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Demographic and experiential correlates of public attitudes towards cell-free fetal DNA screening

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Abstract

This study seeks to inform clinical application of cell-free fetal DNA (cffDNA) screening as a novel method for prenatal trisomy detection by investigating public attitudes towards this technology and demographic and experiential characteristics related to these attitudes. Two versions of a 25-item survey assessing interest in cffDNA and existing first-trimester combined screening for either trisomy 13 and 18 or trisomy 21 were distributed among 3,164 members of the United States public. Logistic regression was performed to determine variables predictive of interest in screening options. Approximately 47% of respondents expressed an interest in cffDNA screening for trisomy 13, 18, and 21, with a majority interested in cffDNA screening as a stand-alone technique. A significantly greater percent would consider termination of pregnancy following a diagnosis of trisomy 13 or 18 (52%) over one of trisomy 21 (44%). Willingness to consider abortion of an affected pregnancy was the strongest correlate to interest in both cffDNA and first-trimester combined screening, although markedly more respondents expressed an interest in some form of screening (69% and 71%, respectively) than would consider termination. Greater educational attainment, higher income, and insurance coverage predicted interest in cffDNA screening; stronger religious identification also corresponded to decreased interest. Prior experience with disability and genetic testing was associated with increased interest in cffDNA screening. Several of these factors, in addition to advanced age and Asian race, were, in turn, predictive of respondents' increased willingness to consider post-diagnosis termination of pregnancy. In conclusion, divergent attitudes towards cffDNA screening - and prenatal options more generally – appear correlated with individual socioeconomic and religious backgrounds and experiences with disability and genetic testing. Clinical implementation and counseling for novel prenatal technologies should take these diverse stakeholder values into consideration.

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Disclosure of interest

None of the authors has a conflict of interest of a financial or other nature. Authors have full control of all primary data and agree to allow the journal to review our data upon request.

Keywords

Cell-free fetal DNA; non-invasive prenatal screening; non-invasive prenatal testing; public attitudes; prenatal genetic counseling

Introduction

Non-invasive screening using cell-free fetal DNA (cffDNA) is poised to transform the practice of prenatal genetic diagnosis and has received significant media and academic attention (Greely, 2011). The benefits of cffDNA screening, which entails the analysis of admixed maternal and fetal DNA circulating in the blood of pregnant women, may include a lack of procedure-related miscarriage risk, early timing of use, and improved sensitivity and specificity over existing screening methods (P. A. Benn & Chapman, 2009; Lo & Chiu, 2012). CffDNA screening for trisomy 21 was introduced commercially in the United States in late 2011 by Sequenom, Inc., and the company expanded screening to include trisomy 13 and 18 detection in early 2012. At least three additional firms located in the United States have introduced similar screening over the past 2 years, covering an increasing number of detectable chromosomal anomalies (Heger, 2012). Ongoing research promises eventual application of cffDNA technology to the detection of single-gene traits and copy number variation across the whole fetal genome (Bianchi, Sehnert, & Rava, 2012; Kitzman et al., 2012; Peters et al., 2011).

Clinical uptake of Sequenom's trisomy test has exceeded the company's initial sales predictions, reaching a projected 120,000 orders in the first year (Heger, 2013). However, uptake to date represents a fraction of the 2,500,000 women who undergo prenatal screening and 200,000 women who receive diagnostic testing in the United States each year (Olney et al., 1995; Palomaki, Knight, McCarthy, Haddow, & donhowe, 1997). It is difficult to predict how changing test indications, performance, cost, and access, the level of familiarity among providers and patients, and the issuance of guidelines by professional organizations, such as recommendations announced by the National Society of Genetic Counselors and the American Congress of Obstetricians and Gynecologists, will affect adoption rates for this technology (P. Benn et al., 2011; "Committee opinion number 545: Noninvasive prenatal testing for fetal aneuploidy," 2012; Devers et al., 2012). Moreover, a growing body of literature demonstrates that the attitudes of pregnant women towards prenatal screening and diagnosis are influenced by a variety of factors, including ethnic and racial identity, age, socioeconomic status, experience with disability, and cultural and religious beliefs, such as those regarding the nature of the condition being tested and the acceptability of termination of pregnancy (Case, Ramadhani, Canfield, & Wicklund, 2007; Kuppermann, Gates, & Washington, 1996; Kuppermann et al., 2011; Rapp, 1998).

Preliminary evidence suggests that uptake of cffDNA screening may stratify along demographic lines; in two previous studies, women who were older, more educated, or of white or Asian race reported greater interest in receiving non-invasive prenatal screening (Tischler, Hudgins, Blumenfeld, Greely, & Ormond, 2011; Zamerowski, Lumley, Arreola, Dukes, & Sullivan, 2001). To date, however, no comprehensive study has been conducted to

determine how these factors are associated with emerging public attitudes towards this technology, particularly in comparison with extant prenatal screening and diagnostic practices. Additionally, while other studies have been limited to women of reproductive age, we survey a sample of individuals representing broad demographic characteristics of the United States general public. Prior research demonstrates that the outlook of the general public towards prenatal technology has multifaceted interplay with the sociocultural and regulatory context in which pregnant women make reproductive decisions (Garcia, Timmermans, & van Leeuwen, 2008b; Kelly & Farrimond, 2012). We provide documentation of public attitudes that may exert influence on pregnant women and their families, healthcare practitioners, technology developers, insurance providers, and policymakers.

