

Population-Based Genetic Screening for Cystic Fibrosis: Attitudes and Outcomes

L. Ioannou^{a, f} J. Massie^{e, g} V. Collins^{a, b} B. McClaren^c M.B. Delatycki^{a, d, f, g}

^aBruce Lefroy Centre for Genetic Health Research, ^bPublic Health Genetics and ^cGenetics Education and Health Research, Murdoch Childrens Research Institute, Parkville, Vic., ^dDepartment of Clinical Genetics, Austin Health, Heidelberg, Vic., ^eDepartment of Respiratory Medicine, Royal Children's Hospital, Parkville, Vic., ^fDepartment of Medicine, Monash University, Clayton, Vic., and ^gDepartment of Paediatrics, University of Melbourne, Parkville, Vic., Australia

Key Words

Attitudes · Carrier screening · Cystic fibrosis · Outcomes · Population screening

Abstract

A population-based cystic fibrosis (CF) carrier screening program was introduced in Victoria, Australia in 2006, and was offered to couples planning a pregnancy or in early pregnancy for a fee. Individuals received pre-test advice from their doctor and through a brochure. Carriers identified received genetic counseling. The aim of this study was to assess the attitudes of people undertaking screening. Between January 2006 and June 2008 all carriers (n = 79) and a randomly selected cohort of non-carriers (n = 162) were invited to participate. A purpose-designed questionnaire explored the following domains: knowledge, recollection and meaning of carrier status, reasons for having screening, anxiety and communication of results to family members. Forty-seven carriers (62%) and 65 non-carriers (41%) returned the questionnaire. Most participants were female (97%) aged 35–39 (46%). The main reasons for choosing screening were the perception of CF as a severe condition and a doctor's recommendation. All carriers correctly recalled their carrier

status and the risk of having a child with CF, while 3 non-carriers (4.7%) were unsure of their carrier status and 12 (22%) incorrectly recalled their residual risk. Carriers answered the knowledge questions correctly more often than non-carriers. There was no difference in anxiety between carriers and non-carriers. The majority of carriers informed relatives of their increased risk of being a carrier. We conclude that participants' attitude towards carrier screening for CF was generally very positive. Our model of screening could be applied on a larger scale.

Copyright © 2010 S. Karger AG, Basel

Cystic fibrosis (CF) is the most common severe autosomal recessive disease in childhood among Caucasians, with a birth prevalence of about 1 in 2,500 live births and a carrier frequency of approximately 1 in 25 [1]. In the state of Victoria, Australia, which has a population of about 5 million, there are approximately 200,000 heterozygous carriers of CF and 20 children with CF born each year [2]. The main clinical features are chronic suppurative lung disease and pancreatic exocrine insufficiency [3]. Although treatments have prolonged life expectancy to the mid thirties, there is no cure for CF. Quality of life,

particularly for individuals with end stage disease, is poor [4].

Carrier screening for CF offers couples who are both carriers reproductive choices regarding the birth of a child with CF and reassurance of the low risk of having an affected child if they are not carriers. The current situation in Australia is that relatives of people with CF or known carriers are offered carrier testing for the known gene mutation in their relative. However, the reality is that more than 95% of CF carriers have no family history of the condition [5]. Population carrier screening refers to the screening of individuals who have no family history of the condition [6]. Remembering that 4% of the Australian population are carriers, population-based carrier screening makes sense [7].

Following the U.S. National Institutes of Health and the American College of Obstetricians and Gynaecologists and the American College of Medical Genetics recommending CF carrier screening [6], a fee-for-service CF carrier screening program was introduced in Victoria, Australia in 2006. However, there has been little exploration of the characteristics of individuals who might choose to have CF carrier screening in Australia. Honnor et al. [8], seeking to gauge test acceptance in the community, offered CF carrier screening in a primary care setting in Western Australia. A similar study was conducted in a variety of different settings in New South Wales including hospitals, workplaces and high schools with good community test acceptance [9].

Here we report the results of a study determining the attitudes towards genetic screening for CF in Victoria, Australia. The aims of this study were to explore reasons for having screening, knowledge of CF, recollection, understanding and impact of carrier status and communication of results to family members.

