



November 2001

DISCUSSION PAPER 46

It's what's expected:
genetic testing for inherited conditions

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1. ABSTRACT

Objective: The development of new genetic technology brings with it responsibility for evaluating the effectiveness and efficiency of testing programs, including gaining an understanding of the value of information. This study examined the factors individuals took into account when making decisions about having a genetic test for Tay Sachs Disease.

Participants, design and setting: Fifteen people participated in an in-depth interview as they attended a clinic for genetic testing. A thematic analysis of the data was undertaken.

Results: Participants were most influenced to have testing by personal factors: e.g. ethnic background and desire to have children. Disease characteristics were also important. The results informed the development of a Stated Preference Discrete Choice (SPDCM) experiment.

Conclusions: Participants were motivated to have testing by a need for reassurance and certainty. Thus, information was an important outcome for them. The results of the SPDCM experiment indicate that participants valued information positively thus providing support for the findings of the qualitative research.

Key words: qualitative research, decision making, value of information, reassurance, certainty.

2. INTRODUCTION

Genetic testing, like many forms of screening, produces information and not health outcomes per se, although the information may enable individuals to take action which will improve their health. Genetic testing to determine individuals' and couples' carrier status, and thence their risk of having children affected with specific autosomal recessive diseases, is already available. With the progression of the Human Genome Project, possibilities for the detection of such genetic mutations are increasing rapidly. The information on carrier status will be translated into health outcomes through couples' decisions to have or not have children; so the information is qualitatively different to other risk factors. Carrier status may bring with it feelings of guilt or blame (1). Knowing both partners are not carriers may bring feelings of relief and reassurance to proceed with pregnancies. Hence understanding the value of information to individuals being tested is important to understanding the value of testing.

There are some circumstances in which information is likely to result in improved health outcomes. First, if the possession of a genetic mutation is associated with certainty (100% probability) with the development of a disorder for which there is an effective intervention, the best case scenario is that the disorder can be prevented or successfully treated. Second, if the possession of a genetic mutation is associated with certainty (100% probability) with the development of a disorder but there is no effective intervention available, prenatal testing can inform reproductive decisions which may lead to improved health outcomes at the population level. However, an individual who discovers that she or he has the genetic abnormality would not experience any health gain.

Third, if the possession of a genetic mutation increases the likelihood (ie the risk) of developing a disorder and there is an effective intervention, some but not all those tested will

experienced improvements in health outcomes. Finally, if the risk of developing the disorder is increased but there is no effective intervention, there is no possibility of health gains (5).

However, the decision to be tested is not just the result of an appraisal of the value of information. People agree to testing without having considered the implications of the results (2). Particularly during pregnancy, individuals may agree to testing without realising they have made a conscious choice (3). There is social pressure for parents to accept testing as part of being good parents (4).

Individuals tested for carrier status prior to conception may use the information in different way: they may select a non-carrier partner, to avoid pregnancy with a carrier partner or to make decisions about pre-natal testing. A decision not to reproduce the abnormal gene will result in a decrease in the incidence of the disorder and an increase in population health outcomes. However, some carrier individuals may proceed with pregnancies knowing that there is a risk that the disorder will be transmitted to the foetus. In this case, there is no change to health outcomes although the parent/s have made a more informed decision (5).

The decisions faced by individuals or couples are made more complex by variation in the severity of disorders, the age of onset and the type and amount of interventions used for monitoring or treatment. Thus, understanding how and why people decide to be tested is important to design effective and sensitive testing programs. Increasingly, new programs are being subject to economic evaluation, and have to be shown to be efficient as well. The usual approach to the economic appraisal of pre-pregnancy and pre-natal testing programs has been in terms of the cost per case of disease prevented (5); but this does not take into account the value of information and hence may not be a valid estimate of the benefits or consequences of

testing. An alternative to cost effectiveness analysis which has been suggested is stated preference discrete choice modelling (6). This alternative requires the analyst to propose the features or attributes which will influence the individual's decision, in this case the decision to be tested or not.

This approach is relatively new in its application in health program evaluation. In most studies, the process by which the attributes were developed is not described. Yet the appropriate selection of the attributes is essential to the validity of the model. Further, the approach requires the collection of survey data. The questions and choices actually posed to respondents need to be phrased in language that they understand.

