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Non-Invasive Prenatal Screening (Nips) Testing Motivations And Informed Decision Making In The Low-Risk Population

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Non-Invasive Prenatal Screening (NIPS) provides a risk assessment for aneuploidies by utilizing cell-free DNA (cfDNA). Recently, it was recommended that NIPS be offered to all pregnant people regardless of a priori risk for aneuploidy. In the absence of an increased risk, alternative motives for electing NIPS, such as for fetal sex disclosure, may arise and result in a less informed decision about proceeding with NIPS. Therefore, our study aimed to characterize low-risk patients' motivations for NIPS election, compare motivations between informed and uninformed decision makers, and determine whether electing NIPS for fetal sex disclosure had any bearing on informed decision making. A survey that included a validated measure of informed choice (MMIC) and questions to assess patients' motivations for NIPS was offered at four UTHealth clinics post genetic counseling. It was found that 44% of participants made an uninformed decision about testing. Participants with private insurers were 5.92 times more likely to make an informed decision (95% CI =1.28-33.05), and participants that self-identified as Black were 9.64 times more likely to make an uninformed decision (CI=0.009-0.737). Informed decision makers scored avoiding invasive procedures higher (p= 0.007) and ranked doing what family/friends desire lower (p = 0.0048) than uninformed decision makers. While most participants scored receiving information about genetic conditions highest, 12% of participants reported fetal sex disclosure as a priority. However, this was not found to be associated with uninformed decision making. Instead,

prioritizing fetal sex was associated with a younger age (p=0.049) and experience with NIPS in previous pregnancies (p=0.034). This study ultimately established shared motivations with the high-risk population, showed no association between fetal sex disclosure motivation and uninformed decision making, characterized participants prioritizing fetal sex, and emphasized the importance of complete pre-test counseling.

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Introduction

The discovery of placentally-derived cell-free DNA (cfDNA) has drastically altered the landscape of prenatal aneuploidy screening [1]. Specifically, Non-Invasive Prenatal Screening (NIPS) adjusts the risk for Down Syndrome, trisomy 18, trisomy 13, and certain sex chromosome abnormalities with greater sensitivity and specificity than serum analyte screening [2] without introducing risk to the fetus. For this reason, NIPS is increasingly utilized over serum screening and invasive diagnostic testing options [3–5].

Upon its commercial release in 2011, NIPS was initially offered only in pregnancies with an increased risk of aneuploidy. Risk factors included advanced maternal age (35 years or older at the time of delivery), the presence of fetal anomalies on ultrasound, history of a prior pregnancy affected by aneuploidy, or a positive maternal serum screen [6]. However, with its growing affordability, accessibility, and evidence of clinical utility since its release [1], NIPS has recently been recommended by the American College of Obstetricians and Gynecologists (ACOG) as a routine screening option for all pregnant people regardless of a priori risk [7]. Given the increasing implementation of NIPS in the last decade, many studies have been performed to better understand the uptake and performance of NIPS.

Furthermore, some studies have aimed to understand the motivations for electing NIPS, primarily in its original target population of advanced maternal age (AMA) patients [8,9]. However, these motivations have yet to be assessed in a low-risk setting, particularly in the context of ACOG's updated recommendations and increasing NIPS uptake by low-risk patients [10]. Low-risk patient motivations for NIPS are of special interest because the absence of substantial aneuploidy risk may suggest that other testing motivations play a significant role in decision making. For instance, the American College of Medical Genetics (ACMG)

has identified fetal sex disclosure as a possible motivator for NIPS and stated that "efforts should be made to deter patients from electing NIPS for the sole purpose of fetal sex identification when a clinical indication is not present" [11]. However, to date, there is limited existing literature exploring low-risk patients' NIPS testing motivations.

Therefore, our study aimed to understand the primary motivations for electing NIPS in low-risk patient populations and whether specific motivations, such as fetal sex disclosure, were more prevalent in the absence of increased aneuploidy risk. It should be noted that the desire to learn fetal sex during pregnancy on its own is not a problem and remains a common practice during pregnancy by way of the second trimester anatomy ultrasound. Rather, the concern lies in the potential of patients electing for NIPS for fetal sex disclosure without understanding the primary purpose of aneuploidy risk assessment, the possibility that any pregnancy can be affected by aneuploidy, and/or the implications of a positive NIPS result. Thus, in attempt to explore this potential misunderstanding, our study included a measure of NIPS informed decision making [9].

Informed decision making is considered a central tenet of genetic counseling [12] and critical for reproductive autonomy [13]. This importance has led to the use of validated multidimensional measures of informed choice (MMIC) to determine informed decision making of patients in a prenatal setting [14]. This measure has since been adapted to assess informed decision-making scores of patients electing or declining NIPS, which was utilized by this study. This measure assesses patients' knowledge of testing, deliberation of testing, and value consistency of uptake decision with attitude toward testing [9]. By incorporating in an informed choice measure, we could explore associations between informed decision making and testing motivations, such as prenatal identification of genetic conditions and fetal

sex disclosure. Potential risks to uninformed decision making, such as overemphasis of NIPS safety and simplicity resulting in screening routinization, increasing social pressures around testing expectations, and undermining of result complexity, have been identified in previous studies [15,16]

In addition to understanding primary motivations for NIPS election in low-risk patients, we also aimed to better understand sub-motivations driving the specific desires for receiving information about genetic conditions and fetal sex. Identifying common sub-motivations in low-risk patients may better inform how genetic condition versus fetal sex information is used during pregnancy and allow for improved pre-test education of patients regarding the benefits and limitations of screening. This could provide valuable perspectives on what should be discussed in more detail for complete pre-test counseling. This could include emphasizing the ability to prepare for a child with a disability as much as providing pregnancy options such as termination [17], and introducing the difference between fetal sex and gender, particularly in consideration of the ritualization of "gender-reveal parties" in Western culture [18].

Determining motivations and sub-motivations for electing NIPS could also aid in the avoidance of adverse outcomes of uninformed decision making. Adverse outcomes can include anxiety resulting from an unexpected positive NIPS result [19], misunderstanding of the non-diagnostic nature of NIPS results, and the unexpected burden of decision making [17]. Therefore, investigating possible correlations with uninformed decision making will aim to alleviate such burdens and contribute to the ultimate goal of maintaining patients' reproductive autonomy through prenatal screening [13].

