

## ORIGINAL ARTICLE

## Exploring prenatal testing preferences among US pregnant individuals: A discrete choice experiment

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**Funding information**

National Society of Genetic Counselors; NIHR Bristol Biomedical Research Centre; Wellcome Trust

**Abstract**

Although there are numerous benefits to diagnostic prenatal testing, such as fetal exome sequencing, there are also consequences, including the possibility of receiving variants of uncertain significance or identifying secondary findings. In this study, we utilized a survey-based discrete choice experiment to elicit the preferences of pregnant people in Northern California for hypothetical prenatal genomic tests. Pregnant individuals were invited to complete the survey through advertisements on social media. Five test attributes were studied: likelihood of getting a result, time taken to receive results, who explains results, reporting of uncertain results, and reporting of secondary findings. The survey also gathered information about the participants' demographics, current and past pregnancies, and tolerance of uncertainty using the IUS-12 scale. Participants were eligible if they were female, currently 24 or more weeks pregnant, and able to read/write enough English or Spanish to complete an online survey. Overall, participants ( $n=56$ ) preferred the option of having a prenatal test over not having a prenatal test ( $p < 0.01$ ) and had substantially higher preferences for tests with the highest likelihood of getting a result ( $p < 0.01$ ). There were also positive preferences for tests that reported secondary findings ( $p = 0.01$ ) and those where results were returned by a genetic specialist (vs. their prenatal provider) ( $p = 0.04$ ). These findings can be used to guide conversations between pregnant individuals and genetics specialists, such as genetic counselors, as they weigh the pros and cons of diagnostic prenatal testing options.

**KEYWORDS**

decision-making, prenatal diagnosis, uncertainty

**1 | INTRODUCTION**

During pregnancy, pregnant individuals face multiple sources of uncertainty, many of which relate to the baby's health and well-being. Routine tests, such as ultrasounds, oftentimes provide reassurance that a pregnancy is developing normally. However,

routine fetal ultrasounds can also detect structural anomalies, which occur in approximately 3% of pregnancies, leading to questions about the baby's development (Centers for Disease Control and Prevention, 2008). When an ultrasound anomaly is detected, parents must decide if they would like to pursue diagnostic testing to gain more information. The decision about whether or not to

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test can be challenging. Many diagnostic tests require an invasive test, either chorionic villus sampling or amniocentesis, which carry a small (<1%) risk of miscarriage (Salomon et al., 2020). If invasive testing is carried out, parents face additional decisions about the type of genomic analysis performed on the sample; these can vary by factors such as diagnostic yield, turnaround time, and clarity of the results. Historically, prenatal genomic testing was limited to the karyotype. With 99% sensitivity and specificity for aneuploidy and a relatively quick turnaround time of less than 2 weeks, karyotyping can reliably detect most pregnancies affected by aneuploidy and large chromosomal deletions/duplications (Jelin et al., 2019). However, aneuploidy and large chromosomal abnormalities explain only about 33% of ultrasound anomalies (Hopkins et al., 2020). In pregnancies with a normal karyotype, chromosomal microarray analysis (CMA), which is currently the most common test used in prenatal diagnosis, improves the diagnostic yield by 8%–12% due to its ability to identify much smaller microdeletions and microduplications in addition to aneuploidies and large chromosomal abnormalities (Patterson et al., 2021; Vestergaard et al., 2013). CMA offers this higher diagnostic yield while still having a turnaround time comparable to that of the karyotype (Jelin et al., 2019). Exome sequencing is a newer technology that examines the coding regions of the genome. This test is being used in prenatal diagnosis with increasing frequency, and studies report diagnostic yields ranging from 10% for unselected groups up to 80% in cohorts with very defined eligibility (Becher et al., 2020; Best et al., 2017).

There are numerous benefits of receiving a definitive diagnosis during pregnancy; these include the ability to counsel parents on prognosis, guide parents through decision-making about pregnancy outcomes, and make plans for delivery and postnatal care (Castleman et al., 2021; Richardson & Ormond, 2018). However, not all prenatal genomic testing results in a diagnosis. Beyond the safety of the procedure, which is paramount for many parents, one major concern with in-depth genomic testing such as CMA or exome sequencing is the range of results that can be produced. Specifically, fetal exome sequencing leads to variants of uncertain significance (VUS) in ~20% of cases, and secondary findings, genetic test results that are not related to the abnormal ultrasound finding, in ~3% of cases (Becher et al., 2020). Rather than providing reassurance, these uncertain results and secondary findings may lead to parental confusion and anxiety (Lou et al., 2020). As the prenatal testing landscape shifts, pregnant individuals must weigh these additional factors while making a decision about what test to undergo. Therefore, it is important for prenatal healthcare providers to understand the general preferences and priorities of pregnant individuals to help guide them through this decision-making process around undergoing prenatal genomic testing.

