Antenatal screening for carriers of cystic fibrosis: randomised trial of stepwise *v* couple screening

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Abstract

Objective—To perform a rigorous comparative evaluation of stepwise and couple approaches to antenatal carrier screening for cystic fibrosis.

Design—Pragmatic randomised trial.

Setting—Hospital antenatal clinic serving a regional population.

Subjects—2002 women (couples) attending for booking antenatal visit at less than 17 weeks' gestation with no family history of cystic fibrosis.

Interventions—Offering counselling and carrier testing for cystic fibrosis, either to women in the first instance (stepwise) or to couples (couple screening).

Main outcome measures—Uptake rates; anxiety; knowledge of cystic fibrosis and carrier status (both partners); attitudes to health, pregnancy, the baby, and screening (both partners); and uptake of carrier testing by relatives.

Results—Uptake of screening was the same for both approaches (90%). After delivery most women remembered test results and their meaning, but 53/253 (21%) of those with negative results of couple testing had forgotten that repeat testing would be advisable if they had a pregnancy with a new partner. With stepwise screening women identified as carriers had high levels of anxiety when results were received (mean anxiety score 52.3). This dissipated with a reassuring partner's result (carriers' mean anxiety score 36.1) to levels similar to those receiving negative results from couple screening. Of those receiving negative results, women who had stepwise screening were significantly less anxious than those who had couple screening (mean score with result 32.1 *v* 35.4, 95% confidence interval for difference -4.7 to -2.1).

Conclusions—Couple screening allows carriers to avoid transient high levels of anxiety, but is associated with more anxiety and false reassurance among most screenees who will test negative. Stepwise screening gives carriers and their relatives genetic information and is, in our opinion, the better method.

Introduction

Cystic fibrosis is a common autosomal recessive disorder which shortens life through chronic lung disease and affects one in 2500 people in Britain. The discovery of the cystic fibrosis gene and its major mutations has made it possible to detect 82-92% of carriers in the British population by using a mouthwash test.¹⁻⁷ As most new cases of cystic fibrosis arise in families with no known affected members carrier screening of the population is the only way to alert most couples at risk before the birth of an affected child. The effectiveness and timing of such screening have been the subjects of recent studies.⁸⁻¹¹ Carrier testing before

conception may allow couples more time to adjust to their increased risk and more reproductive options, including avoiding pregnancy. Pregnant women, however, have a high degree of interest in their own reproduction, have usually chosen their partner, and are readily available for counselling by specialised staff. Prenatal testing is thereby also available for the large number of pregnancies that are unplanned.

Mennie *et al* reported a study of stepwise carrier screening for pregnant women attending hospital for antenatal care.¹⁰ If a carrier was found she and her partner were offered genetic counselling and testing of the partner. Uptake of screening was 71%. Identification of carriers increased maternal distress, although this disappeared when a negative result in her partner became available.¹⁰ In part to avoid such distress and the associated need for counselling, screening of couples was proposed by Wald.¹² Both partners are asked to submit a sample, but only one is tested in the first instance. If a carrier is found the partner's sample is tested. A positive result is issued only if both partners are found to be carriers. If one partner tests negative, even though the other may be a carrier, a negative result is issued to the couple. Couple testing avoids the potential problem of carriers whose partner's test is negative being concerned by the residual 1 in 500 risk that their child is affected, but it fails to inform carriers of their risk with new partners and to warn their families.¹³ The advantages and disadvantages of these two approaches have generated much debate. Livingstone *et al* recently reported a study of the use of routine couple screening in hospital antenatal clinics.¹⁴ They concluded that couple screening was not associated with anxiety in the short term. They did not, however, use a randomised study design, and the measure of anxiety used was not the most sensitive for detecting distress in this group of patients. Pragmatic, as opposed to explanatory, trials seek to establish the most effective treatment for everyday clinical practice, with analysis by intention to treat rather than assessing treatments provided under ideal circumstances.^{15,16} We carried out a pragmatic randomised trial to compare the two methods and to assess knowledge and attitudes of pregnant and delivered women to their babies and their own health.

