HHS Public Access

Author manuscript

Genet Med Open. Author manuscript; available in PMC 2024 December 04.

Published in final edited form as:

Genet Med Open. 2024 ; 2: . doi:10.1016/j.gimo.2024.101890.

Factors affecting couples' decision making about expanded prenatal cell-free DNA screening

Kelsey Mumford[1], **Saskia Hendriks**[1], **Skye Miner**[2], **Chloe O. Huelsnitz**[3,4], **Paul Wakim**[5], **Benjamin E. Berkman**[1,*]

[1]National Institutes of Health Department of Bioethics, Bethesda, MD

[2]RAND Corporation, Boston, MA

[3]National Cancer Institute Division of Cancer Control and Population Sciences, Bethesda, MD

[4]National Cancer Institute Division of Cancer Epidemiology and Genetics, Bethesda, MD

[5]National Institutes of Health Clinical Center Biostatistics and Clinical Epidemiology Service, Bethesda, MD

Abstract

Purpose: To assess intended parents' preferences about expanded prenatal cell-free DNA screening.

Methods: A survey was administered to couples who were pregnant or trying to conceive. Partners within couples were independently asked about willingness to seek prenatal cell-free DNA screening for diseases and traits that varied by severity, treatability, age of onset, and reliability. Additional questions explored couples' decision-making processes and how various factors would affect those decisions.

Results: Respondents (n = 494) were most likely to seek a prenatal genetic test when the test is completely predictive (P value of predictability effect = .0116), for earlier onset (P value of onset effect = .0310), treatable diseases (P value of treatability effect = .0032), and of highest severity (P value of severity effect < .0001). Living in states where termination was not available was not associated with decreased interest in prenatal screening, with 45% reporting that it would make them more likely to seek testing. There was moderate concordance between couples about their

*Correspondence and requests for materials should be addressed to Benjamin E. Berkman, National Institutes of Health Department of Bioethics, 10 Center Drive, Suite 1C118, Bethesda, MD 20892. berkmanbe@mail.nih.gov.

Author Contributions

Conceptualization: B.B., S.H., S.M., C.H., K.M.; Data Curation: K.M., B.B.; Formal Analysis: P.W.; Investigation: K.M., B.B.; Methodology: B.B., P.W.; Resources: P.W.; Software: P.W.; Visualization: K.M., B.B., P.W.; Writing-original draft: K.M., B.B.; Writing-review and editing: K.M., B.B., S.H., S.M., C.H., P.W.

Ethics Declaration

The research protocol was deemed to be exempt from full Institutional Review Board (IRB) review by the NIH Intramural IRB (IRB00011862). The data were deidentified before analysis.

Conflict of Interest

The authors declare no conflicts of interest.

Additional Information

The online version of this article (https://doi.org/10.1016/j.gimo.2024.101890) contains supplemental material, which is available to authorized users.

testing decisions and the majority of pregnant persons (68.8%) and partners (66.7%) desired firm screening recommendations from their doctors.

Conclusion: These data suggest that couples are highly information seeking when presented with all testing options neutrally, but most desire to be presented with firm testing recommendations from their clinician.

Keywords

Bioethics; cfDNA; Prenatal testing

Introduction

Prenatal cell-free DNA (cfDNA) screening for a limited number of serious genetic disorders has been widely adopted in the United States.[1] Expanded prenatal cell-free genome sequencing will likely soon be offered in clinical settings as testing technologies evolve.[2–4] The breadth of newly available prenatal genetic information (eg, adult-onset diseases, nonmedical traits) and the potential for results to be returned before legal limits around pregnancy termination in certain states will raise ethical questions related to whether there should be limits on the information offered to patients and how best to support patients' decision making (eg, preserving a child's right to an open future, genetic determinism).[5]

Existing research about the limited prenatal cfDNA screening currently being offered to patients has shown that pregnant persons and their partners value having the choice to learn about their fetus's genetic risks and tend to hold similar views about prenatal cfDNA screening.[6–11] More recently, studies have investigated the views of obstetrician-gynecologists, pregnant persons, and the general public about the expansion of prenatal cfDNA screening,[12–15] but there has been limited investigation into which specific categories of information partners of pregnant persons would be willing to seek or the factors that affect this decision-making process. Furthermore, limited data describe the preferences of pregnant persons' romantic partners on expansion of prenatal cfDNA screening, despite research which shows that partners want to be involved in the decision-making process,[10] and that pregnant partners value their partners' involvement.[16] Although previous studies investigated couples' decision making about preimplantation genetic diagnosis and current prenatal cfDNA screening, they have largely focused on the reproductive decisions the couples would make rather than on the decision-making process that went into making those decisions,[7,16,17] and many only included couples at high risk for specific genetic diseases.[18,19] In one Nigerian study that did examine couple concordance in decision making, concordance ranged from poor for agreement about wives' amount of power in decision making regarding sexual and reproductive issues to strong on perceptions of each other's references about such issues, suggesting that couples' decision-making concordance can vary considerably across contexts and issues.[20]

Given these gaps in the literature, this article (1) surveys the independent views of both partners about the effect of 4 variables (disease/trait onset, severity, treatability, and test predictiveness) on their willingness to seek a prenatal cfDNA screening test and (2) explores the concordance between partners about willingness to seek testing. Additionally, ancillary

questions were posed to the partners to elicit more detail about how they would make testing decisions. These data can then inform clinicians and policy-makers in the development of guidance to help intended parents navigate decisions about expanded prenatal testing.

Materials and Methods

Population

Study participants were English-speaking, US adult couples who self-reported currently being pregnant or planning to get pregnant in the next 18 months. Participants were recruited from a national Qualtrics panel. To approximate the racial and ethnic demographic distribution of the US population, cohorts were capped based on the proportions reported by 2020 census data. Respondents were excluded if they returned an incomplete survey, filled out the survey in less than 60% of the median time to completion (determined during the survey soft launch), or had substantially discordant responses about the length of their relationship. The sample size needed to detect a 3% difference between partners in a couple for desiring to test for certain genetic information with an alpha of 0.05 and power of 90% was 141 couples. However, given uncertainty surrounding the appropriate effect sizes due to a lack of similar studies in the literature and to enhance our ability to answer secondary research questions, a larger sample was pursued.

