Appendix 1. Pregnant Women's Views about the Ethics of Prenatal Whole Genome Sequencing

Introduction

There are genetic tests today that can tell us about our risk for some diseases. As science continues to advance, we will soon be able to look at all of our genes (called genetic sequencing) to learn how our genes affect our bodies and our health. This kind of genetic testing can provide a lot of information and we are still learning how to use this information to improve health. Genetic testing is now also being used to look at a fetus's genes, by taking a sample of the mother's blood. This kind of test, called non-invasive prenatal testing (NIPT), makes it possible to test a fetus's genes without the risk of miscarriage associated with invasive testing such as amniocentesis and chorionic villus sampling. These tests on the fetus are usually offered to women with certain risk factors such as an abnormal ultrasound or being older than 35 years.

Today, non-invasive prenatal testing (NIPT) is used to look for just a few specific genetic diseases, such as Down's Syndrome or Trisomy 18. But in the future, it will be possible to use NIPT to look at all of the fetus's genes, which will give you and your doctor much more genetic information about your fetus. **Prenatal whole-genome sequencing (PWGS)** will allow parents to learn a huge amount of fetal genetic information. For example, parents will be able to learn whether their fetus has certain disorders caused by changes in a single gene, like cystic fibrosis or sickle cell disease, or may develop a disease later in life, such as breast cancer. In the future, PWGS could allow parents to learn non-health-related information about their fetus, such as eye color and height. It is important to say that much of the information provided by PWGS will involve probabilities or chance; PWGS will not tell parents that their fetus *will definitely* get a certain condition, but rather that their fetus has *some chance* of developing that condition.

PWGS is not yet available in a standard medical setting. However, given public interest in personal genetic testing and the decreasing costs of sequencing, PWGS may soon become part of standard prenatal care.

Survey goal

If you are between 8 and 30 weeks gestational age, we are asking you to help us to prepare for the possible future of PWGS in routine OB/GYN care. Would mothers want to use the test? What sorts of genetic information do parents want to know about their babies, and why? How can we best understand and answer mothers' questions about this new technology? What should we know about how you think and feel about PWGS so doctors can provide the best prenatal test?

Thank you for your time and for sharing your response!

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This research survey is being conducted by researchers at Inova and the National Institutes of Health (NIH).

You will not receive any direct benefit for participating in this study, but your responses to the survey will help make sure that the perspectives of people like you are known, which could be helpful when rules are created for how and when PWGS will be used.

There are no physical risks to you as a result of completing this survey. We will ask you hypothetical questions about genetic diseases. If you have family experience with such a disease, you might find these hypothetical scenarios mildly distressing.

We will not collect any identifying data from you, like your name or email address. Your responses to the survey will not be shared with your doctor.

Participation in this survey is voluntary. Your decision to participate or not participate in this research study will have **no impact on your medical care**. You can stop the survey at any time and for any reason if you do not wish to continue. However, once you have submitted your answers, you may not withdraw responses as there is no way to determine which survey is yours. Your alternative to participation is to not participate.

This survey should take 10-15 minutes to complete and you can take it on your own electronic device (such as a computer, smart phone or tablet) or on paper. You must be 18 years or older and between 8 and 30 weeks gestational age to participate. The survey is available in English or Spanish. If you take the survey electronically (via SurveyMonkey) please do not share the survey link with any friends or family members. Anonymized data from completed surveys will be stored on secure computers employed by the research team. Electronic data will temporarily be stored on SurveyMonkey servers, but will be deleted once the data has been safely transferred to the research team. Paper copies will be secured in a locked filing cabinet until manuscript publication is completed.

You will receive a $10 gift card as compensation for taking this survey.

If you have any questions about this research, please ask the research coordinator who gave you the survey. Alternatively, you can contact the Principal Investigator, Benjamin Berkman, at 301-496-1531.

By continuing you are indicating your willingness to participate.

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1. How many weeks pregnant are you?
    a. 8-20 weeks
    b. 21-30 weeks
    c. 30+ weeks

2. If you have undergone prenatal screening for this or another pregnancy, which of the following statements most closely describes your views on the genetic testing that was conducted?
    a. I was satisfied with the amount of information I learned about my baby.
    b. I wish I could have learned more information about my baby.
    c. I wish I could have learned less information about my baby.
    d. I have never had prenatal genetic testing.