Subjects and Methods

Carrier Screening Program

A population-based CF carrier screening program was implemented in 2006 by Genetic Health Services Victoria (GHSV). CF carrier screening was offered to couples planning a pregnancy or during the early stages of pregnancy by obstetricians and general practitioners [7]. Pre-test information was supplied in the form of a brochure (available at www.cfscreening.com.au). Testing was by cheek swab with the swab posted to the DNA laboratory at GHSV and tested for 12 *CFTR* gene mutations. Both partners were encouraged to undertake testing together, although generally one partner was tested and the other partner was tested only if the first tested individual was identified as a carrier. All carriers underwent free genetic counseling including free cascade testing for

partners and family members. Non-carriers were not offered formal genetic counseling through the program although they could contact the service to discuss their result. Very few did this. Carriers were informed of their carrier result by telephone and either had genetic counseling over the telephone at the time of receiving their result or had face-to-face counseling. The test cost AUD 200 and there is no government or health insurance rebate for the test.

Subjects

All individuals identified as carriers ($n = 79$) and a random sample of non-carriers ($n = 162$) were sent an invitation to participate. Subjects had been screened between January 2006 and June 2008. The non-carriers were randomly selected by choosing every 15th non-carrier in the files to result in a sample of 2 non-carriers for every carrier [10]. Carrier couples were excluded from the study.

Questionnaire

The questionnaire was designed to address the following domains: demographic variables, knowledge of CF, anxiety levels at the time of completing the questionnaire, reasons for participating in screening, recollection of carrier test result and meaning of carrier status. The knowledge questions were sourced from validated surveys assessing the impact of cascade testing on families affected with CF and evaluating school-based Tay Sachs disease genetic screening programs [11]. The anxiety scale used in the questionnaire was the validated, short version of the State Trait Anxiety Inventory (STAI) [12].

The questionnaire was returned in a reply-paid envelope. The questionnaires were identified by a study number allowing reminder letters to be sent to non-responders 3 weeks after the first mail-out. If the questionnaire was not sent back after one reminder no further contact was made.

Analysis

Data analysis was conducted using SPSS Version 16.0. Preliminary descriptive analysis generated frequency data to elicit the description and attitudes of respondents. This was followed by comparisons between groups defined by carrier status. Statistical significance of between-group comparisons were assessed using χ^2 tests of association for categorical variables. Where variables had more than 2 categories, degrees of freedom are given with the χ^2 statistic. As anxiety scores were not normally distributed, box plots of scores are presented for each group, and between-group comparisons were assessed for statistical significance using the Mann-Whitney U test.

This study was approved by the Human Research Ethics Committee of the Department of Human Services, Victoria, Australia (HREC 15/05).

Results

Response

Questionnaires were sent to 241 eligible individuals, 79 carriers and 162 non-carriers. A total of 112 completed questionnaires were received, 47 from carriers, with a re-

Table 1. Demographic characteristics of participants

Demographic	Categories	Participants
Gender n = 112	Male	3 (3%)
	Female	109 (97%)
Age (years) n = 109	25–29	9 (8%)
	30–34	32 (29%)
	35–39	54 (50%)
	>39	14 (13%)
Carrier status n = 112	Non-carrier	65 (58%)
	Carrier	47 (42%)
Highest completed level of education n = 107	Secondary school only	9 (8%)
	Trade/apprenticeship	1 (1%)
	College certificate or diploma	20 (19%)
	University degree	77 (72%)
Current occupation n = 106	Managerial	30 (28%)
	Professional	46 (44%)
	Office duties	13 (12%)
	Skilled/trades	16 (15%)
	Unskilled	1 (1%)
Household income, AUD × 10 ³ n = 104	<60	10 (10%)
	61–80	10 (10%)
	81–100	14 (13%)
	>100	70 (67%)
Partner at time of testing n = 109	Yes	107 (98%)
	No	2 (2%)
Pregnant at time of testing n = 109	Yes	90 (83%)
	No	19 (17%)
Number of children at time of testing n = 107	0	31 (29%)
	1	50 (47%)
	2	20 (19%)
	3 or more	6 (5%)

n = Number of actual responses provided, as not all questions were answered by all participants.

sponse rate of 62%, and 65 from non-carriers, with a response rate of 41%.