Methods

Study Population and Data Collection

Individuals were recruited prospectively from four UTHealth Maternal Fetal Medicine (MFM) clinics in Houston, Texas. English-speaking low-risk patients who received genetic counseling services and elected for NIPS between September 2021 and February 2022 were eligible for this study. Low-risk was defined as any patient whose pregnancy was not determined to be at an increased risk for aneuploidy based on maternal age, ultrasound findings, or family history. Those who conceived via IVF were excluded due to an unrelated research project studying the IVF population that was ongoing during our project's sampling period. Genetic counseling consultations were performed using in-person, telemedicine, or telephone formats. The survey was offered to eligible patients after completion of their genetic counseling appointment via QR code or URL. Study data were collected and managed using REDCap electronic data capture tools hosted at University of Texas Health Science Center Houston [20,21].

The survey utilized a variety of sampling techniques including multiple choice questions, ranking, and Likert scale items. The survey began with a validated MMIC measure [9] which ascertained patients' informed decision-making scores through knowledge, attitude, and deliberation scales. Previous studies validated internal consistency and construct validity for the MMIC measure [9]. Patients' motivations for electing NIPS were assessed through sliding scales that presented motivations previously described in other research studies [8,9]. The survey additionally assessed the desire for alternate screening options and intended use of screening results, with questions specifically targeted toward projected use of fetal sex information. Patient demographics (race, ethnicity, age) and prior experience with NIPS were

also collected. This study was approved by the UTHealth Institutional Review Board (#HSC-MS-21-0464).

Data Analysis

All data were queried through REDCap and compiled into a .csv file that was used for data analysis. R programming (Version 4.1.2, R Core Team, 2021) was utilized for data cleaning and manipulation via base R. All downstream analyses were performed using base R. Statistical significance was set at $p < 0.05$ and graphics were generated using ggplot2 [23].

Informed choice was analyzed by dichotomizing knowledge, deliberation, and attitude scores. Good knowledge was defined as answering at least 8/11 knowledge questions correctly. Poor knowledge was assigned when a patient answered less than 8/11 knowledge questions correctly or provided an incorrect answer when selecting the conditions for which NIPS screens (Down syndrome, trisomy 18, trisomy 13, and sex chromosome abnormalities). A decision was considered deliberated if the midpoint of the scale (more than 18 points) was surpassed. Finally, attitude scores were characterized as either positive (more than 14 points) or negative (less than 10 points). All scores that fell between 10 and 14 were considered neutral and excluded from informed choice calculations. The patient's attitude score was then compared with their choice of pursuing NIPS to generate a value-consistency score. If the patient had a positive attitude about testing and elected NIPS they scored as value consistent; if the patient had a negative attitude score and elected for NIPS, they were coded as value inconsistent. For a patient to qualify as having made an informed decision, their decision must have scored as good knowledge, deliberated, and value consistent. Any deviation from this triad resulted in an uninformed decision-making score. Given that the outcome variable

was either informed or uninformed, it was treated as a dichotomous categorical variable for further analyses.

Motivations for testing were measured using a sliding scale with values ranging from 0 to 100; thus, motivation scores were treated as continuous variables for further analyses. As an exception, question #56 asked the patient to select their highest priority motivation for electing NIPS; this was treated as a categorical variable. Raw scores provided by patients were converted into ranks by assigning a rank of 1 to the motivation with the highest raw score, 2 to the motivation with the second highest score, etc., per patient. For motivations given the same raw score, the same rank was provided, and subsequent, descending scores received the next available rank. For example, when three motivations were all given the score of 100, all motivations received a rank of 1 and the next motivation received a rank of 4, and so on. Both raw and ranked scores were used in data analysis. For additional statistics analyzing motivation raw score and ranked score between informed and uninformed decision makers, Mann Whitney U tests were utilized. To better understand which factors may be contributing to the type of decision made, a logistic regression was utilized where motivation rank, demographic information, and pregnancy history were used as predictor variables, and type of decision made was used as the outcome variable.

Descriptive statistics were used to characterize participant demographics. Variables of interest included race, age, religion/spirituality, insurance, education level, trimester at counseling, and pregnancy history. Comparisons between populations were made using Chi2 and Fischer's exact test, as appropriate.

Results

Participant Characteristics

Out of the 654 pregnant people eligible for our study, 167 participants began the survey (25.5% survey uptake) and 118 participants completed the survey (70.6% completion rate). Responses excluded from analysis included repeat sample submissions (n=3), those who stated they declined NIPS (n=4), patients with a history of high-risk NIPS results (n=1), and neutral attitude participants since they would not be considered in downstream informed decision-making score comparisons (n=10). Ultimately, this gave a final study population of 100 pregnant people who elected NIPS (Figure 1). Our study population was found to be significantly different than the eligible population in that there was a greater presence of "other" insurances ($p=0.0005$), more participants were in their first trimester of pregnancy ($p<0.0001$), and a larger proportion of participants had numerous children from prior pregnancies ($p=0.008$). Our study population was not significantly different than the eligible population for age ($p=0.43$), race ($p=0.07$), and gravida ($p=0.59$). The study population demographics for these participants (Table 1) and their pregnancy history (Table 2) were collected.