One method used to study preferences for specific characteristics of medical interventions, such as genetic tests, is the discrete choice experiment (DCE). In DCEs, study participants are repeatedly asked to choose between two hypothetical alternatives, each of which is described by the same set of attributes fixed at different

### What is known about this topic

There are numerous prenatal genomic tests that are utilized to learn more about the health of a pregnancy. These tests vary by factors including diagnostic yield, turnaround time, and clarity of the results.

### What this paper adds to the topic

Pregnant individuals have preferences for specific factors of prenatal genomic tests, such as whether or not a test includes reporting of secondary findings. Preferences for specific test factors vary by characteristics such as comfort with uncertainty.

levels. Due to the systemic design of the DCE, statistical analyses can infer the participant's preferences for specific levels of the attributes based on their responses to the choice sets (Viberg Johansson et al., 2019). This study aimed to capture the prenatal genomic testing preferences of pregnant individuals in Northern California using an online DCE survey. This preference data can help guide conversations with pregnant people while they make decisions about their pregnancies.

## 2 | METHODS

This study surveyed pregnant individuals in Northern California about their hypothetical prenatal testing preferences using a DCE approach. We utilized a modified survey that was developed for a larger, international study addressing uncertainty in prenatal diagnosis (Buchanan et al., 2022). The design, conduct, and analysis of the DCE survey followed good practice guidelines (Bridges et al., 2011; Lancsar & Louviere, 2008). IRB approval for the survey and all methodology was obtained from Stanford University's Research Compliance Office (Protocol #57961).

### 2.1 | Subjects and recruitment

Eligible participants were individuals of female sex between ages 18 and 47 who were currently 24 or more weeks pregnant and who could read enough English or Spanish to complete an online survey. The eligibility criterion of being 24 or more weeks pregnant was used to prevent any influence the study may have had on participants' pregnancy decisions. At this point in pregnancy, participants were expected to have already undergone routine prenatal testing, including ultrasounds (usually offered through week 20), and no longer had the option to terminate their pregnancies (legal until week 24 in California, where the study was conducted). We

recruited participants in nine Northern California counties (Alameda, Contra Costa, Marin, Napa, San Francisco, San Mateo, Santa Clara, Solano, and Sonoma) through online advertisements on Facebook that linked to the online survey; both the advertisements and survey were available in English and Spanish. Participants reviewed an online consent form and continued to the survey if interested. Once the survey was complete, participants could click a link to a second survey that collected their email address for the provision of \$2 online gift cards as compensation. The survey was open between November 2020 and March 2021.

## 2.2 | Questionnaire design

The survey used in this study was a modified version of the survey designed for the larger, international study, which examined preferences in new parents (having had a child within the past 24 months) in the US, Australia, China, Denmark, the Netherlands, Singapore, Sweden, and the UK (Buchanan et al., 2022). Modifications to the original survey included changes to eligibility and demographic questions to fit the study population and minor changes to questions about the participants' current and past pregnancies. The background information about prenatal testing, the hypothetical situation presented to participants, and the descriptions of the five attributes were not modified from the survey used in the Buchanan et al. (2022) study (Table S1). The ranking of prenatal testing attributes and the DCE choice task component of the survey was also not modified. The modified 50-question survey included four sections: (1) survey eligibility and demographic questions; (2) ranking of prenatal testing attributes and DCE choice tasks; (3) the IUS-12 (Carleton et al., 2007), described below; and (4) questions about the respondent's current and past pregnancies (e.g., use of IVF, prior miscarriages, and use of genetic testing).

Briefly, the attributes studied in the Buchanan et al. (2022) study DCE were selected using a two-phase approach. In Phase 1, potential attributes were gleaned from a literature review and semi-structured interviews with parents and health professionals. In Phase 2, the list of potential attributes was systematically reduced to five: the likelihood of getting a result, the time taken to receive results, who explains results, reporting of uncertain results, and reporting of secondary findings (Hammond et al., 2022). As described in Buchanan et al. (2022), the choice sets were generated using Ngene (Choice Metrics 2018), selecting for a d-efficient design with level balance (each level appears an equal number of times) and no level overlap (no repetition of attributes). This design was based on an 8% opt-out rate.