Method

RANDOMISATION

Two thousand and two couples without a family history of cystic fibrosis attending Aberdeen Maternity Hospital antenatal clinic were randomised in a ratio of 5 to 1 to be offered either stepwise or couple screening. We expected that about 1500 women would accept the offer of a stepwise test, about 300 would accept a couple test, and, of those offered stepwise testing, about 55 would be identified as carriers.¹⁷ This design

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enabled us to estimate the proportion of women who were falsely reassured with a standard error of about 1% for women with negative stepwise results, 3% for negative couple results, and 6% for carriers in the stepwise arm.

Randomisation was performed on a weekly basis with stepwise testing being offered for five consecutive weeks followed by one week of couple screening. This method of randomisation was used to simplify study protocols for laboratory staff, who had to be aware whether or not to await the arrival of a partner's sample before testing.

SCREENING

At recruitment to the study women, and their partners if present, were given an information leaflet and counselling by a study midwife. Women were dissuaded from participating if their partner was not available for testing. Consent forms were completed before tests were carried out. DNA analysis was performed on samples of mouthwash for four cystic fibrosis mutations to allow detection of 92% of carriers in the Grampian population and thus 85% of carrier couples.^{7,18} Positive and negative results were sent to women, their obstetric consultants, and their general practitioners. Carriers (stepwise arm) were contacted by telephone if possible to arrange an early appointment, and were offered counselling and testing of partners with a clinical geneticist. If both partners were found to be carriers, further counselling was provided and prenatal diagnosis was offered via the obstetrician. Carriers were encouraged to inform their families of the genetic risk and of how testing might be obtained if desired.

OUTCOME MEASURES

Outcome measures were uptake of prenatal screening, anxiety, knowledge, perception of genetic risk, attitudes towards the pregnancy and the baby, perception of health, and attitudes to screening. Anxiety was measured by using a six item short form of the state part of the Spielberger state-trait anxiety inventory.¹⁹ The inventory itself is a widely used measure of anxiety that is reliable and sensitive. It has been extensively used in prenatal screening research in the United Kingdom, allowing results from this study to be compared with others. As the original form is 40 items long we used a six item short form to increase compliance with completion. The six item form has been shown to be reliable (reliability coefficient 0.82) and valid, producing scores similar to those produced by the long form.²⁰

Knowledge about cystic fibrosis and carrier status was assessed by using the questions in tables III and IV with either "yes/no/don't know" responses being available or up to four choices. All the questions could be answered with information given during the standardised counselling at recruitment. Perception of genetic risk was measured by using two questions: how likely do you think it is that you are a carrier of cystic fibrosis? and how likely do you think it is that your baby has cystic fibrosis? In response, those being questioned were asked to ring a number from 0 to 7, the words "not at all" being beside the number 0 and "definitely a carrier/has cystic fibrosis" being beside the number 7. Attitudes to pregnancy and the baby were measured with a series of eight point rating scales, previously used in other studies.²¹ Women were asked to consider how they felt about their pregnancy and their baby in response to seven different adjectives and to rate their feelings on a series of eight point scales, which were marked "not at all" beside the figure 0 and "very much" beside the figure 7. The adjectives "fulfilled," "stressed," "pleased," "optimistic," "worried," "uncertain," and "depressed," were considered with respect to the pregnancy, and "uncertain," "confident," "attached," "loving," "maternal," "con-

TABLE I—Baseline data for those offered testing in each arm of study. Figures are numbers (percentages) unless otherwise stated

