)
<i>High school graduate</i>		<b>0.36 (0.15-0.85)</b>	0.76(0.30-1.93)
<i>Some college</i>		0.93 (0.55-1.58)	0.72(0.42-1.25)
<i>College graduate or above</i>		1.00	1.00
<i>Unknown</i>		<b>2.00 (1.41-2.83)</b>	0.83(0.47-1.46)
<b>Insurance</b>	<b>0.030</b>		
<i>Public</i>		1.00	1.00
<i>Private</i>		<b>1.81(1.08-3.03)</b>	1.05(0.64-1.70)
<i>Uninsured/Self-Pay</i>		-	-
<b>Trimester</b>	<b>0.039</b>		
<i>First (<math>\leq 13</math> weeks)</i>		<b>4.71 (2.43-9.13)</b>	1.57(0.75-3.32)
<i>Second (14-26 weeks)</i>		<b>2.10 (1.02-4.29)</b>	1.03(0.55-1.94)
<i>Third (<math>\geq 27</math> weeks)</i>		1.00	1.00

p-values calculated with either  $\chi^2$ , Fisher's exact tests, or two-tailed Student's T-test

Bolded are significant at 95% confidence

\*risk ratio (RR) after adjusting for: perceived risk of invasive testing, belief that testing can find the cause of the ultrasound finding, belief the knowledge of a genetic condition has value, the opinion of family or partner is important to the decision, desire for the medical team to be directive, education, insurance, trimester

**Table 6 -Multivariable Analysis of Facilitated Testing Decision**

	p-value	Crude RR (95% CI)	Adj RR* (95% CI)
<b>Level of concern for a genetic condition</b>	<b>&lt;.001</b>		
<i>Low Concern</i>		<b>0.36 (0.17-0.75)</b>	0.73(0.36-1.47)
<i>High Concern</i>		1.00	1.00
<b>Risk of invasive testing</b>	<b>&lt;.001</b>		
<i>Agree</i>		<b>0.40 (0.24-0.66)</b>	0.68(0.43-1.08)
<i>Disagree</i>		1.00	1.00
<i>Unknown</i>		0.35 (0.06-1.94)	0.28(0.05-1.46)
<b>Genetic testing can explain finding</b>	<b>&lt;.001</b>		
<i>Agree</i>		<b>12.06 (1.75-83.17)</b>	6.10 (0.73-50.90)
<i>Disagree</i>		1.00	1.00
<b>Knowledge is useful at this time</b>	<b>0.002</b>		
<i>Agree</i>		<b>3.18 (1.27-7.95)</b>	1.93(0.81-4.60)
<i>Disagree</i>		1.00	1.00
<i>Unknown</i>		2.75 (0.53-14.28)	1.64(0.26-10.46)
<b>Change in medical management</b>	<b>0.011</b>		
<i>Agree</i>		<b>1.92 (1.09-3.39)</b>	1.27(0.76-2.11)
<i>Disagree</i>		1.00	1.00
<b>Maternal age</b>	<b>0.03</b>	1.03(0.99-1.06)	1.02(0.99-1.05)

p-values calculated with either  $\chi^2$ , Fisher's exact tests, or two-tailed Student's T-test

Bolded are significant at 95% confidence

\*risk ratio (RR) after adjusting for: level of concern for a genetic condition, perceived risk of invasive testing, belief that testing can find the cause of the ultrasound finding, belief the knowledge of a genetic condition has value, testing would change management of the pregnancy, and age

The responses to, 'I believe that genetic testing is being offered in my best interest' and 'I would want my medical team to know if there was a genetic condition before delivery', were excluded from the analyses due to an inadequate comparison group. Only one patient had elected screening after disagreeing with wanting the medical team to know if there was a genetic condition.

The only factors that were significant after multivariable analyses were within the diagnostic cohort: perceived risk of diagnostic testing (RR 0.23, 95% CI 0.10-0.54) and desire for more directive counseling regarding testing (RR 1.53, 95% CI 1.04-2.27), (Table 6).

### *Non-significant Correlates*

Demographic factors including race, marital status, gravidity, parity, previous genetic counseling, and religious belief were not significantly correlated with any testing decision. Factors associated with coping strategy, previous experiences with genetic conditions or disabilities, personal fear of a diagnostic procedure, sufficient information about testing, feeling pressured about testing, and most social support factors (with the exception of the opinion of a partner or family member regarding diagnostic testing) were not correlated with the testing decision in either cohort.

### *Fetal Intervention*

Of the 11 patients who were considering fetal intervention, the majority reported that: they felt genetic testing could explain the ultrasound findings (n=8), the testing would change how they managed their pregnancy (n=8), they would have wanted the medical team to be directive about the genetic testing decision (n=9), and the opinion of their partner or family was important to the genetic testing decision (n=10). All reported the information was useful to them at this time, the testing was offered in their best interest, and they would want the medical team to know if there was a genetic condition. Interestingly, three of the 11 patients who were considering fetal intervention and had diagnostic testing reported that diagnostic testing was too risky to the pregnancy.

## **Discussion**

This study examined a broad range of demographic and psychosocial factors that potentially influence the testing decision in the presence of ultrasound anomalies known to be associated with genetic conditions. Knowledge of influential factors can improve the provision of patient-centered care that incorporates patients' experiences and goals.

### *Risk of Diagnostic Testing*

Unsurprisingly, the risk perception of diagnostic testing had a significant impact on its acceptance. Patients were roughly four times less likely to accept diagnostic testing if they felt it was too

risky to the pregnancy (RR 0.23, 95% CI 0.10-0.54). Multiple studies affirm that the risk for miscarriage and preterm birth negatively influences the uptake or regard of diagnostic testing [2-6, 25, 26].

Conversely, a personal fear of needles or invasive procedures did not reach significance ( $p=.115$ ). This speaks to the salience of the perceived risk to the pregnancy versus the perceived risks of the procedure to oneself.