Survey development

The survey instrument was designed for this study based on a literature review and was revised after feedback by colleagues with survey expertise from the US National Institutes of Health Department of Bioethics. The survey was pilot tested in 10 couples of reproductive age from diverse socioeconomic backgrounds to improve clarity and user comfort. The revised survey was soft launched; 10 couples' responses were analyzed for any systematic confusion about the wording of questions within the survey before further response collection and to establish the speed check exclusion threshold.

In the survey, participants were provided with information about expanded prenatal genome sequencing and how it differs from the prenatal cfDNA screening options currently being offered in the United States (see Supplemental Appendix 1). They were then presented with a series of vignettes that described the characteristics of a hypothetical prenatal cfDNA screening test and were asked whether they would want to have this screen done if it was available (see Supplemental Appendix A). Based on existing literature, 4 variables, each with 3 or 4 levels, were chosen to vary across the vignettes: timing of disease/trait onset (prenatally, in childhood or in adulthood), severity of the disease/trait (fatal, serious, mild, or nonmedical trait), whether the disease/trait can be treated/changed (treatable, partially treatable, or not treatable), and how much certainty the test provides about the disease/trait (100% predictive, highly predictive or somewhat predictive) (Supplemental Table 1).[12,14,21] The power analysis was based on comparing the percentages of those who would agree to seek the information at the different levels of each characteristic of the disease. Each couple was assigned to view 8 randomly drawn vignettes out of 108 possible vignette options (accounting for each scenario of 3 categories with 3 options each and 1 category with 4 options); individuals within each couple received an identical set of vignettes.

Our first primary outcome was the predicted probability of seeking a prenatal genetic test per variable. Our second primary outcome was the degree of partners' concordance about willingness to seek testing. To gain a better understanding of the factors that went into their decision making, additional questions exploring a range of topics unrelated to a specific vignette were asked (ie, whose opinions would be sought, impact of cost and ability to terminate, how they would make decisions with their partners).

Survey dissemination

The survey was administered electronically in February and March 2023 as a single instrument with 2 distinct halves. The pregnant person attested that they would answer the first half of the survey independently and that their partner was immediately available to take the second half of the survey. The partner also attested that they were not the pregnant person and that they were answering independently. Partners were not able to see each other's answers.

Data analysis

A logistic regression model, with clustering of the partners and of the vignettes shown to each couple, was used to determine the effect of vignette variables on the probability of a respondent's willingness to seek each genetic test. Factors included in the model were which partner was responding to the vignette and the onset, severity, treatability, and predictiveness of the test in each vignette. Additionally, a generalized linear model (with clustering of the partners) was fitted to determine the effect of 17 demographic factors on the probability of a respondent's willingness to seek each genetic test. The model was run with all two-way interactions for the demographic factors to determine which to include in the final version. The inclusion of interaction terms in models was based on their *P* value and the corresponding model's QICu (quasi-likelihood under the independence model criteria [simplified]).[22]

To determine the degree of concordance, above and beyond chance, between partners when deciding whether to seek testing, Cohen's kappa values (k) were calculated using kappa statistics for clustered matched-pair data.[23] k of less than 0.2 indicated poor, 0.2 to 0.4 indicated fair, 0.41 to 0.6 indicated moderate, 0.61 to 0.8 indicated good, and 0.81 to 1.0 indicated very good agreement.[24,25] To model whether partners agreed on desiring testing as a function of the vignette variables, a generalized linear model was fitted. To model it as a function of 40 other factors, including partner demographics and responses to other survey questions, 1 at a time, univariable linear models (with clustering of the partners) were created to show whether each factor was associated individually with higher or lower concordance between partners.

Results

Participant characteristics

A total of 969 couples began surveys, and 337 couples returned them fully completed (response rate of 35%). After removing surveys that were completed in less than 60% the

median time to completion (13.5 minutes) and those with discordant responses regarding the length of their relationship (over 10 years difference), the final sample size was 247 couples.

The survey population's median age (35 for pregnant persons/37 for partners) was older than the US median age (30) of the mother at birth (Supplemental Table 2).[26] The race and ethnicity of respondents matched census data, although respondents had higher income and educational backgrounds than the general population.[27,28] Most would not consider termination of pregnancy under any circumstances and, consistent with general population surveys, indicated religion as being important to them.[29]

Willingness to seek expanded prenatal cfDNA screening

Vignette variables' effect—All 4 vignette variables were significantly associated with willingness to seek testing. Respondents were most likely to seek more predictive testing (100% predictive = 87%, highly predictive = 85%, somewhat predictive = 84%, $\chi^2(2) = 8.91$, $P = .0116$) for earlier-onset (childhood = 87%, prenatal = 86%, adult = 84%, $\chi^2(2) = 6.95$, $P = .0310$), treatable diseases (treatable = 87%, partially treatable = 85%, not treatable = 84%, $\chi^2(2)$ 11.49, $P = .0032$) of higher severity (fatal = 88%, significant = 87%, mild = 86%, nonmedical = 81%, $\chi^2(3) = 24.92$, $P < .0001$) (Figure 1).

Reasons for/against testing—Participants were asked why they did or did not prefer testing (Table 1). Although all of the reasons provided for testing were strongly endorsed by respondents who opted for testing, the most frequently endorsed were to see if the fetus is at risk for a disease that runs in the family (94.9% of pregnant persons and 94.9% of partners rated as at least moderately important) and to be able to prepare financially, medically, and/or emotionally for the child (95%/94.3%). 87.1% of pregnant persons and 87.4% of partners who were religious and 90.7% of pregnant persons and 92.8% of partners who previously stated that they would never consider pregnancy termination for any reason still endorsed learning genetic information for the purpose of making termination decisions as being at least moderately important when faced when specific clinical scenarios in the vignettes. The most frequent endorsed reasons for not seeking testing were because they would never consider pregnancy termination based on genetic information (81.6%/75.7%) and concerns about stress and anxiety that they would experience due to learning the test results (71.2%/67.5%).

Demographic factors associated with testing—The demographic factors with the strongest evidence for being associated with a higher probability of a respondent seeking testing (Table 2; $P < .0001$ for all) include: a longer relationship length with their partner ($\chi^2(1) = 37.44$), older age of the respondent ($\chi^2(1) = 23.54$), religion being important ($\chi^2(2) = 21.48$, 90.62% (95% CI [87.64%, 92.94%]) vs 75.66% (95% CI [68.29%, 81.78%]) for not important), and the current pregnancy being planned ($\chi^2(1) = 15.19$, 93.17% (95% CI [90.63. 95.06]) vs 71.13% (95% CI [60.42, 79.91]) if unplanned).