After completing the survey eligibility and demographic questions and prior to completing the DCE portion of the survey, participants were asked to rank the five test attributes, plus one additional attribute (the safety of the test), in order of importance, with 1 being the most important and 6 being the least important. The safety of the test (the lowest risk of miscarriage) was not included in the DCE because all test options were described as "invasive" and carrying a

0.5% risk of miscarriage. Participants were then presented with the following hypothetical situation:

"A pregnant woman goes for her routine 20weeks ultrasound scan at the hospital to check the development of the baby. During the appointment, something is seen on the scan. This may indicate that the baby has a genetic condition. This may impact on the baby's health and/or development. The couple are offered invasive testing to try to find out if the baby has a genetic condition. Invasive tests have a small risk of miscarriage (around 0.5%, or around 1 in 200)."

Following this vignette, participants were asked to complete a total of 13 DCE choice tasks, including one choice task that served as an internal consistency check. The five attributes and their respective levels used to describe the tests are listed in Table 1A. For each choice task, participants chose between the options of Test A, Test B, or "no test". The option of selecting "no test" was then removed, and participants were asked to make a forced choice between Tests A and B (Table 1B).

The 12-item Intolerance of Uncertainty Scale (IUS-12) is an abbreviated version of the 27-item Intolerance of Uncertainty Scale (IUS-27), which was developed by Freeston et al. (1994) to measure intolerance of uncertainty, an important component of worry and anxiety. It has been demonstrated that the IUS-12 highly correlates

TABLE 1 DCE attributes, levels, and example choice set.

(A) DCE attributes and levels		
Attribute	Levels	
Likelihood of getting a result	5%, 30%, 60% of cases	
Time taken to receive a result	1, 2, 4 weeks	
Who explains the result	Genetics specialist, Maternity care provider	
Uncertain results	Reported, Not reported	
Secondary findings	Reported, Not reported	
(B) Example choice set		
Attribute	Test A	Test B
Likelihood of getting a result	30 out of 100 cases (30% of cases)	5 out of 100 cases (5% of cases)
Time taken to receive a result	4 weeks	2 weeks
Who tells you about your result	Maternity care provider	Genetics specialist
Uncertain results	Reported	Not Reported
Secondary findings	Reported	Not Reported
Which test would you prefer?		
Test A <input type="checkbox"/>	Test B <input type="checkbox"/>	No test <input type="checkbox"/>
If "No test" is not an option, which test would you prefer?		
Test A <input type="checkbox"/>	Test B <input type="checkbox"/>	

with the IUS-27 as well as other measures of anxiety and worry, and its reliability and validity have been studied in multiple populations (Carleton et al., 2007; Khawaja & Yu, 2010; Kretzmann & Gauer, 2020; Wilson et al., 2020). The IUS-12 also captures two subscales: prospective intolerance of uncertainty (fear and anxiety based on future events) and inhibitory intolerance of uncertainty (uncertainty inhibiting action or experience). This measure presents 12 statements about uncertainty and collects responses on a 5-point Likert scale ranging from 1 ('not at all characteristic of me') to 5 ('entirely characteristic of me'). The IUS-12 total score is a sum of all responses, with a minimum of 12 and a maximum of 60; the higher the score, the higher the participant's intolerance of uncertainty. A high intolerance of uncertainty score suggests the participant is less comfortable with uncertainty (Carleton et al., 2007). Various studies have reported mean IUS-12 total scores between 25.85 and 38.70 for the general population, scores as low as 19.55 for individuals who screened negative for psychological disorders, and scores between 35.96 and 36.76 for individuals with generalized anxiety disorder and other psychological disorders (Carleton et al., 2007; Khawaja & Yu, 2010; Kretzmann & Gauer, 2020; Wilson et al., 2020). IUS-12 prospective and inhibitory anxiety scores are the sums of responses to the 7 prospective anxiety and 5 inhibitory anxiety statements. The IUS-12 portion of the study was not modified.

The modified survey was translated to Spanish by fluent individuals with clinical genetics backgrounds, then translated back to English to check the accuracy of the translation. Participants were given the option to take the survey in either English or Spanish. The survey was administered via Qualtrics (Version: November 2020–February 2021), which is a survey software used to design, distribute, and analyze surveys online.