Examining this more closely, studies have acknowledged the theory of planned behavior [27] and *a priori* beliefs about diagnostic testing as a primary reason for declining [25, 26, 28]. Individuals who perceive accepting diagnostic testing *a priori* as ‘too risky’ may evaluate testing negatively, thereby diminishing the impact of new information learned during genetic counseling. For example, 23% of patients in our cohort had high concern for a genetic condition yet declined diagnostic testing. If they had a negative *a priori* belief about diagnostic testing, concern for a genetic condition may not override the belief about the risk. Similarly, 26% of individuals declined diagnostic testing and felt diagnostic testing was too risky, despite reporting that the knowledge of a genetic condition would be useful.

Looking beyond the risks of diagnostic testing, it is also important to evaluate other factors that influence a testing decision. It was noted that 22% of patients did not express a desire for prenatal knowledge of a genetic condition, and 36% did not feel it would impact the medical management of the pregnancy. Despite this, 95% of patients had some form of diagnostic or screening test for a genetic condition over the course of their pregnancy. This discrepancy highlights concern for the routinization of cfDNA screening. The “non-invasive” nature of cfDNA is more likely to be perceived as “just a simple blood test”. However, this may result in less informed decision making, increased psychological stress, less provider-patient rapport, and a reduced sense of autonomy [28-32]. Not every family will find value in genetic testing regardless of increased detection, more insurance coverage, or the elimination of risk. Understanding patient values, provider assumptions, and how they can conflict with each other enhances the clinician’s empathy and encourages thoughtful engagement about the genetic testing decision.

### *Value of Knowledge and the Influence of Pregnancy Management*

Patients who reported a prenatal diagnosis would be useful represented a greater proportion of those who accepted diagnostic testing (49.3%) versus those who did not (4.5%,  $p<0.001$ ). This difference became slightly less pronounced when evaluating all testing decisions (57.8% versus 18.2% respectively,  $p=0.002$ ). Thirty of the thirty-eight patients who accepted diagnostic testing indicated that the information would help to inform medical management of their pregnancy.

Of the patients in this study considering fetal intervention, all eleven affirmed that the information was valuable to them and eight stated that it would change the management of their pregnancy. While there are well established fetal interventions for conditions such as lower urinary tract obstructions and open neural tube defects, interventions for single-gene conditions are also being studied. Studies have examined interventions in alpha-thalassemia major [33], severe osteogenesis imperfecta [34], and neonatal lethal Gaucher's disease [35]. This study suggests that more individuals would elect genetic testing if interventions for genetic conditions were available.

Individuals with a higher level of concern for a genetic condition appeared to be more likely to accept any genetic test when examining the fetal center facilitated testing decision. Of those who had increased concern for a genetic condition, 24 had accepted diagnostic testing and 12 had accepted additional screening. Only three individuals elected diagnostic or a screening test respectively when expressing a low concern. This concern level is likely partially dependent upon the risk assessment provided during pretest counseling. For example, copy number variants are detected in 8.1% of pregnancies with ultrasound abnormalities, but the yield varies broadly based on the specific findings, such as the presence of multisystem anomalies [36]. Additionally, the yield of prenatal exome sequencing (ES) can range from 6.2% to 80% based on the indication [37]. Thus, pre-test counseling should entail an accurate risk assessment based on quality prenatal imaging, family history, and studies describing prenatal phenotypes of genetic conditions.

Knowledge of a genetic condition is believed to help families better prepare for the birth of their child. Anecdotally, many providers in the prenatal setting provide this advanced preparation as a rationale for testing. In our cohort, this was echoed by 63% of participants who reported that genetic testing could impact medical management of the pregnancy and 75% who responded that the knowledge of a genetic condition could be useful during the prenatal period. Michie [38], highlighted three possible domains of preparation: clinical activities (such as fetal intervention), social and informational support, and psychological preparation. Preparation can be a unique to each family. Coping mechanisms were evaluated to elucidate whether “problem solvers”, “social support seekers”, or “avoiders”, made different testing decisions, but we did not observe any significant differences that would help inform pre-test discussions. Additional studies are needed to understand how to tailor information that will better prepare families after diagnosis of fetal anomalies.

### *Limitations of Screening*

It is important to consider that 40% of the patients that felt testing could explain the ultrasound finding underwent screening rather than diagnostic testing. While the vast majority of patients (95%) reported they understood the testing options, ensuring that patients know the limitations of screening is important. In a study by Wittman and others, there was concern that some patients misinterpreted negative screen results as definitively negative [39]. Additionally, there is evidence of increased use of cfDNA screening in the presence of ultrasound anomalies [40]. Regardless of advancements in screening, diagnostic CMA remains the recommended first line test in the presence of a fetal anomalies [12]. Further investigation of how patients perceive limitations of screening after discovery of an ultrasound anomaly may be warranted.

### *The Effect of the Medical Team*

A few patients felt that either: ‘testing was *not* being offered in their best interest’ (7%) or felt they ‘*would not* want the medical team to know if there was a genetic condition’ (11%). These patients all declined diagnostic testing and only one accepted screening. However, individuals who reported not



trusting the motives of those offering the testing largely stated they would want their medical team to know if there was a genetic condition. This study was unable to resolve the incongruity of these responses. Further studies of trust in the medical team in the prenatal setting should be pursued in order to elucidate the specific nature of mistrust. Building trust with patients and facilitating healthcare decisions collaboratively helps empower patients not only during their pregnancy but also can influence future healthcare decisions for the child and in future pregnancies [41].

Mistrust can be fostered by a number of factors. Examples of medical mistrust have been associated with race and socioeconomic status [42], fatalism [43], experiential decision making [32, 44, 45] and routinization of prenatal screening [3, 31, 32]. In our study, race was not a significant factor in the testing decision. In looking at educational attainment, a greater proportion of individuals with high school education or less (23% versus 5%) stated that they would not want the medical team to know if there was a genetic condition. Therefore, it appeared that mistrust tracked in our cohort with lower educational attainment rather than race/ethnicity.

Interestingly, wanting the medical team to be more directive in the testing decision was reported by 42% of patients. This remained significant after multivariable analysis. Patients who wanted the testing recommendation of the medical team were more likely to have diagnostic testing (RR 1.52, CI 95% 1.02-2.27). This may represent trust, rapport, and confidence in the care team, but may also be influenced by stress and uncertainty in the context of fetal anomalies. Future studies may wish to explore further why many patients with fetal anomalies want more directive counseling.