Effects of cost and availability of termination on willingness to test—Almost half (42.9%/48.6%) of respondents reported that they would not change their decision to test, regardless of the cost of the test, and only 6.1% of pregnant persons and 8.1% of

partners reported that any testing costs would make them less likely to test (Figure 2C). Additionally, almost half (44.9%/44.5%) reported that the inability to terminate a pregnancy in their state would make them more likely to seek testing, and only 16.2% of pregnant persons and 19.4% of partners reported that inability to terminate in their state would make them less likely to seek testing (Figure 2D).

Directiveness of counseling—The majority of pregnant persons (68.8%) and partners (66.7%) desired firm recommendations from their doctors about the categories of information that the medical community thinks are most appropriate to test for (Figure 2E). Of those that desired firm recommendations, 60.6% of pregnant persons and 60% of partners still wanted to know about their whole range of options, even if they are not recommended. A minority of respondents (10.5%/13.8%) wanted to be given all options so that they could make an independent decision without input from their doctor. Participants generally were most open to being influenced by the opinions of their partner, obstetrician, professional societies, and their parents (Figure 2A). Participants were much less interested in being guided by the opinions of government or religious leaders. Participants were confident that they shared values with their partner and could engage in a rational conversation about making decisions around expanded prenatal testing (Figure 2B).

Concordance between partners

Concordance on seeking testing—The pregnant person and the partner both said they would seek testing in 1557 out of 1976 vignettes; both did not seek testing in 180 vignettes (87.9% total agreement, ie, yes/yes and no/no). There was no significant difference in the likelihood of seeking a test based on which partner was responding to a vignette ($\chi^2(1) = 3.08$, $P = .0793$). On average, the pregnant person and partner agreed on 7 out of 8 vignettes, ranging from 0 to 8 times, with a median of 8 times (63.6% of couples agreed on all 8 vignettes). There was moderate concordance between partners for desiring testing across all vignettes (k = 0.5311, 95% CI [0.4455, 0.6167]). There was no statistically significant difference in the likelihood that a couple would agree on seeking a test because of the severity ($\chi^2(3) = 2.16$, $P = .5407$), treatability ($\chi^2(2) = 0.94$, $P = .6243$), onset ($\chi^2(2) = 4.94$, $P = .0848$), or predictiveness ($\chi^2(2) = 3.42$, $P = .1812$) variables.

Concordance on reasons for/against testing—Concordance on the importance of reasons for or against testing ranged from moderate to poor (Table 1). The highest concordance among reasons for testing, although still moderate, was on seeking testing to prepare financially, medically, and/or emotionally (k = 0.463) and to inform decisions on pregnancy termination (k = 0.426). Of the reasons provided for not seeking testing, couples were moderately concordant about the importance of not trusting the health care system and not wanting testing in general (k = 0.483) and of never considering pregnancy termination due to test results (k = 0.449). Other reasons for or against seeking testing had fair to poor agreement, with the lowest agreement about the idea that it should be up to the future child to make their own decisions about whether to undergo testing (k = 0.136).

Demographic factors associated with concordance on willingness to test—Pregnant persons who self-reported being more religious had higher concordance with

their partners on willingness to test ($\chi^2(2) = 16.82$, $P = .0002$, Table 3). When asked to imagine that pregnancy termination were (hypothetically) illegal in their state, respondents who reported they would be more likely to seek testing, had higher concordance with their partners ($\chi^2(2) = 13.95$, $P = .0009$ for pregnant person and $\chi^2(2) = 14.92$, $P = .0006$ for partner). Other factors being associated with higher concordance included: the pregnant person identifying as Black compared with white ($\chi^2(2) = 11.64$, $P = .0030$), older participant age (pregnant person $\chi^2(1) = 4.16$, $P = .0413$; partner $\chi^2(1) = 4.93$, $P = .0265$), self-reporting the current pregnancy as planned (pregnant person $\chi^2(1) = 5.66$, $P = .0173$; partner $\chi^2(1) = 4.77$, $P = .0289$), and household income (pregnant person $\chi^2(5) = 13.35$, $P = .0203$; partner $\chi^2(5)$ 13.5, $P = .0191$).

Concordance on decision-making process—Partner concordance on the importance of others' opinions and how much they agreed with statements regarding their decision-making process ranged from good (k = 0.61–0.80) to fair (k = 0.21–0.40) agreement (Figure 2A and B). The statements with good concordance were those regarding the lower importance of the opinion of the government (k = 0.674), religious leaders (k = 0.615), and extended family (k = 0.599). There was moderate concordance about the opinions of the partner (k = 0.445) and obstetrician (k = 0.404) being important. Couples showed moderate concordance on the statement that if they could not agree on whether to test, the default should not be to simply not seek testing (k = 0.57) and that they would seek guidance from a doctor or genetic counselor (k = 0.547). There was the least concordance between partners on whether the participant answering the survey would be the primary decision maker on testing decisions (k = 0.282), with the pregnant persons responding "yes" more often than the partners (reflecting agreement that the pregnant person would be the primary decision maker).

Discussion

Although research has examined how individuals interact with existing prenatal cfDNA screening, this exploratory study explored how 4 variables affected each partners' decisions on seeking expanded testing, and the degree of concordance between partners on testing decisions. It also investigated what role various people and factors might play in helping individuals decide which tests to pursue.

How much did respondents want genetic information and what predicted willingness to seek testing?

Consistent with some of the existing literature,[14,30,31] our data showed that pregnant persons and their partners are highly information seeking regardless of the levels of the vignette variables shown. For example, although participants were most likely to seek highly predictive testing for earlier-onset, readily treatable diseases of higher severity, they still said that they would seek testing for adult-onset, nontreatable, or not medically related traits even when the tests themselves were only somewhat predictive. Although there was a moderate preference for more clinically acute information, the fact that respondents were highly information seeking may reflect a broader notion that more information is good within a cultural milieu of continuously increasing data generation and collection.