### 2.3 | Statistical analysis

Data was analyzed using R Software (Version: R 4.0.3) (R Core Team, 2020). Descriptive statistics were used to describe participant

demographic characteristics, IUS-12 responses, and pregnancy details. The DCE choice task data was analyzed using a conditional logit regression model in R, based on methods previously described (Therneau, 2022). As in Buchanan et al. (2022), all attributes were effects-coded to allow estimation of each attribute level given a mean effect of zero, and a constant term was included to model the choice of "no test." The coefficients generated by this model represent the relative preference weights for each attribute level included in the DCE. Positive coefficients indicated a positive preference, and negative coefficients indicated a negative preference. The coefficients were considered statistically significant when  $p < 0.05$ . We hypothesized that coefficients would be positive for the options of Test A and Test B, meaning participants preferred one of the two testing options over the option of no test. We also expected positive coefficients for the highest likelihood of getting a result (60%) and the shortest test turnaround time (1 week). The estimated preference weights were used to determine the relative importance of each attribute by calculating the difference between the highest and lowest preference weights for each attribute. The importance values were then normalized using an attribute-based normalization based on the overall importance of the likelihood attribute (Gonzalez, 2019).

## 3 | RESULTS

### 3.1 | Participant characteristics

In total, 387 individuals clicked the link to open the survey, 103 individuals met eligibility criteria and began the survey, and all surveys that had at least 80% completion, with all the DCE choice tasks completed, were included in the data analysis. This led to a final sample size of 56 individuals (Figure 1). The survey took approximately 17–18 min to complete on average.

The demographic characteristics of the participants are detailed in Table 2. All 56 participants were of female sex, between

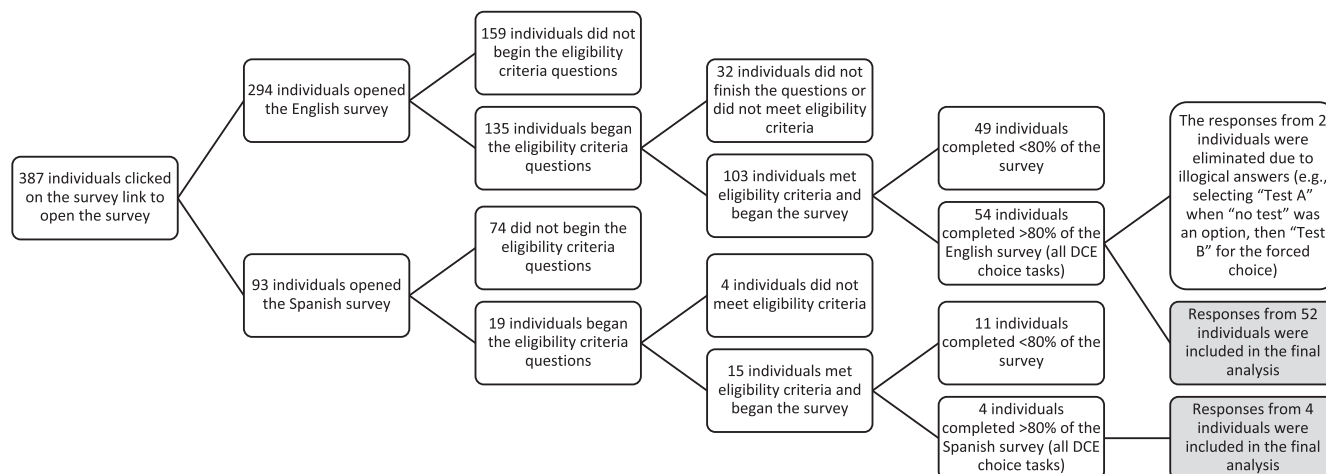


FIGURE 1 Responses included in the final analysis.

TABLE 2 Demographics of study participants.

	Total (n = 56)
Age in years	
Mean (SD)	32.8 (5.07)
Weeks pregnant	
Mean (SD)	27.9 (4.1)
Ethnicity	
White	28 (50.0%)
Asian	17 (30.4%)
Mixed race	6 (10.7%)
Other	4 (7.1%)
Black	1 (1.8%)
Spanish/Hispanic/Latina	
No	47 (83.9%)
Yes	9 (16.1%)
Highest education level	
Less than high school graduate	2 (3.6%)
High school graduate	8 (14.3%)
Some college or university, including associate's degree	7 (12.5%)
University/College degree and above	39 (69.6%)
Religious faith	
None	25 (44.6%)
Christian (any form)	19 (33.9%)
Hindu	5 (8.9%)
Buddhist	1 (1.8%)
Jewish	1 (1.8%)
Muslim	1 (1.8%)
Other	4 (7.1%)
Level of religiosity	
Not very religious	37 (66.1%)
Fairly religious	15 (26.8%)
Very religious	3 (5.4%)
N/A	1 (1.8%)
Number of children (not including current pregnancy)	
0	34 (60.7%)
1	14 (25.0%)
≥2	8 (14.3%)

ages 18 and 47 (mean=32.8years old), and currently pregnant (mean=27.9weeks pregnant). The majority of participants were white (50.0%) or Asian (30.4%) and non-Hispanic (83.9%). Four participants (7.1%) completed the survey in Spanish; since the pattern of preferences did not change when these subjects were removed from analysis, we maintained them in the primary data set.