### *Strengths and Limitations of the Study*

This study examined decision-making in the context of a fetal ultrasound anomaly at a tertiary referral center that serves a racially and socially diverse population. Therefore, a major strength of this study was the ability to assess for attitudes of individuals of more diverse backgrounds. With the exception of those who had accepted testing for fetal intervention, the facilitated testing decision group elected or declined testing at the time of the survey, removing hypothetical decision making relied on in

other studies. Additionally, the genetic counseling unit is staffed by a small, experienced team which limits variability in how pre-test counseling is provided.

The small sample size limited the ability to resolve factors with smaller effect sizes, limiting our comparison groups. Additionally, resolution of the data was lost by compressing survey categories. Another limitation was the inability to capture decision making that happened prior to arrival at the fetal center, as was the case for many individuals who had aneuploidy screening before arriving at the fetal center. Lastly, while the coping strategy survey was validated [23], the survey utilized to assess decision-making factors was not.

### *Future Directions*

Additional research is needed to explore how families utilize the information gained through genetic testing, particularly as genetic information becomes increasingly accessible through cfDNA screening. Our study demonstrates the need for more research regarding trust and perception of the care team and how they will use prenatal genetic testing results. Lastly, expanding the survey cohort may further refine the impact and relative weight of some of the factors that have been explored in this research.

### **Conclusion**

This study highlights the impact of perceived risk on the uptake of genetic testing in a high-risk setting and emphasizes how decision-making factors may be complex and unique to individual patients. How providers communicate the value of testing and what can be done with this information will be critical, particularly as testing expands in breadth and depth. Additionally, it is important to explain the limitations of cfDNA screening given the majority of patients in this study declined diagnostic testing despite having an increased risk for a genetic condition. Lastly, trust in the medical team is critical to consider both in the impact on testing uptake and the overall care of these high-risk pregnancies. In the rapidly evolving landscape of genetic testing, understanding these individual factors, building trust and rapport with patients, and tailoring the counseling to patients' needs are essential.

## Appendix

### Appendix A – Four-Point Likert Tables

**Table 7a- Diagnostic Testing Decision and Decision-Making Factors (Four-Point Likert)**

	<b>Total (n=99)</b>	<b>%</b>	<b>Yes (n=38)</b>	<b>%</b>	<b>No (n=61)</b>	<b>%</b>	<b>p- value</b>
<b>Rate your level of concern for a genetic condition</b>							<b>0.315</b>
<i>None</i>	10	10.1	3	7.9	7	11.5	
<i>Minimal</i>	25	25.3	7	18.4	18	29.5	
<i>Some</i>	26	26.3	9	23.7	17	27.9	
<i>A great deal</i>	38	38.4	19	50.0	19	31.1	
<b>Describe your experience or amount of interaction with individuals with special needs, physical or intellectual disabilities or genetic conditions</b>							<b>0.056</b>
<i>None</i>	20	20.2	4	10.5	16	26.2	
<i>Minimal</i>	37	37.4	18	47.4	19	31.1	
<i>Some</i>	23	23.2	6	15.8	17	27.9	
<i>A great deal</i>	19	19.2	10	26.3	9	14.8	
<b>I feel that invasive testing (amniocentesis or CVS) is too risky to the pregnancy</b>							<b>&lt;.001</b>
<i>Strongly Agree</i>	18	18.2	1	2.6	17	27.9	
<i>Agree</i>	30	30.3	4	10.5	26	42.6	
<i>Disagree</i>	44	44.4	31	81.6	13	21.3	
<i>Strongly Disagree</i>	3	3.0	1	2.6	2	3.3	
<i>Unknown</i>	4	4.0	1	2.6	3	4.9	
<b>I have a fear of needles and/or invasive procedures</b>							<b>0.241</b>
<i>Strongly Agree</i>	14	14.1	6	15.8	8	13.1	
<i>Agree</i>	35	35.4	9	23.7	26	42.6	
<i>Disagree</i>	28	28.3	14	36.8	14	23.0	
<i>Strongly Disagree</i>	22	22.2	9	23.7	13	21.3	
<b>I feel that genetic testing could explain what caused the ultrasound finding in my pregnancy</b>							<b>0.021</b>
<i>Strongly Agree</i>	23	23.2	14	36.8	9	14.8	
<i>Agree</i>	53	53.5	20	52.6	33	54.1	
<i>Disagree</i>	20	20.2	4	10.5	16	26.2	
<i>Strongly Disagree</i>	3	3.0	0	0.0	3	4.9	
<b>I feel that I understood the genetic testing options and was able to make an informed choice</b>							<b>0.305</b>
<i>Strongly Agree</i>	46	46.5	21	55.3	25	41.0	
<i>Agree</i>	49	49.5	17	44.7	32	52.5	
<i>Disagree</i>	3	3.0	0	0.0	3	4.9	
<i>Strongly Disagree</i>	1	1.0	0	0.0	1	1.6	
<b>If there was a genetic condition, I would like to know about it before delivery</b>							<b>&lt;.001</b>
<i>Strongly Agree</i>	40	40.4	24	63.2	16	26.2	
<i>Agree</i>	35	35.4	13	34.2	22	36.1	
<i>Disagree</i>	22	22.2	1	2.6	21	34.4	
<i>Strongly Disagree</i>	0	0.0	0	0.0	0	0.0	
<i>Unknown</i>	2	2.0	0	0.0	2	3.3	

p-values calculated using a  $\chi^2$  or Fisher's exact test (bolded significant at  $p < 0.05$ )