The purpose of this study is to assess expected interest in cffDNA screening for trisomy 13, 18, and 21 among the general public of the United States in order to understand how the technology may be received by diverse stakeholders. We utilize demographic data and information regarding personal experience with parenthood, disability, and genetic testing to predict who expresses interest in undergoing cffDNA screening. We additionally query interest in existing prenatal screening methods and attitudes towards the consideration of termination following detection of trisomy in order to place cffDNA screening into the existing, complex framework of prenatal diagnosis and care.

Methods

Instrumentation

A 25-question web-based survey was designed to address attitudes towards cffDNA screening in relation to existing first-trimester combined screening and diagnostic technologies. The survey was grounded in concepts and questions posed in the literature and through previous empirical research conducted by our team (Sayres, Allyse, Norton, & Cho, 2011). A broader team of bioethics scholars reviewed this survey for readability and content.

Two versions of the survey were developed - one addressing screening for trisomy 13 and 18 and the other addressing screening for trisomy 21 – and approximately half of respondents were randomly assigned to receive each version. This dichotomy of trisomy 13 and 18 and trisomy 21 as test conditions was used to establish whether the difference in morbidity and mortality associated with these conditions influenced respondents' attitudes toward prenatal screening. We chose to use two versions to maintain a short expected length of completion (fewer than ten minutes); our sample size for each version was calculated to allow us sufficient power to perform the statistical analyses presented herein. Aside from the short descriptions of either trisomy 13 and 18 or trisomy 21 provided (see Figure 1), each version included identical sets of questions. The survey provided information about the features and costs of each screening method, including cffDNA and existing first-trimester combined screening (see Figure 2, (Malone et al., 2005)). Respondents were asked to consider questions in the appropriate prenatal context, i.e. making decisions for either themselves or a loved one. Two questions addressed respondent interest in cffDNA screening in addition to or instead of existing screening methods and whether respondents would consider termination of pregnancy following prenatal detection of trisomy 13 or 18

and trisomy 21. The survey included fifteen questions soliciting respondents' demographic information and personal experiences that may be relevant to their attitudes towards prenatal genetic screening, including prior experience with mental illness or physical disability and doctor-ordered or purchased genetic testing. Eight additional questions regarding other aspects of respondents' interest in prenatal screening are considered in a separate manuscript (Allyse, Sayres, Goodspeed, & Cho, 2013).

Approximately two hundred individuals (one hundred individuals for the trisomy 13 and 18 version and one hundred individuals for the trisomy 21 version) completed a pilot version of the survey to ensure readability and comprehension. Following minor revisions, final versions of the survey were distributed and completed by approximately three thousand additional respondents.

Procedures

We contracted with a web-based survey provider, Zoomerang, to send this survey to a sample of adults ages eighteen years and older on the company's user panel, which is designed to represent the primary demographic features of the United States general public. Zoomerang contacted individuals on their panel via electronic mail with a web link to the survey and permitted responses until a specified number of complete response sets are collected. Zoomerang ensured that a random, non-overlapping sample of its panel members would be invited to complete each of the two versions of the survey. To ensure the validity of responses, Zoomerang reviewed the quality of prospective panelists in advance and de-duplicated responses using digital fingerprinting. Respondents were compensated for their time and effort through the web-based survey provider; our research team did not directly communicate with the respondents or provide compensation. The Stanford University Institutional Review Board approved the exempt status of this study and waived informed consent procedures.

Data analysis

We downloaded individual responses, identified by a unique code assigned by the survey provider, through a secure website. Responses were numerically coded and statistical analysis was performed using version 20.0 of the SPSS Standard Statistics package.

Logistic regression analyses were performed to determine whether demographic and experiential indicators correlated to interest in prenatal screening and consideration of pregnancy termination following trisomy detection, adjusting for whether respondents were asked about trisomy 13 and 18 or trisomy 21. To determine whether the demographic and experiential predictors were robust, we conducted multivariate regression analyses combining all significant predictive variables. For all statistical analyses, α is set to 0.05; p-values greater than 0.05 are reported as "not significant". Responses to trisomy 13 and 18 and trisomy 21 versions of the survey were compared using chi-square and Mann-Whitney tests for categorical and ordinal data respectively; these findings are reported in a separate manuscript (Allyse et al., 2013).

Results

Demographic and experiential characteristics

We received 3,164 responses to our survey: 1,657 for trisomy 13 and 18 and 1,507 for trisomy 21. Because the survey provider rendered the web link to the survey inactive after a predetermined number of responses, we cannot know how many individuals received the survey but chose not to complete it or did not complete it before the web link closed. Some respondents did not answer all demographic and experiential questions, and thus sample size varies slightly by question (see Tables I and II). All 3,164 respondents provided answers to all questions regarding interest in various forms of prenatal screening.

