

5-2020

Factors That Impact Uptake Of Carrier Screening By Male Reproductive Partners Of Female Prenatal Patients

Wendi Betting

Follow this and additional works at: https://digitalcommons.library.tmc.edu/utgsbs_dissertations



Part of the [Congenital, Hereditary, and Neonatal Diseases and Abnormalities Commons](#), and the [Genetics Commons](#)

Recommended Citation

Betting, Wendi, "Factors That Impact Uptake Of Carrier Screening By Male Reproductive Partners Of Female Prenatal Patients" (2020). *Dissertations and Theses (Open Access)*. 999.
https://digitalcommons.library.tmc.edu/utgsbs_dissertations/999

This Thesis (MS) is brought to you for free and open access by the MD Anderson UTHealth Houston Graduate School at DigitalCommons@TMC. It has been accepted for inclusion in Dissertations and Theses (Open Access) by an authorized administrator of DigitalCommons@TMC. For more information, please contact digcommons@library.tmc.edu.

FACTORS THAT IMPACT UPTAKE OF CARRIER SCREENING BY MALE
REPRODUCTIVE PARTNERS OF FEMALE PRENATAL PATIENTS

by

Wendi Nicole Betting, BS

APPROVED:

Meagan Choates, MS, CGC
Advisory Professor

Lauren Murphy, MS, CGC

Malorie A. Jones, MS, CGC

Jessica Corredor, MS, CGC

Jacqueline Parchem, MD

APPROVED:

Dean, The University of Texas
MD Anderson Cancer Center UTHHealth Graduate School of Biomedical Sciences

FACTORS THAT IMPACT UPTAKE OF CARRIER SCREENING BY MALE
REPRODUCTIVE PARTNERS OF FEMALE PRENATAL PATIENTS

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

Wendi Nicole Betting, BS
Houston, Texas

May, 2020

FACTORS THAT IMPACT UPTAKE OF CARRIER SCREENING BY MALE REPRODUCTIVE PARTNERS OF FEMALE PRENATAL PATIENTS

Wendi Nicole Betting, BS

Advisory Professor: Meagan Choates, MS, CGC

Carrier screening is a genomic technology that is used to identify individuals who are carriers of autosomal recessive conditions. Despite published recommendations, the majority of male partners do not complete carrier screening after their female partner is identified to be a carrier. Previous studies have examined reasons why women elect or decline carrier screening, but there have been few published studies that examine factors that influence a male partner's decision to elect or decline carrier screening, particularly when the female has been identified as a carrier. The aim of the study was to determine the factors that influence the uptake of carrier screening in male partners at several clinics within an academic medical center. Data was ascertained via a novel survey. Of the 98 patients included in the analysis, more than half of the male partners did not attend the initial counseling session (57/98, 58%), but the partner being present at the initial genetic counseling session was significantly associated with his uptake of carrier screening ($p=0.001$). The only other significant factor included the male partner placing increased importance on wanting to be able to plan for the future ($p=0.006$). Of the couples where the female was identified to be a carrier ($n=21$), 18 (86%) of them indicated that the male partner would pursue screening if the female screened positive. However, only 5 males ultimately completed carrier screening (28%). The study confirms that despite published recommendations and original intentions of the patient and/or her partner to follow such recommendations, the majority of male partners are not completing carrier screening after their

female partner screens positive for an autosomal recessive condition. Future studies should examine barriers to partner screening and investigate methods to increase the utility of prenatal carrier screening.

TABLE OF CONTENTS

Approval Sheet.....	i
Title Page.....	ii
Abstract.....	iii
Table of Contents.....	v
List of Illustrations.....	vi
List of Tables.....	vii
Abbreviations.....	viii
Introduction.....	1
Methods.....	3
<i>Study Design and Participants</i>	3
<i>Data Analysis</i>	5
Results.....	7
<i>Participant Enrollment and Carrier Screening Uptake</i>	7
<i>Demographic Factors Associated with Partner Carrier Screening Uptake</i>	10
<i>Partner Likert Measure Responses</i>	12
<i>Paired Patient and Partner Couple Likert Measure Responses</i>	16
<i>Impact of Disease Severity and Presence on Newborn Screen on CS Uptake</i>	16
<i>Electronic Surveys</i>	17
Discussion.....	18
<i>Strengths and Limitations</i>	23
<i>Future Directions</i>	23
Bibliography.....	25
Vita	28

LIST OF ILLUSTRATIONS

FIGURE 1: Participant Ascertainment and Survey Distribution Scheme

FIGURE 2: Patient and Partner Carrier Screening Uptake

FIGURE 3: Partner Likert Responses

LIST OF TABLES

TABLE 1: Characteristics of Patients Enrolled in the Study

TABLE 2: Patients who were Identified as Carriers of Autosomal Recessive Conditions

TABLE 3: Characteristics of Partners Enrolled in the Study

TABLE 4: Partner Likert Responses of Partners that Elected Versus Did Not Elect Carrier
Screening

TABLE 5: Partner Likert Responses of Partners that Elected Simultaneous Carrier Screening
Versus Did Not Elect Simultaneous Carrier Screening

ABBREVIATIONS

ACOG: American College of Obstetricians and Gynecologists

CS: Carrier Screening

MFM: Maternal Fetal Medicine

IQR: Interquartile Range

AR: Autosomal Recessive

INTRODUCTION

Carrier screening is a genomic technology that is used to identify individuals who are carriers of autosomal recessive conditions. If an individual is found to be a carrier of an autosomal recessive condition, it typically does not have any direct clinical impact on the individual's health (1). Rather, knowing this information can be utilized for family planning decisions and/or postnatal preparation. If both partners are found to be carriers of the same condition, there is a 25% chance that their offspring would be affected with the condition, and a variety of reproductive options both prior to and during an ongoing pregnancy could be pursued to either minimize or better understand this risk (1, 2).

The American College of Obstetricians and Gynecologists (ACOG) recommends that information about carrier screening be offered to all pregnant women, but states that ideally, carrier screening should be offered prior to pregnancy, as this allows for more reproductive options to be considered (1, 3). Additionally, ACOG recommends that when an individual is found to be a carrier of an autosomal recessive condition, their reproductive partner should pursue carrier screening to clarify the couple's reproductive risk (1, 2, 4). Concurrent screening can be considered depending on gestational age, partner availability, and patient preference (1, 2, 4).