**Table 7b- Diagnostic Testing Decision and Decision-Making Factors (Four-Point Likert)**

	Total (n=99)	%	Yes (n=38)	%	No (n=61)	%	
<b>The opinion of my partner or family member is important in helping me decide whether to have genetic testing</b>							<b>0.049</b>
<i>Strongly Agree</i>	44	44.4	21	55.3	23	37.7	
<i>Agree</i>	37	37.4	15	39.5	22	36.1	
<i>Disagree</i>	16	16.2	2	5.3	14	23.0	
<i>Strongly Disagree</i>	2	2.0	0	0.0	2	3.3	
<b>The opinion of a friend is important in helping me decide whether to have genetic testing</b>							<b>0.03</b>
<i>Strongly Agree</i>	1	1.0	0	0.0	1	1.6	
<i>Agree</i>	18	18.2	8	21.1	10	16.4	
<i>Disagree</i>	59	59.6	27	71.1	32	52.5	
<i>Strongly Disagree</i>	21	21.2	3	7.9	18	29.5	
<b>My religious faith influenced my genetic testing decision</b>							0.200
<i>Strongly Agree</i>	9	9.1	6	15.8	3	4.9	
<i>Agree</i>	14	14.1	3	7.9	11	18.0	
<i>Disagree</i>	48	48.5	19	50.0	29	47.5	
<i>Strongly Disagree</i>	28	28.3	10	26.3	18	29.5	
<b>My belief in the spiritual influenced my genetic testing decision</b>							0.176
<i>Strongly Agree</i>	7	7.1	4	10.5	3	4.9	
<i>Agree</i>	16	16.2	4	10.5	12	19.7	
<i>Disagree</i>	46	46.5	22	57.9	24	39.3	
<i>Strongly Disagree</i>	29	29.3	8	21.1	21	34.4	
<i>Unknown</i>	1	1.0	0	0.0	1	1.6	
<b>Genetic testing would conflict with my faith</b>							0.248
<i>Strongly Agree</i>	0	0.0	0	0.0	0	0.0	
<i>Agree</i>	4	4.0	0	0.0	4	6.6	
<i>Disagree</i>	54	54.5	22	57.9	32	52.5	
<i>Strongly Disagree</i>	40	40.4	15	39.5	25	41.0	
<i>Unknown</i>	1	1.0	1	2.6	0	0.0	
<b>I believe that genetic testing is being offered in my best interest</b>							<b>0.003</b>
<i>Strongly Agree</i>	35	35.4	20	52.6	15	24.6	
<i>Agree</i>	57	57.6	17	44.7	40	65.6	
<i>Disagree</i>	6	6.1	0	0.0	6	9.8	
<i>Strongly Disagree</i>	0	0.0	0	0.0	0	0.0	
<i>Unknown</i>	1	1.0	1	2.6	0	0.0	
<b>I would want my medical team to know if there was a genetic condition before delivery</b>							<b>&lt;.001</b>
<i>Strongly Agree</i>	40	40.4	25	65.8	15	24.6	
<i>Agree</i>	49	49.5	13	34.2	36	59.0	
<i>Disagree</i>	10	10.1	0	0.0	10	16.4	
<i>Strongly Disagree</i>	0	0.0	0	0.0	0	0.0	
<b>If there was a genetic condition, it would change the way I medically manage my pregnancy</b>							<b>0.021</b>
<i>Strongly Agree</i>	22	22.2	14	36.8	8	13.1	
<i>Agree</i>	41	41.4	16	42.1	25	41.0	
<i>Disagree</i>	26	26.3	6	15.8	20	32.8	
<i>Strongly Disagree</i>	10	10.1	2	5.3	8	13.1	

p-values calculated using a  $\chi^2$  or Fisher's exact test (bolded significant at p<0.05)

**Table 7c- Diagnostic Testing Decision and Decision-Making Factors (Four-Point Likert)**

	<b>Total (n=99)</b>	<b>%</b>	<b>Yes (n=38)</b>	<b>%</b>	<b>No (n=61)</b>	<b>%</b>	
<b>If there was a genetic condition, it would change the way I feel about my pregnancy</b>							0.188
<i>Strongly Agree</i>	9	9.1	4	10.5	5	8.2	
<i>Agree</i>	19	19.2	9	23.7	10	16.4	
<i>Disagree</i>	46	46.5	19	50.0	27	44.3	
<i>Strongly Disagree</i>	24	24.2	5	13.2	19	31.1	
<i>Unknown</i>	1	1.0	1	2.6	0	0.0	
<b>I did not feel pressured to undergo genetic testing</b>							0.862
<i>Strongly Agree</i>	45	45.5	19	50.0	26	42.6	
<i>Agree</i>	46	46.5	16	42.1	30	49.2	
<i>Disagree</i>	6	6.1	2	5.3	4	6.6	
<i>Strongly Disagree</i>	2	2.0	1	2.6	1	1.6	
<b>I feel that I had adequate input from the medical team in making a decision about genetic testing</b>							0.451
<i>Strongly Agree</i>	45	45.5	20	52.6	25	41.0	
<i>Agree</i>	53	53.5	18	47.4	35	57.4	
<i>Disagree</i>	1	1.0	0	0.0	1	1.6	
<i>Strongly Disagree</i>	0	0.0	0	0.0	0	0.0	
<b>I feel that I had adequate input from family and friends in making a decision about genetic testing</b>							0.180
<i>Strongly Agree</i>	28	28.3	12	31.6	16	26.2	
<i>Agree</i>	50	50.5	20	52.6	30	49.2	
<i>Disagree</i>	18	18.2	4	10.5	14	23.0	
<i>Strongly Disagree</i>	2	2.0	2	5.3	0	0.0	
<i>Unknown</i>	1	1.0	0	0.0	1	1.6	
<b>I would have liked the genetic counselor or doctor to tell me if I should get genetic testing or not</b>							0.224
<i>Strongly Agree</i>	9	9.1	4	10.5	5	8.2	
<i>Agree</i>	33	33.3	17	44.7	16	26.2	
<i>Disagree</i>	49	49.5	15	39.5	34	55.7	
<i>Strongly Disagree</i>	8	8.1	2	5.3	6	9.8	

p-values calculated using a  $\chi^2$  or Fisher's exact test (bolded significant at  $p < 0.05$ )