Detail	Stepwise screening (minimum n=1513*)	Couple screening (minimum n=330*)
Mean (SD) age (years):		
Women	27.6 (4.82)	27.9 (4.72)
Partners	29.9 (5.68)	30.1 (5.59)
Marital status:		
Married	1190 (79)	269 (81)
Living together	224 (15)	45 (14)
Single	99 (6)	16 (5)
No of children:		
None	761 (50)	179 (54)
One	550 (36)	117 (36)
Two	163 (11)	28 (8)
More than two	42 (3)	6 (2)
Partner present at antenatal visit?		
Yes	840 (51)	188 (52)
No	796 (49)	173 (48)
Gestation (weeks):		
6-8	60 (4)	15 (4)
9-12	938 (58)	193 (54)
13-16	618 (38)	149 (41)
17+	13 (1)	3 (1)
Social class‡ (woman's occupation):		
I	83 (6)	16 (5)
II	405 (27)	100 (30)
IIIN	621 (41)	135 (41)
IIIM	156 (10)	35 (11)
IV	124 (8)	25 (8)
V	73 (5)	13 (4)
Other (for example, students)	23 (2)	3 (1)
Not classified	34 (1)	4 (1)
Related to someone with cystic fibrosis?:		
Yes‡	10 (1)	2 (1)
No/don't know	1507 (99)	327 (99)
Know someone with cystic fibrosis?		
Yes	255 (17)	51 (16)
No	1254 (83)	279 (84)
Heard of cystic fibrosis?:		
Yes	1377 (91)	304 (92)
No	135 (9)	26 (8)

*Data for age, gestation, and social class were available for all women (1638) and most partners (361).

†1980 HMSO classification of occupations.

‡Relations were cousins (five), second cousins (four), father in law (one), sister in law (one).

cerned," and "detached" were considered with respect to the baby. Responses were then summarised in two scores; one for negative attitudes to pregnancy and one for negative attitudes to the baby, produced by reversing the negative responses and then adding the component scores, giving a worst score of 28. Perception of health was measured with a five item questionnaire relating to past, present, and future health. The responses were summarised in a score with the score for the most pessimistic view of health being 5 and the most optimistic score possible 24.²² Attitudes to screening were assessed with the questions in table VIII.

QUESTIONNAIRES

Women received self completion questionnaires at the time of recruitment, with test results, and after delivery (not sent to 93 women because of loss of pregnancy or baby, or new address unknown). Women's knowledge and attitudes were assessed at recruitment and after delivery, with the other outcomes being assessed at each time point. Partners received questionnaires at recruitment and after delivery regarding knowledge, perception of genetic risk, and attitudes to screening. An additional questionnaire was sent to carriers after their partner's result was available. After delivery carriers were also asked about the number of relatives they had informed. These results are expressed as the ratio of the number of relatives told (siblings/parents/aunts or uncles/cousins) over total number of relatives.

STATISTICAL ANALYSIS

Two group comparisons for continuous variables with a normal distribution were made by using Student's *t* test. Categorical data were analysed by the χ^2 test. Differences in "with test result" anxiety scores were confirmed by using analysis of covariance

(multiple regression) to adjust for baseline anxiety scores. An economic analysis will be reported elsewhere.

Results

Randomisation—There was little difference in the ages of women or partners between the two arms of the study, nor in social class, economic status, race, number of children, or reproductive intentions (table I). Response rates for the women's questionnaires were 1844/2002 (92%) at recruitment, 1642/2002 (82%) with the test result, 42/48 (88%) with the partner's result, and 1470/1908 (77%) after delivery. Partners' response rates were 1421/2002 (71%) at recruitment and 1413/1908 (74%) after delivery.

Screening—Stepwise testing was offered to 1641 women, of whom 1487 (91%) accepted a test. Twelve women were found to have a family history of cystic fibrosis; extra counselling and appropriate mutation analysis were performed. Forty eight carriers were identified and offered genetic counselling and testing of their partners. Samples from partners were provided in all but one instance, that carrier having refused to take any further part in the study. Three carriers' partners were not available at the time of counselling but provided postal samples. One carrier couple was identified. Couple screening was offered to 361 couples, of whom 321 (89%) provided two samples. Nineteen (5%) couples did not provide a sample from the man. One couple received a positive result. Of the 320 couples given negative results, 11 included one partner who was a carrier. Both of the carrier couples identified by the study elected to have prenatal diagnosis; both fetuses were unaffected.