It may also reflect the fact that the respondents did not consider, or may not agree with, the notion that is widely held in the academic bioethics literature that pediatric genetic testing should generally be limited to tests for medically actionable, early-onset diseases to preserve the children's ability to make genetic testing decisions for themselves as an adult.[5,12,32–35] If further research suggests that the desire to seek information reflects a lack of consideration of the ethical salience of differentiating between categories of information, this would highlight an important opportunity for pretest counseling. If these results reflect a normative disagreement with bioethics commentators, this should be carefully considered. Finally, the fact that the scope of expanded prenatal cfDNA screening was recently reduced in The Netherlands because of the limited clinical implications of reporting rare autosomal trisomies and patient decisional regret further suggests that establishment of ethical guardrails related to the scope of prenatal screening in the United States might be an appropriate way to check market forces that will likely align with parental demand for more expansive genetic testing options.[36]

Our data surprisingly (given the correlation between higher religiosity and negative views on pregnancy termination[37]) demonstrated that those who reported religion as being important to them were more likely to seek testing than those who rated it as unimportant. More specifically, those who were religious or stated that they would never consider pregnancy termination were still fairly likely to endorse the importance of learning genetic information for the purpose of making termination decisions. This is not consistent with a previous finding that people who would not consider termination were generally less likely to seek prenatal genetic information.[14] Future work is needed to elucidate if the availability of expanded prenatal genetic information is shifting people's views on the range of acceptable reproductive decisions, or if views on pregnancy termination are firmer in the abstract (ie, when respondents were asked whether they would ever consider termination) than in the concrete (ie, decision making regarding a specific vignette). Furthermore, given the new categories of information that will be available through expanded prenatal testing, it will be important to investigate who is seeking which kinds of information and the reasons underlying those decisions. Existing literature that has focused on exploring testing for a very limited number of serious, early-onset diseases (eg, Down syndrome) will still be helpful as a baseline but should be reevaluated and expanded as new categories of prenatal genetic information become available to couples.[16,17]

How much partner concordance was there about seeking testing and reasons for seeking testing?

Given the massive amount of information that could be revealed by prenatal genome sequencing, there have been questions about how to manage the clinical encounter in which choices are made about which findings to seek. Navigating these complicated and ethically challenging decisions (eg, concerns about a child's right to an open future)[5,12] will be difficult under the best of circumstances but could be even harder if couples disagree. Generally, our findings suggested only moderate concordance. (The kappa statistic takes agreement by chance into account, making even 90% overall concordance fall into the moderate category.) Our data suggest that younger and lower income couples and those with

unplanned pregnancies might be less likely to agree on testing decisions, which could inform the development of additional resources for these couples.

Although couples moderately agreed on testing decisions overall, their concordance on their reasons for seeking (or not seeking) testing was only fair to low-moderate. Of the reasons with relatively higher (moderate) concordance, our findings are consistent with previous results showing that pregnant persons seek prenatal testing for preparation purposes and do not seek testing because of concerns about results causing stress or anxiety.[14] Interestingly, although partners similarly agreed on the importance of preparation, they were only half as likely as their pregnant partners to rate stress/anxiety as important. This could be because the genetic information learned could draw into question whether to consider pregnancy termination, and although both partners would typically have input into this decision, the emotional impact associated with making this choice is felt more strongly by the pregnant person whose body is directly affected by this decision.[38]

How will couples make decisions about expanded prenatal genetic testing?

Some have suggested that patients should be given an extensive menu of testing options in a nondirective manner to maximize patient autonomy.[39] Furthermore, the long-standing view in genetic counseling has been to present information to patients in a nondirective manner.[40,41] Our findings, however, suggest that couples desire more substantive guidance from their providers about which types of testing to pursue and would seek guidance from a doctor or genetic counselor over that of friends, family, the government, or religious leaders if they could not agree on what testing to seek. Our findings suggest that professional society guidance (eg, grouping prenatal genetic information into bins for providers to either recommend, not recommend, or present neutrally) could help to make testing decisions more manageable and to avoid information overload for the potential parents. Although the creation of this kind of guidance will be difficult, and potentially controversial, studies such as this one can provide evidence about the testing options that couples will (or will not) seek, and the varying reasons supporting these decisions. These data also highlight that intended parents seem to be information seeking, raising questions about how best to counsel patients regarding decision making about expanded prenatal testing.

Limitations

There are several potential limitations to the exploratory survey methodology. The pregnant person could have filled out both portions of the survey, although identity attestations and speed checks were utilized to mitigate this risk. Survey questions could have also been interpreted differently by respondents (particularly in the context of nuanced concepts, such as the distinction between testing, screening, and diagnosis), although cognitive interviewing was performed before survey distribution, and examples were provided to limit this possibility. The survey also asked respondents to make somewhat idealized hypothetical decisions, which could differ from the decisions they would actually make in a clinical setting, in which diseases can differ in the severity of their phenotypic expression and when severity cannot always be ascertained before birth. The current political climate surrounding pregnancy termination and social desirability bias[42] could have also resulted in underreporting of willingness to terminate a pregnancy. There are also potential limitations

to the respondent sample characteristics. Although the sample was representative by race and ethnicity, on average, it had a higher age and socioeconomic status than the general population—factors that are associated with increased use of prenatal cfDNA screening[8] and could limit the generalizability of the findings. Additionally, the relatively low response rate of our sample due to the number of responses that required elimination given quality concerns could result in a nonresponse bias and could also limit generalizability. However, this limitation reflects the challenge of sampling couples together using a survey format and having the larger sample size than necessary helps to mitigate these concerns. We also did not ask demographic questions about the sex, gender, or sexual orientation of respondents, which could limit generalizability. A potential limitation of the data flows from the fact that there was limited variability between couples (ie, most respondents sought testing), making it more difficult to identify statistically significant associations. We explicitly asked couples not to discuss the questions with each other while taking the survey and did not collect data about whether they had discussed prenatal genetic testing before the survey, but any previous or concurrent discussion could also have affected concordance. Finally, although we collected data from 337 couples, which is more than the 141 we initially calculated that we would need, we cannot ascertain that the sample size required for all analyses was adequate from a power analysis perspective.

Conclusion

Given the steady historical expansion of prenatal genetic testing and the recent rapid evolution of sequencing technology, it seems very likely that expanded prenatal cell-free genome sequencing will soon become clinically available. Data from projects such as this one can help to inform the thoughtful implementation of this potential paradigm shift that raises a range of ethical questions. Our data suggest that couples are largely information seeking but strongly desire expert help to guide them through the complicated clinical decision-making process about which kinds of information to seek. This will likely involve the challenging reexamination of how some long-held ethical norms should be applied in the context of this emerging technology. Couples' views were moderately concordant, which is somewhat reassuring but presents an opportunity to better understand and mitigate the particular areas in which disagreement could arise. Finally, our data suggest some surprising interactions between the shifting reproductive landscape and desire to access prenatal genetic testing (ie, that individuals identifying as religious or as against pregnancy termination in the abstract indicated that they would consider using information garnered from expanded cfDNA testing to inform termination decisions), which would benefit from further investigation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This work was completed as part of the authors' official duties as employees or fellows of the US National Institutes of Health (NIH) Clinical Center. The NIH had no role in the analysis, writing of the manuscript, or the

decision to submit it for publication. The views expressed are the authors' and do not represent the Clinical Center, the NIH, or the US Department of Health and Human Services.