Respondent demographic characteristics are summarized in Table I. A nearly equal proportion of females and males participated, and ages of respondents spanned cohorts from 18 to 24 years to 65 years and older. Most respondents identified as non-Hispanic and white. A majority of respondents had attended some college or had a college degree; income brackets from under $25,000 to $100,000 and higher were well-represented among respondents. Nearly all respondents carried some form of health insurance. Various denominations of Christianity, and particularly Catholicism, were the most frequently identified religious affiliations. However, one-fifth of participants did not identify with a religion, and many self-reported as “not religious” or “not very religious”.

We asked respondents about five life experiences that might affect their interest in prenatal genetic screening; our findings are summarized in Table II. Greater than one-half of respondents were parents. Many reported personal experience with disability, as either they or someone close to them had experienced physical disability or mental illness or disability. Respondents were asked whether they had experience undergoing genetic testing with several examples of said tests provided to them. Approximately one-tenth of respondents stated that they had had a doctor order a genetic test for them, and fewer noted that they had purchased a genetic test for themselves or a loved one.

Expressed interest in prenatal screening

Respondents were asked to consider whether they would be interested in cffDNA or first-trimester combined screening, or both, for trisomy 13 and 18 or trisomy 21. As denoted in Figure 3, 38% of respondents to the survey on trisomy 13 and 18 expressed interest in only cffDNA screening, and 8% expressed interest in both cffDNA and first-trimester combined screening, for a sum of 46% demonstrating interest in cffDNA testing. By contrast, 42% of those responding to the trisomy 21 version preferred only cffDNA screening. and 5% showed an interest in both cffDNA and first-trimester combined screening; a total of 47% of individuals documented interest in cffDNA screening for trisomy 21. Of note, 31% and 29% respectively stated that they were not interested in any screening for trisomy 13 and 18 or trisomy 21. The only significant difference between respondents being asked about screening for trisomy 13 and 18 and trisomy 21 was the rates of individuals who noted interest in both cffDNA and combined screening, with a greater interest in both screening options when queried regarding trisomy 13 and 18 ($\chi^2(1, N=2202)=10.601$, $p=0.001$).

Consideration of termination of pregnancy

Respondents were asked whether they would consider termination of pregnancy following a diagnosis of fetal trisomy 13 or 18 or trisomy 21. As highlighted in Figure 4, 52% of those surveyed about trisomy 13 and 18 and 44% of those surveyed about trisomy 21 indicated that they would contemplate pregnancy termination following prenatal diagnosis. The discrepancy in rates of consideration of termination following trisomy diagnosis constitutes a statistically significant difference between responses to the trisomy 13 and 18 and trisomy 21 versions of the survey ($\chi^2(1, N=2962)=18.775$, $p<0.001$).

Demographic and experiential predictors of interest in screening

Using logistic regression analyses adjusting for the two versions of the survey, we determined the demographic or experiential characteristics that were predictive of respondents' expressed interest in cffDNA screening or in any prenatal screening.

Table III highlights the significant predictors of interest in cffDNA screening for trisomy. Greater educational attainment (odds ratio (OR)=1.171, $p<0.001$), higher household income (OR=1.271, $p<0.001$), and health insurance coverage (OR=1.594, $p<0.001$), were positively predictive of interest. Additionally, individuals who identified as Jewish were more likely to be interested cffDNA screening (OR=2.020, $p=0.003$), although self-reported level of religiosity corresponded negatively to a preference for screening (OR=0.886, $p=0.013$). Prior experience with genetic testing – either doctor-ordered (OR=1.499, $p=0.010$) or purchased (OR=1.591, $p=0.013$) – significantly predicted interest in cffDNA screening. Finally, respondents who were more likely consider termination of pregnancy following detection of fetal trisomy were more likely to note interest in cffDNA screening (OR=1.619, $p<0.001$).

A multivariate logistic regression analysis containing each of these eight variables indicated adjusted significant relationships between interest in cffDNA screening and household income (OR=1.232, $p<0.001$) and interest in cffDNA screening and consideration of abortion (OR=1.451, $p<0.001$). No other variables remained predictive in this model.

Table IV displays factors that are predictive of interest in any form of trisomy screening including cffDNA screening, first-trimester combined screening, or both. Again, greater educational attainment (OR=1.137, $p<0.001$), higher household income (OR=1.179, $p<0.001$), and insurance coverage (OR=1.477, $p<0.001$) positively predicted interest in prenatal screening. Respondents identifying as American Indian or Alaskan Native (OR=0.470, $p=0.003$) or Evangelical Protestant (OR=0.480, $p<0.001$) expressed less interest in screening, while those who identified as Jewish (OR=3.260, $p<0.001$) or as unaffiliated with a religion (OR=1.263, $p=0.017$) were more likely to express an interest in screening. Reported level of religiosity corresponded to lower interest in prenatal screening (OR=0.793, $p<0.001$). Personal experience with physical disability (OR=1.274, $p=0.006$) and doctor-ordered (OR=1.932, $p<0.001$) or purchased (OR=2.031, $p<0.001$) genetic tests positively predicted interest in prenatal screening. Finally, respondents who would contemplate abortion following detection of fetal trisomy were significantly more likely to indicate interest in screening (OR=8.270, $p<0.001$).