Since the purpose of carrier screening is to inform couples about potential reproductive outcomes, the clinical utility of carrier screening relies on the availability and willingness of both the patient and her male partner to elect and complete carrier screening (1). Previous studies have examined reasons that influence a woman's decision to elect or decline carrier screening (3, 5-10), but there have been few published studies that examine factors that influence a male's decision to pursue carrier screening, particularly when an increased risk for an autosomal recessive condition has been established (11). A retrospective study by Giles

Choates et al. found that only 38% of males completed carrier screening after their female partner was found to be a carrier of an autosomal recessive condition (12). Male partner uptake of carrier screening was primarily associated with lower parity and younger gestational age of the female patient, but more specific factors affecting this low rate could not be ascertained by the authors due to the retrospective nature of the study (12). This incomplete follow-through may ultimately undermine the impact of carrier screening on patient management and risk assessment, and likely is a source of wasted healthcare dollars and provider time. To have a better understanding of the clinical utility of carrier screening, knowledge of more specific factors that influence a male partner's decision to elect carrier screening is imperative. Exploring these factors may provide insight into barriers to male partner screening, which can then allow for improved clinical utility. This study thus aimed to determine what factors influence the uptake of carrier screening in reproductive couples and to identify potential deterrents to uptake of carrier screening in male partners using a survey tool, particularly when an increased risk for an autosomal recessive condition has been established.

METHODS

Study Design and Participants

Individuals were recruited to participate in this prospective study from four UTHealth Maternal Fetal Medicine (MFM) practices in Houston, TX between July 31, 2019 and January 31, 2020. Participants were eligible for the study if they met with a prenatal genetic counselor for either prenatal or preconception genetic counseling, were over 18 years of age, English-speaking, not known to be a carrier of an autosomal recessive disorder, and elected carrier screening during the genetic counseling appointment. Individuals who previously had negative carrier screening were eligible as long as they elected a panel with additional conditions. The carrier screening practices of the UT MFM clinics have been previously described (12). Traditional carrier screening was defined as panels that include autosomal recessive conditions recommended by ACOG (cystic fibrosis, spinal muscular atrophy, hemoglobinopathies, Tay-Sachs disease, Canavan disease, familial dysautonomia, Bloom syndrome, Fanconi anemia, Gaucher disease, Niemann-Pick disease, mucopolysaccharidosis type IV, and hexosaminidase A deficiency.) Expanded carrier screening is defined as panels that include autosomal recessive conditions beyond those recommended by ACOG (1, 12).

The participant ascertainment and survey distribution scheme are outlined in Figure 1.

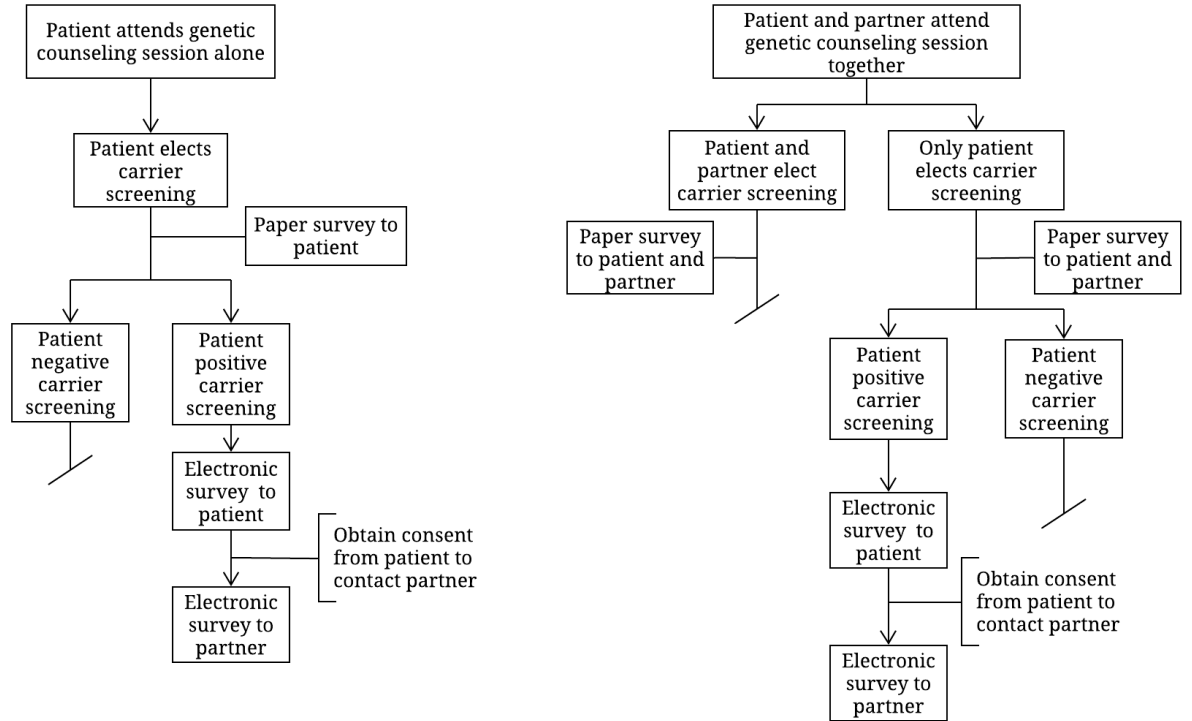


Figure 1: Participant Ascertainment and Survey Distribution Scheme

Women who elected to participate in the study are referred to as “patient” and their male reproductive partner are referred to as “partner.” Individuals who attended the genetic counseling session alone, elected carrier screening, and elected to participate in the study, were asked to complete a novel survey asking about their intent to notify their partner about their carrier screening, their intent to ask their partner to pursue carrier screening if the patient was found to be a carrier of a condition, and factors that influenced the patient’s decision to elect carrier screening, presented via a Likert measure. If a patient presented to the genetic counseling appointment with her partner, both the patient and her partner were invited to complete a novel survey that asked about factors impacting their decision to elect either simultaneous or sequential carrier screening presented via a Likert measure, depending on their testing decision.

Couples who elected sequential testing were also asked about their intent to get the partner screened if the patient was found to be a carrier of an autosomal recessive condition. Self-reported and/or partner-reported demographic data was collected for all groups.

Patients who were found to be a carrier of at least one autosomal recessive condition were sent an electronic follow-up survey if her partner did not elect simultaneous testing. The survey asked patients if they communicated the result to their partner, if their partner elected carrier screening, and about factors that the patients thought had an impact on their partner's decision to elect or decline carrier screening. After completion of the electronic survey, patients were sent an additional electronic survey for their partner to complete. The electronic survey asked partners if they ultimately elected carrier screening and asked about factors that influenced their decision to elect or decline carrier screening presented via a Likert measure. This study was approved by the UTHealth Institutional Review Board (#HSC-MS-19-0475).