Funding

This work was funded by the Intramural Research Program of the NIH Clinical Center.

Data Availability

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

References

1. Allyse MA, Wick MJ. Noninvasive prenatal genetic screening using cell-free DNA. JAMA. 2018;320(6):591–592. 10.1001/jama.2018.9418 [PubMed: 30073283]
2. Kitzman JO, Snyder MW, Ventura M, et al. Noninvasive whole-genome sequencing of a human fetus. Sci Transl Med. 2012;4(137): 137ra76. 10.1126/scitranslmed.3004323
3. International Society for Prenatal Diagnosis, Society for Maternal and Fetal Medicine, Perinatal Quality Foundation. Joint position statement from the International Society for Prenatal Diagnosis (ISPD), the Society for Maternal Fetal Medicine (SMFM), and the Perinatal Quality Foundation (PQF) on the use of genome-wide sequencing for fetal diagnosis. Prenat Diagn. 2018;38(1):6–9. 10.1002/pd.5195 [PubMed: 29315690]
4. Liu P, Vossaert L. Emerging technologies for prenatal diagnosis: the application of whole genome and RNA sequencing. Prenat Diagn. 2022;42(6):686–696. 10.1002/pd.6146 [PubMed: 35416301]
5. Donley G, Hull SC, Berkman BE. Prenatal whole genome sequencing: just because we can, should we? Hastings Cent Rep. 2012;42(4):28–40. 10.1002/hast.50
6. Biesecker BB. The psychological well-being of pregnant women undergoing prenatal testing and screening: a narrative literature review. Hastings Cent Rep. 2019;49(suppl 1):S53–S60. 10.1002/hast.1017 [PubMed: 31268571]
7. van Schendel RV, Kleinveld JH, Dondorp WJ, et al. Attitudes of pregnant women and male partners towards non-invasive prenatal testing and widening the scope of prenatal screening. Eur J Hum Genet. 2014;22(12):1345–1350. 10.1038/ejhg.2014.32 [PubMed: 24642832]
8. Di Mattei V, Ferrari F, Perego G, Tobia V, Mauro F, Candiani M. Decision-making factors in prenatal testing: a systematic review. Health Psychol Open. 2021;8(1):2055102920987455. 10.1177/2055102920987455
9. Lund ICB, Becher N, Petersen OB, Hill M, Chitty L, Vogel I. Preferences for prenatal testing among pregnant women, partners and health professionals. Dan Med J. 2018;65(5):A5486.
10. Laberge AM, Birko S, Lemoine ME, et al. Canadian pregnant women's preferences regarding NIPT for Down syndrome: the information they want, how they want to get it, and with whom they want to discuss It. J Obstet Gynaecol Can. 2019;41(6):782–791. 10.1016/j.jogc.2018.11.003 [PubMed: 30738740]
11. Watanabe M, Matsuo M, Ogawa M, et al. Genetic counseling for couples seeking noninvasive prenatal testing in Japan: experiences of pregnant women and their partners. J Genet Couns. 2017;26(3):628–639. 10.1007/s10897-016-0038-7 [PubMed: 27830353]
12. Bayefsky MJ, White A, Wakim P, et al. Views of American OB/GYNs on the ethics of prenatal whole-genome sequencing. Prenat Diagn. 2016;36(13):1250–1256. 10.1002/pd.4968 [PubMed: 27862072]
13. Fisher CF, Birkeland LE, Reiser CA, et al. Alternative option labeling impacts decision-making in noninvasive prenatal screening. J Genet Couns. 2020;29(6):910–918. 10.1002/jgc4.1191 [PubMed: 31793699]
14. Sullivan HK, Bayefsky M, Wakim PG, et al. Noninvasive prenatal whole genome sequencing: pregnant women's views and preferences. Obstet Gynecol. 2019;133(3):525–532. 10.1097/AOG.0000000000003121 [PubMed: 30741804]

15. van der Meij KRM, van de Pol QYF, Bekker MN, et al. Experiences of pregnant women with genome-wide non-invasive prenatal testing in a national screening program. Eur J Hum Genet. 2023;31(5):555–561. 10.1038/s41431-022-01248-x [PubMed: 36481825]

16. Carroll FE, Al-Janabi H, Flynn T, Montgomery AA. Women and their partners' preferences for Down's syndrome screening tests: a discrete choice experiment. Prenat Diagn. 2013;33(5):449–456. 10.1002/pd.4086 [PubMed: 23533095]

17. Birko S, Ravitsky V, Dupras C, et al. The value of non-invasive prenatal testing: preferences of Canadian pregnant women, their partners, and health professionals regarding NIPT use and access. BMC Pregnancy Childbirth. 2019;19(1):22. 10.1186/s12884-018-2153-y [PubMed: 30630440]

18. Hershberger PE, Pierce PF. Conceptualizing couples' decision making in PGD: emerging cognitive, emotional, and moral dimensions. Patient Educ Couns. 2010;81(1):53–62. 10.1016/j.pec.2009.11.017 [PubMed: 20060677]

19. Severijns Y, Heijmans MWF, de Die-Smulders CEM, et al. The effects of an online decision aid to support the reproductive decision-making process of genetically at risk couples-A pilot study. J Genet Couns. 2023;32(1):153–165. 10.1002/jgc4.1631 [PubMed: 36056622]

20. John ME, John EE, Sylvia EE. Husband-wife agreement and concordance on sexual decision making, positive self management and Health Promotion among couples living with HIV in Calabar, Nigeria. Nur Primary Care. 2018;2(3):1–6. 10.33425/2639-9474.1065

21. Kalia SS, Adelman K, Bale SJ, et al. Recommendations for reporting of secondary findings in clinical exome and genome sequencing, 2016 update (ACMG SF v2.0): a policy statement of the American College of Medical Genetics and Genomics. Genet Med. 2017;19(2):249–255. 10.1038/gim.2016.190 [PubMed: 27854360]