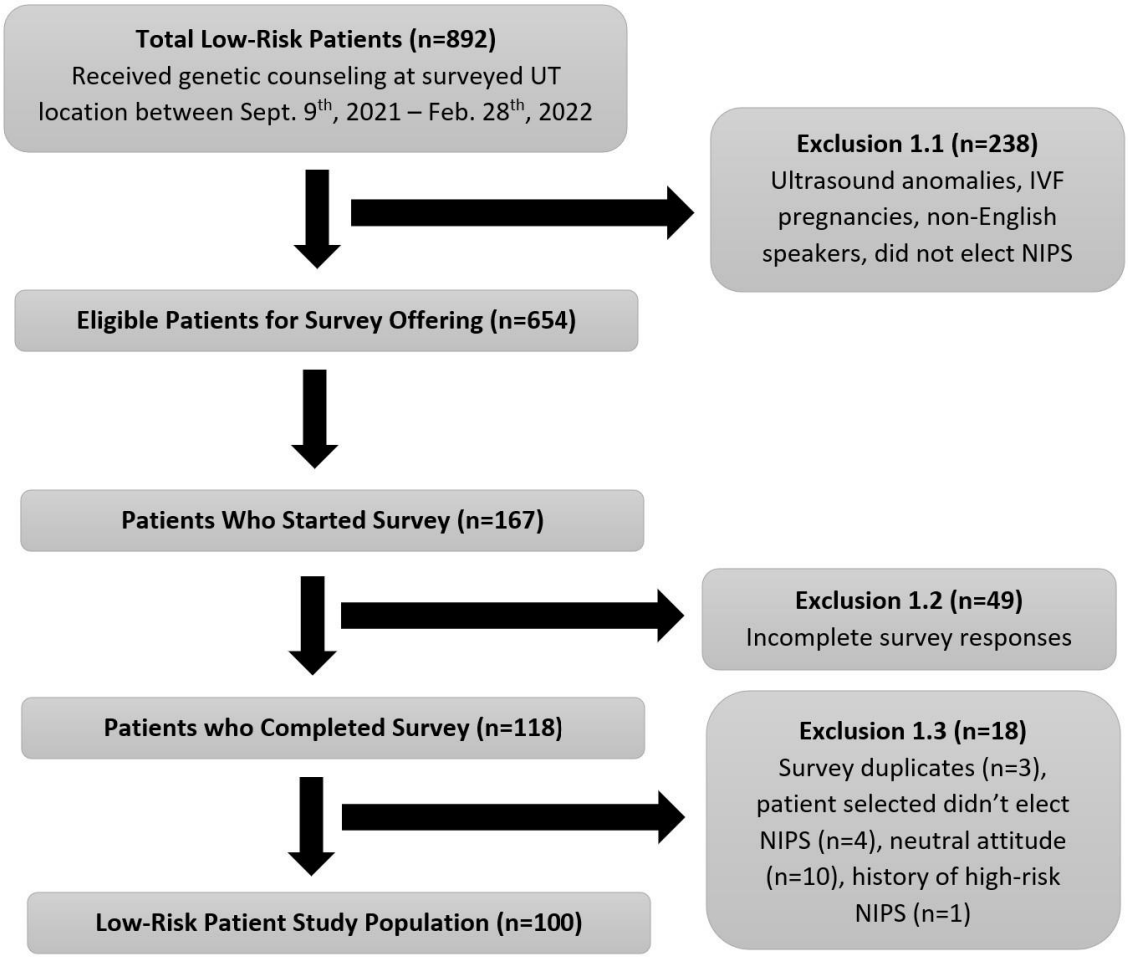

Figure 1. Participant Exclusion Criteria Flowchart.

Table 1. Summary of Low-Risk Sample Population

Item	Number in Sample Population (% total)
Race	
White	26 (26%)
Black	16 (16%)
Hispanic	39 (39%)
Asian	14 (14%)
Other	5 (5%)
Age	
15-20	6 (6%)
21-30	61 (61%)
31-34	33 (33%)
Religion/Spirituality	
Very religious/spiritual	26 (26%)
Somewhat religious/spiritual	54 (54%)
Not very religious/spiritual	11 (11%)
Not at all religious/spiritual	9 (9%)
Insurance	
Medicaid	44 (44%)
Private insurance	43 (43%)
Other	13 (13%)
Education Level	
Some high school	3 (3%)
High school graduate	24 (24%)
Some college	21 (21%)
College graduate	32 (32%)
Graduate school	20 (20%)

Table 1. Study Participant Demographics.

Table 2. Summary of Sample Population's Pregnancy History

Item	Number in Sample Population (% total)
Trimester at Counseling	
First Trimester	87 (87%)
Second Trimester	12 (12%)
Third Trimester	1 (1%)
First pregnancy	
Yes	30 (30%)
No	70 (70%)
Number of prior pregnancies	
One	18 (25.7%)
Two	25 (35.7%)
Three	15 (21.4%)
More than three	12 (17.1%)
Living Children	
Zero	5 (7.1%)
One	42 (60%)
Two	14 (20%)
Three	5 (7.14%)
Four	3 (4.3%)
Seven	1 (1.4%)
NIPS in previous pregnancies	
Yes	39 (55.7%)
No	24 (34.3%)
Unsure	7 (10%)
Results of previous NIPS	
Low-risk/Normal	38 (97.4%)
Unsure	1 (2.5%)
Previous pregnancy with genetic condition*	
No	70 (100%)
Previous pregnancy with birth defect**	
Yes	1 (1.4%)
No	69 (98.5%)

* Examples for genetic conditions included Down Syndrome, trisomy 13, trisomy 18, Turner syndrome, XXX, XXY, and XYY

** Examples for birth defects included cleft lip, clubfoot, and heart defect

Table 2. Study Participant Pregnancy History.

Informed Decision-Making Score

Utilizing the criteria outlined by the MMIC Validated Measure for NIPS [9] it was found that 56% of participants made an informed decision about NIPS election, whereas 44% of participants did not. Within the uniformed decision makers, it was found that 95.5% received a score of poor knowledge, 6.8% received a score of value inconsistency, and 11.4% received a score of non-deliberated. The most common group of uninformed decision makers (81.8%) received a designation of poor knowledge, value consistent, and deliberated. However, among those with poor knowledge (n = 44), 10 participants (22.7%) only received such a designation because of incorrectly answering the question regarding the conditions for which NIPS analyzes; they had otherwise received a knowledge score of 8 or more by answering the remaining questions correctly. The questions that most contributed to poor knowledge assignments resulting in uninformed decision-making scores included those related to the conditions for which NIPS analyzes (n=35/44, 79.5%), the potential for inconclusive results (n= 31/44, 70.5%), and the risks associated with chorionic villus sampling and amniocentesis (n= 36/44, 81.8%).

Additionally, the results of the logistic regression showed significance for the raw score provided for information about genetic conditions, insurance, and race. It found that for every unit increase in the raw score provided for information about genetic conditions, the odds of making an informed decision increases by 5% (OR=1.05, 95% CI= 1.01-1.10). For insurance, participants that had private insurance were 5.92 times more likely to make an informed decision (95% CI =1.28-33.05) and for race, participants that self-identified as Black were 9.64 times more likely to make an uninformed decision (CI=0.009-0.737).