Following a multivariate regression analysis of these twelve predictors, six variables remained significantly predictive: income (OR=1.091, p=0.044); self-identification as American Indian or Alaskan Native (OR=0.409, p=0.009), Evangelical Protestant (OR=0.606, p=0.001), or Jewish (OR=2.304, p=0.029); and willingness to consider termination of pregnancy (OR=8.213, p<0.001). Lack of religious affiliation remained significant but with reversed directionality: respondents who reported a lack of religious affiliation were less likely to articulate interest in prenatal screening in this model (OR=0.747, p=0.047). No other variables were predictive.

Demographic and experiential predictors of consideration of termination of pregnancy

We used similar logistic regression models, standardizing for the two versions of the survey, to determine which demographic or experiential variables were predictive of respondents' willingness to consider termination of pregnancy following prenatal detection of trisomy 13 or 18 and trisomy 21.

Table V illustrates the characteristics that were significantly predictive of consideration of termination following prenatal trisomy detection. Respondents who were older (OR=1.079, p=0.001), more educated (OR=1.136, p<0.001), or had higher household incomes (OR=1.181, p<0.001) were more likely to contemplate termination of pregnancy under these circumstances. While respondents identifying as Asian were more likely to indicate a willingness to consider abortion after prenatal detection of trisomy (OR=1.854, p<0.001), self-identification as black or African-American corresponded with a lower likelihood of considering abortion (OR=0.685, p<0.001). Respondents identifying as Evangelical Protestant (OR=0.358, p<0.001) or Mormon (OR=0.502, p=0.009) were also less likely to find pregnancy termination following trisomy detection acceptable, whereas those who identified as Jewish (OR=2.510, p<0.001) or unaffiliated with a religious tradition (OR=2.381, p<0.001) were more likely to consider this option. Higher levels of religiosity (OR=0.553, p<0.001) and parenthood (OR=0.853, p=0.035) were negatively predictive of consideration of abortion. On the other hand, experience with genetic testing – both doctor-ordered (OR=1.498, p=0.002) and purchased (OR=1.916, p<0.001) – corresponded with increased likelihood of considering termination of pregnancy.

Logistic regression analysis of these thirteen predictive characteristics demonstrated that older age (OR=1.222, p<0.001), higher household income (OR=1.148, p<0.001), and identification as Asian (OR=1.763, p=0.004), Evangelical Protestant (OR=0.490, p<0.001), Jewish (OR=1.673, p=0.035), or religiously unaffiliated (OR=1.297, p=0.033) remained significantly predictive. Religiosity (OR=0.554, p<0.001), parenthood (OR=0.656, p<0.001), and experience with either doctor-ordered (OR=1.628, p=0.006) or purchased (OR=1.777, p=0.005) genetic tests additionally continued to be significant in this multivariate analysis. The other adjusted variables were no longer significantly predictive.

Discussion

Expected interest in ffDNA screening and consideration of termination of pregnancy

In this study, we provide evidence of attitudes among members of society who are not necessarily women of reproductive age but still influence prenatal decision-making via complex interpersonal, social, cultural, and political relationships. Overall, our results illustrate a substantial interest in cffDNA screening for trisomy 13, 18, and 21 among the general public of the United States, consistent with the growing body of literature in this realm (Kelly & Farrimond, 2012; Kooij, Tymstra, & Berg, 2009; Sayres et al., 2011; Tischler et al., 2011; Yotsumoto et al., 2012; Zamerowski et al., 2001). While cffDNA screening for trisomy is not currently standard of care, its role in supplementing (rather than supplanting) existing prenatal screening mechanisms in high-risk populations is supported by at least four professional societies (P. Benn et al., 2011; “Committee opinion number 545: Noninvasive prenatal testing for fetal aneuploidy,” 2012; Devers et al., 2012). A majority of respondents who reported interest in some form of screening expressed a preference for cffDNA screening as a replacement for first-trimester combined screening, with a fraction of individuals indicating that they would be interested in both screening techniques. These results are consistent with a recent qualitative study of early adopters of cffDNA screening, in which women reported a belief that cffDNA screening provided a better alternative to conventional means of first- and second-trimester screening, which were deemed ‘unnecessary,’ with highly variable sensitivity and specificity rates (Yi, Hallowell, Griffiths, & Yeung Leung, 2013). In fact, one study showed that, of cffDNA screens for trisomy 21 performed in the first year following introduction, 14% were performed for women either as a primary screen or following a negative first-trimester screen. These data lend further credence to our finding that many individuals may make use of cffDNA screening in a manner at odds with current professional recommendations by foregoing recommended first-or second-trimester screens or obtaining cffDNA screening even in the event of a negative result from these conventional screening techniques (Poon et al., 2013). Thoughtful and thorough genetic counseling represents one means of ensuring that pregnant women receive prenatal screening that aligns with their values and professional practices.