For 34 of the participants (60.7%), their current pregnancy was their first pregnancy, and there was not a statistically significant difference in the number of children prior to the current pregnancy between older and younger mothers (Student's *t*-test,  $p=0.26$ ).

Thirty-nine of the participants (72.2%) reported having undergone Down syndrome screening in their current or past pregnancies, but only one participant reported having undergone an invasive test (amniocentesis/CVS). Eleven participants (20.4%) reported that they had previously received prenatal test results that caused uncertainty. No participants reported receiving results about the baby's health that led them to terminate a pregnancy. Eight participants (14.8%) reported using in vitro fertilization to achieve current or past pregnancies, and six participants (11.1%) reported being affected by or being related to someone affected by a genetic condition (Table S2).

### 3.2 | Intolerance of uncertainty

Fifty-four participants completed the IUS-12 (Table S3); IUS-12 total scores ranged from 20 to 53. The mean IUS-12 total score was 33.0 (SD=8.0), and the mean prospective and inhibitory anxiety scores were 21.4 (SD=4.5) and 11.5 (SD=4.4), respectively.

### 3.3 | Ranking of prenatal test attributes

The majority of participants ranked safety (87.5%) or the greatest likelihood of getting a result (73.2%) as their first or second priority (Table S4).

### 3.4 | DCE coefficients

Overall, coefficients for Test A and Test B were positive, suggesting participants preferred the hypothetical option of prenatal testing over not testing ( $p<0.01$ ). Participants chose the "no test" option 22.53% of the time. This opt-out rate was heavily influenced by seven participants who chose "no test" for all choice tasks before they were required to choose Test A or Test B in the "forced choice" task. Coefficients were positive for tests with a 60% likelihood of getting a result ( $p<0.01$ ), tests where results were returned by a genetic specialist ( $p=0.04$ ), and those that reported secondary findings ( $p=0.01$ ). This suggests participants preferred the hypothetical options of tests with the highest likelihood of getting a result, those where results were returned by a genetic specialist over their maternity care provider, and tests that reported additional information. Participants had negative preferences for tests with the lowest likelihood of getting a result ( $p<0.01$ ). Participants did not have a statistically significant preference for tests that reported uncertain findings, suggesting they did not significantly favor receiving or not receiving VUS (Table 3). The relative importance of each test attribute was determined and displayed in Figure 2. The substantial difference in relative importance between the likelihood of getting a result and all other attributes indicates that participants would trade off other prenatal test attributes, such as a shorter time taken to receive a result, for an increase in the likelihood of getting a result. The analysis was repeated excluding the

seven participants who chose “no test” for all choice tasks, and the results mirrored those described above (Table S5).

## 4 | DISCUSSION

Overall, this sample of pregnant individuals in California preferred the hypothetical option of having a prenatal genomic test over not having a prenatal test and specifically preferred prenatal tests with the highest likelihood of getting a result. Analysis also showed positive preferences for hypothetical tests that reported secondary findings and those that had results returned by a genetic specialist.

TABLE 3 DCE findings.

	Coefficient value	SE	p-Value
Alternative specific constant for Test A	0.43	0.11	0.00***
Alternative specific constant for Test B	0.35	0.11	0.00**
Likelihood (60%)	1.04	0.09	0.00***
Likelihood (30%)	-0.07	0.08	0.33
Likelihood (5%)	-0.97	0.10	0.00***
Time (1 week)	0.10	0.08	0.23
Time (2 weeks)	-0.06	0.08	0.46
Time (4 weeks)	-0.04	0.08	0.65
Who (genetic specialist)	0.11	0.05	0.04*
Who (maternity care provider)	-0.11		
Uncertain results (reported)	0.02	0.05	0.74
Uncertain results (not reported)	-0.02		
Secondary findings (reported)	0.14	0.05	0.01**
Secondary findings (not reported)	-0.14		

Note: Significance codes: <0.0001 (\*\*\*), <0.001 (\*\*), <0.05 (\*).  $n = 56$ .