Demographic Variables

Demographic features of the cohort are presented in table 1. Most respondents were female (97%) with only 3 males (3%) participating in the study. Of the 112 participants, 98% had a partner and 83% were pregnant at the time of being offered CF carrier screening.

Reasons for Having Screening

Participants were asked to rate factors that influenced their decision to participate in CF carrier screening on a 5-point Likert scale, 1 being 'did not influence' and 5 be-

ing 'strongly influenced'. For analysis, points 1 and 2 were combined to form the category 'did not influence', the middle point 3 was neutral and points 4 and 5 were combined to form the category 'influenced' (fig. 1).

The most influential factor for participating in CF carrier screening was the perception that CF is a severe disease (72%) followed by their doctor's recommendation (58%). Partner's opinion towards CF carrier screening was influential for 45 participants (41%) while 44 participants (40%) indicated their partner's opinion did not influence their decision. The majority of participants (87%) stated that their perception of being a carrier of CF was not an influencing factor in participating in screening.

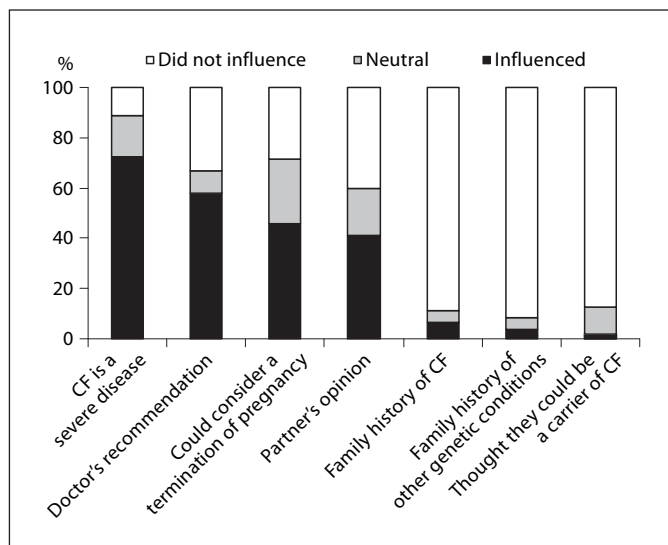


Fig. 1. Level of influence of various factors in the decision to participate in CF carrier screening.

Knowledge of Carrier Status

All 47 carriers (100%) correctly recalled their carrier screening result while 3 (5%) non-carriers were unsure of their carrier screening result. Participants were asked in an open-ended question to explain their CF carrier screening test result with respect to their risk of having a child with CF (table 2). Seventeen carriers (42%) responded that their risk of having a child with CF was dependent on their partner's result, while 9 (22%) carriers stated that they had an increased or high risk of having a child with CF. Thirty-three non-carriers (60%) responded that their risk of having a child with CF was low, while 12 (22%) stated that they have no risk of having a child with CF.

Knowledge of CF

Participants were asked to answer 15 questions regarding CF and carrier screening (fig. 2). They were required to select 1 of 3 options: true, false, unsure. There were 4 knowledge questions in which less than 50% of both carriers and non-carriers were correct. These were: (a) if no gene change is found they cannot be a carrier; (b) CF test can identify all carriers; (c) carriers usually have a family history; (d) affects more males than females.

Five of the fifteen questions were answered correctly significantly more frequently by carriers compared with non-carriers. These were: (a) a carrier couple can have a

Table 2. Meaning of results with respect to risk of having a child with CF

	n	%
<i>Carriers</i>		
Dependent on partner's result	17	41.5
Increased or high risk	9	21.9
1 in 500	8	19.5
Low risk	5	12.2
Child could be a carrier	2	4.9
<i>Non-carriers</i>		
Low risk	33	60.0
No risk	12	21.8
At ease	6	11.0
Don't know	2	3.6
1 in 500	1	1.8
Child could be a carrier	1	1.8

n = Number of actual responses provided, as not all questions were answered by all participants.

child who does not have CF ($\chi^2 = 8.52$, $p < 0.01$); (b) CF test can identify all CF carriers ($\chi^2 = 4.48$, $p = 0.03$); (c) if only one parent is identified as a carrier there is still a small chance of having a child with CF ($\chi^2 = 6.76$, $p = 0.01$); (d) need to be screened for CF carrier status every time you have a baby ($\chi^2 = 4.50$, $p = 0.03$); (e) partner determines risk as couple ($\chi^2 = 7.88$, $p = 0.01$). No questions were answered correctly more often by non-carriers than carriers.