Initial studies of uptake have demonstrated that, when offered as a second-tier screening test following a positive first- or second-trimester screening result, 39% of women elected to undergo cffDNA screening for trisomy 21 (Chetty, Garabedian, & Norton, 2013). While not directly comparable to our results, as we asked about cffDNA and first-trimester combined screening as separate options without a pre-determined sequence, the figure that we obtained −47% - highlights significant interest in cffDNA technology for trisomy detection. However, almost one-third of individuals were not interested in either cffDNA or first-trimester combined screening, which is consistent with previously reported levels of refusal of prenatal testing (Palomaki et al., 1997). Interest in cffDNA screening was significantly stronger for the detection of trisomy 13 and 18, most likely due to the increased severity of symptoms of these conditions over trisomy 21. Perhaps surprisingly, however, overall interest in receiving some form of screening did not vary with the targeted trisomy, suggesting that there exists a cohort among which prenatal information is not valued.

Willingness to consider abortion and several socioeconomic variables, including income, educational attainment, and health insurance status, robustly predicted the reported interest in prenatal screening (Dormandy, Michie, Hooper, & Marteau, 2005). These findings hold true with respect to interest in cffDNA screening specifically, which is consistent with a previous pilot study of expected uptake among pregnant women (Tischler et al., 2011). We also found that individuals identifying with certain races or religions were more or less likely to express a desire for prenatal screening; these results may be explained by the unique history and positioning of different racial or religious communities within the biomedical establishment, in addition to specific sociocultural and religious stances towards the moral status of abortion (Rapp, 1998). For example, Jewish individuals may be more likely to accept prenatal genetic testing because of their increased familiarity with preconception testing for carrier status of the gene for Tay Sachs disease (Kaback, 2000).

Interestingly, the findings that experience with genetic testing is positively associated with interest in screening and religiosity is negatively associated with interest run counter to the findings of a smaller previous study of pregnant women in which experience of genetic testing and self-reported levels of religiosity were not significant predictors of expressed interest in non-invasive prenatal screening (Tischler et al., 2011). It is, however, not surprising that individuals demonstrating prior acceptance of genetic testing - particularly when ordered by a physician - may be more comfortable receiving further genetic information in the context of pregnancy, either because they believe in the intrinsic value of information or they are more comfortable following doctor recommendations (Press & Browner, 1997). Additionally, stronger adherents to religions that forbid the termination of a pregnancy may be less likely accept information about a fetus if they feel that the knowledge is unlikely to change their prenatal decision-making and will only produce anxiety (Markens, Browner, & Press, 1999).

Along these lines, approximately half of respondents indicated a willingness to consider termination of a pregnancy following prenatal detection of trisomy 13 or 18 and trisomy 21. Of note, there is a significant increase in the percentage of respondents with an interest in any form of prenatal screening for trisomy 13 and 18 or trisomy 21 (69% and 71%, respectively) over the percentage who would consider termination (52% and 44%, respectively). This finding provides support for the presence of factors other than termination of pregnancy in motivation for receiving prenatal testing, such as reassurance or preparation for an affected child (Garcia, Timmermans, & van Leeuwen, 2008a; Parens & Asch, 2000; Suter, 2002). The rate of consideration of pregnancy termination is greater in the context of trisomy 13 and 18, which have higher levels of intrauterine lethality and infant mortality than trisomy 21 (Rasmussen, Wong, Yang, May, & Friedman, 2003). Overall, our figures are significantly lower than actual rates of termination reported in the literature, suggesting that speculation on whether termination of pregnancy would be permissible under hypothetical circumstances does not align with how prospective parents confronting such decisions actually act (Drugan et al., 1990). Moreover, our study is taken from a sample of the general public in the United States, and this population likely differs from the samples of other studies, which have mostly been limited to recently pregnant women who are receiving prenatal care. Thus, our study may better reflect the attitudes of individuals who are not able to or who would choose not to receive prenatal care.

Our findings that older maternal age, greater socioeconomic status, identification with particular races and religions, decreased strength of religious beliefs, and prior experience with genetic testing correspond to willingness to contemplate abortion following prenatal trisomy detection concord with previous research (Choi, Van Riper, & Thoyre, 2012; Kuppermann et al., 2011; Natoli, Ackerman, McDermott, & Edwards, 2012). Our data add to existing mixed evidence regarding the willingness of individuals who already have children to consider termination of pregnancy, by demonstrating that parents may be less likely to contemplate this option (Kramer et al., 1998). On one hand, individuals with existing children may not be as inclined to have more children, particularly children requiring elevated attention and resources. However, parents may also believe that love for one's children is unconditional and recognize that all children, and not just those with trisomy, will place significant demands on their lives. Regardless, provision of unbiased informational materials and expanded access to pre- and post-natal care may allow prospective parents of all classes to make prenatal decisions that best align with their personal values.