Anxiety—At recruitment those offered couple

TABLE II—Mean (SD) anxiety scores* of women at different time points. Note that different numbers of women answered each questionnaire so minimum number answering is given

Timing of scores	Stepwise screening (minimum n=carriers 34; negative results 1072)	Couple screening (minimum n=250)	Difference between arms (95% confidence interval for difference in means)
At recruitment:			
Overall	32.7 (10.1)	34.2 (10.9)	-1.50 (-2.81 to -0.19)
With result:			
Overall	32.8 (10.7)	35.4 (11.5)	-2.67 (-4.04 to -1.30)
Carriers	52.3 (14.4)	N/A	
Negative result	32.1 (9.9)	35.4 (11.5)	-3.36 (-4.66 to -2.06)
With partner's result:			
Carriers	36.1 (13.5)	N/A	0.68 (-3.13 to 4.49)†
After delivery:			
Overall	31.2 (9.7)	32.0 (10.3)	-0.78 (-2.14 to 0.58)
Carriers	32.3 (10.7)		
Negative result	31.2 (9.7)	32.0 (10.3)	-0.82 (-2.18 to 0.54)

*Anxiety score derived from six item short form of state part of Spielberger state-trait anxiety inventory (worst score = 100).²⁰

†Comparison made with negative couple results.

NA=not applicable.

TABLE III—Women's and partners' understanding of their own results after delivery, by study arm, and test result. Figures are numbers (percentages) of group giving correct response to question

Question (correct response in brackets)	Stepwise screening				Couple screening (Negative results)	
	Carriers		Negative results		Women (n=253)	Partners (n=248)
	Women (n=36)	Partners (n=35)	Women (n=1092)	Partners (n=1067)		
Did you/your partner have a cystic fibrosis carrier test? (Yes)	36 (100)	34 (97)	1081 (99)	960 (90)	250 (99)	238 (96)
What was the result of your own test?	36 (100)	N/A	1081 (99)	N/A	243 (96)	246 (99)
Was your partner found to be a carrier?	36 (100)	34 (97)	N/A	1046 (98)	N/A	N/A
If you had a pregnancy in future with a different partner would you need to have another carrier test? (no for stepwise, yes for couple)	29 (81)		732 (67)		200 (79)	179 (72)
Would your new partner need to have a carrier test? (carriers and couples yes)	34 (94)	N/A	N/A	N/A	200 (79)	179 (72)

N/A=not applicable.

TABLE IV—Women's and partners' knowledge about cystic fibrosis and carrier status at different times. Figures are numbers (percentage) giving correct response

General knowledge questions on cystic fibrosis (correct response)	At recruitment		After delivery	
	Women (n=1841)	Partners (n=1427)	Women (n=1470)	Partners (n=1457)
If both parents are cystic fibrosis carriers can they have a normal baby? (Yes)	1546 (84)	1126 (79)	1147 (78)	1078 (74)
Which sex is more likely to be carriers? (Equally likely)	1565 (85)	941 (66)	779 (53)	627 (43)
What proportion of British people are carriers? (1/25)	1638 (89)	1140 (80)	N/A	N/A
Are all carriers related to someone with cystic fibrosis? (No)	1418 (77)	898 (63)	N/A	N/A

N/A=not applicable.

testing were slightly more anxious than those offered stepwise testing (table II), but this difference was of borderline significance ($P=0.02$). On receipt of negative test results women from the couple screening arm were significantly more anxious than women from the stepwise arm ($P<0.001$). This difference was still present when analysis of covariance was used to correct for differences in anxiety score at recruitment ($F_{11362}=19.2$, $P<0.001$). Women identified as carriers in the stepwise arm had very high levels of anxiety, but this dissipated after receiving a negative result for their partners. Anxiety levels of carriers were then similar to those of women with a negative couple result. After delivery there was no difference in anxiety between groups, and anxiety levels were lower than at recruitment.