Low-risk Patients' Motivations for NIPS Election

When asked to identify the single most important factor when deciding to elect NIPS, 85 participants (85%) chose information about genetic conditions, 12 participants (12%) chose information about fetal sex, two participants (2%) chose following their doctor's recommendations, and one participant (1%) chose avoiding an invasive procedure. The majority of individuals that identified fetal sex information as a priority were between the ages of 21-30 years old (n=9; 75%), were in the first trimester (n=12; 100%), had been pregnant before (n=9; 75%), and had done NIPS in a previous pregnancy with low-risk/normal results (n=8; 88.9%). When compared to individuals who did not prioritize fetal sex disclosure, the fetal sex prioritizing group (n=12) was significantly younger (p=0.049) and had more experience with NIPS in previous pregnancies (p=0.034).

When differentiated based on decision-making score, 49 informed decision makers (87.7%) and 36 uninformed decision makers (81.8%) identified genetic condition information as the priority; seven informed decision makers (12.3%) and five uninformed decision makers (11.36%) identified fetal sex information as the priority for NIPS election. These differences were not significant (p = 0.2685).

When patients were asked to assign a numerical value to the importance of each motivation, it was found that receiving information about genetic conditions was given the highest score (median = 100) followed by insurance coverage of NIPS (median = 86). Informed decision makers were more likely to score avoiding an invasive procedure higher (median = 87.5) than uninformed decision makers (median = 50; p= 0.007). Of note, there were not significant differences in raw scores for receiving genetic condition information (p=

0.57) or receiving fetal sex information (p = 0.93) between decision makers. Raw scores for each motivation can be found in Figure 2.

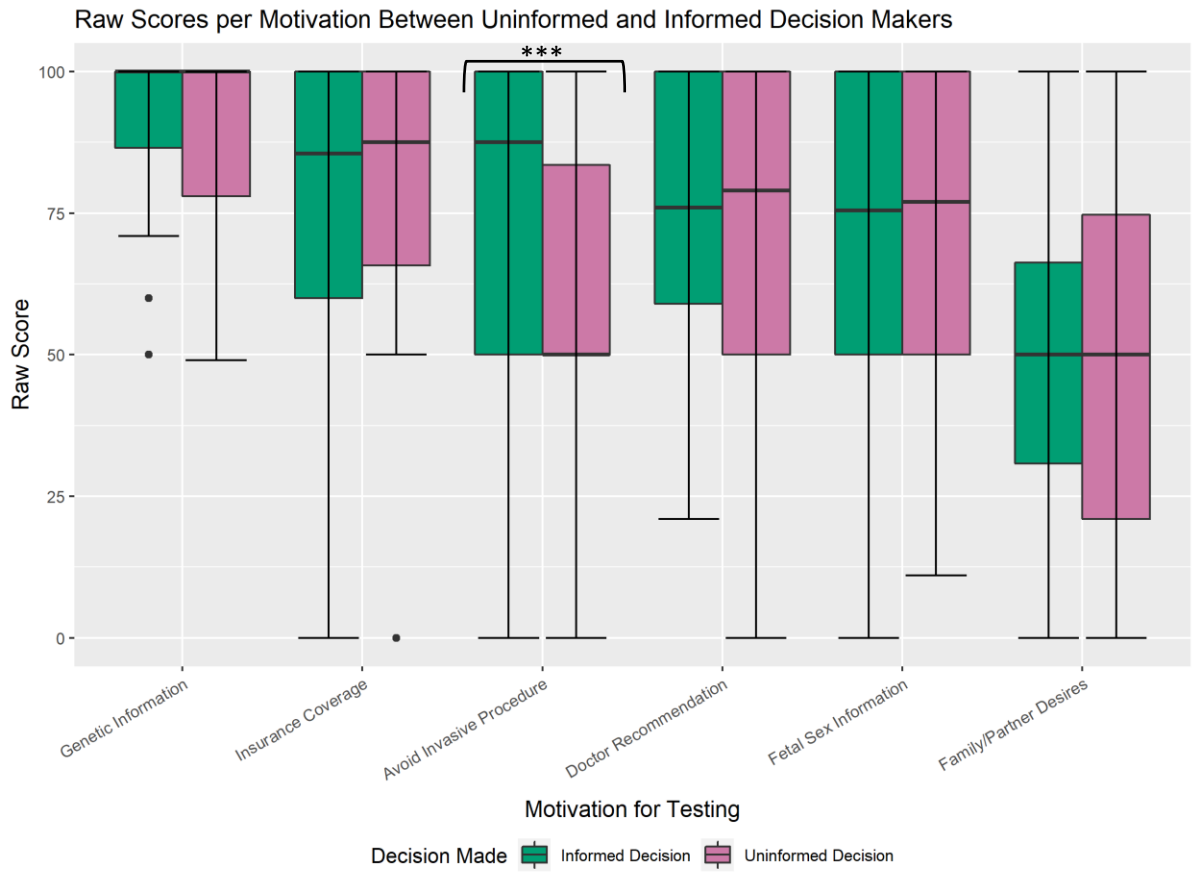

Figure 2. Motivations for NIPS by Raw Score.

When the raw scores were assigned a rank per participant and compared between decision makers, we found that doing what the family and partner desires was ranked lower by informed decision makers (median = 5) versus uninformed decision makers (median = 4; p = 0.0048). Receiving genetic condition information received the highest rank (median rank = 1) followed by insurance coverage (median rank = 2) for both decision maker types. Of note, informed decision makers ranked fetal sex information lower (median = 3) than

uninformed decision makers (median = 2), but this comparison was not significant (p =0.24). Ranks for each motivation can be found in Figure 3.