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3. A new type of genetic testing called genome sequencing may be offered to pregnant women in the near future. Genome sequencing can offer a variety of types of results that may predict future health risks for the developing baby, but can also reveal results that cannot yet be clearly understood.

   Prenatal whole-genome sequencing (PWGS) could reveal a wide range of genetic information about your baby. Which of the following categories of information would you want regarding your baby?

➢ Life-threatening conditions *beginning in adulthood* that have treatment options (e.g., breast cancer)
(please select one)

Definitely **Probably** **Probably not** **Definitely not**

There might be many reasons why you would want to learn about this category of genetic information, but please select the *single most important* factor.

I would want the information…

a. to prepare financially, medically, or psychologically for a child with special needs.
b. to inform decisions about having future children.
c. to inform a decision about whether to end the pregnancy.
d. just to know it, but would not act on the information.

There might be many reasons why you would not want to learn about this category of genetic information, but please select the *single most important* factor.

I would not want the information because…

a. it is not relevant for my reproductive decision-making since I would not consider ending a pregnancy.
b. I would worry that the information would increase my stress or the stress of my family.
c. I want to respect my future child's privacy; this is the kind of information that he/she should be allowed to learn his/herself upon reaching adulthood.
d. I want to retain a sense of mystery about my child.
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Prenatal whole-genome sequencing (PWGS) could reveal a wide range of genetic information about your baby. Which of the following categories of information would you want regarding your baby?

- Fatal congenital conditions that result in death shortly after birth (e.g., Tay-Sachs disease)
  (please select one)

Definitely **Probably** **Probably not** **Definitely not**

*If you selected **definitely** or **probably**, please answer below*

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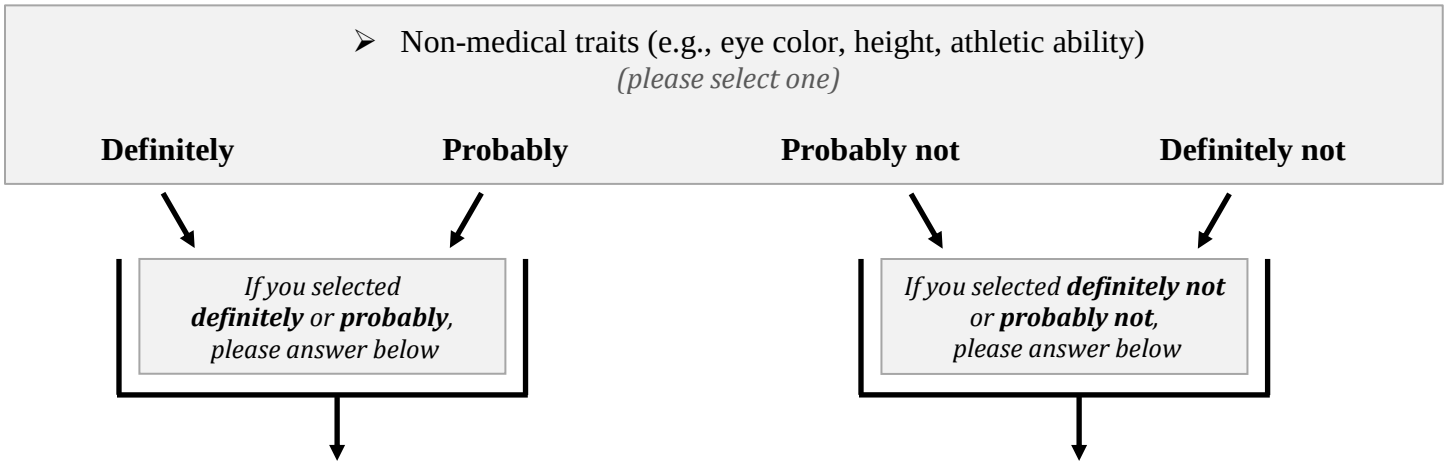