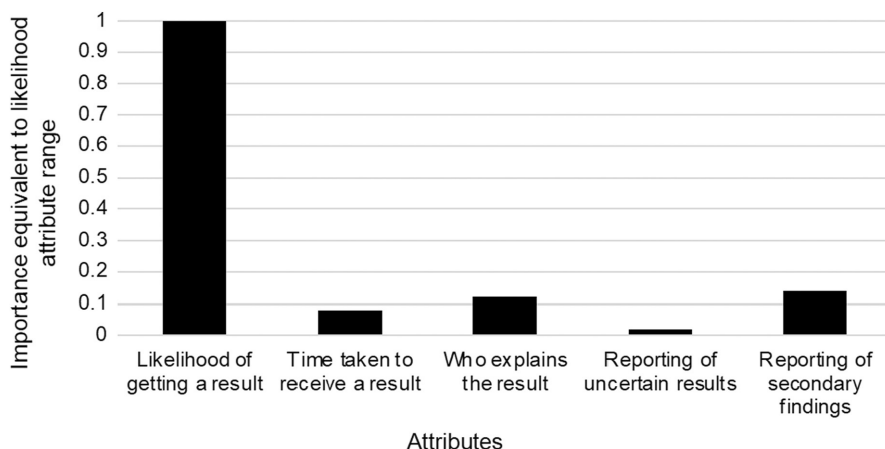


FIGURE 2 Relative importance of each test attribute. The attributes are displayed as a proportion of the “likelihood of getting a result” attribute at 60%. The substantial difference in relative importance between the likelihood of getting a result and all other attributes indicates that participants would trade off other prenatal test attributes, such as a shorter time taken to receive a result, for an increase in the likelihood of getting a result.

However, when the relative weight of participants' preferences was considered, respondents appeared to be willing to substitute any of the other test attributes for an increase in the likelihood of getting a result. These findings were supported by participants' responses to the ranking task, which showed that safety was the most important factor to participants, followed by the likelihood of getting a result. The importance of safety when considering prenatal testing options is likely a factor in why, despite the significant preferences for having a prenatal test, participants chose “no test” 22.53% of the time (compared to 7%–10% of the time in our international study). This may be reflective of the fact that the participants in this study were pregnant at the time of completing the survey and may therefore be more risk-averse when it comes to invasive testing. A decline rate of around 20% for invasive testing among high-risk pregnant individuals has been observed in other studies (Spencer, 1999). This finding is also in line with previous DCE studies looking at prenatal tests for Down syndrome that show women emphasize test safety when making decisions (Beulen et al., 2015; Hill et al., 2012, 2016). Future studies are needed to explore how varying levels of safety (e.g., amniocentesis sampling vs hypothetical cfDNA-based exome sequencing) might be traded off for varying diagnostic yields.

### 4.1 | Practice implications

Although the tests described in the DCE choice tasks were not representative of actual available testing options, the preference data from this study suggests many pregnant individuals would prefer prenatal tests with a higher diagnostic yield, irrespective of differences in the other test attributes. This is consistent with the preference data from the international study of parental prenatal testing preferences, where the key attribute affecting preferences was the test with the highest diagnostic yield (Buchanan et al., 2022). Prior studies have also demonstrated that parents in the US and UK want as much information as possible from prenatal testing, including secondary findings (Quinlan-Jones et al., 2017; Wou et al., 2018). As more data points to both the utility and preference for exome sequencing in the prenatal space, it is essential to consider a variety of clinical and ethical implications.

First, pre-test counseling must set parents' expectations appropriately. The reported diagnostic yield of prenatal exome sequencing varies greatly depending on the inclusion criteria and methodology of various studies (Best et al., 2017; Mellis et al., 2022). High diagnostic yields (up to 80%) are reported in studies that only include prenatal exome sequencing performed for fetuses with multiple structural anomalies, especially in those with brain malformations (Best et al., 2017). Higher diagnostic yields are also seen in studies where trio exome analysis (with both parents) was performed compared to only analyzing the fetal DNA (Yates et al., 2017). A much lower diagnostic yield (3.6%) was reported in a study of fetuses with isolated anomalies, including increased nuchal translucency and cystic hygroma (Wapner et al., 2017). To guide expectations, information provided around the "likelihood of getting a result" should be tailored to each pregnancy as much as is possible depending on the number and type of fetal anomalies identified and the parents' willingness to provide samples for trio exome sequencing. Expectations around test turnaround time must also be considered. Although the attribute "time taken to receive a result" was not the key attribute for decision-making for participants in this study, the processing time for exome sequencing samples is an important consideration when discussing options available to parents once they receive results (Best et al., 2017; Wou et al., 2018).

