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The impact of population based screening for carriers of cystic fibrosis

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Abstract

The purpose of the study was to evaluate the short term effects of population based screening for carriers of cystic fibrosis. The outcome measures included perceptions of health, anxiety, and understanding of test results. Those adults aged between 18 and 45, registered with a general practice in Inner London, who accepted the offer of carrier testing, completed questionnaires before testing, upon receipt of results, and three months later. Full data were obtained from 427 with negative test results and 14 carriers.

Receipt of results had no effect upon perceptions of health or perceived risk of having an abnormal baby. Those receiving a positive test result were significantly more anxious upon receipt of this result. By three months, this anxiety had dissipated. While knowledge of the test improved from before to after testing, by three months there was some decay. Although the residual risk among those with a negative result of being a carrier was given as 1:135, at least 17% of those receiving a negative result incorrectly believed that they were at no risk of having a child with cystic fibrosis. Five of the 14 receiving a positive result erroneously believed that their results meant that they probably, but not definitely, carried the gene for cystic fibrosis. In the longer term the greatest problem of population screening would appear to be one of false reassurance rather than anxiety. Longer term studies are needed to determine how well carrier status information is retained, and how carriers and carrier couples plan and respond to pregnancy and how much understanding they retain of their test results.

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Screening can cause harm as well as good. The most common unintended adverse effects are sustained raised levels of anxiety, and false reassurance. These are evident across a wide range of screening programmes.[1] The psychological effects need to be considered in the evaluation of any screening programme, first to determine the extent of both benefits and harm, and, second, to determine how unwanted effects might be avoided in future programmes.

Cystic fibrosis (CF) is the most common autosomal recessive disease among northern Europeans, with 1:25 being known carriers. Hitherto the great majority of carriers only discovered their carrier status after having an affected child. The cloning of the gene in 1989 makes population based carrier detection feasible. We set up a screening programme in which CF carrier testing was offered to all adults of reproductive age registered with a primary care health centre. As well as determining uptake of the test[2] we have studied the psychological consequences of participation in the screening programme. These results are reported in this paper.

The psychological effects of the inability to provide a definitive negative result also need to be determined as only about 85% of the mutations are easily identified.[3,4] The majority of studies of the effects of gene carrier testing have been conducted into screening for Tay-Sachs and sickle cell diseases in North America. The most frequently studied effects of carrier testing are the emotional consequences and, in particular, anxiety. Some degree of anxiety is evident both in the short and longer term for those who are found to carry a gene for a recessive condition.[5,6] This effect is more marked in men than in women.[5] From these studies, however, it is not possible to determine the extent to which some of these adverse effects may be prevented by the provision of counselling both before and after testing. The cognitive and behavioural consequences of genetic testing have rarely been studied. In a recent cross sectional study of those who had undergone carrier testing for Tay-Sachs disease, we found that carriers had a less optimistic view of their health in the future compared with those who had received a negative test result.[7] How carriers detected in these screening programmes use the information about their carrier status in any decisions they may make concerning reproduction has not yet been the subject of formal study.

The purpose of the current study is to evaluate the short term effects of population based screening for carriers of cystic fibrosis. The outcome measures include perceived health, anxiety, and understanding of test results.

Material and methods

SAMPLE

Those eligible for testing for the cystic fibrosis gene included all patients aged 18 to 45 registered with an inner London general practice (n = 5529).[2] All 5529 were approached; 957 patients were tested, 637 females and 320 males.

THE BOOKLETS

Two brief booklets were written for participants in the screening programme, one for all participants, the other for those receiving a positive test result.

Booklet I: "Have you heard of cystic fibrosis?"

This booklet begins with a brief description of cystic fibrosis. The booklet explains that the disease is inherited by children from parents who carry a gene for cystic fibrosis. This explanation is followed by (1) a definition of the term carrier; (2) carrier incidence in the population; (3) how testing for the gene is conducted by mouth wash. A telephone number for further information was also included.

Booklet II: "What does it mean to be a carrier of cystic fibrosis?"

The booklet describes the symptoms and prognosis of cystic fibrosis. It is emphasised that carriers will not develop cystic fibrosis. Genes and how they are passed on to children are described, using words and diagrams. A brief description of the reproductive options available to carrier couples are listed. Also included is a contact telephone number and advice on having partners and relatives tested.

Readability of booklets

This was assessed using the "Readability Yardstick".[8] The booklets scored 67 and 68 respectively, meaning that about 83% of the population can be expected to understand them.