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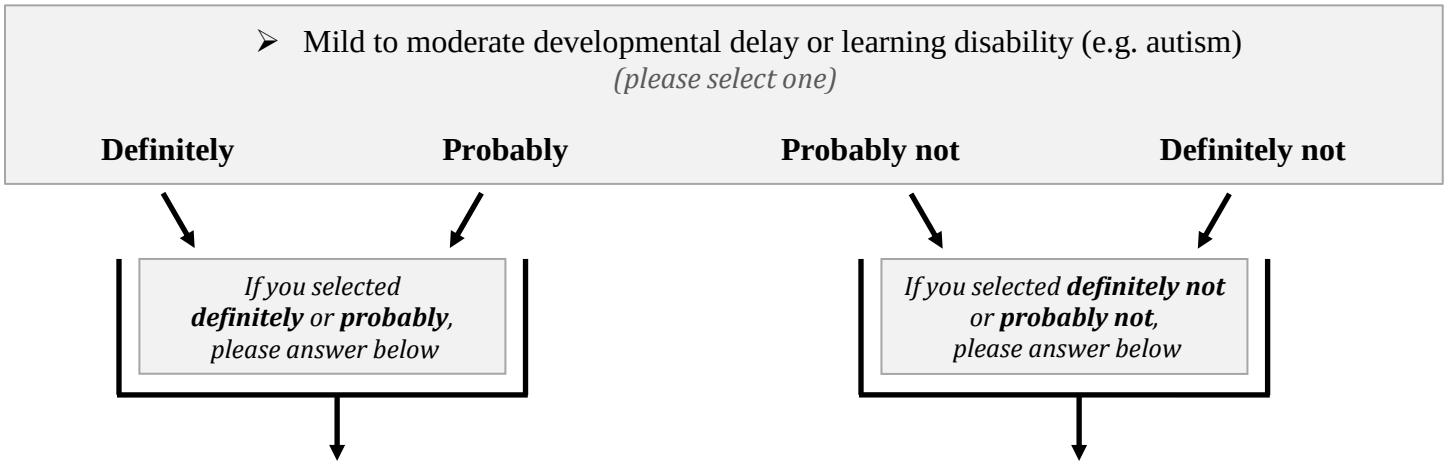

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- Moderate increased risk of a common disease that can be treated (e.g., heart disease)
  (please select one)