Study limitations

To determine whether our sample was representative of the general United States public, we compared the demographic data of respondents to those available from the United States Census of 2010 and the Pew Religious Landscape Survey of 2008 using chi-square goodness-of-fit tests with $\alpha=0.05$. We appear to have under-sampled males ($\chi^2(1, N=3164)=15.590$, $p<0.001$), individuals of Hispanic or Latino ($\chi^2(1, N=2962)=173.432$, $p<0.001$) and Black or African-American ($\chi^2(1, N=3164)=74.912$, $p<0.001$) identities, and those affiliated with Evangelical ($\chi^2(1, N=3157)=469.142$, $p<0.001$) or other ($\chi^2(1, N=3157)=147.939$, $p<0.001$) denominations of Protestantism. Additionally, distributions of age ($\chi^2(5, N=3164)=166.340$, $p<0.001$), household income ($\chi^2(4, N=3164)=140.058$, $p<0.001$), and educational attainment ($\chi^2(4, N=3164)=469.694$, $p<0.001$) varied significantly from findings of the Census. Additionally, a web-based survey available only in English will not be accessed by individuals who do not have access to the internet or who cannot read and write in English. Moreover, it is impossible in this format to assess whether there existed biases among responders or non-responders. However, given the significant proportion of respondents choosing to receive no prenatal screening or who are opposed to termination following a diagnosis of trisomy despite our sample's skew towards individuals historically more likely to do so, it is possible that we have nonetheless underrepresented these values while taking account of a wide range of public attitudes.

Our findings are contingent on the descriptions of trisomy 13, 18, and 21 and the features and costs of different prenatal screening options that were provided. This fact highlights the necessity of providing potential parents with genetic counseling educational materials that address the concerns and questions surrounding screening and post-screening decision-making. It is highly likely that, over time, as the performance and cost of cffDNA screening improve, insurers will begin to cover screening for a greater number of indications, physicians will recommend screening under more circumstances, and the public will become more familiar with the availability of this technology. The realization of these prospects may

lead to increased acceptance of cffDNA testing for trisomy 13, 18, and 21 beyond what is suggested in this study.

Practice implications

This is the first large study of perspectives of the United States public on cffDNA screening for trisomy 13, 18, and 21. There appears to be significant interest in this method of screening as a supplement or replacement for existing prenatal screening mechanisms, increasing the likelihood that uptake will continue to increase rapidly as the technology become more widely publicized, more widely available, less costly, and more widely covered by insurers. However, this does not negate the urgent need for healthcare providers, professional organizations, regulators, third-party payers, and other policymakers to consider the various ethical aspects of cffDNA screening, such as assurance of analytic and clinical utility, proper informed consent procedures, availability of nondirective genetic counseling, access by broad patient populations, and non-discrimination and continued support and resources for individuals living with disabilities (P. A. Benn & Chapman, 2010; Kent, 2008; Lewis, Hill, Skirton, & Chitty, 2012). Additionally, stakeholders involved in implementing cffDNA screening must be respectful of individuals who choose not to receive screening or who decide against termination of pregnancy based on diagnostic results and the social and cultural structures that may influence prenatal decisions (Lewis, Silcock, & Chitty, 2013). Test developers and providers should employ measures that encourage pregnant women and their families to make informed decisions about cffDNA screening grounded in their personal values, such as by developing and distributing unbiased educational materials and supporting access to screening by medically underserved populations. Pregnant women should be made aware of the availability and utility of diagnostic testing, including amniocentesis and chorionic villus sampling, that may be recommended in the case of a positive result of any form of prenatal screening. As our ability to non-invasively detect other chromosomal anomalies, copy number variants, and inherited or de novo polymorphisms in a fetus continues to improve, we must incorporate attitudes of the general public into the translational process early and often to ensure that this technology aligns with the priorities of its diverse stakeholders (Kitzman et al., 2012).

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Description of trisomy 21 provided to respondents

Trisomy 21 (also known as Down syndrome) is a genetic condition, meaning that it can occur in a fetus very early in a pregnancy. People with Down syndrome often have learning disabilities, an increased risk for some heart and lung diseases, and distinct physical characteristics. Not all individuals with Down syndrome have the same symptoms. Some have very severe symptoms while some have very mild symptoms. In the United States, individuals with Down syndrome live an average of 60 years and can lead fulfilling lives with proper care and resources. However, these individuals do have special needs, often have trouble supporting themselves financially, and may face social discrimination.

Description of trisomy 13 and 18 provided to respondents

Trisomy 13 (also known as Patau syndrome) and trisomy 18 (also known as Edwards syndrome) are genetic conditions, meaning that they can occur in a fetus very early in a pregnancy. Approximately 50% of pregnancies with trisomy 13 or 18 result in miscarriage or stillbirth. Of babies born with trisomy 13 or 18, about 90 out of 100 die within the first year of life. Others may survive into their teenage years but often have severe cognitive impairment, medical problems, and physical disabilities. Although there are support groups to help families and children with trisomy 13 or 18, there are no treatments or cures for either of these conditions.