**Table 8a- Facilitated Testing Decision and Decision-Making Factors (Four-Point Likert)**

	<b>Total (n=88)</b>	<b>%</b>	<b>Yes (n=42)</b>	<b>%</b>	<b>No (n=46)</b>	<b>%</b>	<b>p-value</b>
<b>Rate your level of concern for a genetic condition</b>							<b>&lt;.001</b>
<i>None</i>	9	10.2	4	9.5	5	10.9	
<i>Minimal</i>	19	21.6	2	4.8	17	37.0	
<i>Some</i>	25	28.4	13	31.0	12	26.1	
<i>A great deal</i>	35	39.8	23	54.8	12	26.1	
<b>Describe your experience or amount of interaction with individuals with special needs, physical or intellectual disabilities or genetic conditions</b>							<b>0.15</b>
<i>None</i>	19	21.6	5	11.9	14	30.4	
<i>Minimal</i>	33	37.5	19	45.2	14	30.4	
<i>Some</i>	22	25.0	10	23.8	12	26.1	
<i>A great deal</i>	14	15.9	8	19.0	6	13.0	
<b>I feel that invasive testing (amniocentesis or CVS) is too risky to the pregnancy</b>							<b>&lt;.001</b>
<i>Strongly Agree</i>	17	19.3	5	11.9	12	26.1	
<i>Agree</i>	28	31.8	8	19.0	20	43.5	
<i>Disagree</i>	36	40.9	26	61.9	10	21.7	
<i>Strongly Disagree</i>	3	3.4	2	4.8	1	2.2	
<i>Unknown</i>	4	4.5	1	2.4	3	6.5	
<b>I have a fear of needles and/or invasive procedures</b>							<b>0.049</b>
<i>Strongly Agree</i>	12	13.6	8	19.0	4	8.7	
<i>Agree</i>	32	36.4	10	23.8	22	47.8	
<i>Disagree</i>	26	29.5	12	28.6	14	30.4	
<i>Strongly Disagree</i>	18	20.5	12	28.6	6	13.0	
<b>I feel that genetic testing could explain what caused the ultrasound finding in my pregnancy</b>							<b>&lt;.001</b>
<i>Strongly Agree</i>	21	23.9	15	35.7	6	13.0	
<i>Agree</i>	47	53.4	26	61.9	21	45.7	
<i>Disagree</i>	17	19.3	1	2.4	16	34.8	
<i>Strongly Disagree</i>	3	3.4	0	0.0	3	6.5	
<b>I feel that I understood the genetic testing options and was able to make an informed choice</b>							<b>0.154</b>
<i>Strongly Agree</i>	41	46.6	23	54.8	18	39.1	
<i>Agree</i>	43	48.9	19	45.2	24	52.2	
<i>Disagree</i>	3	3.4	0	0.0	3	6.5	
<i>Strongly Disagree</i>	1	1.1	0	0.0	1	2.2	
<b>If there was a genetic condition, I would like to know about it before delivery</b>							<b>&lt;.001</b>
<i>Strongly Agree</i>	36	40.9	27	64.3	9	19.6	
<i>Agree</i>	28	31.8	10	23.8	18	39.1	
<i>Disagree</i>	22	25.0	4	9.5	18	39.1	
<i>Strongly Disagree</i>	0	0.0	0	0.0	0	0.0	
<i>Unknown</i>	2	2.3	1	2.4	1	2.2	

p-values calculated using a  $\chi^2$  or Fisher's exact test (bolded significant at  $p < 0.05$ )

**Table 8b- Facilitated Testing Decision and Decision-Making Factors (Four-Point Likert)**

	Total (n=88)	%	Yes (n=42)	%	No (n=46)	%	p-value
<b>The opinion of my partner or family member is important in helping me decide whether to have genetic testing</b>							0.189
<i>Strongly Agree</i>	40	45.5	23	54.8	17	37.0	
<i>Agree</i>	31	35.2	14	33.3	17	37.0	
<i>Disagree</i>	15	17.0	4	9.5	11	23.9	
<i>Strongly Disagree</i>	2	2.3	1	2.4	1	2.2	
<b>The opinion of a friend is important in helping me decide whether to have genetic testing</b>							0.977
<i>Strongly Agree</i>	1	1.1	0	0.0	1	2.2	
<i>Agree</i>	16	18.2	8	19.0	8	17.4	
<i>Disagree</i>	51	58.0	25	59.5	26	56.5	
<i>Strongly Disagree</i>	20	22.7	9	21.4	11	23.9	
<b>My religious faith influenced my genetic testing decision</b>							0.196
<i>Strongly Agree</i>	9	10.2	7	16.7	2	4.3	
<i>Agree</i>	13	14.8	4	9.5	9	19.6	
<i>Disagree</i>	42	47.7	19	45.2	23	50.0	
<i>Strongly Disagree</i>	24	27.3	12	28.6	12	26.1	
<b>My belief in the spiritual influenced my genetic testing decision</b>							0.377
<i>Strongly Agree</i>	7	8.0	5	11.9	2	4.3	
<i>Agree</i>	15	17.0	5	11.9	10	21.7	
<i>Disagree</i>	40	45.5	21	50.0	19	41.3	
<i>Strongly Disagree</i>	25	28.4	11	26.2	14	30.4	
<i>Unknown</i>	1	1.1	0	0.0	1	2.2	
<b>Genetic testing would conflict with my faith</b>							0.159
<i>Strongly Agree</i>	0	0.0	0	0.0	0	0.0	
<i>Agree</i>	4	4.5	0	0.0	4	8.7	
<i>Disagree</i>	47	53.4	22	52.4	25	54.3	
<i>Strongly Disagree</i>	36	40.9	19	45.2	17	37.0	
<i>Unknown</i>	1	1.1	1	2.4	0	0.0	
<b>I believe that genetic testing is being offered in my best interest</b>							<.001
<i>Strongly Agree</i>	21	23.9	21	50.0	9	19.6	
<i>Agree</i>	20	22.7	20	47.6	31	67.4	
<i>Disagree</i>	6	6.8	0	0.0	6	13.0	
<i>Strongly Disagree</i>	0	0.0	0	0.0	0	0.0	
<i>Unknown</i>	1	1.1	1	2.4	0	0.0	
<b>I would want my medical team to know if there was a genetic condition before delivery</b>							<.001
<i>Strongly Agree</i>	33	37.5	25	59.5	8	17.4	
<i>Agree</i>	45	51.1	16	38.1	29	63.0	
<i>Disagree</i>	10	11.4	1	2.4	9	19.6	
<i>Strongly Disagree</i>	0	0.0	0	0.0	0	0.0	

p-values calculated using a  $\chi^2$  or Fisher's exact test (bolded significant at p<0.05)