Definitely **Probably** **Probably not** **Definitely not**

*If you selected **definitely** or **probably**, please answer below*

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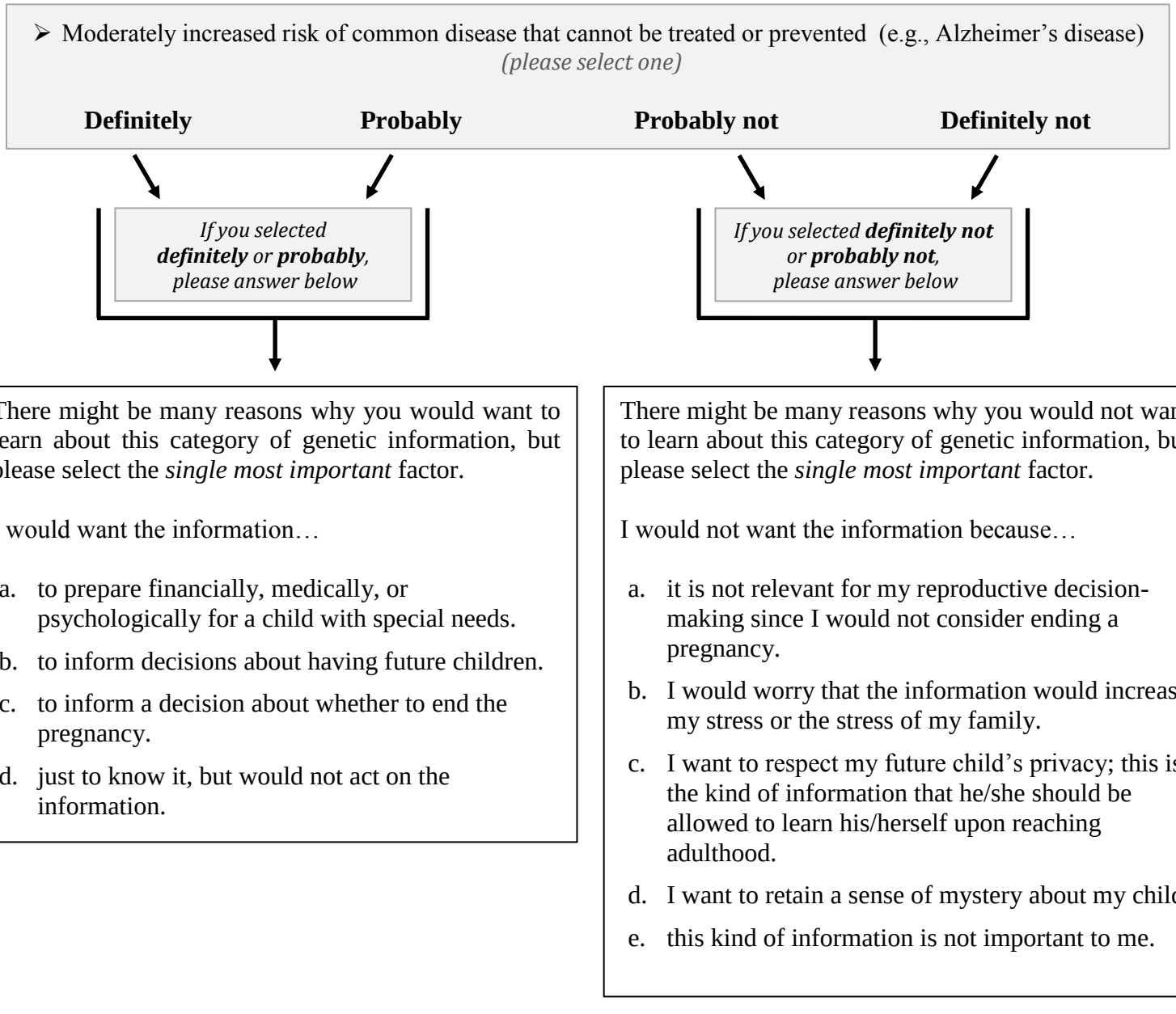

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- Fatal conditions *beginning in adulthood* that result in early death (e.g., Huntington's disease)
  (please select one)

Definitely **Probably** **Probably not** **Definitely not**

*If you selected **definitely** or **probably**, please answer below*

There might be many reasons why you would want to learn about this category of genetic information, but please select the *single most important* factor.