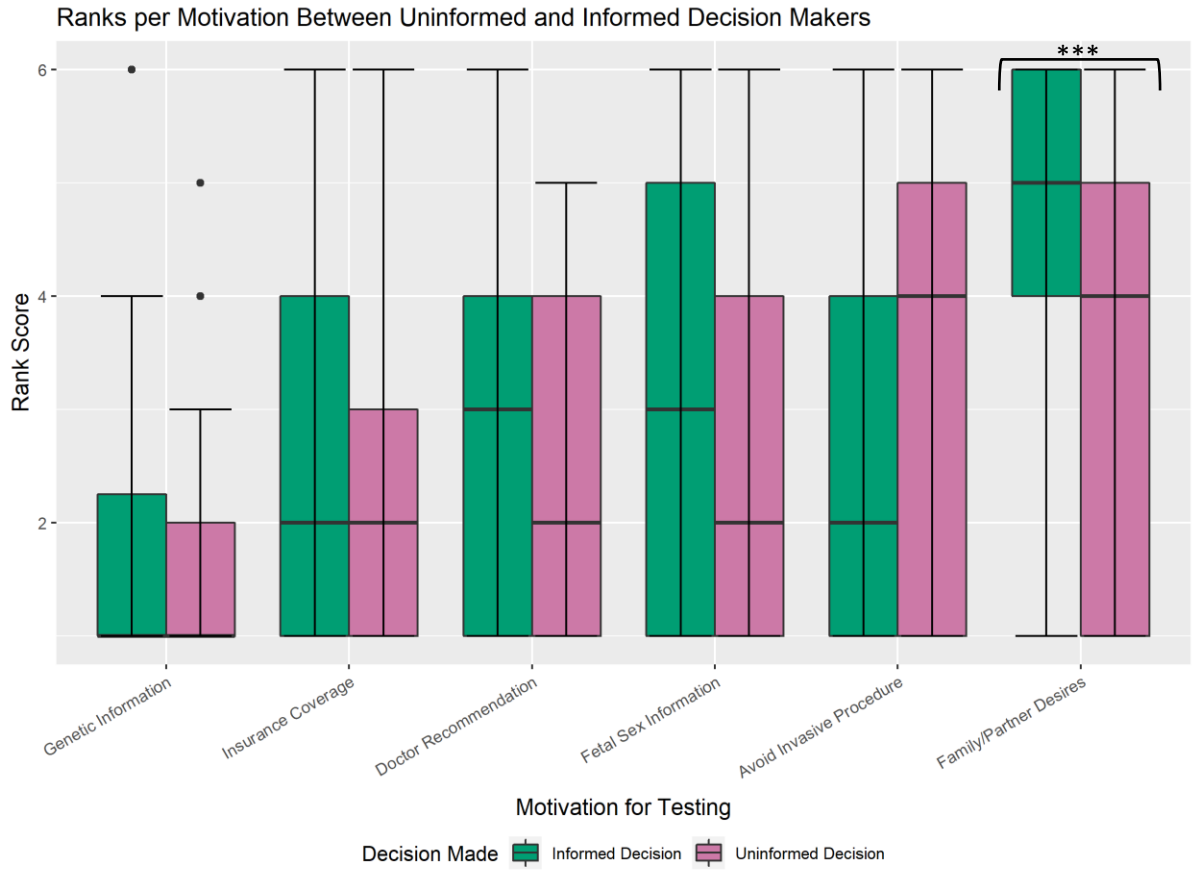

Figure 3. Motivations for NIPS by rank.

In attempt to better understand the group of individuals that ranked fetal sex information as a highest priority (n=42/100, 42%), we looked further at their ranks for all other motivations. Of these participants, only 7 exclusively ranked fetal sex as their #1 priority; the remainder assigned at least one other motivation the same raw score (and thus rank) as determining fetal sex by NIPS. Specifically, 30 (71.4%) gave genetic condition information the same raw score, as did 21 participants (50%) who gave doing what the doctor

recommends, 20 participants (47.6%) who gave insurance coverage of testing, 18 participants (42.9%) who gave avoiding invasive procedure, and 15 participants (35.7%) who gave doing what friends and family desire as the same #1 rank. In the subpopulation of individuals that exclusively ranked fetal sex first (n = 7) insurance coverage was the most commonly ranked second highest motivation (n=4; 57.1%), followed by genetic condition information (n=2; 28.6%), and avoiding an invasive procedure (n=1; 14.3%).

Low-risk Patients' Sub-Motivations for NIPS Election

To provide more context for motivations related to receiving information about genetic conditions and fetal sex, participants were asked to provide a sliding scale score for sub-motivations for NIPS election. For sub-motivations regarding receiving information about genetic conditions, the following received a median score of 100: planning for the baby's arrival, providing reassurance around the health of the pregnancy, preventing unexpected news later in pregnancy, and easing anxiety (Figure 4). Sub-motivations for receiving information about fetal sex were scored as follows: receiving information about sex chromosome genetic conditions (median = 100), bonding with the pregnancy (median = 90), picking out names for the baby (median = 82.5), and buying clothing and nursery decorations (median = 66.5) (Figure 5). There were not any significant differences in sub-motivations for receiving genetic condition or fetal sex information through NIPS between decision maker types.

For the group of participants that identified fetal sex disclosure as their highest priority when electing NIPS (n=12, 12%), it was found that all sub-motivations for finding out fetal sex information were scored higher when compared to the entire study population, except for the sub-motivation of receiving information about sex chromosome genetic

conditions (median=97), but this was not a significant difference (p=0.129). Each sub-motivation for fetal sex information received the following median scores: bonding with the pregnancy (median=98.5), planning a baby shower (median=83), buying clothing and nursery decorations (median=98), planning a gender reveal (median=90.5), and picking out names (median=99). Of note, within this group most sub-motivations for receiving genetic condition information, except for making decisions about continuing the pregnancy of not (median=50), were scored above a median of 90.