Data Analysis

Descriptive statistics were used to characterize the participants. Variables of interest were compared using Mann-Whitney-U test, t-test, and Fisher's exact test as appropriate. The male partners' demographic characteristics were primarily used in the data analysis. Variables of interest included partner age, gestational age at the time of the patient's screening, the partner's education level, whether this was the couple's first child together, the partner's insurance, the partner's race/ethnicity, whether the couple identified as the same race, whether the partner was present at the initial genetic counseling session, and whether the partner elected carrier screening. Variables of interest were compared between partners who elected carrier screening and those that did not. Additionally, Likert responses between the patient and her partner as well as between partners who did and did not elect carrier screening were compared using Wilcoxon signed-rank test and Mann-Whitney-U test, respectively. Fisher analyses were

performed to determine if disease severity, determined using a modified version of the disease severity algorithm developed by Lazarin et al. or the presence of the disorder on the Texas Newborn Screen (NBS) impacted uptake of partner carrier screening (13). Due to the small sample size, Lazarin's algorithm was modified from four disease severity categories to two. The categories profound and severe were grouped together and moderate and mild were grouped together. Statistical analyses were conducted using Stata (StataCorp, College Station, Texas) with statistical significance set at $p < 0.05$. The interquartile range (IQR) is presented as the 25th to 75th percentile. Given the low sample size of the electronic survey respondents, we present some descriptive data without statistical analysis.

RESULTS

Participant Enrollment and Carrier Screening Uptake

Of the 291 patients who elected carrier screening, 101 (34.7%) were enrolled in the study. Three individuals were excluded from analysis, due to cancelled test order, sample failure, and pregnancy loss. Of the 98 patients who were analyzed, 57 (58.2%) attended the initial genetic counseling session without their partner. The majority of patients were multigravida (n= 64, 65.3%) and presented to genetic counseling during the first trimester of pregnancy (n= 82, 83.7%). Patient characteristics are shown in Table 1.

Characteristic	Total Patients (n=98)
<i>Patient age, Mean in years</i>	29.9 (5.6)
<i>Patient race/ethnicity</i>	
Hispanic, White	25 (25.5)
Non-Hispanic, White	33 (33.7)
Asian	12 (12.2)
African American	21 (21.4)
Self Reported Other	7 (7.2)
<i>Gestational age</i>	
1st Trimester	82 (83.7)
2nd Trimester	16 (16.3)
<i>Parity</i>	
Nulliparous	46 (46.9)
<i>Gravidity</i>	
Primigravida	34 (34.7)
Multigravida	64 (65.3)
Data shown as mean (SD) or n (%)	

Table 1: Characteristics of Patients Enrolled in the Study

The type of carrier screening panel the patient elected at the initial genetic counseling appointment was relatively evenly split between traditional carrier screening panels (52%) and expanded carrier screening panels (48%). In total, 30 (30.6%) women were identified to be a carrier of at least one autosomal recessive condition. Twenty-one of these patients either attended the initial genetic counseling session alone or with a partner that did not elect simultaneous screening. The conditions for the 21 patients are described in Table 2.

Condition(s)	Partner Tested?	Severity of Condition ⁺
USH2A-Related Disorders	No	Profound or Severe
Maple Syrup Urine Disease Type 1A	No	Profound or Severe
Medium-Chain Acyl-CoA Dehydrogenase (MCAD) Deficiency	No	Profound or Severe
Wilson Disease	No	Profound or Severe
Smith-Lemli-Opitz Syndrome and Congenital Disorder of Glycosylation (MPI-related)	No	Profound or Severe
Medium-Chain Acyl-CoA Dehydrogenase (MCAD) Deficiency	No	Profound or Severe
Leber Congenital Amaurosis	No	Moderate or Mild
Spinal Muscular Atrophy	No	Profound or Severe
Spinal Muscular Atrophy SNP (Increased Carrier Risk) g.27134T>G	Yes- Not a carrier	Moderate or Mild
Spinal Muscular Atrophy SNP (Increased Carrier Risk) g.27134T>G	Yes- Not a carrier	Moderate or Mild
Spinal Muscular Atrophy SNP (Increased Carrier Risk) g.27134T>G	No	Moderate or Mild
Cystic Fibrosis and Cystic Fibrosis Poly-T Tract Variant c.1210-34TG[12]T[5]	Yes- Not a carrier	Profound or Severe
Cystic Fibrosis Poly-T Tract Variant c.1210-34TG[12]T[5]	No	Moderate or Mild
Cystic Fibrosis	No	Profound or Severe
Cystic Fibrosis Poly-T Tract Variant c.1210-34TG[11]T[5]	No	Moderate or Mild
Cystic Fibrosis Poly-T Tract Variant c.1210-34TG[11]T[5]	No	Moderate or Mild
Galactosemia (Duarte variant) and	No	Moderate or Mild
Cystic Fibrosis Poly-T Tract Variant c.1210-34TG[12]T[5]	No	Moderate or Mild
Aspartylglucosaminuria and Cystic Fibrosis Poly-T Tract Variant c.1210-34TG[12]T[5]	No	Profound or Severe
Silent Alpha-Thalassemia	Yes- Not a carrier	Moderate or Mild
Silent Alpha-Thalassemia	No	Moderate or Mild
Silent Alpha-Thalassemia	No	Moderate or Mild
Silent Alpha-Thalassemia	Yes- Not a carrier	Profound or Severe*

⁺ Based on most severe condition

* Severity differs from other silent alpha-thalassemia cases because partner identified as Asian

Table 2: Patients who were Identified as Carriers of Autosomal Recessive Conditions

A total of 19 (19.4%) partners elected carrier screening. Among partners who attended the initial genetic counseling appointment, 14/41 (31.4%) elected simultaneous carrier screening and 2/7 (28.6%) returned for carrier screening after the female patient was identified as a carrier. When the patient attended the initial genetic counseling session alone and was identified as a carrier, 3/14 (21.4%) partners returned to complete their carrier screening. Of the 21 patients that either attended the initial genetic counseling session alone or with a partner that did not elect simultaneous screening, 18 (85.7%) of the patients or partners indicated on the survey that they would pursue carrier screening for the partner if the patient was identified to be a carrier. However, only 5 of the 18 (27.8%) ultimately followed through with screening.

For couples who underwent sequential testing, the average number of days between the patient's result disclosure session and the partner's blood draw was 53.3 days (n=3, SD 43.8 days) for those partners who were not present at the initial genetic counseling session, and 14 days (n=2, SD 0 days) for those who were present at the session.

Two couples, who both elected simultaneous screening, were determined to be carriers of the same condition. One couple was known to be consanguineous. No other at-risk couples were identified. Figure 2 illustrates patient and partner carrier screening uptake.