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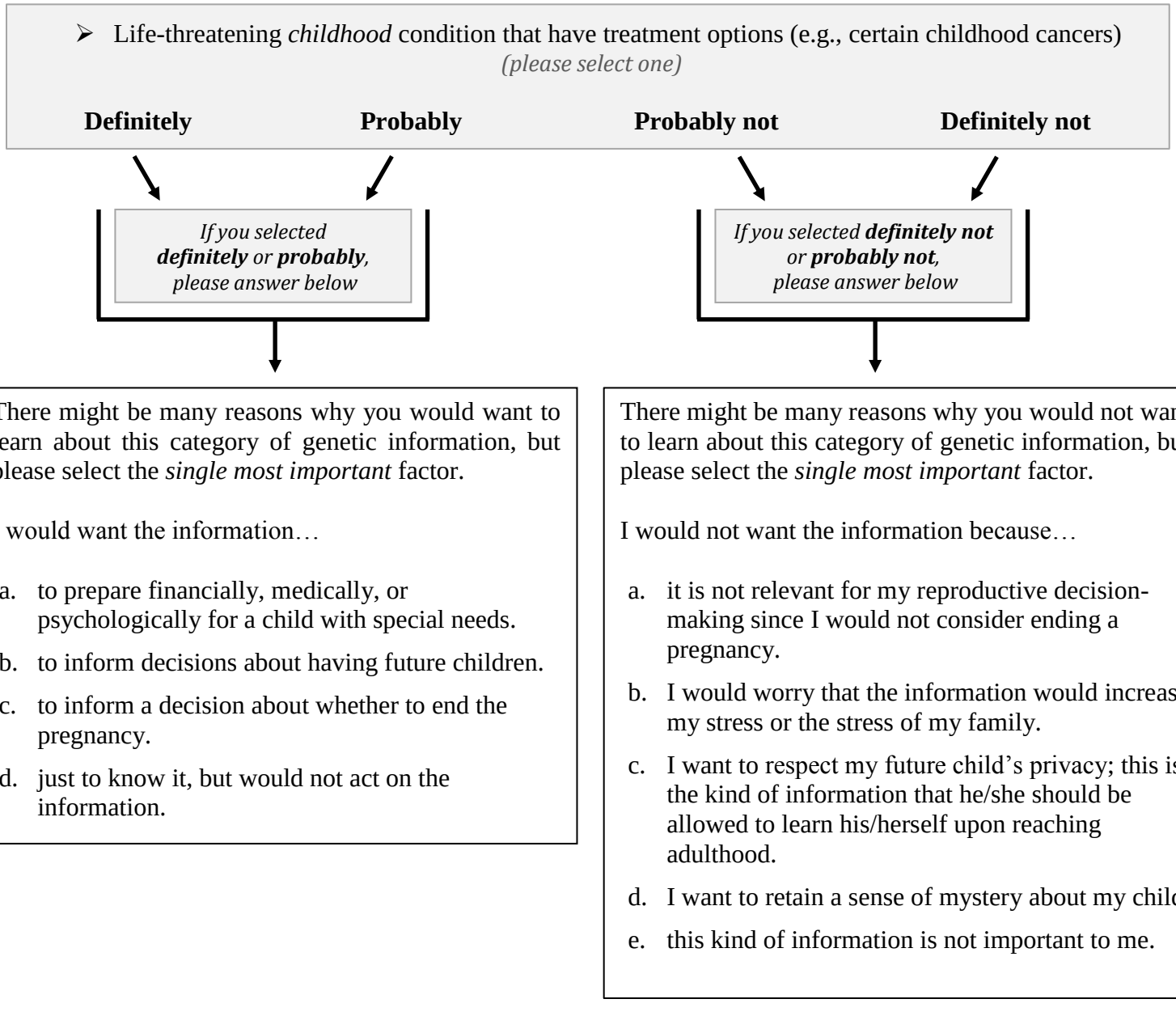

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4. Consider this scenario: Before getting tested, you and your doctor are discussing the kinds of genetic information that you might learn about your baby. You can choose to test for some kinds of information and not other kinds of information. In making a decision about which categories of information to choose, how much help would you want from your doctor?

    a. **Firm Recommendations:** I would like my doctor to present clear recommendations about the categories of information that the medical community thinks are most appropriate to test for.
    b. **Firm Recommendations, Plus All Options.** I would like my doctor to present clear recommendations about the categories of information that the medical community thinks are most appropriate, but I would also want to know about my whole range of options even if they are not recommended.
    c. **All Options, Joint Decision.** I would not want my doctor to give me clear recommendations about what to do. I would want to learn about my whole range of options, and then would make a decision together with my doctor.
    d. **All Options, Independent Decision.** I would not want my doctor to give me clear recommendations about what to do. I would want to learn about my whole range of options, and then I would make the decision on my own, or with my significant other/family.

5. Consider this scenario: You are discussing with your OB/GYN what information you would like to learn about your baby through PWGS. You have heard that some genetic information can tell you whether your child is likely to have autism. You mention this possibility to your doctor and she explains that while dozens of genes have a possible connection to autism, no single gene, or handful of genes, can definitively predict whether your baby will have autism.

    Would you still want to know the results for these genes, which are possibly connected to autism?

    On the scale, marking 1 means that you would definitely want to know, marking 5 means that you definitely would not want to know. Marking 3 means that you are neutral about knowing or not knowing. Please mark the number on the scale that best reflects your opinion.

Definitely would want to know 1 2 3 4 5 Definitely would not want to know

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6. Please rate to what extent you agree or disagree with the following statements.

   a. The more information parents have about their baby's genes, the better.

Strongly disagree	Somewhat disagree	Neither agree or disagree	Somewhat agree	Strongly agree

   b. Parents should be able to access all *medically relevant* genetic information that they want to know.

Strongly disagree	Somewhat disagree	Neither agree or disagree	Somewhat agree	Strongly agree

   c. Parents should be able to access all *non-medical* genetic information that they want to know. Non-medical information might include eye color or height.