Anxiety

The STAI scores for carriers ranged from 20 to 60, with a median of 33, while the STAI scores for non-carriers ranged from 20 to 70, with a median of 30. There was no significant difference for anxiety scores in carriers compared to non-carriers ($p = 0.56$).

Attitudes towards Screening

The attitudes towards screening are presented in table 3. Most carriers (98%) and non-carriers (87%) believe the best time to offer CF carrier screening is before pregnancy. Significantly more carriers (94%) than non-carriers (41%) recommended carrier screening to others ($\chi^2 = 31.88$, $p < 0.01$). The vast majority of both carriers (96%) and non-carriers (97%) stated that if they had their time again they would still have CF carrier screening.

Fig. 2. Percentage of participants who correctly answered each CF knowledge question according to carrier status. * $p < 0.05$ for comparison of percent correct in carriers versus non-carriers using χ^2 tests. The correct answer is provided in parentheses (T = true, F = false).

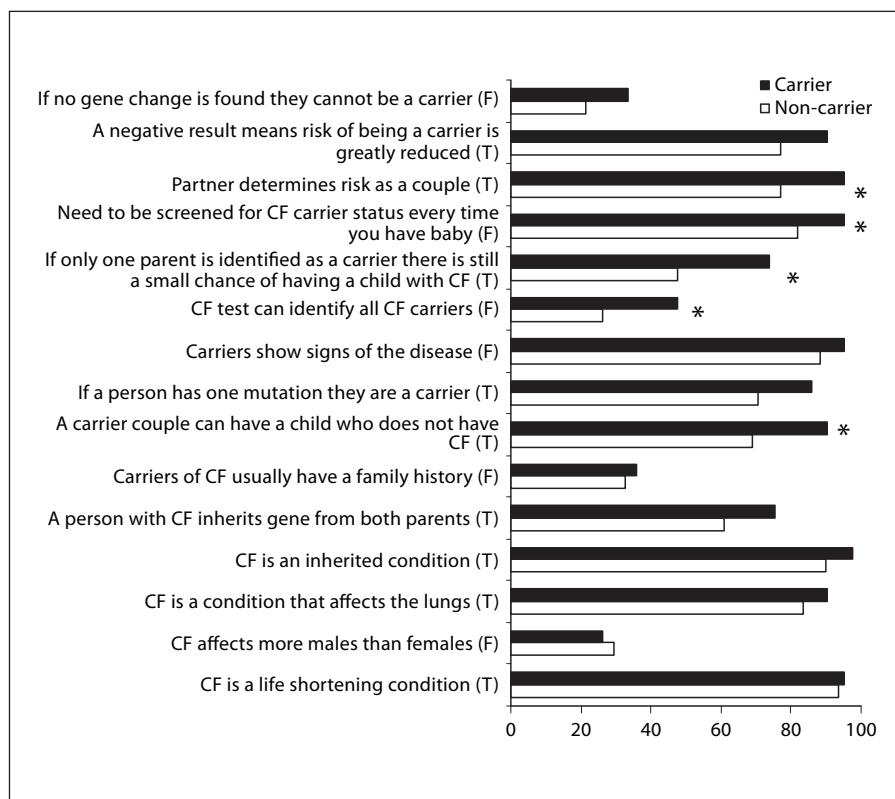


Table 3. Attitudes towards screening according to carrier status

	Categories	Carrier n (%)	Non-carrier n (%)
Best time to offer n = 108	Before pregnancy	46 (98%)	53 (87%)
	During pregnancy	0 (0%)	4 (6.5%)
	Unsure	1 (2%)	4 (6.5%)
Recommended to others n = 111	Yes	44 (94%)	26 (41%)
	No	3 (6%)	37 (58%)
	Unsure	0 (0%)	1 (1%)
If had time again would do again n = 110	Yes	45 (96%)	61 (97%)
	No	1 (2%)	1 (1.5%)
	Unsure	1 (2%)	1 (1.5%)

n = Number of actual responses provided, as not all questions were answered by all participants

Attitudes of Carriers to Family Communication and Testing

Forty-five (96%) of the carriers informed 95 family members of their result (table 4). Sixteen carriers (34%) reported that they had relatives who had been tested.