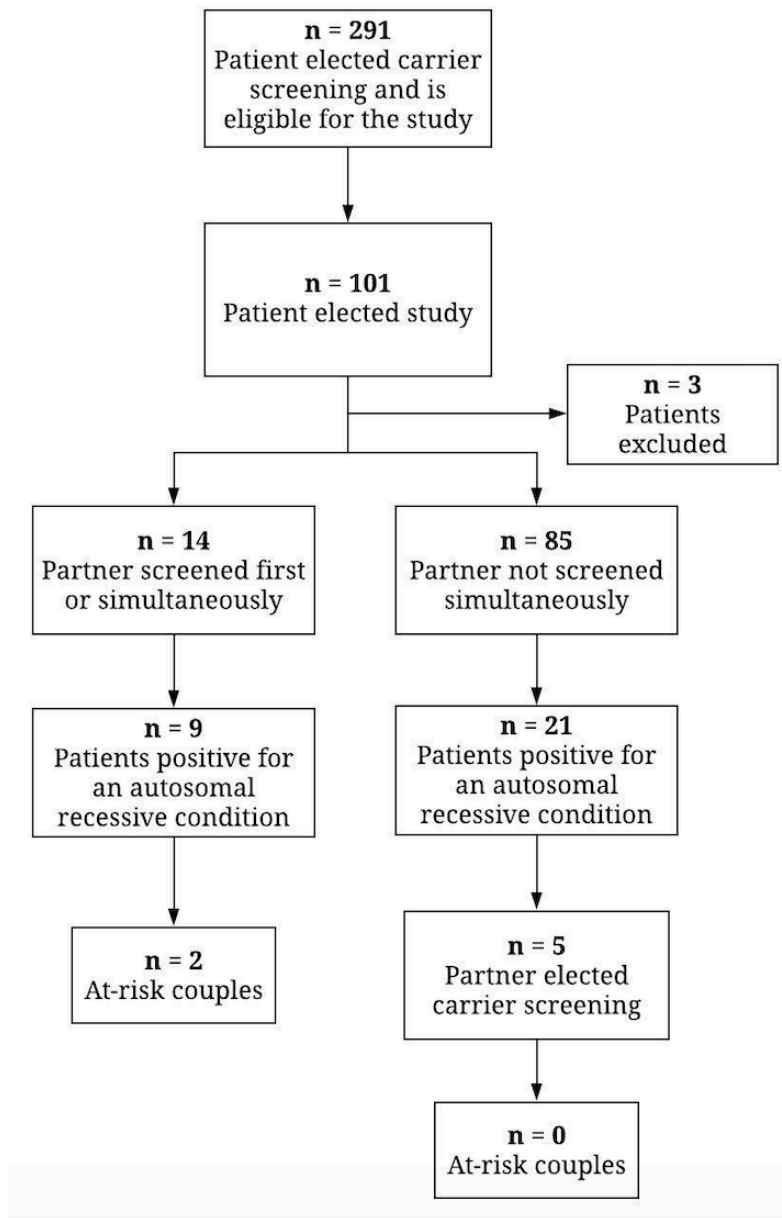


Figure 2: Patient and Partner Carrier Screening Uptake

Demographic Factors Associated with Partner Carrier Screening Uptake

Demographic characteristics for the partners are presented in Table 3.

n (%), unless noted* ⁺	Total Partners (n=98)	Elected CS (n=19)	Did not elect CS (n=79)	p-value
<i>Partner age, Mean in years (SD)</i>	31.0 (6.4)	32.7 (3.8)	30.4 (6.9)	0.22
<i>Gestational age, Median in weeks (IQR)</i>	12.1 (11.1-13.1)	12 (11.4-12.9)	12 (11.1-13.3)	0.864
<i>Partner race/ethnicity</i>				0.09
Hispanic, White	21 (22.6)	5 (23.8)	16 (76.2)	
Non-Hispanic, White	33 (35.5)	4 (12.1)	29 (87.9)	
African American	21 (22.6)	3 (14.4)	18 (85.6)	
Asian	12 (12.9)	6 (50)	6 (50)	
Self Reported Other	6 (6.4)	1 (16.7)	5 (83.3)	
<i>Is the partner the same race as the patient?</i>				0.794
Yes	75 (76.5)	15 (20)	60 (80)	
No	18 (18.4)	4 (22.2)	14 (77.8)	
Unknown	5 (5.1)	0 (0)	5 (100)	
<i>Partner education level</i>				0.287
Less than college degree	51 (57.3)	8 (15.7)	43 (84.3)	
College degree or higher	38 (42.7)	10 (26.3)	28 (73.7)	
<i>Is this the couple's first child together?</i>				0.296
Yes	60 (61.2)	14 (23.3)	46 (76.7)	
<i>Was the partner at the initial GC session?</i>				0.001
Yes	41 (41.8)	16 (39)	25 (61)	
<i>Partner insurance</i>				0.134
Private	61 (68.5)	16 (26.2)	45 (73.8)	
Self pay	24 (27)	2 (8.3)	22 (91.7)	
Other	4 (4.5)	1 (25)	3 (75)	

* Categories do not sum to column totals because of individual non-response.

⁺ Values in parentheses are percentages across the row

Table 3: Characteristics of Partners Enrolled in the Study

The majority of partners reported having less than a college degree (n= 51, 57.3%), having private insurance (n=61, 68.5%), being the same race/ethnicity as their partner (n=75, 76.5%), and reported that it was their first child with the patient (n=60, 61.2%). The partner's attendance at the initial genetic counseling session was the only significant difference observed between partners who did and did not elect carrier screening (p=0.001). If the partner was present at the initial genetic counseling session, the rate of carrier screening uptake was 39% (n=16/41) compared to the overall partner carrier screening uptake rate of 19.4%. Additionally, while no statistically significant differences were observed in the partner's race/ethnicity between partners who did and did not elect carrier screening, six (50%) partners that reported

Asian race elected carrier screening and accounted for 31.6% of the entire partner population that elected carrier screening. Other partner characteristics including education level, type of insurance, number of previous children with the patient, and gestational age of the patient were not significant predictors of male carrier screening uptake.

Partner Likert Measure Responses

Overall, the most commonly reported reasons in the carrier screening decision-making process for partners were “I like to know as much information as possible” (92.1% selecting moderately or extremely important), “I want to know if I am at risk of having a child with an autosomal recessive condition” (86.5 % selecting moderately or extremely important), and “I want to be able to plan for the future” (84.2% selecting moderately or extremely important). Factors including the genetic counselor or doctor recommending carrier screening, affordability of carrier screening, and the patient wanting the partner to be screened, were not reported as being as influential in the decision-making process (Figure 3).