Figure 1.

Description of trisomy 13, 18, and 21 provided to respondents

	Risk	Timing	Detection rate	Accuracy	Cost
CffDNA screening	Uses a blood draw from mother with no risk to fetus	Can be done about 3 months into pregnancy	Almost always right (detects 98 out of 100 cases) 2 out of 100 times, says fetus does not have trisomy when it actually does	Almost never wrong 1 out of 100 times, says fetus has trisomy when it actually does not	With no insurance, $2000 With insurance, about $250
First-trimester combined screening	Uses a blood draw from mother with no risk to fetus	Can be done about 3 months into pregnancy	Often right (detects 85 out of 100 cases) 15 out of 100 times, says fetus does not have trisomy when it actually does	Rarely wrong 5 out of 100 times, says fetus has trisomy when it actually does not	With no insurance, $250 With insurance, about $20

Figure 2.
Description of cffDNA and first-trimester combined screening provided to respondents

Figure 3.

Interest in first-trimester combined screening and cffDNA screening for trisomy (N=3133)

* Interest in both forms of screening varied significantly between trisomy 13 and 18 and trisomy 21 (p=0.001).

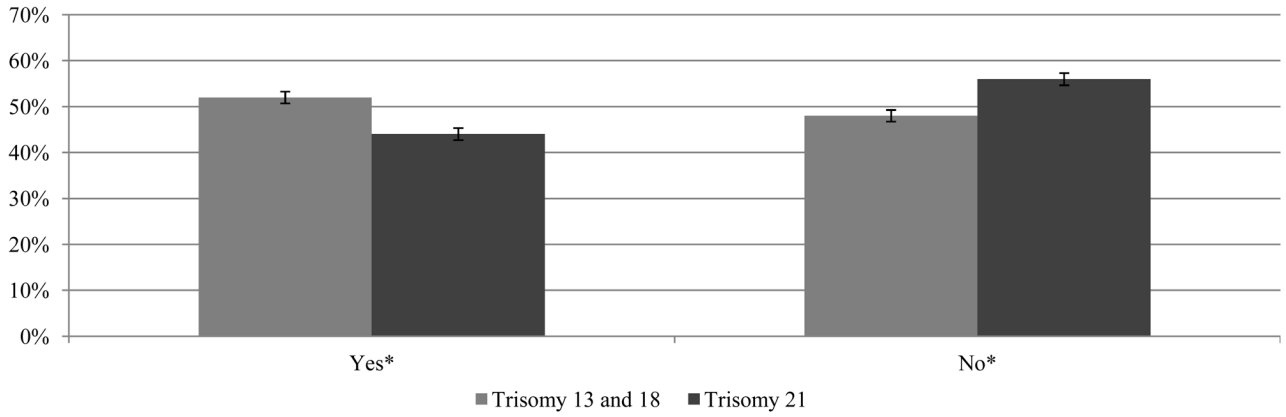

Figure 4.

Consideration of termination of pregnancy following detection of trisomy (N=2962)

* Consideration of termination of pregnancy varied significantly between trisomy 13 and 18 and trisomy 21 ($p<0.001$).

Table I

Demographic characteristics of respondents (N=3164)*

Gender	
Female	55% (1739)
Male	45% (1425)
Age	
18 to 24 years	14% (451)
25 to 34 years	22% (710)
35 to 44 years	22% (700)
45 to 54 years	16% (510)
55 to 64 years	10% (330)
65 years and over	15% (463)
Ethnicity	
Hispanic or Latino	7% (219)
Not Hispanic or Latino	93% (2743)
Race†	
American Indian or Alaska Native	2% (64)
Asian	6% (194)
Black or African-American	8% (264)
Native Hawaiian or Pacific Islander	1% (21)
White	84% (2642)
Educational attainment	
Some high school	2% (71)
High school diploma	19% (596)
Some college	31% (967)
College diploma	34% (1072)
Graduate school diploma	14% (458)
Household income	
Under $25,000	20% (641)
$25,000 to $49,999	28% (887)
$50,000 to $74,999	23% (727)
$75,000 to $99,999	14% (449)
$100,000 and over	15% (460)
Health insurance status	
Insured	86% (2692)
Not insured	14% (452)
Religion†	
Catholic	23% (728)

Evangelical Protestant	10% (303)
Other Protestant	17% (538)
Mormon	2% (69)
Jewish	4% (127)
Buddhist	1% (31)
Muslim	1% (19)
Unaffiliated	22% (692)
Religiosity	
Very religious	22% (639)
Somewhat religious	41% (1226)
Not very religious	21% (611)
Not religious	16% (486)

* Values reported as % (#). For select questions, N<3164.

† Participants may select any number of responses; thus percentages may not add to 100%.