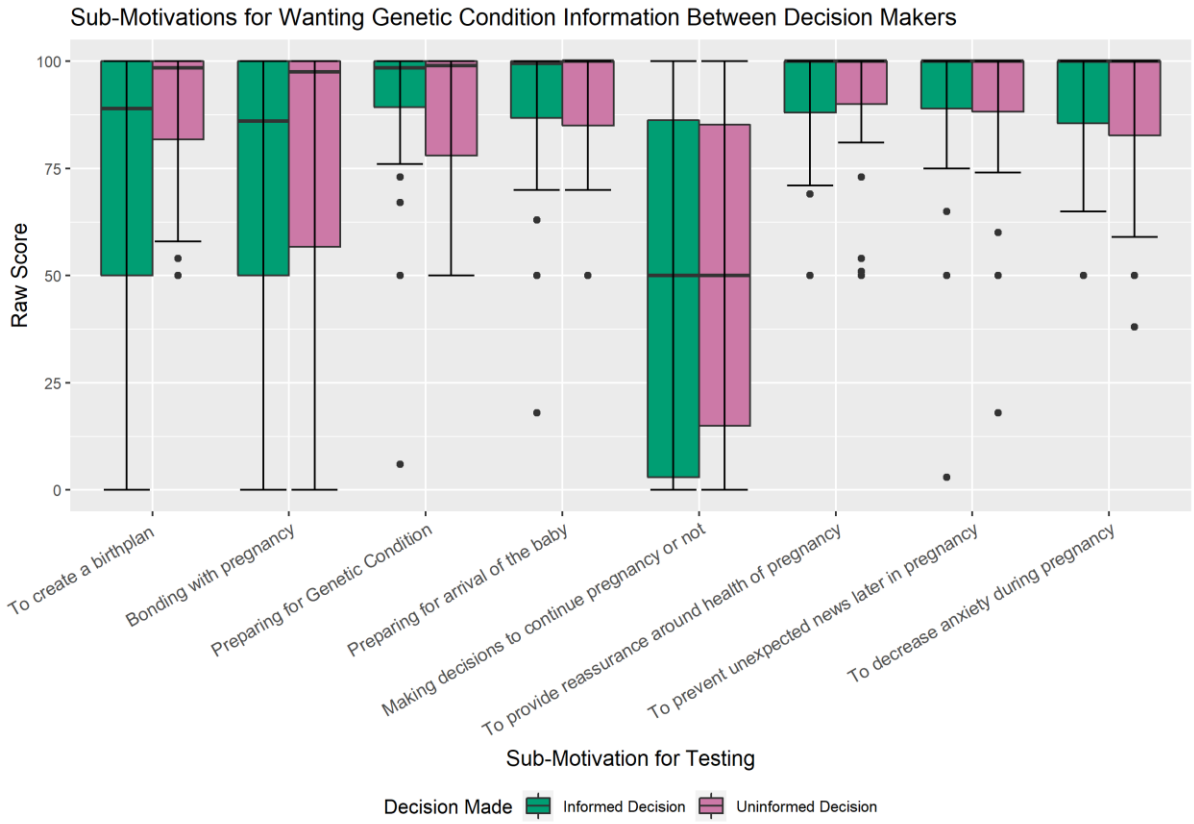

Figure 4. Sub-motivations for genetic condition information.

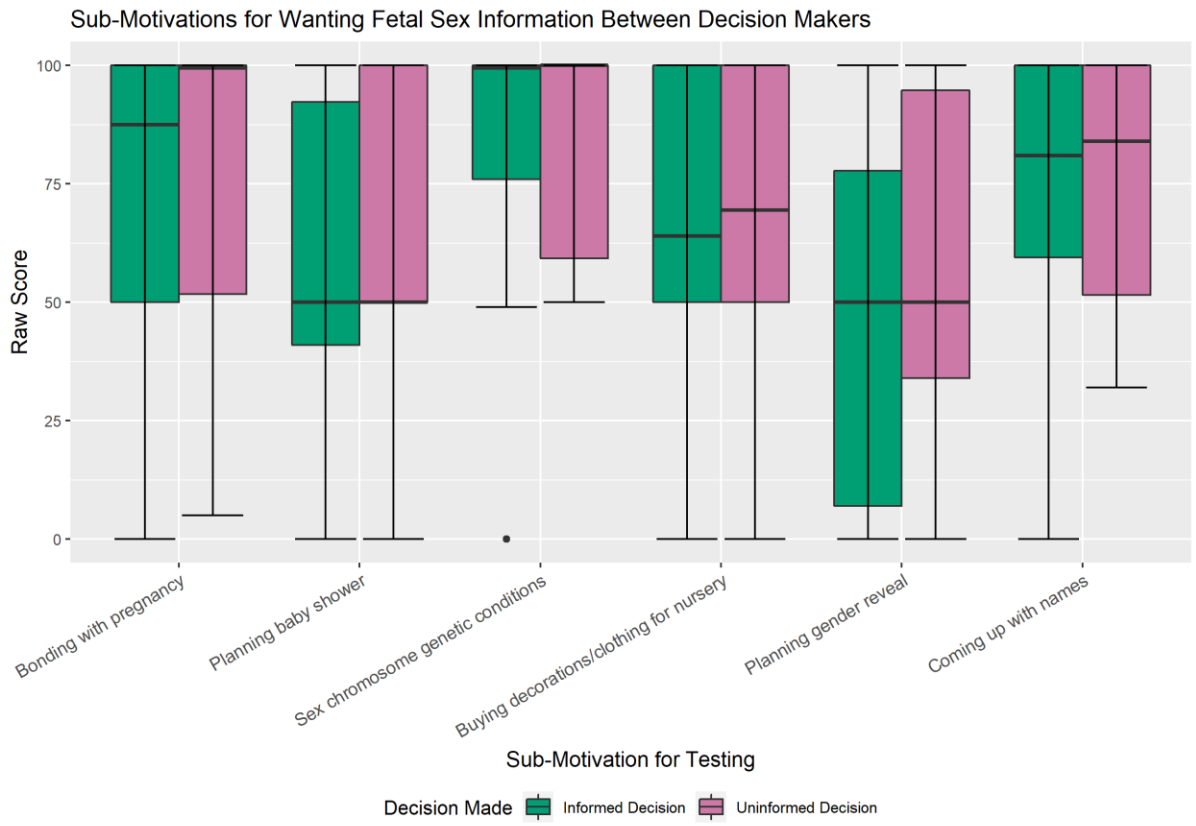

Figure 5. Sub-motivations for fetal sex information**.**

Other Testing Preferences and Intended Plans for NIPS Results

When participants were asked if they would prefer to have a test that looked only at fetal sex but did not provide a risk assessment for genetic conditions, most participants selected that they would not prefer such a test (n=82; 82%), while seven participants (7%) selected that they would prefer this test instead of NIPS. Eleven participants (11%) said they were unsure. Of the seven participants that preferred a stand-alone sex prediction test, one (14.2%) was an informed decision maker and six (85.7%) were uninformed decision makers, however this difference was not significant (p=0.059). Next, participants were asked if they would prefer to have a test that only provided a risk assessment for genetic conditions but did not provide fetal sex. Responses showed that most participants (n=72; 72%) said they would not prefer such a test, however 11 participants (11%) said they would prefer this test, and 16

participants (16%) said they were unsure, however this difference was not significant (p=0.29). Finally, participants were asked to detail their intended use of fetal sex information from NIPS (Table 3). For the participants that chose fetal sex disclosure as their priority for testing (n=12), most reported that they did not already know the sex of the baby (n=11, 91.67%). Of that group, they planned to learn the sex of the baby from NIPS results (n=10, 90.9%) or a gender reveal (n=1, 9.1%), and planned to share fetal sex with family and friends through word of mouth/online posts (n=5, 45.5%) or a gender reveal (n=6, 54.5%).