Discussion

This is the first study to evaluate participants in a population-based CF carrier screening program in Australia. Most participants were women and already pregnant

Table 4. Communication of increased risk of carrier status to family

	Categories	n (%)
Informed family n = 47	Yes	45 (96%)
	No	2 (4%)
Informed who* n = 45	Parent/s	34 (76%)
	Sibling/s	41 (91%)
	Aunt/uncle	7 (16%)
	Cousin/s	13 (29%)
Informed why n = 44	Childbearing age/ planning pregnancy	22 (50%)
	Awareness/interest	7 (16%)
	At risk	6 (14%)
	Implications for next generation	4 (9%)
	Support/advice	3 (7%)
	Other	2 (4%)
Family tested n = 47	Yes	16 (34%)
	No	27 (58%)
	Unsure	4 (8%)
Tested* n = 16	Parent/s	5 (31%)
	Sibling/s	11 (69%)
	Aunt/uncle	0 (0%)
	Cousin/s	1 (6%)
	Other	2 (13%)

n = Number of actual responses provided by carriers, as not all questions were answered by all carriers. * Carriers could select more than one response.

at the time of screening. They generally chose to be screened because of a perception that CF is a serious disease and because of a recommendation by their doctor. Carriers recalled their result and its implications better than non-carriers, probably due to their result being more significant and because of the additional genetic counseling received. Carriers were not more anxious as a result of the screening test than non-carriers. Most carriers informed members of their family of their increased risk of being a CF carrier, and many relatives followed through with cascade family testing. Despite most being pregnant at the time of testing, participants recommended carrier screening should be undertaken prior to conception.

The majority of participants in this study were well educated, affluent women between 30 and 40 years of age. The demographics of our participants reflect the setting in which screening is offered, mainly through private ob-

stetricians and some shared care general practitioners. This may have implications for generalizability of our results to the Australian population. The cost of AUD 200 is likely to have been a barrier to some. Similarly, the lack of government support may be an indication to some people that CF carrier screening is not necessary. Most people tested were women, reflecting attendance at prenatal medical visits and a sense of responsibility for testing. Most participants had no children or only one child at the time of screening. This is in keeping with evidence that women without children are more likely to have screening than those with children [8]. This may be due to women with children without CF believing that they are not at risk.

The main reason participants stated they had CF carrier screening was the perception that CF is a severe disease. It is unclear whether many knew about CF prior to the offer of screening and it is likely the severity was judged from the pre-test information brochure. The attitude of the treating doctor was also an important factor in the decision to screen. Higher uptake of screening is associated with an active offer of screening from the treating doctor, which includes providing the CF information pack and discussing screening, while lower uptake is associated with a passive offer of screening, which involves including information on CF screening with the other information pamphlets provided [13]. This was cited as a key factor by McClaren et al. [14] who interviewed pregnant women and their partners regarding factors that may influence their decision to have CF carrier screening. In a study exploring the attitudes of non-pregnant couples towards the offer of free CF carrier screening, Clayton et al. [13] found that the most influential factors in participating in screening were the opinions of both doctor and partner. However, less than half of participants in our study stated that their partner's opinion influenced their decision to have screening. The findings of our study may reflect the fact that women often attend obstetrician appointments unaccompanied by their partner. This was noted by Wald et al. [15] who found that 46% of women in their study attended obstetrician appointments alone.