Table II

Experiential characteristics of respondents (N=3164)*

Experience as a parent	
Yes	59% (1877)
No	41% (1287)
Experience with physical disability	
Yes	30% (938)
No	68% (2145)
I don't know	3% (81)
Experience with mental illness or disability	
Yes	35% (1105)
No	62% (1963)
I don't know	3% (96)
Experience with doctor-ordered genetic test	
Yes	9% (293)
No	82% (2596)
I don't know	9% (271)
Experience with purchased genetic test	
Yes	6% (204)
No	85% (2659)
I don't know	9% (276)

*Values reported as % (#). For select questions, N<3164.

Table III

Predictors of interest in cffDNA screening for trisomy (N=3164)

Demographic or experiential variable	Odds ratio	Wald χ^2 statistic	p-value*
Gender			N.S.
Age			N.S.
Ethnicity			
Hispanic or Latino			N.S.
Race			
American Indian or Alaska Native			N.S.
Asian			N.S.
Black or African-American			N.S.
Native Hawaiian or Pacific Islander			N.S.
White			N.S.
Educational attainment	1.171	20.476	<0.001†
Household income	1.271	46.866	<0.001
Health insurance status	1.594	12.816	<0.001†
Religion			
Catholic			N.S.
Evangelical Protestant			N.S.
Other Protestant			N.S.
Mormon			N.S.
Jewish	2.020	8.689	0.003†
Buddhist			N.S.
Muslim			N.S.
Unaffiliated			N.S.
Religiosity	0.886	6.192	0.013†
Experience as a parent			N.S.
Experience with physical disability			N.S.
Experience with mental illness or disability			N.S.
Experience with doctor-ordered genetic test	1.499	6.671	0.010†
Experience with purchased genetic test	1.591	6.231	0.013†
Consideration of pregnancy termination	1.619	24.908	<0.001

*N.S.=not significant. All p-values are reported using logistic regressional analysis adjusting for whether respondents were queried regarding trisomy 13 and 18 or trisomy 21.

†This predictive variable does not remain significant in a multivariate logistic regression of all individually significant predictors of interest.

Table IV

Predictors for interest in any prenatal screening for trisomy (N=3164)

Demographic or experiential variable	Odds ratio	Wald χ^2 statistic	p-value*
Gender			N.S.
Age			N.S.
Ethnicity			
Hispanic or Latino			N.S.
Race			
American Indian or Alaska Native	0.470	8.836	0.003
Asian			N.S.
Black or African-American			N.S.
Native Hawaiian or Pacific Islander			N.S.
White			N.S.
Educational attainment	1.137	17.847	<0.001†
Household income	1.179	29.422	<0.001
Health insurance status	1.477	13.309	<0.001†
Religion			
Catholic			N.S.
Evangelical Protestant	0.480	35.527	<0.001
Other Protestant			N.S.
Mormon			N.S.
Jewish	3.260	18.090	<0.001
Buddhist			N.S.
Muslim			N.S.
Unaffiliated	1.263	5.724	0.017
Religiosity	0.793	30.812	<0.001†
Experience as a parent			N.S.
Experience with physical disability	1.274	7.445	0.006†
Experience with mental illness or disability			N.S.
Experience with doctor-ordered genetic test	1.932	17.143	<0.001†
Experience with purchased genetic test	2.031	13.498	<0.001†
Consideration of pregnancy termination	8.270	432.907	<0.001

*N.S.=not significant. All p-values are reported using logistic regressional analysis adjusting for whether respondents were queried regarding trisomy 13 and 18 or trisomy 21.

† This predictive variable does not remain significant in a multivariate logistic regression of all individually significant predictors of interest.

Table V

Predictors for consideration of termination of pregnancy following trisomy detection (N=3164)

Demographic or experiential variable	Odds ratio	Wald χ^2 statistic	p-value*
Gender			N.S.
Age	1.079	10.977	0.001
Ethnicity			
Hispanic or Latino			N.S.
Race			
American Indian or Alaska Native			N.S.
Asian	1.854	15.486	<0.001
Black or African-American	0.685	7.768	<0.001†
Native Hawaiian or Pacific Islander			N.S.
White			N.S.
Educational attainment	1.136	20.482	<0.001†
Household income	1.181	34.760	<0.001
Health insurance status			N.S.
Religion			
Catholic			N.S.
Evangelical Protestant	0.358	54.586	<0.001
Other Protestant			N.S.
Mormon	0.502	6.897	0.009†
Jewish	2.510	20.089	<0.001
Buddhist			N.S.
Muslim			N.S.
Unaffiliated	2.381	87.394	<0.001
Religiosity	0.553	213.935	<0.001
Experience as a parent	0.853	4.450	0.035
Experience with physical disability			N.S.
Experience with mental illness or disability			N.S.
Experience with doctor-ordered genetic test	1.498	9.806	0.002
Experience with purchased genetic test	1.916	17.225	<0.001

* N.S.=not significant. All p-values are reported using logistic regressional analysis adjusting for whether respondents were queried regarding trisomy 13 and 18 or trisomy 21.

† This predictive variable does not remain significant in a multivariate logistic regression of all individually significant predictors of consideration of termination.