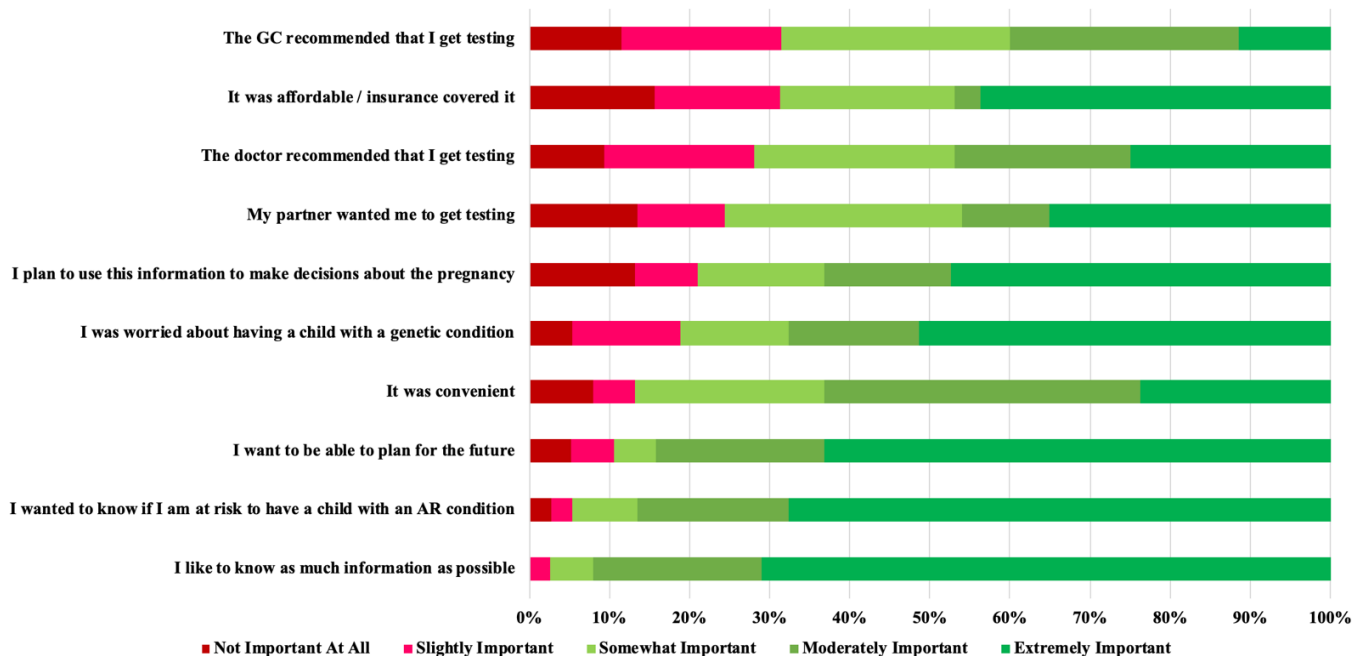


Figure 3: Partner Likert Responses

We were interested to determine if partners who elected carrier screening ranked any factors as being more influential than partners who did not elect carrier screening. The Likert distribution was significantly different for “I want to be able to plan for the future” between the two groups. The respondents that elected carrier screening were more likely to assign moderate or extreme importance to this factor (n=16/16, 100%) compared to those that did not elect carrier screening (n=16/22, 72.8%), (p=0.006). Similar trends of higher levels of importance in decision making were assigned to “I am worried about having a child with a genetic condition,” “The genetic counselor recommended that I get testing,” and “I plan to use this information to make decisions about the pregnancy” by the partners who elected carrier screening (n= 13/16, 82%; n=8/15, 53%; and n=12/16, 75%, respectively) compared to those that did not elect carrier screening (n= 12/21, 57.1%; n=6/20, 30%; and n=12/22, 54.5%, respectively.) However, these trends failed to reach statistical significance (p = 0.068, p = 0.093, and p=0.109, respectively.) (Table 4).

	Elected CS, n (%)						Did Not Elect CS, n (%)						p-value
	Not Important at all	Slightly Important	Somewhat Important	Moderately Important	Extremely Important	Total n	Not Important at all	Slightly Important	Somewhat Important	Moderately Important	Extremely Important	Total n	
It was convenient	1 (6.3)	2 (12.5)	4 (25)	4 (25)	5 (31.2)	16	2 (9.1)	0 (0)	5 (22.7)	11 (50)	4 (18.2)	22	0.926
My partner wanted me to get testing	2 (12.5)	2 (12.5)	6 (37.5)	0 (0)	6 (37.5)	16	3 (14.3)	2 (9.5)	5 (23.8)	4 (19.1)	7 (33.3)	21	0.824
The doctor recommended that I get testing	1 (7.1)	2 (14.3)	4 (28.6)	2 (14.3)	5 (35.7)	14	2 (11.1)	4 (22.2)	4 (22.2)	5 (27.8)	3 (16.7)	18	0.381
I like to know as much information as possible	0 (0)	0 (0)	0 (0)	3 (18.8)	13 (81.2)	16	0 (0)	1 (4.6)	2 (9.1)	5 (22.7)	14 (63.6)	22	0.187
It was affordable / my insurance covered it	3 (25)	1 (8.3)	3 (25)	0 (0)	5 (41.7)	12	2 (10)	4 (20)	4 (20)	1 (5)	9 (45)	20	0.637
I wanted to know if I am at risk to have a child with an autosomal recessive condition	0 (0)	0 (0)	0 (0)	3 (20)	12 (80)	15	1 (4.5)	1 (4.5)	3 (13.7)	4 (18.2)	13 (59.1)	22	0.116
The GC recommended that I get testing	1 (6.7)	1 (6.7)	5 (33.3)	6 (40)	2 (13.3)	15	3 (15)	6 (30)	5 (25)	4 (20)	2 (10)	20	0.093
I was worried about having a child with a genetic condition	0 (0)	2 (12.5)	1 (6.2)	2 (12.5)	11 (68.8)	16	2 (9.5)	3 (14.3)	4 (19)	4 (19)	8 (38.2)	21	0.068
I want to be able to plan for the future	0 (0)	0 (0)	0 (0)	2 (12.5)	14 (87.5)	16	2 (9.1)	2 (9.1)	2 (9.1)	6 (27.2)	10 (45.5)	22	0.006
I plan to use this information to make decisions about the pregnancy	1 (6.3)	1 (6.3)	2 (12.5)	2 (12.5)	10 (62.4)	16	4 (18.2)	2 (9.1)	4 (18.2)	4 (18.2)	8 (36.3)	22	0.109

Values in parentheses are percentages across the row

Table 4: Partner Likert Responses of Partners that Elected Versus Did Not Elect Carrier

Screening (CS)

Likert responses were also compared between partners who attended the initial session and did not elect carrier screening and those that elected simultaneous carrier screening to determine if factors differed between these two groups. The Likert distribution was significantly different for “I was worried about having a child with a genetic condition” between the two groups. The respondents that elected simultaneous carrier screening were more likely to assign moderate or extreme importance to this factor (n=12/13, 92%) compared to those that did not elect simultaneous carrier screening (n=13/24, 54%), (p=0.018). Respondents that elected simultaneous carrier screening were also more likely to assign moderate or extreme importance to the factor “I want to be able to plan for the future” (n=13/13, 100%) compared to those that

attended the initial genetic counseling session, but did not elect simultaneous carrier screening (n=19/25, 76%), (p=0.007). Additionally, Likert distribution was significantly different for “The genetic counselor recommended that I get testing” between the two groups. The respondents that elected simultaneous carrier screening were more likely to assign moderate or extreme importance to this factor (n=7/12, 59%) compared to those that were present at the initial genetic counseling session but did not elect simultaneous carrier screening (n=7/23, 31%), (p=0.04) (Table 5).