Second, pre-test counseling must address the clinical and ethical implications of findings unrelated to the primary test indication, including secondary and incidental findings. The American College of Medical Genetics and Genomics practice guidelines for the reporting of secondary findings in adult exome sequencing are relatively clear—secondary findings should be reviewed in detail during pre-test counseling, and individuals should be given the option to opt in or out. These guidelines also suggest how secondary findings should be handled for exome sequencing in children, recommending the child's best interest be prioritized and ethical points, such as preserving the child's autonomy, be considered (Miller et al., 2021). More recently, the International Society for Prenatal Diagnosis released an updated position statement on prenatal exome sequencing, acknowledging that there is no current international consensus on reporting secondary findings. This statement recommends that if secondary findings are offered, parents are consented individually, and findings for the fetus reflect serious childhood conditions (Van den Veyver et al., 2022). Discussions about reporting secondary findings in the prenatal space are ethically more complex due to the possibility of the results influencing parents' decisions to terminate a pregnancy. Pregnant individuals in this study hypothetically preferred to receive secondary findings; however, the survey did not include any information on the ethical debate surrounding this topic. If secondary findings are offered, pre-test counseling should thoroughly cover the risks and benefits (Van den Veyver et al., 2022). For example, if the trio exome increases diagnostic yield, based on this study's findings, parents would likely prefer this option. However, they then must consider the implications of secondary findings on their own health (Thompson et al., 2018). Even with proper counseling, secondary findings can be unsettling, especially when they

are the only outcome from a trio exome (Thompson et al., 2018). While dealing with the emotional impact of an uncertain pregnancy, parents may struggle in learning their own genetic risks.

Third, in-depth genomic testing will undoubtedly lead to VUS, and pre-test counseling must prepare parents for dealing with either results that themselves hold uncertainty or the uncertainty of having chosen not to receive all results. Unlike the international DCE that was conducted and prior studies of parents who have undergone the prenatal exome process (Buchanan et al., 2022; Lou et al., 2020; Wou et al., 2018), this study did not demonstrate a clear preference for or against the reporting of uncertain results in hypothetical genomic prenatal tests. Wou et al. (2018) reported that most parents who had prenatal exome sequencing wanted to know about the results even if their providers were not certain of the significance of the results. The exome sequencing in that study, however, did not include secondary findings or uncertain results, so these parents' opinions are both retrospective and hypothetical. Lou et al. (2020) interviewed parents who had received uncertain CNV results and reported that parents worried about the significance of the result but eventually adjusted to the information using various coping strategies. Long-lasting impacts of the uncertain results were also reported, including increased alertness to the child's progression through development (Lou et al., 2020). While it is likely that the incidence of VUS will decrease as variant interpretation improves (Mone et al., 2018), current practice may be best dealt with on a per-case basis depending on each parent's comfort with different types of uncertainty. As individuals with a higher intolerance of uncertainty may be drawn to exome sequencing to resolve their uncertainty, pre-test counseling for exome sequencing may discuss uncertain results as a "risk." Even for individuals who feel they have a lower intolerance of uncertainty, it may prove beneficial to discuss how anxiety normally fluctuates throughout pregnancy (da Costa et al., 1999). As anxiety and intolerance of uncertainty have been linked, there may be similar fluctuations in intolerance of uncertainty during pregnancy.

As exome sequencing is offered prenatally with increasing frequency, various studies are addressing how these challenges are best dealt with in the real world. For example, in Denmark, early implementation of exome sequencing led to a revised consent form, now stating that only pathogenic and likely pathogenic variants that likely explained the fetal phenotype and secondary findings relevant to the immediate health of the fetus or future pregnancies will be reported (Becher et al., 2020). Protocols are likely to continue to evolve as the prenatal space adapts to this new technology, however, as this study's DCE data support, one critical element must be included: thorough pre- and post-test counseling by trained genetics professionals.

## 4.2 | Study limitations

This study is limited by its small sample size, inadequate diversity (majority white, highly educated, non-Hispanic participants), and

restricted geographic location. This study's sample is also largely agnostic, with 66.1% of participants reporting that they are "not very religious." Prior studies have shown that religious beliefs influence pregnancy decisions in the US (Frohworth et al., 2018), and this was likely not captured in this sample. Furthermore, the participants' gender identities were not collected, preventing the identification of differences in preferences between cis women, trans men, and individuals of other gender identities. Responses to all questions on a page were required in order for participants to move forward to the next section of the survey, which may have limited the information collected. Given the sensitive nature of questions about demographics and past pregnancies, participants may have dropped off the survey if not given the ability to opt out of answering a question or may have provided an incorrect answer. The DCE methodology has additional limitations, including that it does not offer insight into why participants answered the way they did (e.g., Why did pregnant individuals prefer the reporting of secondary findings but have no preference for reporting uncertain results?). Future qualitative research is needed to explore these questions further. The study is also hypothetical in nature, which may affect the authenticity of participant responses and may not reflect the decisions made by people in real life.