Therefore, an important step in designing and framing such evaluations is gaining an understanding of the experiences of individuals who make decisions about participating in testing. Qualitative research is particularly suited to exploratory assessments where the objective is to understand why people behave as they do. Its techniques of data collection and analysis aim to elicit the meanings people apply to events and situations occurring in their lives and to provide insights into the beliefs and attitudes underlying their behaviour (7). Thus it provides a useful first step in identifying the appropriate outcomes for economic evaluation.

This discussion paper reports the results of qualitative research undertaken with a sample of people attending a Sydney hospital for genetic testing. The aims of the research were to:

- ❑ explore the factors which influenced participants' decisions to undergo genetic testing and
- ❑ assess the benefits, risks and burdens of any decision

3. BACKGROUND

Participants attended the Wolper Jewish hospital (Sydney, NSW) intending to be tested for Tay-Sachs Disease (TSD). However, the genetics testing program operating at the hospital also offers people the opportunity to be tested for three other inherited conditions: cystic fibrosis (CF); Canavan disease and Fanconi anaemia. Individuals or couples can choose to have one test or any combination of the four tests available. They can also choose to be tested and to receive their results as an individual or as a couple. While those who receive their individual results learn their own carrier status, those who choose the couple option do not receive individual results, but learn their status as a couple. Thus, if both are non-carriers or if one person only is a carrier, the couple will be told that, as a couple, they are unlikely to have a child with the condition/s they have been tested for. Only when both members of a couple are carriers will they be told that there is a one-in-four chance that a pregnancy will result in the birth of an affected child.

TSD is an autosomal recessive neurodegenerative disease, characterised by an accumulation of gangliosides throughout the body, resulting in progressive neurological dysfunction and death (8). Infants born with TSD usually die between the ages of three and five. Adolescent- or adult-onset TSD are less severe forms of the disease and do not always result in death. TSD is most prevalent in the Jewish Ashkenazi population (Jewish individuals of Central and Eastern European descent). Such individuals have a 1 in 25 chance of being carriers of TSD compared to a 1 in 250 chance for non-Ashkenazi Jewish people and the general population (9)).

CF is also an autosomal recessive disorder. It affects multiple organs and varies in the severity with which it is manifested in individuals, but is usually fatal by age 30 (10). The

disease is characterised by repeated respiratory infections, pulmonary obstruction and pancreatic insufficiency, resulting in increasing and often prolonged periods of severe handicap. Thus, CF is likely to have a measurable impact on an individual's quality as well as length of life and result in comparatively high consumption of health care services and products. Carrier rates for CF vary between 1 in 25 and 1 in 30 (11).

Canavan disease is similar in its manifestation to TSD. It is an autosomal recessive neurodegenerative condition which is more common among people of Ashkenazi Jewish descent, who have a 1 in 40 chance of being a carrier, compared to a 1 in 400 chance for the general population.

Fanconi anaemia is an autosomal recessive disorder characterised by severe anaemia, immune system failure and malformations of other body systems including the skin and bones. It is not restricted to any particular ethnic or regional group. The carrier rate in the population is 1 in 500.

4. METHODS

People attending the Wolper Jewish Hospital for genetic testing for TSD were asked by the genetic counsellor administering the test(s) whether they would be willing to participate in a short face-to-face interview about the factors that influenced their decision to have genetic testing. A list of the questions (including prompts) used as the basis for the interview are shown in Appendix One. Testing is offered once a month at the hospital and all people who attended between November 1999 and March 2000 were approached to participate. Of the 22 people attending during this time, 15 agreed. The reasons for non-participation were overwhelmingly time-related. Fifteen people were interviewed; four couples and seven individuals (all women). It should be noted that the seven individuals were all members of couples who had made a decision not to be tested as a couple. All couples who agreed to be interviewed were interviewed together.

All interviews were transcribed and a thematic analysis was carried out (12). The analysis was undertaken by the first author (MH) using the following steps:

1. After listening to the tapes and reading the transcriptions a list of issues raised by the respondents was produced;
2. The transcriptions were searched for “significant statements” (i.e. statements made by respondents which were directly relevant to the issues, including opinions, preferences and assumptions);
3. The statements were interpreted. This can also be described as moving from what was said to what was meant;
4. The meanings were clustered into broader categories called themes;

5. Using the themes as a framework, the “results” were described in detail, using direct quotes from the interviews to illustrate the points being made.