**Table 8c- Facilitated Testing Decision and Decision-Making Factors (Four-Point Likert)**

	<b>Total (n=88)</b>	<b>%</b>	<b>Yes (n=42)</b>	<b>%</b>	<b>No (n=46)</b>	<b>%</b>	<b>p-value</b>
<b>If there was a genetic condition, it would change the way I medically manage my pregnancy</b>							<b>0.008</b>
<i>Strongly Agree</i>	19	21.6	15	35.7	4	8.7	
<i>Agree</i>	36	40.9	17	40.5	19	41.3	
<i>Disagree</i>	24	27.3	7	16.7	17	37.0	
<i>Strongly Disagree</i>	9	10.2	3	7.1	6	13.0	
<b>If there was a genetic condition, it would change the way I feel about my pregnancy</b>							<b>0.863</b>
<i>Strongly Agree</i>	9	10.2	4	9.5	5	10.9	
<i>Agree</i>	18	20.5	10	23.8	8	17.4	
<i>Disagree</i>	39	44.3	17	40.5	22	47.8	
<i>Strongly Disagree</i>	22	25.0	11	26.2	11	23.9	
<b>I did not feel pressured to undergo genetic testing</b>							<b>0.288</b>
<i>Strongly Agree</i>	41	46.6	21	50.0	20	43.5	
<i>Agree</i>	40	45.5	18	42.9	22	47.8	
<i>Disagree</i>	5	5.7	1	2.4	4	8.7	
<i>Strongly Disagree</i>	2	2.3	2	4.8	0	0.0	
<b>I feel that I had adequate input from the medical team in making a decision about genetic testing</b>							<b>0.133</b>
<i>Strongly Agree</i>	40	45.5	23	54.8	17	37.0	
<i>Agree</i>	47	53.4	19	45.2	28	60.9	
<i>Disagree</i>	1	1.1	0	0.0	1	2.2	
<i>Strongly Disagree</i>	0	0.0	0	0.0	0	0.0	
<b>I feel that I had adequate input from family and friends in making a decision about genetic testing</b>							<b>0.448</b>
<i>Strongly Agree</i>	25	28.4	13	31.0	12	26.1	
<i>Agree</i>	45	51.1	19	45.2	26	56.5	
<i>Disagree</i>	15	17.0	7	16.7	8	17.4	
<i>Strongly Disagree</i>	12	13.6	2	4.8	0	0.0	
<i>Unknown</i>	1	1.1	1	2.4	0	0.0	
<b>I would have liked the genetic counselor or doctor to tell me if I should get genetic testing or not</b>							<b>0.168</b>
<i>Strongly Agree</i>	8	9.1	4	9.5	4	8.7	
<i>Agree</i>	25	28.4	15	35.7	10	21.7	
<i>Disagree</i>	48	54.5	18	42.9	30	65.2	
<i>Strongly Disagree</i>	7	8.0	5	11.9	2	4.3	

p-values calculated using a  $\chi^2$  or Fisher's exact test (bolded significant at  $p < 0.05$ )



## Appendix B – Coping Strategy Results

**Table 9 - Coping Strategy Indicator and Testing Decision**

Diagnostic					FTD			
	Total (n=99)	Yes (n=38)	No (n=61)	p- value	Total (n=88)	Yes (n=42)	No (n=46)	p- value
<b>Problem Solving*</b>				0.55				0.47
<i>Low</i>	2	1	1		2	1	1	
<i>Average</i>	56	23	32		45	22	23	
<i>High</i>	38	14	25		38	19	19	
<i>Unknown</i>	3	0	3		3	0	3	
<b>Social Support Seeking</b>				0.053				0.83
<i>Very Low</i>	1	0	1		1	1	0	
<i>Low</i>	12	1	11		12	5	7	
<i>Average</i>	51	25	26		43	21	22	
<i>High</i>	30	11	19		28	14	14	
<i>Unknown</i>	5	1	4		4	1	3	
<b>Avoidant</b>				0.48				0.17
<i>Low</i>	12	3	9		9	2	7	
<i>Average</i>	49	22	27		44	24	20	
<i>High</i>	22	6	16		21	7	14	
<i>Very High</i>	10	5	5		9	6	3	
<i>Unknown</i>	6	2	4		5	3	2	

p-values calculated using a  $\chi^2$  or Fisher's exact test (bolded significant at  $p < 0.05$ )

\*No respondents had a rating of 'very low' in problem solving

## Bibliography

- [1]Saucier JB, Johnston D, Wicklund CA, Robbins-Furman P, Hecht JT, Monga M. Racial-ethnic differences in genetic amniocentesis uptake. *Journal of Genetic Counseling*. 2005;14(3):189-95.
- [2]Marteau TM, Kidd J, Cook R, Michie S, Johnston M, Slack J, Shaw RW. Perceived risk not actual risk predicts uptake of amniocentesis. *British Journal of Gynaecology*. 1991;98(3):282-6.
- [3]Tercyak KP, Bennett Johnson S, Roberts SF, Cruz AC. Psychological response to prenatal genetic counseling and amniocentesis. *Patient Education and Counseling*. 2001;43(1):73-84.
- [4]Markens S, Browner CH, Press N. 'Because of the risks': how US pregnant women account for refusing prenatal screening. *Social Science & Medicine*. 1999;49(3):359-69.
- [5]Hill M, Fisher J, Chitty LS, Morris S. Women's and health professionals' preferences for prenatal tests for Down Syndrome: a discrete choice experiment to contrast noninvasive prenatal diagnosis with current invasive tests. *Genetics in Medicine*. 2012;14(11):905-13.
- [6]Beulen L, Grutters JPC, Fass BHW, Feenstra I, Groenewoud H, van Vugt JMG, Bekker MN. Women's and healthcare professionals' preferences for prenatal testing: a discrete choice experiment. *Prenatal Diagnosis*. 2015;35(6):549-57.
- [7]Larion S, Warsof SL, Romary L, Mlynarczyk M, Peleg D, Abuhamad AZ. Uptake of noninvasive prenatal testing at a large academic referral center. *American Journal of Obstetrics & Gynecology*. 2014;211(6):651.e1-e7.
- [8]Williams J, Rad S, Beauchamp S, Ratousi D, Subramaniam V, Farivar S, Pisarska MD. Utilization of noninvasive prenatal testing: impact on referrals for diagnostic testing. *American Journal of Obstetrics and Gynecology*. 2015;213(1):102e1-e6.
- [9]Hui L, Hutchinson B, Poulton, A, Halliday J. Population-based impact of noninvasive prenatal screening on screening and diagnostic testing for fetal aneuploidy. *Genetics in Medicine*. 2017;19(12):1338-45.
- [10]Stevens BK, Noblin SJ, Chen, H-Y, Czerwinski, J, Friel LA, Wagner, C. Introduction of cell-free DNA screening is associated with changes in prenatal genetic counseling indications. *Journal of Genetic Counseling*. 2019;28(3):692-9.