MEASURES

(1) *Emotional outcomes*

(*A*) *Anxiety*. This was assessed using a short form of the state scale of the Spielberger State-Trait Anxiety Inventory.[9]

(*B*) *Responses to test results*. These were assessed using a list of 11 feelings: surprised, happy, upset, pleased, healthy, worried, guilty, unhealthy, depressed, relieved, and indifferent. Respondents were asked to tick the words that best described their feelings about their test results at the time of completing the questionnaire.

(2) *Perception of health*

This was assessed using a five item scale, assessing perceptions of current, past, and future health.[7]

(3) *Perceived risk of having a child with an abnormality*

This was assessed using a nine point visual analogue scale, marked at one end "not at all likely", and at the other "extremely likely".

(4) *Knowledge of cystic fibrosis carrier testing*

This was measured using three questions with a multiple choice format, assessing knowledge of the implications for carriers' health of being a carrier, and likelihood of carriers having affected children (appendix 1).

(5) *Understanding test results*

This was measured using a multiple choice question (appendix 2).

(6) *Reproductive intentions*

These were assessed only in those receiving a positive test result. Carriers were asked about their intended uses of prenatal diagnosis and termination of affected pregnancies if their partners were also carriers.

PROCEDURE

Those eligible for inclusion in the population based screening programme were approached in one of six ways.[2] All were given a leaflet describing the test. The 957 who accepted the offer of testing had at least a 10 minute period of discussion with the study nurse counsellor (GD) before giving a mouthwash sample for analysis.

All results were sent by post within three weeks of testing. Recipients of positive results were sent more detailed information on the implications of being a carrier and were invited to make an appointment for further counselling. Questionnaires were completed before the test, upon receipt of the test result, and three months after the results. Six of those receiving a positive test result were interviewed six months after receipt of their test results.

Results

Twenty-eight of those participating in the screening programme received a positive result. The numbers returning questionnaires before and after testing were 681 (73%) of those receiving a negative result, and 23 (82%) of those receiving a positive result. At three months these numbers were 656 (69%) and 18 (64%) respectively. Analyses were carried out on those who had completed all three questionnaires: 467 of those receiving negative test results, and 14 of those receiving positive results.

The immediate responses of those receiving negative test results are presented in table 1.

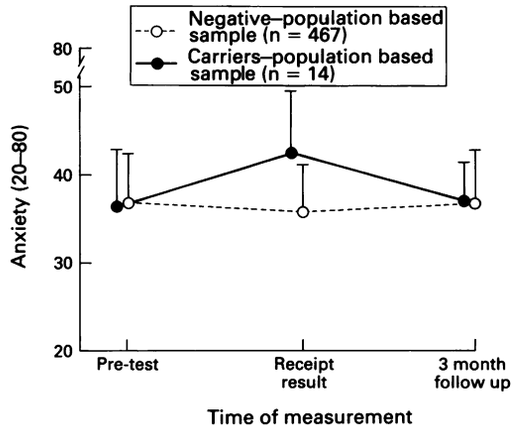
The most frequently chosen adjectives to describe reactions to a negative test result were pleased, happy, and relieved. The next most frequently chosen adjective was healthy. Those receiving positive results were more likely to respond initially with feeling of surprise and upset.

Upon receipt of test results, those receiving a positive result were significantly more anxious than those receiving a negative result; three months later this difference was no longer apparent (repeated measures MANOVA: $F(2,958) = 3{\cdot}8$, $p < 0{\cdot}024$) (figure).

Receipt of negative or positive results had no evident effects upon perceptions of

Table 1 Responses to results of carrier testing

	Positive result (carriers) (n=14)		*Negative result (carrier risk 1/135 see text) (n=467)*	
	Receipt of test result No	*3/12 follow up No*	*Receipt of test result No (%)*	*3/12 follow up No (%)*
Surprised	8	8	7 (2)	3 (1)
Happy	0	0	155 (33)	139 (30)
Upset	4	1	1 (0)	1 (0)
Pleased	3	3	341 (73)	308 (66)
Healthy	4	2	52 (11)	46 (10)
Worried	1	0	1 (0)	1 (0)
Guilty	1	0	1 (0)	1 (0)
Unhealthy	1	0	1 (0)	0 (0)
Depressed	1	0	1 (0)	1 (0)
Relieved	2	1	140 (30)	87 (19)
Indifferent	1	3	39 (8)	63 (14)



Anxiety in those receiving positive and negative test results in population based screening.