Strongly disagree	Somewhat disagree	Neither agree or disagree	Somewhat agree	Strongly agree

   d. It is appropriate for physicians to provide their opinion about the kinds of genetic information that parents should learn about their babies.

Strongly disagree	Somewhat disagree	Neither agree or disagree	Somewhat agree	Strongly agree

   e. The state or federal government should decide what categories of fetal genetic information can and cannot be returned.

Strongly disagree	Somewhat disagree	Neither agree or disagree	Somewhat agree	Strongly agree

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7. Are there any circumstances in which you would choose to end a pregnancy?
    a. Yes
    b. Yes, but only in very limited circumstances
    c. No

8. Do you already have children?
    a. Yes
    b. No

9. Are you planning to have additional children after your current pregnancy?
    a. Yes
    b. No

10. Do you have a child or close relative with a genetic disease or developmental disorder?
    a. Yes
    b. No

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11. Age
    a. 20 or under
    b. 21-25
    c. 26-30
    d. 31-35
    e. 36-40
    f. 41-45
    g. Over 45

12. Race/Ethnicity (check all that apply)
    a. White
    b. Hispanic or Latino
    c. Black or African American
    d. Asian
    e. American Indian or Alaska Native
    f. Native Hawaiian or Other Pacific Islander
    g. Middle Eastern
    h. Prefer not to answer

13. How important would you say religion is in your life?
    a. Not important at all
    b. A little bit important
    c. Somewhat important
    d. Very important
    e. Extremely important

14. Education level
    a. Less than high school degree
    b. High school or GED degree
    c. Some college but no degree
    d. Associate degree
    e. Bachelor degree
    f. Graduate degree

15. Marital status
    a. Single
    b. Married or long-term partner

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16. Household income
    a. Less than $24,999
    b. $25,000 to $49,999
    c. $50,000 to $74,999
    d. $75,000 to $99,999
    e. $100,000 to $149,999
    f. $150,000 to $199,999
    g. $200,000 or more
    h. Prefer not to answer

17. **Familiarity with Complex Genetic Terms**

The words below are words that patients in the genetics clinic sometimes struggle with. The first question after the word asks how familiar you are with each word. Marking "7" on the scale reflects that you strongly agree, marking "1" on the scale means that you strongly disagree. Please circle the number that best reflects your opinion. The second question asks you to choose the best word which fills in the blank.

Genetic
I am familiar with this term:

Strongly disagree 1 2 3 4 5 6 7 Strongly Agree

Genetics is the study of how living things receive common traits from previous _____.
    a. generations
    b. experiences
    c. exposures
    d. geminations

Chromosome
I am familiar with this term:

Strongly disagree 1 2 3 4 5 6 7 Strongly Agree

A chromosome contains all of our _____ material.
    a. genetic
    b. digestive
    c. cellular
    d. brain

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Susceptibility
I am familiar with this term:

Strongly disagree 1 2 3 4 5 6 7 Strongly Agree

Susceptibility to a disease means you _____ get the disease.

a. eventually will
b. definitely will
c. might
d. will never

Mutation
I am familiar with this term:

Strongly disagree 1 2 3 4 5 6 7 Strongly Agree

A mutation is a change in your _____ .

a. intestine
b. skin
c. DNA
d. blood

Variation
I am familiar with this term:

Strongly disagree 1 2 3 4 5 6 7 Strongly Agree

Having variation in the genetic code will lead to disease _____ .

a. all of the time
b. some of the time
c. never
d. only in animals

Abnormality
I am familiar with this term:

Strongly disagree 1 2 3 4 5 6 7 Strongly Agree

_____ is abnormal.

a. A trachea
b. Brown hair
c. Trisomy
d. Blood pressure

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Heredity
I am familiar with this term:

Strongly disagree 1 2 3 4 5 6 7 Strongly Agree

Heredity is the transfer of characteristics from _____ .

a. the environment to the person
b. the sick to the healthy
c. parent to child
d. teacher to student

Sporadic
I am familiar with this term:

Strongly disagree 1 2 3 4 5 6 7 Strongly Agree

A genetic disease that occurs without _____ is considered sporadic.

a. symptoms
b. a family history
c. a diagnosis
d. medication

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