- [11]Friel LA, Czerwinski JL, Singletary CN. The impact of noninvasive prenatal testing on the practice of maternal-fetal medicine. *American Journal of Perinatology*. 2014;31(9):759-64.
- [12]Rose N, Kaimal AJ, Dugoff L, Norton ME, American College of Obstetricians and Gynecologists' Committee on Practice Bulletins-Obstetrics CoG, & Society for Maternal-Fetal Medicine. Screening for fetal chromosomal abnormalities: ACOG Practice Bulletin, Number 226. *Obstetrics and Gynecology*. 2020;136(4):e48-e69.
- [13]Committee Opinion No.682: Microarrays and next-generation sequencing technology: The use of advanced genetic diagnostic tools in obstetrics and gynecology. *Obstetrics & Gynecology*. 2016;128(6):e262-e8.
- [14]Lord J, McMullan DJ, Eberhardt RY, Rinck G, Hamilton SJ, Quinlan-Jones E, Prigmore E, Keelagher R, Meellis R, Mellis R, Robart S, Berry IR, Chandler KE, Cilliers D, Cresswell L, Edwards SL, Gardiner C, Henderson A, Holden ST, Homfray T, Lester T, Lewis RA, Newbury-Ecob R, Prescott K, Quarrell OW, Ramsden SC, Roberts E, Tapon D, Tooley MJ, Vasudevan PC, Weber AP, Wellesley DG, Westwood P, White H, Parker M, Williams D, Jenkins L, Scott RH, Kilby MD, Chitty LS, Hurles ME, Maher ER, Consortium PAGE. Prenatal exome sequencing analysis in fetal structural anomalies detected by ultrasonography (PAGE): a cohort study. *Lancet*. 2019;393(10173):747-57.
- [15]Petrovski S, Aggarwal V, Giordano JL, Stosic M, Wou K, Bier L, Spiegel E, Brennan K, Stong N, Jobanputra V, Ren Z, Zhu X, Mebane C, Nahum O, Wang Q, Kamalakaran S, Malone C, Anyane-Yeboah K, Miller R, Levy B, Goldstein DB, Wapner RJ. Whole-exome sequencing in the evaluation of fetal structural anomalies:a prospective cohort study. *Lancet*. 2019;393(10173):758-67.
- [16]Mone F, Eberhardt RY, Morris RK, Hurles ME, McMullan DJ, Maher ER, Lord J, Chitty LS, Giordano JL, Wapner RJ, Kilby MD, CSC. COngenital heart disease and the Diagnostic yield with Exome sequencing (CODE) study: prospective cohort study and systematic review. *Ultrasound Obstetrics and Gynecology*. 2021;57(1):43-51.
- [17]Gil MM, Giunta G, Macalli EA, Poon LC, Nicolaides KH. UK NHS pilot study on cell-free DNA testing in screening for fetal trisomies: factors affecting uptake. *Ultrasound Obstetrics and Gynecology*. 2015;45(1):67-73.

- [18]Richards EG, Sangi-Haghepeykar H, McGuire AL, Van den Veyver IB, Fruhman G. Pregnant patients' risk perception of prenatal test results with uncertain fetal clinical significance: ultrasound versus advanced genetic testing. *Prenatal Diagnosis*. 2015;35(12):1213-7.
- [19]Lostchuck E, Poulton A, Halliday J, Hui L. Population-based trends in invasive prenatal diagnosis for ultrasound-based indications: two decades of change from 1994 to 2016. *Ultrasound Obstetrics and Gynecology*. 2019;53(4):503-11.
- [20]Wapner RJ, Marin CL, Levy B, Ballif BC, Eng CM, Zachary JM, Savage M, Platt LD, Saltzman D, Grobman WA, Klugman S, Scholl T, Simpson JL, McCall K, Aggarwal VS, Bunke B, Nahum O, Patel A, Lamb AN, Thom EA, Beaudet AL, Ledbetter DH, Shaffer LG, Jackson L. Chromosomal microarray versus karyotyping for prenatal diagnosis. *New England Journal of Medicine*. 2012;367(23):2175-84.
- [21]Patel A, Costello JM, Backer CL, Pasquali SK, Hill KD, Wallace AS, Jacobs JP, Jacobs ML. Prevalence of non-cardiac and genetic abnormalities in neonates undergoing cardiac surgery: analysis of the Society of Thoracic Surgeons congenital heart surgery database. *The Annals of Thoracic Surgery*. 2016;102(5):1607-14.
- [22]Nunley PB, Hashmi SS, Johnson A, Ashfaq M, Farach LS, Singletary CN, Stevens BK. Exploring the predicted yield of prenatal testing by evaluating a postnatal population with structural abnormalities using a novel mathematical model. *Prenatal Diagnosis*. 2021;41(3):354-61.
- [23]Amirkhan JH. A factor analytically derived measure of coping: The Coping Strategy Indicator. *Journal of Personality and Social Psychology*. 1990;59(5):1066-74.
- [24]QuickFacts: Harris County, Texas. United States Census Bureau2020.
- [25]Grinshpun-Cohen J, Miron-Shatz T, Rhee-Morris L, Briscoe B, Pras E, Towner D. A priori attitudes predict amniocentesis uptake in women of advanced maternal age: A pilot study. *Journal of Health Communication*. 2015;20(9):1107-13.
- [26]Chen A, Tenhunen H, Torkki P, Heinonen S, Lillrank P, Stefanovic V. Considering medical risk information and communicating values: a mixed method study of women's choice in prenatal testing. *PLoS One*. 2017;12(3).