	Partner Attended Session and Did Not Elect Simultaneous CS, n (%)						Partner Attended Session and Elected Simultaneous CS, n (%)						p-value
	Not Important at all	Slightly Important	Somewhat Important	Moderately Important	Extremely Important	Total n	Not Important at all	Slightly Important	Somewhat Important	Moderately Important	Extremely Important	Total n	
It was convenient	2 (8)	1 (4)	6 (24)	11 (44)	5 (20)	25	1 (7.7)	1 (7.7)	3 (23.1)	4 (30.7)	4 (30.8)	13	0.822
My partner wanted me to get testing	4 (16.7)	2 (8.3)	6 (25)	4 (16.7)	8 (33.3)	24	1 (7.7)	2 (15.3)	5 (38.5)	0 (0)	5 (38.5)	13	0.974
The doctor recommended that I get testing	3 (14.3)	4 (19)	6 (28.6)	5 (23.8)	3 (14.3)	21	0 (0)	2 (18.2)	2 (18.2)	2 (18.2)	5 (45.4)	11	0.08
I like to know as much information as possible	0 (0)	1 (4)	2 (8)	6 (24)	16 (64)	25	0 (0)	0 (0)	0 (0)	2 (15.4)	11 (84.6)	13	0.158
It was affordable / my insurance covered it	3 (13.6)	4 (18.2)	5 (22.7)	1 (4.6)	9 (40.9)	22	2 (20)	1 (10)	2 (20)	0 (0)	5 (50)	10	0.847
I wanted to know if I am at risk to have a child with an autosomal recessive condition	1 (4.2)	1 (4.2)	3 (12.5)	5 (20.8)	14 (58.3)	24	0 (0)	0 (0)	0 (0)	2 (15.4)	11 (84.6)	13	0.077
The GC recommended that I get testing	4 (17.4)	6 (26.1)	6 (26.1)	5 (21.7)	2 (8.7)	23	0 (0)	1 (8.3)	4 (33.3)	5 (41.7)	2 (16.7)	12	0.04
I was worried about having a child with a genetic condition	2 (8.3)	4 (16.7)	5 (20.8)	4 (16.7)	9 (37.5)	24	0 (0)	1 (7.7)	0 (0)	2 (15.4)	10 (76.9)	13	0.018
I want to be able to plan for the future	2 (8)	2 (8)	2 (8)	7 (28)	12 (48)	25	0 (0)	0 (0)	0 (0)	1 (7.7)	12 (92.3)	13	0.007
I plan to use this information to make decisions about the pregnancy	4 (16)	2 (8)	5 (20)	4 (16)	10 (40)	25	1 (7.7)	1 (7.7)	1 (7.7)	2 (15.4)	8 (61.5)	13	0.202

Values in parentheses are percentages across the row

Table 5: Partner Likert Responses of Partners that Elected Simultaneous Carrier Screening (CS)
Versus Did Not Elect Simultaneous Carrier Screening

Paired Patient and Partner Couple Likert Measure Responses

We explored that agreement between patient and partner responses, which we hypothesized may influence testing decisions. No significant differences between patient and partner Likert responses were identified when analyzing both couples where the partner elected carrier screening and those where partners did not elect carrier screening. Overall, agreement between the patient and the partner ranged from 30.6% (11/36) to 70.3% (26/35). Patients were more likely to assign a higher level of importance to the factor “I want to be able to plan for the future” compared to their male partners, however, this trend failed to reach statistical significance ($p = 0.057$). Further analysis of the paired Likert responses from couples where the partner did not elect carrier screening indicated that patients in this cohort assigned a higher importance to the factor “I want to be able to plan for the future” compared to their male partners ($p=0.02$). Alternatively, there was not a significant difference in level of importance assigned to this factor between couples in which the partner elected carrier screening ($p= 0.564$).

Impact of Disease Severity and Presence on Newborn Screen on Uptake of Carrier Screening

We hypothesized that the severity of the disease detected on the patient’s carrier screening would affect the likelihood of partner testing. Therefore, we classified diseases using a modified version of the disease severity algorithm developed by Lazarin et al. Disease severity was not associated with partner carrier screening uptake ($p=0.550$) (13).

Additionally, we hypothesized that partners may be less likely to pursue screening if the condition was screened for via the Texas Newborn Screening program. The presence of the condition on the Texas Newborn Screen was not associated with partner carrier screening uptake ($p=0.344$).

Electronic Surveys

Electronic surveys were sent to the 21 patients who were found to be a carrier of an autosomal recessive condition whose partner did not elect simultaneous screening. Four patients (19%) completed the electronic survey. One patient's partner elected carrier screening and completed his separate online survey; three partners neither elected carrier screening nor completed his online survey. The three patients whose partners did not pursue carrier screening were asked to indicate on a Likert scale the extent to which they thought certain factors contributed to their partner's decision to decline carrier screening. Two out of three (66.7%) of respondents indicated extreme importance for the following factors: "I do not think he is a carrier of the condition" and "He does not think he is a carrier of the condition." One patient also indicated extreme importance to "The results would not influence the management of the pregnancy," while the other two patients indicated that factor was not important at all. Additionally, one respondent indicated that her partner did not get carrier screening because "Further testing not done because carrier result would only impact male child and sex of baby was determined female." This participant was a carrier of a cystic fibrosis poly T tract polymorphism that may lead to infertility in males but is otherwise not considered to be disease-causing. None of the 3 patients indicated that they believed factors such as religious beliefs, not having a family history of the condition, the partner being scared that he is a carrier of the condition, or the partner forgetting to go in for testing had any impact on their partner's decision to decline carrier screening.

The one partner that completed the electronic survey indicated that he elected carrier screening because "The test was affordable/my insurance covered it" as the factor that had the biggest impact on him electing carrier screening. He also indicated extremely high importance to the factor "It was convenient to send my sample in for testing."

DISCUSSION

Uptake of sequential carrier screening for males whose female reproductive partner was identified to be a carrier of a condition was 23.8%. This rate is similar to what has been previously reported in the literature (12). The results of the study continue to suggest that despite recommendations put forth by ACOG (1, 5), the majority of male partners are not completing carrier screening, even when the patient is found to be a carrier for an autosomal recessive condition, and even if the patient or partner stated that it was their intention to have this performed.