Knowledge of carrier status and perception of genetic risk—After delivery most women and their partners remembered their results, remembered some facts about cystic fibrosis and carrier status, and perceived their own genetic risk appropriately (tables III-V). There was no significant difference in perception of the baby's risk of cystic fibrosis between the two methods. Of those receiving negative results, however, 160 (21%) of the women in the stepwise group and 23 (13%) of the women in the couple group perceived incorrectly that they had no risk of being a carrier, and 145 (19%) of the stepwise group and 30 (17%) of the couple group perceived incorrectly that they had no risk of having a baby with cystic fibrosis. There was no significant difference between these groups in the proportions of those incorrectly perceiving their baby to have no risk of cystic fibrosis ($P=0.9$). After delivery, but not before, partners had a significantly greater perception of their own carrier risk than did women ($P<0.01$). This was appropriate for partners in the stepwise arm but inappropriate in the couple arm. After delivery, partners' perception that their baby might have cystic fibrosis was greater than women's (both arms of the study, $P<0.01$). Of 253 women with negative couple results, 53 (21%) were unaware that repeat testing would be required with a new partner.

Negative attitudes to pregnancy and the baby—Carriers had more negative attitudes towards their pregnancies and their babies on receipt of results (table VI). Once a partner's negative result was available, carriers' attitudes towards the baby were slightly more positive than those of women receiving negative results (mean difference in scores 2.1, 95% confidence interval 1.2 to 3.0). There were no differences between attitudes of the two groups receiving negative results.

Perception of own health—No significant differences were found in perceptions of health between arms or between carriers and those receiving negative stepwise results at any time point (table VII).

Attitudes towards screening, prenatal diagnosis, and termination of pregnancy—Most women and their partners believed that carrier screening for cystic fibrosis should

TABLE V—Women's and partners' perception of genetic risk at different time point by study arm. Figures are mean (SD) score*

Perception of risk question	Stepwise screening		Couple screening	
	Women (minimum n=carriers 35; negative results 1089)	Partners (minimum n=carriers 35; negative results 1069)	Women (minimum n=251)	Partners (minimum n=245)
How likely do you think it is that you are a carrier?:				
At recruitment:				
Overall	2.1 (0.9)	2.0 (0.9)	2.0 (0.9)	2.0 (1.0)
With results:				
Carriers	6.6 (1.0)		N/A	
Negative results	1.5 (0.9)		1.9 (0.9)	
After delivery:				
Carriers	6.7 (1.3)	2.5 (1.4)	N/A	N/A
Negative results	1.4 (1.0)	3.0 (1.0)	1.6 (1.0)	2.6 (1.0)
How likely do you think it is that your baby has cystic fibrosis?:				
At recruitment:				
Overall	1.9 (0.9)	1.8 (0.9)	1.9 (0.8)	1.8 (0.9)
With results:				
Carriers	3.2 (1.1)		N/A	
Negative results	1.5 (0.9)		1.7 (0.9)	
With partner's results:				
Carriers	2.0 (1.7)		N/A	
After delivery:				
Carriers	1.6 (1.2)	2.5 (1.4)	N/A	N/A
Negative results	1.5 (1.0)	3.0 (1.0)	1.5 (0.9)	2.6 (1.0)

*Score on eight point rating scale: 0=impossible, 7=definitely a carrier/has cystic fibrosis.

TABLE VI—Women's attitudes to pregnancy and the baby at different times by study arm. Figures are mean (SD) scores

Timing of attitude questions	Stepwise screening (minimum n=carriers 34; negative results 1047)	Couple screening (minimum n=263)	Difference between arms (95% confidence interval for difference in means)
Attitude to pregnancy scores (worst score=28):			
At recruitment:			
Overall	5.5 (3.3)	5.7 (3.6)	-0.2 (-0.6 to 0.3)
With result:			
Overall	5.4 (3.4)	5.5 (3.6)	-0.1 (-0.5 to 0.3)
Carriers	7.7 (4.2)		
Negative result	5.3 (3.6)	5.5 (3.6)	-0.2 (-0.6 to 0.2)
With partner's result:			
Carriers	4.9 (3.2)	N/A	-0.6 (-1.8 to 0.6)*
After delivery	N/A	N/A	N/A
Attitude to baby scores (worst score=28):			
At recruitment:			
Overall	7.9 (2.7)	8.2 (2.8)	-0.3 (-0.6 to 0.0)
With result:			
Overall	7.9 (2.7)	8.0 (2.7)	-0.2 (-0.5 to 0.2)
Carriers	9.0 (2.8)		
Negative result	7.8 (2.7)	8.0 (2.7)	-0.2 (-0.6 to 0.1)
With partner's result:			
Carriers	5.7 (4.4)	N/A	-2.3 (-3.3 to -1.3)*
After delivery:			
Overall	4.0 (2.7)	4.2 (3.0)	-0.0 (-0.7 to 0.1)
Carriers	4.2 (3.1)	N/A	
Negative result	4.0 (2.7)	4.2 (3.0)	-0.3 (-0.7 to 0.1)