- [27]Azjen I. The theory of planned behavior. *Organizational Behavior and Human Decision Processes*. 1991;50(2):179-211.
- [28]Vergani P, Locatelli A, Biffi A, Ciriello E, Zagarella A, Pezzullo JC, Ghidini A. Factors affecting the decision regarding amniocentesis in women at genetic risk because of age 35 years or older. *Prenatal Diagnosis*. 2002;22(9):769-74.
- [29]Suter SM. The routinization of prenatal testing. *American Journal of Law & Medicine*. 2002;28(2-3):233-70.
- [30]Potter BK, O'Reilly N, Etchegary H, Howley H, Graham ID, Walker M, Coyle D, Chorny Y, Cappelli M, Boland I, Wilson BJ. Exploring informed choice in the context of prenatal testing: findings from a qualitative study. *Health Expectations*. 2008;11(4):355-65.
- [31]Cernat A, De Freitas C, Majid U, Trivedi F, Higgins C, Vanstone M. Facilitating informed choice about non-invasive prenatal testing (NIPT): a systematic review and qualitative meta-synthesis of women's experiences. *BMC Pregnancy and Childbirth*. 2019;19(27).
- [32]Montgomery S, Thayer ZM. The influence of experiential knowledge and societal perceptions on decision making regarding non-invasive prenatal testing (NIPT). *BMC Pregnancy and Childbirth*. 2020;20(630).
- [33]Kreger EM, Singer ST, Witt RG, Sweeters N, Lianoglou B, Lal A, Mackenzie TC, Vichinsky E. Favorable outcomes after in utero transfusion in fetuses with alpha thalassemia major: a case series and review of the literature. *Prenatal Diagnosis*. 2016;36(13):1242-9.
- [34]Le Blanc K, Götherström C, Ringdén O, Hassan M, McMahon R, Horwitz E, Anneren G, Axelsson O, Nunn J, Ewald U, Nordén-Lindeberg S, Jansson M, Dalton A, Åström E, Westgren M. Fetal mesenchymal stem-cell engraftment in bone after in utero transplantation in a patient with severe osteogenesis imperfecta. *Transplantation*. 2005;79(11):1607-14.
- [35]Massaro G, Mattar CNZ, Wong AMS, Sirka E, Buckley SMK, Herbert BR, Karlsson S, Perocheau DP, Burke D, Heales S, Richard-Londt A, Brandner S, Hueebecke M, Priestman DA, Platt FM, Mills K, Biswas A, Cooper JD, Chan JKY, Cheng SH, Waddington SN, Rahim AA. Fetal gene therapy for neurodegenerative disease of infants. *Nature Medicine*. 2018;24(9):1317-23.

- [36]Donnelly JCP, Lawrence D, Rebarber A, Zachary J, Grobman WA; Wapner RJ. Association of copy number variants with specific ultrasonographically detected fetal anomalies. *Obstetrics & Gynecology*. 2014;124(1):83-90.
- [37]Best S, Wou K, Vora N, Van der Veyver IB, Wapner R, Chitty LS. Promises, pitfalls and practicalities of prenatal whole exome sequencing. *Prenatal Diagnosis*. 2018;38(1):10-9.
- [38]Michie M. Is preparation a good reason for prenatal genetic testing? Ethical and critical questions. *Birth Defects Research*. 2020;112(4):332-8.
- [39]Wittman AT, Hashmi SS, Mendez-Figueroa H, Nassef S, Stevens B, Singletary, CN. Patient perception of negative noninvasive prenatal testing results. *American Journal of Perinatology Reports*. 2016;6(4):e391-e406.
- [40]Al Toukhi S, Chitayat D, Keunen J, Roifman M, Seaward G, Windrim R, Ryan G, Van Mieghem T. Impact of introduction of noninvasive prenatal testing on uptake of genetic testing in fetuses with central nervous system anomalies. *Prenatal Diagnosis*. 2019;39(7):544-8.
- [41]Bohnhorst B, Ahl T, Peter C, Pirr S. Parents' prenatal, onward, and postdischarge experiences in case of extreme prematurity: When to set the course for a trusting relationship between parents and medical staff. *American Journal of Perinatology*. 2015;32(13):1191-7.
- [42]Benkert R, Cuevas A, Thompson HS, Dove-Meadows E, Knuckles D. Ubiquitous yet unclear: A systematic review of medical mistrust. *Behavioral Medicine*. 2019;45(2):86-101.
- [43]García E, Timmermans DRM, van Leeuwen E. Women's views on the moral status of nature in the context of prenatal screening decisions. *Journal of Medical Ethics*. 2011;37(8):461-5.
- [44]Janvier A, Farlow B, Wilfond BS. The experience of families with children with trisomy 13 and 18 in social networks. *Pediatrics*. 2012;130(2):293-8.
- [45]Pivetti M, Montali L, Simonetti G. The discourse around usefulness, morality, risk and trust: A focus group study on prenatal genetic testing. *Prenatal Diagnosis*. 2012;32(12).

**Vita**

Lukas Daniel Kruidenier completed high school at Greeley West High School in Greeley, Colorado in 2006. He attended the University of Northern Colorado in Greeley, Colorado for four years and graduated in 2010 with a Bachelor of Arts degree in Psychology with a minor in sociology. He performed his post-baccalaureate studies in Biology at Metropolitan State University of Denver in Colorado from 2013-2017. He entered The University of Texas MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences in 2018 and graduated with his Masters in Genetic counseling in May 2021. Lukas is currently employed at Seattle Children's Hospital as a pediatric genetic counselor.

Permanent address:

2201 4<sup>th</sup> Ave Apt 219

Seattle, Washington 98121