While previous studies have examined reasons why women elect or decline carrier screening, our study differs as it focuses on assessing specific factors that impact a male partner's decision to elect carrier screening. Previous studies have assessed factors that impact a woman's decision to pursue carrier screening and found that doctors recommending carrier screening, perception of certain autosomal recessive conditions as severe diseases, and wanting to prepare seem to influence decision making (7-9). Our study examined similar factors in the male population and found that influential factors in the decision-making process included wanting to know information, wanting to be able to plan for the future, and wanting to know if their child would have an autosomal recessive condition. Additionally, partners that elected carrier screening assigned more importance to "I want to be able to plan for the future" than partners that did not elect carrier screening. While not statistically significant, partners who elected carrier screening tended to assign more importance to the factors "I plan to use this information to make decisions about the pregnancy" and "I was worried about having a child with a genetic condition," compared to partners that did not pursue carrier screening. Our study suggests that individuals often elect carrier screening because they want to be able to plan for

the future, while those who decline may be less inclined to use the information to inform choices about the pregnancy.

Other earlier studies in female prenatal and preconception patients revealed that factors that influence a woman's decision to decline carrier screening include having no family history of a genetic condition, perception that the chance to be a carrier is small, not planning to make pregnancy decisions based on the results, not wanting to know the information, lack of interest, and potential causes of worry or anxiety (5, 6, 8-10). Similarly, for those that completed our electronic survey, the belief that the partner was not a carrier of the patient's condition seemed to influence the couple's decision to decline his screening. These perceptions held by the patient and/or her partner make us wonder that, despite counseling on the carrier frequency and/or couple's empiric reproductive risk for a particular condition, personal perceptions of risk and the notion that "it's never going to be me" (10) may be the most important misconception to correct to improve partner uptake.

Previous studies looking at uptake of carrier screening in the male partner population found that partner uptake of carrier screening was influenced by gestational age and parity (12). Our study examined partner demographic characteristics, including gestational age at the time of the initial genetic counseling visit and number of children with the current partner, which was used as a proxy for parity, and did not find that either of those factors were significant predictors of carrier screening uptake in partners. Differences between our findings and existing literature may be due to sample ascertainment, as previous data was acquired via chart review, while this study was a survey. Additionally, we found no significant difference in uptake across partner education level, partner race/ethnicity, partner insurance type, or partner age, suggesting that partner uptake is uniformly lacking across all demographic groups. Other factors that have previously been hypothesized to play a role in partner carrier screening uptake including

affordability and convenience of sample collection were not determined to be an influential factor in this study (12). Furthermore, partner uptake in potentially at-risk couples was not predicted by severity of the condition that the patient was found to be a carrier for, or the presence of the condition on the Texas Newborn Screen.

What we did find was that partner screening was significantly higher among those who attended the initial genetic counseling appointment. We speculate that partners who are engaged in the initial conversation about carrier screening likely have a better understanding of carrier screening, including the recommendation to pursue carrier screening if the patient is identified to be a carrier of a condition. Previous literature has documented that lack of interest in carrier screening may be linked to lack of awareness and knowledge (14, 15).

Additionally, we found that the partner's attendance at the genetic counseling session may reduce the wait time between result disclosure of the patient's positive result and the partner's sample collection for at-risk couples who elect sequential testing. Partners who attended the genetic counseling session on average waited 14 days between the patient's initial result disclosure and partner sample collection (n=2). Partners who did not attend the genetic counseling session on average waited 53.3 days between the patient's initial result disclosure and partner sample collection (n=3). Although this was a small sample size, partners who attended the initial genetic counseling session received final results, and thus risk clarification, sooner than partners who did not attend the initial genetic counseling session. However, this may reflect ascertainment bias, as partners that attend a genetic counseling session may be inherently more engaged and interested in this aspect of the pregnancy. If the goal is to increase uptake of carrier screening in the partner population, and better adhere to time constraints often placed on decision-making during pregnancy, measures such as encouraging partners to attend obstetric or genetic counseling appointments with the patients may be beneficial.

Differences in patient and partner views may also influence uptake of partner carrier screening. Our study observed that patients want to use information from carrier screening to plan for the future more than their partners who did not elect carrier screening. This discrepancy in the perceived value of carrier screening among couples may be partially responsible for the lack of follow-up of carrier screening by the male. Previous studies were unable to comment on whether males not completing carrier screening was patient- or partner-driven (12). However, this difference in perceived importance about planning for the future may suggest that another barrier to male partner carrier screening completion lies with the male's perceptions about the value of or need for carrier screening itself. When possible, it may be fruitful to explore both the patient and the partner's views on carrier screening during pre-test counseling in order to uncover any potential discrepancies in priorities prior to testing. However, in order to explore these views, the partner's attendance is required, which has already been determined by this study to be associated with increased carrier screening uptake.

The study confirmed that there is a discrepancy between guideline recommendations and uptake of carrier screening by male partners, which ultimately depreciates the overall utility of carrier screening. From this cohort, a complete assessment could not be provided to over half of potentially at-risk couples. Alternatively, from this cohort, only 2 at-risk couples were identified by carrier screening, one of which was a consanguineous couple whose a priori risk to be carriers of the same autosomal recessive condition was expected to be higher than the general population. Previous studies have highlighted the burden on healthcare costs and provider time caused by the current landscape of carrier screening (12, 14, 16). This study again supports that the utility of carrier screening is hindered by incomplete uptake by male partners. Debate exists regarding the best way to implement carrier screening and some have argued that offering screening only to couples, rather than to individuals, maximizes clinical utility and minimizes

provider time (14, 17). We found that partners that attended the initial genetic counseling appointment and elected simultaneous carrier screening were more likely to assign moderate or extreme importance to the factor “The genetic counselor recommended that I get testing” compared to the partners that attended but did not elect simultaneous genetic counseling ($p=0.04$). This suggests that some genetic counselors may be promoting simultaneous carrier screening due to its acknowledged benefits. Further exploration of this topic including the cost benefit or risk of promoting simultaneous carrier screening is warranted.

Additionally, future practices and guidelines may consider advocating for the partner’s presence at medical appointments when possible. It is important to acknowledge that some women may not have a reproductive partner that is available to pursue testing due to a variety of reasons including lack of adequate insurance, not being involved in the pregnancy, or unclear paternity. Alternatively, presence of the partner may be a luxury that some couples simply cannot afford, such as in cases where the male cannot be excused from work to attend the patient’s appointment(s). With the expansion of genetic screening availability and affordability, the hope would be that testing could transcend these adversities, but if carrier screening hinges on partner attendance, this may highlight an example of health disparity for some families.

Barriers to clarifying reproductive risk due to lack of paternal testing may be reduced as technology continues to advance. Recently, a non-invasive screen that tests cell-free DNA (cfDNA) for a select number of autosomal recessive conditions was introduced to the United States market. The screen is able determine if a female is a carrier for a small subset of conditions and reflexes to analyze cell-free DNA to determine if the pregnancy is at a high or low risk to be affected with the autosomal recessive condition, if the patient is identified to be a carrier (18). cfDNA screening for recessive conditions has been available in the United Kingdom and other countries for several years. While traditional carrier screening methods

remain standard of care, new carrier screening technology may be able to provide more accurate risk assessments for women whose partner is not able to pursue screening.