Table 3. Summary of Plans for Fetal Sex Information

Item	Number (% total)
Did you know the fetal sex coming into the appointment?	
Yes	7 (7%)
No	93 (93%)
Do you plan to find out the fetal sex during pregnancy?	
Yes	88 (94.6%)
No	3 (3.2%)
Unsure	2 (2.1%)
How do you plan to find out the fetal sex?	
From NIPS results	51 (57.9%)
"Gender" Reveal *	30 (34.1%)
Ultrasound	2 (2.3%)
Unsure	5 (5.7%)
Do you plan to share fetal sex with friends/family?	
Yes	82 (93.2%)
No	2 (2.3%)
Unsure	4 (4.5%)
How do you plan to share fetal sex with friends/family?	
Word of mouth/online post	41 (50%)
"Gender" reveal *	36 (43.9%)
Unsure	5 (6.1%)

* "Gender reveal" reflects language used in free responses and does not represent that NIPS discloses gender

Table 3. Summary of knowledge of fetal sex and intended use of fetal sex information.

Discussion

Understanding patients' perception and understanding of NIPS is paramount for appropriate and complete patient education and informed decision making. Given the updated ACOG recommendation to offer NIPS to all pregnant people regardless of a priori risk [7], importance was placed on understanding low-risk patients' motivations for electing NIPS. Specifically, we aimed to identify motives in the absence of increased risk of aneuploidy, such as fetal sex determination.

Our study confirmed that motivations for NIPS election initially observed in AMA patients, such as importance placed on genetic condition information [8,9] and insurance coverage [24], are also factors that are important for NIPS selection in the low-risk population. This suggests that regardless of a patient's a priori risk, similar pre-test counseling on the advantages and disadvantages of NIPS compared to invasive diagnostic testing can be performed. Additionally, the importance placed on insurance coverage recognizes existing financial barriers resulting from selective public and private insurer coverage of low-risk NIPS. For instance, pregnant people covered by private insurers because they do not qualify for public insurance, but still experience socioeconomic hardship, may be prevented from accessing care. Moreover, public insurer plans vary on low-risk NIPS coverage between states, further exacerbating the existing adversities experienced by populations requiring healthcare support. This emphasizes the necessity of discussing available financial assistance and self-pay options in pre-test sessions, while recognizing that these options may lessen, but not eliminate, financial barriers contributing to healthcare disparities [6].

Furthermore, there may be additional nuances with pre-test counseling in the low-risk setting when specifically considering individuals who made an uninformed decision to

proceed with NIPS. Utilizing the MMIC validated measure, informed decision makers were more likely to score avoiding an invasive procedure higher than uninformed decision makers. This result is representative of the existing knowledge that patients place high importance on test safety and avoidance of pregnancy risks [25] when selecting a prenatal screen, but identifies a difference between understanding of, or the value placed on, test safety between decision makers. Furthermore, uninformed decision makers tended to rank doing what family and friends desire higher than informed decision makers. This could introduce an additional component to decision making that goes outside the scope of information provided in the NIPS pre-test discussion therefore requiring more in-depth pre-test counseling and shared decision making.

Additionally, several sub-motivations for genetic condition information were also identified as important by participants, such as preparing for a pregnancy affected with a genetic condition, preparing for delivery, providing reassurance, decreasing anxiety, and preventing unexpected news later in pregnancy. This highlights the necessity of a discussion on various uses of positive NIPS results during pre- and post-test sessions. This can include providing access to options for subsequent decision making through changes to the proposed pregnancy and/or birth plan, consideration of diagnostic procedures, election of pregnancy termination, or preparation for raising a child affected with a genetic condition [16]. Therefore, the potential choices that may become available from learning about genetic information should be diverse, but cognizant of the patient's self-described values.

When the decision to undergo NIPS is primarily driven by the desire to learn fetal sex, concern for uninformed decision making increases. Therefore, the purpose of this study was to not only identify the motivations for NIPS election in the low-risk patient population,

but also to determine if electing NIPS primarily for learning fetal sex was associated with uninformed decision making. This study did not identify a significant difference in fetal sex scores and ranks between informed and uninformed decision makers, but a group that elected NIPS primarily for fetal sex disclosure was identified. As a result, this shows that the ACMG recommendation to deter from NIPS election for the basis of fetal sex disclosure [11], has not been entirely upheld. However, in the absence of a negative effect on decision making, it begs to question the purpose behind adherence to this recommendation and demands a deeper understanding of this patient population.

Existing literature on potential harms of early fetal sex disclosure detail potential for sex selection [15,26], sex-driven bonding during the trimester with the highest risk of miscarriage [27], and parental assumption of gender norms from fetal sex information [28]. While the intent behind this recommendation may be to enforce ethical and social considerations of electing NIPS solely for learning fetal sex, targeted restriction of fetal sex information by NIPS in the presence of an otherwise informed understanding of genetic condition information could be perceived as paternalistic gatekeeping of fetal sex information by prenatal care providers. As a result, if motive for NIPS is questioned, specific guidelines may need to be outlined on which non-medical sub-motivations for fetal sex information may require gatekeeping. If motive is not questioned, more detailed conversations on the considerations of learning fetal sex may need to be had. Our study began to understand the potential sub-motivations driving fetal sex information desires (i.e., shopping for nursery decorations, clothing, and picking out names), but additional studies could provide a more in depth understanding of this group.