The research was undertaken with the approval of the University of Sydney Human Ethics Committee.

5. RESULTS

In this section, the themes emerging from participants' descriptions of decision making related to genetic testing are reported. Each theme is illustrated by one or more quotes. After each quote the participant is identified as either female (F) or male (M) and by whether she/he was part of a couple (C) or attended for testing alone (S).

TSD is a particular problem for Jewish people

Almost all participants had known about TSD for a long time, including its effect on children and families and the fact that a genetic test is available. A few were able to describe being taught about it at school, others claimed that it was knowledge passed on to them by their family. Two responses illustrate this:

I have known about it for a very long time. Probably since we were kids (M,C).

I've known about it for a long time, I think initially through my studies (M,S).

Despite their good general understanding of TSD, all participants appreciated the detailed information supplied by the testing program about the diseases being tested for and the tests on offer. This was described by participants as information which did not affect the decision they had made (i.e. to have the test) but which made the process of having the test easier.

That is, it assisted their decisions about whether to have the test as an individual, as individuals within a couple separately or as a couple together and of how they would receive the results. In this way, such information may have enhanced their perception that they were doing the right thing in having a test. Some typical responses were:

It [the information] didn't influence my decision [to be tested] but it made the process easier. It was good to have someone who knew a bit about it to have a talk with them on the phone (M, C).

We'd made our decision [to have the test] but we wanted to hear what it was about as well (F, C).

We always intended to be tested

Many participants claimed that their decision to be tested was a long-standing one. That is, they had always known that they would have the test – it was just a matter of deciding when. Some people described some personal knowledge or family link with TSD (a relative born with TSD or a friend of the family having a child with TSD) as being the catalyst for their (and sometime their family's) expectations that they would be tested. However, others described the decision to get married or to have children as the (short-term) trigger which prompted them to investigate the test. The following responses illustrate these factors in the decision making process:

I have a history of one case [of TSD] in my family plus my sister and my cousin had the test (M,C).

It's sort of an expectation really, getting married and having the test (F,S).

It's [having the test] been on my mind, and we're getting married in five weeks and just decided to have the test (M,C).

We wouldn't have the test if we weren't thinking about having a baby (F,C).

Whenever the decision was made, it was often made on the advice of others – parents (usually mothers), prospective spouses, friends or doctors were mentioned:

Because they're concerned as a family, my parents and her [fiancee's] parents said have you had your Tay-Sach's test (M,C).

We have got some friends who have had the test. It's pretty common among our peer group (M,C).

There were probably two or three couples I knew who said they were going to do it [have the test].

After that, it was natural [to consider having the test] (F,C).

Well, my gynaecologist [advised her to have the test]. I actually called her to tell her I was pregnant and she called me and told me to go for a Tay-Sach's test (F,S).

Many people insisted that the decision making process they undertook was neither complicated nor drawn out. Their attitude was “the test is available, it seems to apply to me, why not have it?”

I didn't think [about getting tested], I just made a decision to get tested because I was worried about the implications of the disease [TSD] (M,C).

It was a simple decision that we were going to do it (F,C).

It's better to know the risks

Almost all the participants cited the desire to be relieved of worry about their risk of passing TSD to their children as the major reason for having the test.

Because we want to have a baby so before we fall pregnant we want to know if we are at risk (M,C).

It's part of becoming pregnant, first of all being tested (F,S).

It's [the benefits of the test] reassurance I've done everything I can to prevent it [TSD] (F,C).

Whatever you can do to neutralise those concerns [about having an affected child] gives you more peace of mind (M,C).

The results will give me peace of mind hopefully. It you're going to have kids you might as well check it out (M,C).

A related aspect which was also mentioned was the desire to know their status (and thus be certain of it and hence their risk of passing the disease on).

We're very health conscious and very grateful for the medical technologies that are available and we plan to take full advantage of them to find out our status (F,C).

A number of people described the test as one part of a process of elimination – this (and other tests) were their contribution to doing all they could to ensure the birth of a healthy child:

It [the test] fitted in with my character of being cautious and doing the best things possible to have a healthy child (M,C).