Strengths and Limitations

This study contributes valuable findings to a currently limited body of literature that is working to elucidate factors that impact uptake of carrier screening of males in the prenatal and preconception patient population. A strength of this study was that it was conducted at an academic medical institution that serves a demographically diverse population. The population studied was diverse in both racial and socioeconomic makeup and thus, the results may be generalizable to the entire population.

Limitations to this study include its small sample size and use of novel surveys that have not been validated. Additionally, an aim of this study was to identify factors that impact uptake in at-risk males whose female partner was found to be a carrier of an autosomal recessive condition. Due to low uptake of the partner follow-up survey, we were not able to adequately analyze this aim. Of the 21 couples where the patient was found to be a carrier, 18 (85.7%) indicated that they would pursue carrier screening for the partner if the patient was identified to be a carrier. However, only 5 partners ultimately followed through with the testing. Due to low uptake of the follow-up survey we were not able to capture how the decision-making process changed over time. In order to truly understand what is driving the decision-making process for at-risk couples, it is necessary to collect complete data from couples after one partner has been identified to be a carrier.

Future Directions

Future studies should explore factors that impact uptake of carrier screening in male partners whose female reproductive partner is known to be a carrier of an autosomal recessive condition. Focusing on carrier screening uptake in male partners of at-risk couples may provide

more robust information about factors that influence uptake in situations where ACOG guidelines are more immediately pertinent (1).

BIBLIOGRAPHY

1. Obstetricians, A. C. o., and Gynecologists. 2017. Committee opinion No. 691: carrier screening for genetic conditions. *Obstet Gynecol* 129: e41-e55.
2. Edwards, J. G., G. Feldman, J. Goldberg, A. R. Gregg, M. E. Norton, N. C. Rose, A. Schneider, K. Stoll, R. Wapner, and M. S. Watson. 2015. Expanded carrier screening in reproductive medicine—points to consider: a joint statement of the American College of Medical Genetics and Genomics, American College of Obstetricians and Gynecologists, National Society of Genetic Counselors, Perinatal Quality Foundation, and Society for Maternal-Fetal Medicine. *Obstetrics & Gynecology* 125: 653-662.
3. Gregg, A. R., and J. G. Edwards. 2018. Prenatal genetic carrier screening in the genomic age. In *Seminars in perinatology*. Elsevier. 303-306.
4. Pletcher, B. A., and M. Bocian. 2006. Preconception and prenatal testing of biologic fathers for carrier status. *Genetics in Medicine* 8: 134-135.
5. Ioannou, L., J. Massie, S. Lewis, B. McClaren, V. Collins, and M. Delatycki. 2014. ‘No thanks’—reasons why pregnant women declined an offer of cystic fibrosis carrier screening. *Journal of community genetics* 5: 109-117.
6. Gilmore, M. J., J. Schneider, J. V. Davis, T. L. Kauffman, M. C. Leo, K. Bergen, J. A. Reiss, P. Himes, E. Morris, and C. Young. 2017. Reasons for declining preconception expanded carrier screening using genome sequencing. *Journal of genetic counseling* 26: 971-979.
7. Ioannou, L., J. Massie, V. Collins, B. McClaren, and M. Delatycki. 2010. Population-based genetic screening for cystic fibrosis: attitudes and outcomes. *Public Health Genomics* 13: 449-456.

8. Plantinga, M., E. Birnie, K. M. Abbott, R. J. Sinke, A. M. Lucassen, J. Schuurmans, S. Kaplan, M. A. Verkerk, A. V. Ranchor, and I. M. van Langen. 2016. Population-based preconception carrier screening: how potential users from the general population view a test for 50 serious diseases. *European Journal of human genetics* 24: 1417-1423.
9. Ekstrand Ragnar, M., T. Tydén, U. Kihlbom, and M. Larsson. 2016. Swedish parents' interest in preconception genetic carrier screening. *Upsala journal of medical sciences* 121: 289-294.
10. Propst, L., G. Connor, M. Hinton, T. Poorvu, and J. Dungan. 2018. Pregnant women's perspectives on expanded carrier screening. *Journal of genetic counseling* 27: 1148-1156.
11. Vuthiwong, C., P. Panichkul, and P. Punpuckdeekoon. 2012. Causes and attitude of husbands toward thalassemic carrier screening test when their partners have abnormal screening tests. *J Med Assoc Thai* 95: S162-S167.
12. Giles Choates, M., B. K. Stevens, C. Wagner, L. Murphy, C. N. Singletary, and A. T. Wittman. 2020. It takes two: uptake of carrier screening among male reproductive partners. *Prenatal Diagnosis* 40: 311-316.
13. Lizarin, G. A., F. Hawthorne, N. S. Collins, E. A. Platt, E. A. Evans, and I. S. Haque. 2014. Systematic classification of disease severity for evaluation of expanded carrier screening panels. *PLoS One* 9.
14. Kraft, S. A., D. Duenas, B. S. Wilfond, and K. A. Goddard. 2019. The evolving landscape of expanded carrier screening: challenges and opportunities. *Genetics in Medicine* 21: 790-797.

15. Holtkamp, K. C., E. M. Vos, T. Rigter, P. Lakeman, L. Henneman, and M. C. Cornel. 2017. Stakeholder perspectives on the implementation of genetic carrier screening in a changing landscape. *BMC health services research* 17: 146.
16. Delatycki, M. B., F. Alkuraya, A. Archibald, C. Castellani, M. Cornel, W. W. Grody, L. Henneman, A. S. Ioannides, E. Kirk, and N. Laing. 2020. International perspectives on the implementation of reproductive carrier screening. *Prenatal diagnosis* 40: 301-310.
17. Janssens, S., D. Chokoshvili, D. Vears, A. De Paepe, and P. Borry. 2017. Attitudes of European geneticists regarding expanded carrier screening. *Journal of Obstetric, Gynecologic & Neonatal Nursing* 46: 63-71.
18. Tsao, D. S., S. Silas, B. P. Landry, N. P. Itzep, A. B. Nguyen, S. Greenberg, C. K. Kanne, V. A. Sheehan, R. Sharma, and R. Shukla. 2019. A novel high-throughput molecular counting method with single base-pair resolution enables accurate single-gene NIPT. *Scientific reports* 9: 1-14.

VITA

Wendi Nicole Betting attended high school at Darlington School in Rome, Georgia. Upon graduation in 2011, she moved to Lexington, Virginia to attend Washington and Lee University, where she received her Bachelor of Science in Neuroscience in May 2015. After graduation, she worked as a clinical research assistant at Genomes2People in Boston, Massachusetts. In August of 2018, she began pursuing her graduate degree at the University of Texas MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences Genetic Counseling Program.

Permanent address:

244 Huntley Avenue

Charlottesville, Virginia 22903