Furthermore, there are limitations in the comparisons between this study and the international study by Buchanan et al. (2022). Most importantly, the recruitment methods were different between the two studies. In the Buchanan et al. (2022) study, potential participants were people who were already signed up with a marketing company, while in this study, participants were invited to take part in a survey in isolation through Facebook. The survey used in this study was also slightly longer, as there were some additional demographic questions added to the version of the survey used in the Buchanan et al. (2022) study. For these reasons, participants in the Buchanan et al. (2022) study may have been more inclined to complete the online survey. These methodological differences may explain the variance in attrition rate between the two studies, which was 85% (331/387) in this study compared to 43% (951/2190) in the Buchanan et al. (2022) study.

Lastly, data collection took place during the COVID-19 pandemic, and this could have influenced people's intolerance of uncertainty in unknowable ways.

## 5 | CONCLUSION

This study highlights the importance of diagnostic yield, or a prenatal test's "likelihood of getting a result," to pregnant individuals in the US when considering hypothetical prenatal genomic testing options. This strong preference, which overshadowed preferences for any other prenatal test attribute in this study, suggests that pregnant individuals may choose prenatal genomic tests that provide the most information, including information that is unexpected or uncertain. Here, we expose a potential conflict: people who are seeking clarity by selecting tests with the highest

diagnostic yield may request testing that leads to uncertain information. This underscores the importance of ensuring individuals are forewarned that prenatal genomic tests may not result in a diagnostic finding and may lead to further uncertain results. Such results might not help in pregnancy decision-making and may lead to anxiety due to unresolved uncertainty. Genetic and obstetric specialists should therefore include conversations about tolerance of uncertainty in their pre-test counseling with pregnant individuals seeking prenatal genomic testing. Moving forward, as new screening options enter the market, such as non-invasive prenatal testing (NIPT) with deletion/duplication and whole genome detection capabilities, additional anticipatory guidance by genetics specialists may help pregnant people make the best decisions for themselves during their pregnancies. Furthermore, there is a continuing need for additional education for both providers and patients on the range of possible results from this type of screening. Even if a screening or test option is touted as being highly accurate, the clinical implications of the results may still be unclear and/or unactionable as we continue to understand the impact of genetic variants on human health.

## AUTHOR CONTRIBUTIONS

**Jennifer Siranosian:** Conceptualization, Methodology, Software, Formal analysis, Investigation, Data Curation, Writing – Original draft preparation and Reviewing and Editing, Visualization, Funding acquisition. **Celine Lewis:** Conceptualization, Methodology, Writing – Reviewing and Editing, Funding acquisition. **Melissa Hill:** Conceptualization, Methodology, Writing – Reviewing and Editing, Validation. **Kelly E. Ormond:** Conceptualization, Methodology, Writing – Reviewing and Editing, Supervision. Author Jennifer Siranosian confirms that they had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. All of the authors gave final approval for this version to be published and agreed to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

## ACKNOWLEDGMENTS

This project was completed in partial fulfillment of the first author's degree requirements. Funding was provided by the National Society of Genetic Counselors Prenatal Special Interest Group for this project. The broader international project from which this study was derived (Buchanan et al., 2022) was funded by a Small Grant in Humanities and Social Science from the Wellcome Trust, a research charity based in London, UK (Celine Lewis, PI). Celine Lewis is funded by an NIHR Advanced Fellowship (NIHR300099). The views expressed are those of the author(s). Open access funding provided by Eidgenössische Technische Hochschule Zurich. Jehannine Austin served as action editor on this paper.

## CONFLICT OF INTEREST STATEMENT

Jennifer Siranosian, Celine Lewis, Melissa Hill, and Kelly E. Ormond declare that they have no conflict of interest.



## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## ETHICS STATEMENT

Human studies: This study was reviewed and approved by the Stanford University's Research Compliance Office (Protocol #57961). All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000.

Informed consent: Implied informed consent was obtained for individuals who voluntarily completed the online survey and submitted their responses.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

**How to cite this article:** Siranosian, J., Lewis, C., Hill, M., & Ormond, K. E. (2023). Exploring prenatal testing preferences among US pregnant individuals: A discrete choice experiment. *Journal of Genetic Counseling*, 00, 1–10. <https://doi.org/10.1002/jgc4.1777>