*Carriers' scores compared with negative couple results. Carriers' scores compared with negative stepwise results were as follows: Pregnancy—difference 2.3 (1.3 to 3.4), baby—difference 1.1 (0.3 to 2.0).

be generally available, although in pregnancy only 486 women (32%) and 437 partners (30%) thought they would have a termination if they learned that their fetus was affected by cystic fibrosis. After delivery of an unaffected child, women were less likely to favour termination than in early pregnancy (table VIII). Carriers were more likely to favour termination.

Spread of genetic information—Of 35 carriers in the stepwise arm who completed an extra questionnaire after delivery, all had told some relatives their result (four telling all, 11 most, and 20 a few). The mean proportion of relatives told was 1.0 for siblings, 0.94 for parents, 0.37 for aunts and uncles, and 0.23 for cousins. Fifteen months after completion of recruitment to the study, 18 relatives of carriers have attended for genetic counselling and carrier testing.

Discussion

Both methods of screening worked well in practice. Very few partners did not provide samples when a woman had elected to be tested; all partners of carriers except for one provided samples. Stepwise screening

required more staff time, but couple screening required slightly more laboratory organisation to pair samples. Although not formally measured, stepwise testing was more demanding for counselling and laboratory staff. Uptake of screening was the same for both approaches (90%), suggesting that having some form of test was important rather than the actual process of testing. Uptake of testing was higher in this study than previously reported but was similar to the local uptake rate for the triple test (Down's syndrome and spina bifida).^{10 14}

Although carriers detected in pregnancy had very high levels of anxiety before results from their partners were available, levels of anxiety after receipt of a negative result for the partner (one in 500 risk or less) were similar to those of women given a negative couple test result. All those couples tested were subjected to slightly but significantly increased anxiety. Thus, once carriers have received partners' results, there is no benefit for them from non-disclosure. Although those in the couple arm had a slightly higher anxiety level at recruitment (perhaps because women found getting a sample from their partner stressful), the differences in anxiety between those with negative results on receipt of these results were still present if recruitment scores were taken into account. In either arm of the study any excess anxiety seemed to dissipate after delivery.

Similar proportions of both groups with negative results perceived that their baby had no risk of being affected by cystic fibrosis (17% v 15%). Only 200 (79%) women couple tested remembered that testing would be necessary in a pregnancy with another partner (despite a leaflet and an oral explanation). In contrast, nearly all the carriers (34/36, 94%) were aware that a new partner should be tested. Thus overall, couple screening is associated with more misunderstanding of results.

Eighteen relatives of 48 carriers attended for testing during the study period, but we found that most carriers had informed their siblings and sometimes more distant relatives of their results. More informed relatives may yet come forward for testing when considering or during a pregnancy. The personal and resource implications of informing relatives, however, have not been evaluated. The number of people having children with more than one partner is increasing, so knowledge of carrier status may be useful for future pregnancies. Informed carriers have the opportunity of new partners being tested before conception, thus increasing reproductive choice.

Carriers (whose partners tested negative) did not perceive their baby to be more at risk of cystic fibrosis than those women who had tested negative, although they realised there was some residual risk of the baby

TABLE VII—Women's perception of health* at different time points by study arm. Figures are mean (SD) scores

Timing of perception	Stepwise screening (minimum n=carriers 36; negative results 1084)	Couple screening (minimum n=252)
At recruitment:		
Overall	16.1 (1.6)	16.0 (1.6)
With result:		
Overall	15.8 (1.6)	15.8 (1.6)
Carriers	15.6 (1.4)	N/A
Negative result	15.8 (1.6)	15.8 (1.6)
With partner's result:		
Carriers	15.7 (1.4)	N/A
After delivery:		
Overall	15.9 (1.7)	15.8 (1.8)
Carriers	15.8 (1.4)	N/A
Negative result	15.9 (1.8)	15.8 (1.8)

*Perception of health score derived from responses to questions published elsewhere.²² Score calculated by adding score for each response after recoding of negative attitudes as positive attitudes (most pessimistic view of health score 5, most optimistic view of health score 24). N/A=not applicable.