It's a process of elimination. You eliminate all the things that are likely to cause problems (M,C).

It will be an extra precaution I've taken and I don't have to worry if I do have children (F,S).

A few participants described how they would use the information from the test to make another set of decisions (i.e. to try to become pregnant or to have an amniocentesis).

If you are going to be having further tests or about doing an amniocentesis you should be able to time things appropriately (F,C).

If there is a positive [test] it means we can take whatever the steps are to make an informed choice about what the future holds (F,C).

As they had come for testing, it is likely that all participants believed that the potential benefits of the test (i.e. increased certainty, peace of mind and the knowledge that they had done the right thing) outweighed any negative aspects. However, a few were able to cite factors which were or might be a barrier to having the test. These included the fact that it involved having a blood test, knowledge that a negative result would not completely eliminate their chances of having a child with TSD, fear of the results and the cost of the test(s).

I don't really like having my blood taken, it is just a physical concern (F,S).

Well [I'll] never be sure [that I won't have a child with TSD], I think [genetic counsellor] says they give you statistics like 99.5% sure (F,S).

Naturally, you worry that you might test positive (F,C).

It is quite expensive so I think the cost can be a barrier for people. When we saw the cost it makes you think twice about having all four tests (F,C).

A moral responsibility to prevent suffering

Almost all participants mentioned the "horrific" nature of TSD and their desire not to put a child through such suffering or to bear the brunt of such suffering themselves as one of the reasons they had decided on testing.

I think having a baby born into this world that's going to go through any kind of pain and then die young --I wouldn't want to put a child through that (F,C).

Knowing I could be the carrier of a disease which will render my child dead within two years – it's a pretty frightening thought (M,C).

A number of people also mentioned a feeling of responsibility to the wider community, and, in particular, their responsibility to do the right thing by the Jewish community.

I think if you have a chance of preventing or decreasing the genetic disease in your local community, it should be tackled (M,C).

It's better for everyone in the Jewish community in the long run – maybe eventually find a cure (F,S).

Consequences of testing

While the consequences of any positive results were referred to by about half the participants, most were unwilling to discuss details of their decisions if they were to find out they that they were carriers of the TSD gene. While one or two referred to pre-natal testing as the next logical step, others referred to the next steps as decisions they would only consider if they had to.

[We would consider] having further tests or about doing an amniocentesis (F,C).

It [a positive test] may not change the fact that we try and have a baby but it will mean that we can prepare ourselves better for the potential consequences (M,C).

I suppose we'll find out first if it was positive and then we will see what steps to take (F,C).

If [wife] is positive as well, then it'll be a real dilemma, what to do. A real dilemma (M,C).

While many people had discussed having the test with family members, only a few considered that the results of their test would be important for family members. This may have been because the discussions were likely to have been with older members of the family

(e.g parents) and they perceived that the results were applicable to younger members who were likely to have children.

Some people stated that they would only pass on the results if they were positive i.e. that either individually or as a couple, they were carriers of the gene for TSD.

I think if it came back that I was [a carrier], I think it will be useful for relatives to know and be tested (F,S).

6. DISCUSSION AND CONCLUSIONS

It has been proposed that a number of factors are likely to influence individuals' decisions to undergo genetic testing. These include the characteristics of the disease (i.e. the age of onset, prognosis, severity), the characteristics of the test (e.g. level of discomfort, predictability) and personal characteristics (e.g. age, level of education). The participants in this study were most influenced by personal factors such as their Jewish ancestry and desire to have children as well as by the characteristics of TSD as a fatal disease predominantly affecting infants. The characteristics of the test were less important to participants. Two or three people mentioned the distasteful nature of blood tests, but also denied that this characteristic had ultimately influenced their decision, although it may have delayed their having the test. Approximately the same number mentioned that they were aware that the test was not a perfect predictor of their chances of having an affected child, but, as with their dislike of blood tests, believed that the benefits of the test outweighed this negative aspect.

Participants in this research were largely motivated to have genetic testing by a desire to eliminate some of the risk associated with having a child, that is, by their need for reassurance and certainty. Thus the value of information was an important component of the decision to be tested. Some also believed that the testing program could benefit the wider community of Jewish people, indicating that feelings of social responsibility and altruism were also important in their decision making. Participants were more likely to be encouraged or expected to have the tests by members of their family and community than by health professionals.