22. Beal D. Information criteria methods in SAS® for multiple linear regression models. Paper presented at: Proceedings of the Fifteenth Annual Conference of the SouthEast SAS Users Group; Hilton Head, SC. 2007. Accessed September 18, 2024. https://analytics.ncsu.edu/sesug/2007/SA05.pdf

23. Yang Z, Zhou M. Kappa statistic for clustered matched-pair data. Stat Med. 2014;33(15):2612–2633. 10.1002/sim.6113 [PubMed: 24532251]

24. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics. 1977;33(1):159–174. 10.2307/2529310 [PubMed: 843571]

25. Kwiecien R, Kopp-Schneider A, Blettner M. Concordance analysis: part 16 of a series on evaluation of scientific publications. Dtsch Ärztebl Int. 2011;108(30):515–521. 10.3238/arztebl.2011.0515 [PubMed: 21904584]

26. Morse A. Stable fertility rates 1990–2019 mask distinct variations by age. USCensus.gov. Accessed September 18, 2024. https://www.census.gov/library/stories/2022/04/fertility-rates-declined-for-younger-women-increased-for-older-women.html?utm_campaign=20220406msacos1ccstors&utm_medium=email&utm_source=govdelivery

27. Census Bureau releases new educational attainment data. U.S. Government Publishing Office. Accessed September 18, 2024. https://www.census.gov/newsroom/press-releases/2022/educational-attainment.html

28. Semega J, Kollar M. Income in the United States: 2021. Current population report. USCensus.gov. Accessed September 18, 2024. https://www.census.gov/content/dam/Census/library/publications/2022/demo/p60-276.pdf

29. U. S. public becoming less religious. Pew Research Center. Accessed September 18, 2024. https://www.pewresearch.org/religion/2015/11/03/u-s-public-becoming-less-religious/

30. Wou K, Weitz T, McCormack C, et al. Parental perceptions of prenatal whole exome sequencing (PPPWES) study. Prenat Diagn. 2018;38(11):801–811. 10.1002/pd.5332 [PubMed: 30035818]

31. Kalynchuk EJ, Althouse A, Parker LS, Saller DN Jr, Rajkovic A. Prenatal whole-exome sequencing: parental attitudes. Prenat Diagn. 2015;35(10):1030–1036. 10.1002/pd.4635 [PubMed: 26151551]

32. Ross LF, Saal HM, David KL, Anderson RR. American Academy of Pediatrics, American College of Medical Genetics and Genomics. Technical report: ethical and policy issues in genetic testing and screening of children. Genet Med. 2013;15(3):234–245. 10.1038/gim.2012.176 [PubMed: 23429433]

33. Committee on Bioethics. Committee on Genetics, and, American College of Medical Genetics and, Genomics Social, Ethical, Legal Issues Committee. Ethical and policy issues in genetic testing and screening of children. Pediatrics. 2013;131(3):620–622. 10.1542/peds.2012-3680 [PubMed: 23428972]

34. Garrett JR, Lantos JD, Biesecker LG, et al. Rethinking the "open future" argument against predictive genetic testing of children. Genet Med. 2019;21(10):2190–2198. 10.1038/s41436-019-0483-4 [PubMed: 30894702]

35. Miner SA, Similuk M, Jamal L, Sapp J, Berkman BE. Genomic tools for health: secondary findings as findings to be shared. Genet Med. 2022;24(11):2220–2227. 10.1016/j.gim.2022.07.015 [PubMed: 35980380]

36. WBO: the non-invasive prenatal test (NIPT) as a population screening to: the Minister of Health, Welfare and Sport. Health Council of the Netherlands. Accessed January 31, 2024. https://www.healthcouncil.nl/documents/advisory-reports/2023/02/20/population-screening-act-non-invasive-prenatal-testing-nipt-as-a-national-population-screening-programme

37. Newport F. Personal religiosity and attitudes toward abortion. Gallup. May 13, 2022. Accessed September 18, 2024. https://news.gallup.com/opinion/polling-matters/392648/personal-religiosity-attitudes-toward-abortion.aspx

38. Lee AM, Lam SK, Sze Mun Lau SM, Chong CSY, Chui HW, Fong DYT. Prevalence, course, and risk factors for antenatal anxiety and depression. Obstet Gynecol. 2007;110(5):1102–1112. 10.1097/01.AOG.0000287065.59491.70 [PubMed: 17978126]

39. Chen SC, Wasserman DT. A framework for unrestricted prenatal whole-genome sequencing: respecting and enhancing the autonomy of prospective parents. Am J Bioeth. 2017;17(1):3–18. 10.1080/15265161.2016.1251632

40. Jamal L, Schupmann W, Berkman BE. An ethical framework for genetic counseling in the genomic era. J Genet Couns. 2020;29(5):718–727. 10.1002/jgc4.1207 [PubMed: 31856388]

41. Schupmann W, Jamal L, Berkman BE. Re-examining the ethics of genetic counselling in the genomic era. J Bioeth Inq. 2020;17(3):325–335. 10.1007/s11673-020-09983-w [PubMed: 32557217]

42. Mueller J, Kirstein M, VandeVusse A, Lindberg LD. Improving abortion underreporting in the USA: a cognitive interview study. Cult Health Sex. 2023;25(1):126–141. 10.1080/13691058.2022.2113434 [PubMed: 36007884]