Table 2 Understanding of test results

	Positive results (carrier) (n=14)		*Negative results (carrier risk 1/135) (n=467)*	
	Receipt of test result No	*3/12 follow up No*	*Receipt of test result No (%)*	*3/12 follow up No (%)*
Correct	10	9	435 (93)	379 (81)
Incorrect	3	5	29 (6)	77 (17)
Don't know	1	0	3 (1)	11 (2)

health or perceptions of risk of having an abnormal baby (repeated measures MANOVAs: $F(2,958)=1{\cdot}74$, $p=0{\cdot}2$, $F(2,958)=2{\cdot}7$, $p=0{\cdot}1$).

Overall knowledge about the test improved from before to after participation (Wilks Lamda approx $F(2,474)=13{\cdot}8$, $p<0{\cdot}001$) (table 2). However, univariate analyses showed that between receipt of the test results and the three month follow up, those receiving a negative test result showed a significant decay in knowledge ($t=2{\cdot}67$, df -466, $p=0{\cdot}008$) whereas carriers showed a trend towards improved knowledge ($t=-1{\cdot}96$, df $=9$, $p=0{\cdot}08$).

A certain amount of misunderstanding was evident, however. For example, three months after testing, five of the 14 carriers did not correctly understand that their test results meant that they were *definitely* carriers of a gene for CF. Seventeen percent of those receiving a negative result incorrectly believed that they were *definitely not* carriers.

Indeed, for those receiving a negative test result, understanding significantly decreased from receipt of result to the three month follow up (χ^2 30·1, df $=1$, $p<0{\cdot}01$). There was no change in understanding for those receiving a positive result ($\chi^2=0{\cdot}18$, df $=1$, $p=$ NS).

There were no significant associations between understanding of test results, anxiety, or perceptions of health.

Those receiving a positive test result were asked how they might react to the offer of prenatal diagnosis if their partners were also carriers. Seven intended to undergo prenatal testing and to have a termination if the fetus were found to be affected. One would have the test, but not a termination; one other stated that she would not have testing. Five did not know how they would respond.

Discussion

The results of this study suggest that in the short term there are relatively few adverse effects of population based screening for cystic fibrosis. The raised anxiety upon receipt of a positive test result had dissipated by three months. In the longer term, the greater problem would appear to be one of false reassurance. Although the residual risk of being a carrier among those with a negative result was given as 1:135, at least 17% of those receiving a negative result incorrectly believed that they were at no risk of having a child with cystic fibrosis. This risk was given both before and after testing in writing, and verbally during pretest counselling. One third of those receiving a positive result erroneously believed that their results meant that they probably but not definitely carried the gene for cystic fibrosis. Both groups therefore took a somewhat optimistic view of the facts presented to them.

The finding of temporarily raised anxiety among carriers is similar to the results in two other recent studies of CF carrier testing.[10 11] Of more concern are the misunderstandings about the meaning of test results in one fifth of those with negative test results and one third of those with positive test results.

The causes of these misunderstandings may be the result of several psychological phenomena, explained below.

First, it may be the result of forgetting. People's recall of any information declines over time, including medical information.[12] Even between the time of receiving test results and three months later there is a significant decrement in understanding of the meaning of negative test results. One factor influencing recall is motivation. Misunderstanding of results may have arisen because people were not highly motivated to undergo testing in the first place, and hence may have had relatively little interest in their results. Evidence to support this comes from people's responses to the offer of testing. While 70% accepted an offer when made face to face, the majority failed to return on another day for the test.[2]

A further possible explanation for the apparent misunderstanding of test results may be that recall of results follows the use of a cogni-

tive heuristic or rule of thumb that allows the essence of the meaning of the test result to be retained without having to recall the somewhat complex details. For those receiving negative test results, a residual risk of 1:135 of being a carrier is so small as to be unworthy of action, conferring a sense of "I am not at risk, and therefore my result means I am definitely not a carrier". For those receiving positive results, believing that this means only a likelihood of being a carrier may represent an acknowledgement of the possibility as opposed to the certainty that carriers have affected children.

Finally, the tendency for results to be misremembered in a direction that underplays a person's risk is similar to a more general and well described tendency for people to be optimistic in appraising their health as well as other personal attributes.[13] This has been seen as a self-serving bias, defending the person against the possibilities of misfortune.