No test is 100% sensitive and specific. Couples where both partners are identified as carriers can still have unaffected children (3 in 4 chance); and two partners told they are not carriers

can still have rare mutations that will produce affected children. The extent to which the value of information is influenced by the certainty attached to that information is worth further investigation.

Although the potentially negative aspects of testing, including the possibility of a positive test and cost were mentioned by a few participants, testing was widely regarded as beneficial. This result is not surprising as the sample of respondents was limited to people who had already decided to be tested. People who had considered testing but decided against it and non-Jewish people may have a different perspective on the factors influencing their decisions about genetic testing. Nonetheless, the study provides important insights into how the recipients of testing perceived the potential positive and negative consequences of the tests.

As alluded to in the Introduction, the results of this study informed the design of a Stated Preference Discrete Choice experiment which aimed to elicit preferences for screening for Tay-Sachs disease and cystic fibrosis and to value benefits beyond carrier detection. The attributes chosen for the SPDCM survey included carrier risk, disease severity, proportion of other people tested, rate of false negatives, cost and doctor recommendation. The survey was completed by 471 adults in metropolitan Sydney (261 representatives of the general population and 210 Ashkenazi Jewish people).

The results indicated that individuals were prepared to pay for testing, and to pay more for test results with a lower false negative rate, implying a positive value for information.

Interestingly, individuals were more likely to be tested the more prevalent testing was in the community, counter to the idea of the economic rational self-interested decision-maker.

Preferences were also sensitive to doctor's recommendation and carrier risk, and were

affected by individuals' stage of life. In addition to providing evidence about uptake of screening for these particular conditions, the results inform more general models of participation in screening programs and add to understanding of the consumer's utility function. Thus, they have both clinical and policy relevance in terms of showing the potential uptake of testing in response to alterations to the testing program (13).

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8. APPENDIX ONE:

Research Study into “How individuals make decisions about and assess the benefits and burdens of genetic testing”.

Questions for participants

First of all, can you tell me how you found out about the test for Tay-Sachs disease?

What made you think that you might get tested?

What were the sorts of things which helped (are helping) you make a decision about having a test?

(If had test) Were there any particular factors which influenced your decision?

[for example, influence of family, friends, health professionals, probability of being at risk, disease characteristics, accuracy of test results]

(If not had test) What sorts of things are you taking into account as you think about whether or not to have testing? [for example, influence of family, friends, health professionals, probability of being at risk, disease characteristics, accuracy of test results]

(if already decided/tested) **Could you describe the process you went through in thinking about whether or not to have the (genetic disorder) test?**

Took time to think things over?

Gathered information about disease/mode of inheritance/test (e.g. read books, pamphlets, the Internet etc.)?

Sought opinions of others (experts/family/others)

Discussed the implications of the results?

What was/were the most important factor/s which influenced your decision to have the test? What was done to help you in making the decision? Could anything else have been done?

Did the way you were treated or the manner of the health professionals make any difference? How?

Did you have any worries or concerns about having the test?

(If yes) why/how are the worries/concerns not as important as the benefits of the test?

(If yes) what, if anything, could have (or did) relieved any worries/concerns you have/had?

Could you describe the positive or good things about having the results of the (genetic disorder) test?

Certainty

Reassurance

Information and knowledge

Effect on family members

Could you describe any negative/bad things about having the results of the (genetic disorder) test?

Residual risk

Guilt

Anxiety/stress/depression

Effect on family members

What have (will) the test results told (tell) you?

How have (will) the results been (be) useful to you?

**Have (Do you think) the results been (will be) useful to other members of your family?
How?**

(if undecided about being tested) **What sort of process are you going through in making the decision?**

- Gathering information
- Getting advice/opinions
- Discussion of the implications of being tested
- Weighing up the pros and cons of being tested

Do you have any worries or concerns about the test or the results you might receive?

(If yes) why/how are the worries/concerns not as important as the benefits of the test?

(If yes) what, if anything, could have (or did) relieved any worries/concerns you have/had?

Is there anything else you want to tell me about making these decisions?

Thank you very much for participating in this study.