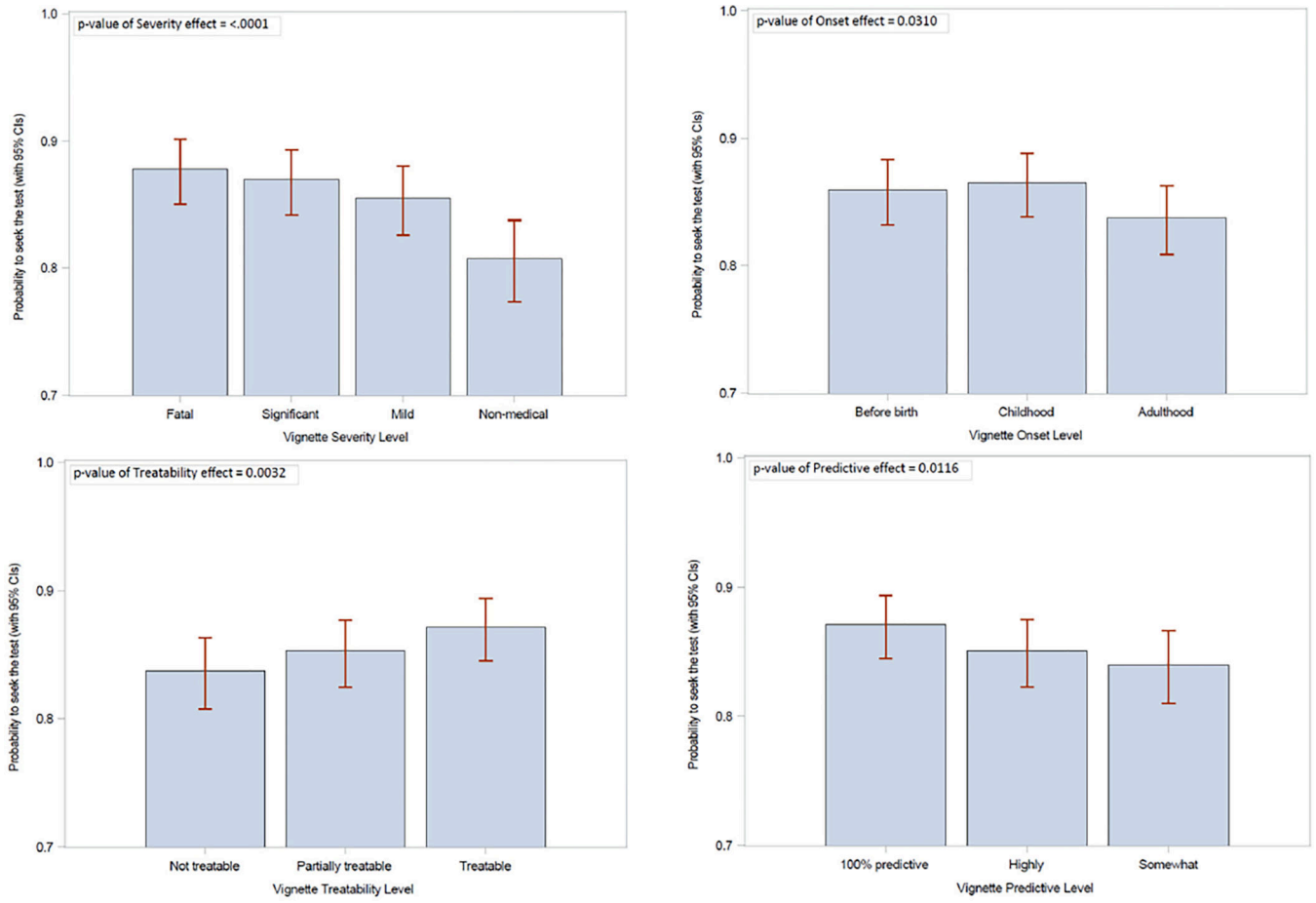

Figure 1.
Effect of vignette levels on willingness to seek a predictive genetic screen.

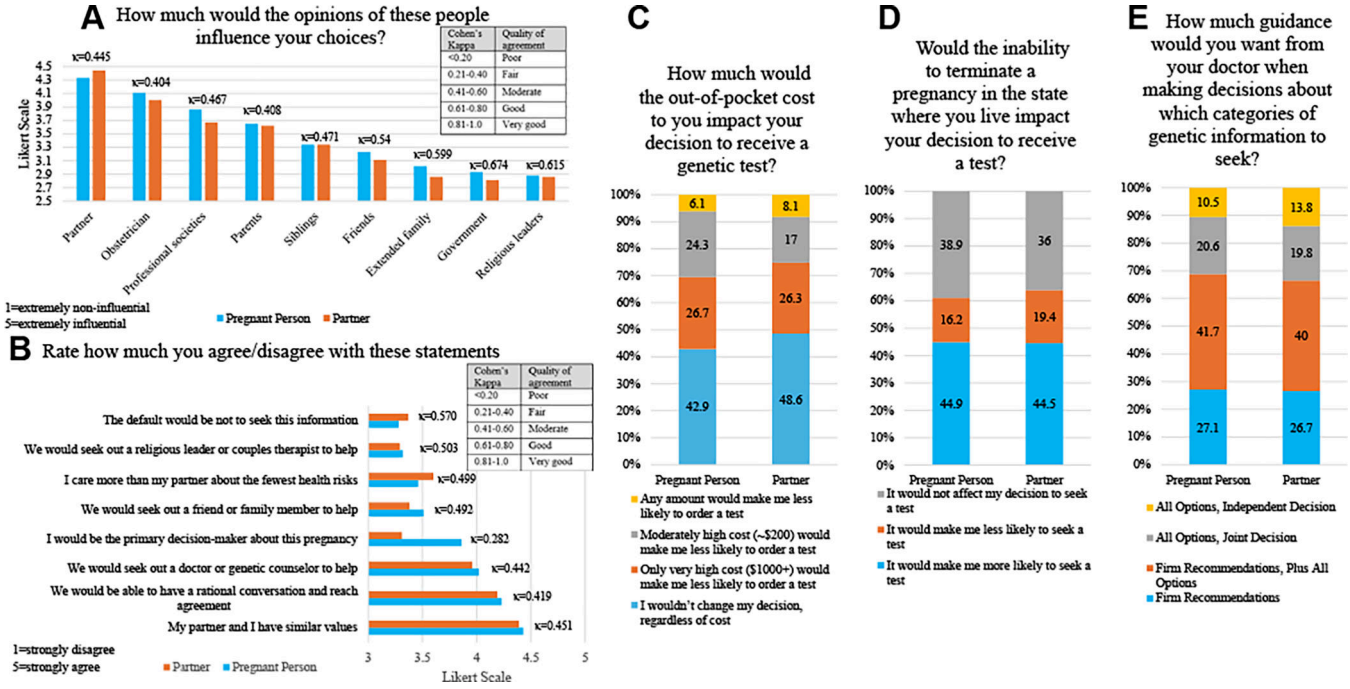

Figure 2.

Questions regarding decision-making process between partners.