Aside from these psychological mechanisms, a cause of and solution to these misunderstandings may lie in the counselling people received before and after testing. The meaning of all test results was emphasised in the written information and the information provided verbally before testing, and in the letters conveying test results. Given the primary care setting of the study, one way of addressing the decrease in understanding is for health professionals to use consultations as an opportunity to discuss and check understanding of any test results.

We did not confirm an earlier finding of reduced optimism in future health among carriers. This could be because of many differences between the two studies: time since carrier detection, nature of conditions being screened for, method of screening. There was some evidence, however, that for some people undergoing screening called into question their general health. So, for example, 10% of those receiving a negative result on the population based screening programme described feeling healthy upon receipt of their results. One of the carriers, herself a health professional, considered attributing previous ailments to carrying the gene:

"I wondered if the fact that I have a number of allergies may be a tenuous link in a way . . . And when I have a cold it tends to go to my chest . . ." (0505).

Many of those found to be carriers were uncertain about how they would respond when actively contemplating pregnancy. Although not assessed formally, it became apparent during interviews with six of the carriers that their understanding of CF was extremely limited. The amount of information provided in the study about CF was brief and similar to that provided in other reported studies.*[10 11] It is evident, however, that probably largely as a result of this, people were poorly informed about the nature and severity of the disease. Most carriers overestimated the severity of cystic fibrosis. The information provided in the study information booklet given to all those tested stated that even with intensive treatment people with the disease usually died in early adulthood. While this is arguably a rather pessimistic picture of the outcome for children born now with CF,[14] the understanding of most carriers was even more gloomy.

In response to a question asking how much she knew about CF, one carrier responded:

"It affects the lungs, and it's quite distressing for the children in that they can't breathe properly and they don't survive into adulthood. I'm not actually very clear if it affects the brain or not . . . I wondered if there was a lack of oxygen or something and it was related to that." (0014).

Another, in response to a question about the life expectancy of someone with CF replied:

"I'd seen someone (with CF) who is 26; that was very unusual. I would have thought it was just childhood really, about 5 or 6 years old or a bit older but not reaching into adulthood." (0650).

Another in response to the same question:

"I believe it is no longer than 12. . . . But mainly it's 2 to 5 years." (1103).

Given that perceived burden is an important predictor of the use of prenatal diagnosis and termination of pregnancy,[15] it is important that those undergoing testing are given more information about the condition for which they are found to be carriers.

The main reason for offering carrier detection to the general population and not just to those who are pregnant is that if carrier couples learn that they carry the mutated gene before pregnancy, then they have more reproductive options, including the option not to have children. It has also been suggested that it allows more time to decide whether to undergo prenatal testing outside of the emotional intensity that characterises pregnancy. While we now know the initial responses of non-carriers to testing, longer term studies are needed to determine how well carrier status information is retained, and how carrier couples, in particular, plan and respond to pregnancy, and whether there are residual anxieties about carrier status.

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* Description of the symptoms and severity of cystic fibrosis were included in both information booklets.

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Appendix 1 Questions on knowledge of carrier status and disease transmission

Format of questions: multiple choice.

(1) A carrier for cystic fibrosis is a person who:
  (a) has one cystic fibrosis gene, is healthy but needs to have regular medical check ups.
  (b) has one cystic fibrosis gene, is healthy but needs to follow a strict diet
  (c) has one cystic fibrosis gene, is healthy, and *will not* develop the disease.
  (d) has one cystic fibrosis gene, is healthy, and *will* develop the disease.
  (e) don't know.

  Correct answer (c).

(2) A baby can only develop cystic fibrosis if *both* parents pass on the gene for cystic fibrosis:
  (a) true
  (b) false
  (c) don't know

  Correct answer (a).

(3) If *both* parents have the cystic fibrosis gene they can have a baby *without* cystic fibrosis:
  (a) true
  (6) false
  (c) don't know

  Correct answer (a).

Appendix 2 Understanding of test result

(1) Receipt of a negative result.
  If a person received a negative result on testing for the cystic fibrosis gene, this means that:
  (a) s/he is *definitely* not a carrier.
  (b) s/he is *unlikely* to be a carrier.
  (c) don't know.
  (d) other (specify . . .).

(2) Receipt of a positive result.
  If a person receives a *positive* result after having the test for the cystic fibrosis gene, this means that:
  (a) s/he is *definitely* a carrier.
  (b) s/he is *likely* to be a carrier.
  (c) don't know.
  (d) other (specify . . .).