To expand on the potential misinformation of gender assumption from NIPS, our study identified an emerging trend of fetal sex information utilization for gender reveals. The advent of gender reveals in and of itself provides concern for the misunderstanding of gender versus sex, and which of these NIPS provides. Fetal sex is defined as the biological sex provided by the presence or absence of a Y chromosome, whereas gender is a sociocultural construct rooted in identity, masculinity, and femininity [29]. Therefore, NIPS provides, at most, the chromosomal sex of the fetus. Even so, potential sex chromosome discordance with internal and/or external genitalia provides additional considerations for the patient's interpretation of NIPS fetal sex results [30]. As a result, inclusion of an explanation of gender versus sex and potential limitations of fetal sex results should be considered for NIPS pre-test counseling.

Finally, the difference between informed decision making, informed choice, and informed consent, the legitimacy and consistency of informed measures, and whether informed choice is attainable when offering NIPS, deserves further attention. Informed decision making refers to the pre-decision deliberation that leads to an informed choice, which incorporates a patient's understanding of and attitude towards medical options. In literature about NIPS, informed choice has been used preferentially over informed consent when pertaining to patients' decision about prenatal screening. This is likely because informed choice values both accepting or rejecting NIPS equally with the overarching goal of reproductive autonomy, whereas the use of informed consent can show bias towards one outcome, or decision, recommended by the medical provider. The separation of each of these terms has been argued both for [31,32] and against [33] in previous literature.

Furthermore, previous studies have shown that certain informed decision-making skills (i.e., knowledge) may be more easily measured, and therefore overexpressed, due to the dichotomization of correct versus incorrect answers. Whereas other equally as important skills (i.e., deliberation and attitude) may not be as easily measured through more arbitrary cutoffs and receive less weight in informed choice calculations [34]. Moreover, the utilization of a knowledge component in informed choice measures may not accurately reflect if an informed choice was made. This is because knowledge scores may be directly affected by pre-determined decisions about NIPS from materials outside of pre-test counseling, unspoken inferences made from information given in pre-test counseling, and the effect of education overload on information retention and performance on knowledge-based measures.[33] Given that the designation of poor knowledge would result in an uninformed decision, the incorporation of knowledge components may overrepresent populations as uninformed although their reproductive autonomy, through decisions grounded in deliberation and value consistency, is maintained. Better measures of such skills may be imperative for a more complete understanding of patient decision making for continued improvement of the medical provider and patient pre-test experience.

Future Directions

Results showed a substantial number of individuals making uniformed decisions following pre-test genetic counseling in general. Given this outcome occurred after patients received complete pre-test counseling with a genetic counselor, this pattern may be further exacerbated under other methods of test offering that provide less involved pre-test counseling. Therefore, this result lays the framework for future studies to investigate other causes of, or correlations with, uninformed decision making. For instance, investigating

informed decision making in patients who receive pre-test education that does not include consultation with a genetic counselor (e.g. online modules, pre-test education with OB/GYN) could produce more generalizable data that may identify factors that were not recognized in this study.

Additionally, both our study and the previous study utilizing the MMIC measure [9] did not survey non-English speaking patients. Therefore, future studies could aim to study non-English patients electing for NIPS by providing multiple translations of the MMIC measure. Furthermore, follow-up after results disclosure with patients that elected for NIPS for fetal sex determination could provide valuable insight into the entire experience of a patient prioritizing fetal sex.

Study Limitations

It is important to recognize variables of our research study that may have hindered the full potential of the results or reduced applicability to a broader clinical context. This study was conducted only with patients that received pre-test genetic counseling with a genetic counselor for prenatal screening options. These consultations typically entail a 30-minute discussion of the patient's risk for genetic conditions and a detailed explanation of the risks, benefits and limitations of prenatal aneuploidy and carrier screening. We are aware that low-risk patients are not typically seen by a genetic counselor, so pre-test counseling and knowledge score reflections may not be representative of the general population where pre-test counseling, if any, is performed during an OB appointment[35]. Although the results of this and future studies focusing on pre-test counseling performed by genetic counselors can be simplified and applied in the OB setting, they do not serve as direct representations of the success and efficacy of such initiatives.

Furthermore, the research survey was distributed to patients following the genetic counseling session. Therefore, the patient may have been swayed to provide values that were more reflective of the information covered in the genetic counseling session (e.g. information about genetic conditions) instead of what their pre-counseling motivations may have been (e.g. fetal sex prediction). It is also possible that those who would have elected NIPS solely to learn fetal sex, after a full pre-test counseling session, decided that this screen was not in line with their values and opted out of NIPS. These perspectives and motivations for declining NIPS were not captured in this study. Finally, the clinics in which the survey was distributed are teaching clinics in which genetic counseling students are often leading sessions. Therefore, there is likely an additional variable of inconsistency between each session, potentially owing to the higher count of uninformed decision makers compared to previous studies [9].

Lastly, our study did not collect complete information about participant's socioeconomic status. Given the results of the logistic regression pointing to insurance and race as predictors of the decision made, it is imperative to recognize the modifier effects of socioeconomic status on each of these variables. Therefore, information about gross household income, occupation, resource availability, and household size and composition should be included in any future studies.

Conclusions

Overall, our study was able to establish that low-risk patients' motivations for proceeding with NIPS are mostly consistent with previously identified motivations for NIPS in the high-risk population. Most low-risk patients prioritized genetic condition information and identified insurance coverage as a common secondary motivator for testing, regardless of

if they were informed or uninformed decision makers. Instead, differences between decision makers were demonstrated in the value placed on testing safety through avoidance of invasive procedures and the influence of family and friend desires. Together, these identified similarities with the high-risk population and differences between decision makers confirms the necessity of complete pre-test counseling on the benefits and limitations of NIPS for low-risk patients. Furthermore, the identification of a low-risk group prioritizing fetal sex was identified, but this motivation was not associated with uninformed decision making. Therefore, pre-test counseling, when fetal sex is identified as a motivator, should emphasize the primary purpose of aneuploidy risk assessment and the difference between sex and gender, but not necessarily result in NIPS deterrence. Finally, future studies should weigh different variables that may better predict decision making, such as pre-testing model and socioeconomic status, as well as take a critical look at how and if informed choice can be accurately measure in the prenatal patient population.

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