TABLE VIII—Attitudes after delivery of all women and their partners to screening for cystic fibrosis

Question	No (%) of women (n=1470)	No (%) of partners (n=1457)
Should cystic fibrosis screening be generally available?:		
Yes	1426 (97)	1399 (96)
No/don't know	4 (3)	58 (4)
When should testing be done?:		
Birth	368 (25)	423 (29)
Age 13/16	382 (26)	379 (26)
Age ≥ 18 years	235 (16)	189 (13)
Antenatal clinic	485 (33)	466 (32)
Who should be tested in the first instance?:		
Both individually	778 (53)	829 (57)
Couples	469 (32)	465 (32)
Women	219 (15)	160 (11)
Men	4 (0.3)	3 (0.2)
Would you recommend carrier testing to a pregnant friend?:		
Yes	1235 (84)	1151 (79)
No	73 (5)	117 (8)
Don't know	162 (11)	189 (13)
If you and your partner were both found to be carriers in pregnancy:		
Would you ask for tests to be done on the baby?:		
Yes	1338 (91)	1326 (91)
No	59 (4)	44 (3)
Don't know	73 (5)	87 (6)
Would you have a termination if the baby was found to have cystic fibrosis?:		
Yes	323 (22)*	437 (30)
No	1073 (73)	408 (28)
Don't know	74 (5)*	612 (42)

*At time of test results 486 (32%) women stated they would have termination if fetus had cystic fibrosis; 395 (26%) said they would not; and 639 (42%) were undecided. Responses significantly different from those after delivery ($P < 0.01$).

being affected. The possibility that carriers would be more pessimistic about their own health was not confirmed. Pregnant women and their partners considered that carrier testing for cystic fibrosis should be available, but long term studies are required to assess how carriers will use their genetic information. Women from this study have been recruited to an ongoing long term follow up of carriers detected by the recent United Kingdom studies of population based cystic fibrosis screening (coordinated by Theresa Marteau).

Among those with negative results, couple testing was associated with more anxiety and false reassurance than stepwise testing. Women seemed to find residual doubt about their carrier status acceptable if it was due to technical reasons like the deficiencies of the test itself, but non-disclosure of potentially useful information seemed less acceptable. These findings contrast with those of Livingstone *et al.*¹⁴ We consider that the anxiety measure used in this study is more suitable than the general health questionnaire and the randomised design allows appropriate comparison to be made between alternative treatments. Stepwise screening did not seem to affect adversely carriers'

perception of their health and gave them information for themselves and their families. Carriers were, however, subjected to high levels of anxiety for a short period. Testing both partners to allow simultaneous disclosure of results might prevent much of this anxiety while allowing results to be available for other pregnancies, but additional resources would be needed.

In our opinion, stepwise screening is the better of the two methods compared as although carriers do experience transiently high levels of anxiety, the method is associated with less anxiety and false reassurance for most screenees. Additionally detected carriers and their families are given information for future pregnancies, although the long term benefits and costs of this knowledge are yet to be assessed.

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Key messages

- Most antenatal screening tests are associated with anxiety in those with positive results and false reassurance in those with negative results, so finding the best way to offer screening is important
- This study compares the stepwise and couple approaches to antenatal screening for carriers of cystic fibrosis
- With stepwise screening carriers experience transiently high levels of anxiety that dissipate when the partner's negative result becomes available
- Carriers identified by stepwise screening inform most of their siblings about their genetic risk
- Couple screening is associated with more anxiety and more false reassurance among most screenees, who will have negative results
- On balance, the authors judge stepwise screening to be the better method