Table 1

Reasons for/against wanting a specific prenatal cfDNA screening test

Reasons (A = Pregnant Person; B = Partner)	Not At All Important A/B% (A/Bn)	Slightly Important A/B% (A/Bn)	Moderately Important A/B% (A/Bn)	Very Important A/B% (A/Bn)	Extremely Important A/B% (A/Bn)	Cohen's Kappa Value
Importance of Reasons for Wanting a Specific Test (*n* = 1715/1638)						
To prepare financially, medically, and/or emotionally	1.3/1.4 (22/23)	3.7/4.3 (64/70)	13.7/11.8 (235/193)	36.2/37.5 (621/615)	**45.1/45.0 (773/737)**	**0.463**
To learn the information for the sake of knowing it	1.5/1.9 (25/31)	6.6/7.7 (114/126)	18.3/20.0 (313/328)	35.3/33.3 (605/546)	**38.4/37.1 (658/607)**	**0.370**
To inform decisions on pregnancy termination	8.1/6.5 (139/107)	6.1/7.0 (105/114)	14.3/16.1 (245/264)	32.5/35.6 (557/583)	**39.0/34.8 (669/570)**	**0.426**
To inform future decisions about how and when to get pregnant	2.9/3.7 (50/60)	6.8/6.4 (116/105)	13.5/15.0 (231/245)	35.9/33.2 (615/544)	**41.0/41.8 (703/684)**	**0.401**
To see if the fetus is at risk for a disease that runs in the family	0.6/1.2 (11/19)	4.5/3.9 (77/64)	11.9/13.3 (204/218)	34.3/35.9 (588/588)	**48.7/45.7 (835/749)**	**0.353**
Importance of reasons for not wanting a specific test (*n* = 261/338)						
I would never consider terminating a pregnancy because of the test	10.0/12.4 (26/42)	8.4/11.8 (22/40)	21.8/27.8 (57/94)	23.0/18.0 (60/61)	**36.8/29.9 (96/101)**	**0.449**
I would feel stress or anxiety due to the test	11.1/15.7 (29/53)	17.6/16.9 (46/57)	22.2/30.2 (58/102)	**26.4/24.3 (69/82)**	22.6/13.0 (59/44)	**0.201**
It is up to the future child to make their own decisions about testing	11.5/13.6 (30/46)	16.1/16.9 (42/57)	**31.4/31.4 (82/106)**	25.3/23.1 (66/78)	15.7/15.1 (41/51)	**0.136**
To retain a sense of mystery about the future child	13.8/14.8 (36/50)	18.0/17.2 (47/58)	**33.3/28.7 (87/97)**	22.6/24.3 (59/82)	12.3/15.1 (32/51)	**0.213**
Concern about who might gain access to the genetic information	16.9/23.4 (44/79)	23.8/16.0 (62/54)	**24.9/31.7 (65/107)**	21.1/21.9 (55/74)	13.4/7.1 (35/24)	**0.305**
I would feel that I was "playing God"	18.0/22.5 (47/76)	18.0/12.4 (47/42)	**26.1/28.4 (68/96)**	24.5/20.7 (64/70)	13.4/16.0 (35/54)	**0.323**
Concern about potential social implications	18.0/21.9 (47/74)	21.1/21.9 (55/74)	**25.7/32.5 (67/110)**	25.3/16.6 (66/56)	10.0/7.1 (26/24)	**0.237**
Mistrust of health care and not wanting screening in general	23.8/22.8 (62/77)	15.7/12.4 (41/42)	**26.1/25.7 (68/87)**	18.4/21.0 (48/71)	16.1/18.0 (42/61)	**0.483**

Bolded cells indicate the most common response for each option.

Table 2

Demographic variables that are associated with a higher probability of seeking testing

Explanatory Variable	Unadjusted *P* Value
Impact of inability to terminate a pregnancy in the state that they live on respondent's decision to receive a test	<.0001
Respondent's length of relationship with partner	<.0001
Age of respondent	<.0001
Importance of religion to respondent	<.0001
Respondent's response to whether the current pregnancy was planned	<.0001
Frequency that respondent attends religious services	.0001
Respondent's reporting of household income	.0002
Respondent's reporting of status of relationship with partner	.0005
Education level of respondent	.0029
Race of respondent	.0065
Respondent's response to how many children they have (not including a current pregnancy)	.0089
Political affiliation of respondent	.0114
Respondent's response to whether the current pregnancy was wanted	.2363
Respondent's response to whether the current pregnancy has been stressful	.5028
Ethnicity of respondent	.5062
Whether there are any circumstances under which the respondent would consider terminating a pregnancy	.5577
Respondent's response to how many children they would like to have in total	.8909

Table 3

Factors predicting concordance between partners on responses to vignettes (from univariable analyses)

Explanatory Variable	Unadjusted *P* Value
Importance of religion to pregnant person	.0002
Impact of inability to terminate a pregnancy in their state on partner's decision to test	.0006
Impact of inability to terminate a pregnancy in their state on pregnant person's decision to test	.0009
Race of pregnant person	.0030
Pregnant person's response to length of relationship with partner	.0107
If there are circumstances under which the partner would consider terminating a pregnancy	.0131
Partner's response to length of relationship with pregnant person	.0137
Pregnant person's response to whether the current pregnancy was planned	.0173
Partner's reporting of household income	.0191
Pregnant person's reporting of household income	.0203
Importance of religion to partner	.0249
Age of partner	.0265
Partner's response to whether the current pregnancy was planned	.0289
Partner's response to whether he and his partner have similar values	.0322
Age of pregnant person	.0413
Political affiliation of pregnant person	.0429
Same frequency of pregnant person and partner religious service attendance	.0456
Education level of pregnant person	.0514
Race of partner	.0613
Frequency that partner attends religious services	.0624
Frequency that pregnant person attends religious services	.0903
Timing of disease/trait onset in vignettes	.0936
Political affiliation of partner	.0953
Pregnant person's response to whether the current pregnancy has been stressful	.1400
Education level of partner	.1406
Pregnant person and partner choosing the same political affiliation	.1559
Pregnant person's response to whether her and her partner have similar values	.1653
Certainty of genetic test results in vignettes	.1675

Explanatory Variable	Unadjusted *P* Value
Pregnant person and partner choosing the same level for importance of religion	.1925
If there are circumstances under which the pregnant person would consider terminating a pregnancy	.1966
Pregnant person's response to whether the current pregnancy was wanted	.2082
Partner's response to how many children he has (not including a current pregnancy)	.2285
Partner's response to whether the current pregnancy was wanted	.2967
Difference in age between the pregnant person and partner	.4774
Partner's response to whether the current pregnancy has been stressful	.4803
Pregnant person's response to how many children she has (already born)	.4810
Pregnant person and partner choosing the same education level	.5091
Severity of disease/trait in vignettes	.5695
Treatability of disease/trait in vignettes	.6670
Pregnant person and partner choosing the same race	.7164
Pregnant person's response to length of relationship with partner	.8740
Partner's response to length of relationship with pregnant person	.8792