We hypothesized that the perception that individuals were likely to be carriers of CF would be an important factor in choosing to be screened based on the findings of Fang et al. [16]. However, this was not the case. Henneman et al. [17] presented similar findings from a study of pre-conception carrier couple screening. Interestingly the uptake of cascade family testing for CF carriers following the diagnosis of CF by newborn screening for CF has

been poor even though relatives are at high risk of being carriers [18]. The consideration of pregnancy termination in certain circumstances was an influential factor for nearly half of the participants in this study. Similarly, Levenkron et al. [19] found that pregnant women who had CF carrier testing had an accepting attitude towards pregnancy termination.

The recollection of carrier status was high for both carriers and non-carriers despite a time lag between testing and questioning of over 12 months in many instances. Carriers had better knowledge of CF and screening than non-carriers. The most important point was the lack of understanding about residual risk by non-carriers. Residual risk is covered in the pre-test brochure but also may not be easily understood by those being screened. Carriers received genetic counseling whereas non-carriers did not and this is the most likely reason for the better knowledge of the former group.

We showed that there was no difference in anxiety levels between carriers and non-carriers at the time of completing the questionnaire. This is an important finding as an argument against population-based carrier screening is the detection of carriers who may consider they have the disease or who may remain anxious about the result. The low level of anxiety shown by carriers is likely to be a reflection of the genetic counseling they received. Levenkron et al. [19] found that the anxiety levels after receiving a positive test result (carrier) was significantly reduced following genetic counseling.

We found that having been through screening, most participants felt that the best time to offer CF carrier screening is before pregnancy. This is a common finding from other studies [19–21], however, preconception carrier screening is difficult to achieve. This is because of the low attendance at general practice of healthy young women (and men) with most people attending for pregnancy advice when already pregnant. Furthermore, while intention to participate in screening has been shown to be high it has been associated with low uptake rates [21]. In an exploration of attitudes to carrier screening in Australia, McClaren et al. [14] found that unless already pregnant, testing for CF was not considered relevant to many.

The majority of carriers in the present study reported that they had recommended carrier screening to others. Although the positive endorsement of our program was less by non-carriers, only one carrier and one non-carrier regretted their decision to participate in CF carrier screening. It is likely that carriers, who received additional genetic counseling, recognized the importance of

screening. The low numbers regretting involvement with screening is a positive reflection of the pre-test information and informed decision to participate and deal with the consequences of the result. In a similar study concerned with test acceptance and follow-up one year after screening, Levenkron et al. [19] studied 124 carriers and showed that while the majority of carriers would recommend CF screening to others, 12% regretted their decision to participate in the program due to anxiety and stress while waiting for their partner's result. By contrast, Henneman et al. [22] reported that all carriers identified in their study would make the same decision to participate in screening.

Most carriers identified in our population-based program informed family members of their increased risk of being a CF carrier. The main reason for passing information to at risk relatives was the age of the relative and their reproductive plans, with relatives of childbearing age or those planning a pregnancy being the most likely to have been informed. Ormond et al. [23] found the main reason for disclosure of genetic information is a close bond with the relative and is dependent on the relationship status, with the main reason for non-disclosure being that the relative is not in a significant relationship. Despite many carriers telling at-risk family members about CF screening, only 16 carriers reported that family members had undergone testing. This is likely to be the lowest estimate of tested relatives as participants may have been unaware of their relatives' testing status. Ormond et al. [23] also found that while the passing of information or recommendation by carriers to at-risk relatives is high, the screening of these relatives as a result of this information or recommendation is low. This is similar to the low rate of cascade family testing after newborn screening for CF in Australia [18].

There are a few limitations of this study. Our program is based on fee-for-service testing and not every obstetrician or shared care general practitioner informs their patients of the availability of CF carrier testing. As such, the target population for this study is not likely to be representative of the Australian population. The overall response rate was just under 50%. Although this is generally considered a satisfactory response rate for this type of study, where individuals are approached by mail without prior knowledge of the study, it was not possible to determine how representative the responders were of the total tested population. There is very limited information available on non-responders.

Our program of population-based carrier screening for CF can safely identify carriers without inducing un-

necessary anxiety and enable them to pass this information on to relatives. We would recommend pre-conception carrier screening where possible. With government funding, this model of screening could be applied on a larger scale enabling equity of access.

Acknowledgements

We thank Agnes Bankier, Vicki Petrou and the GHSV CF laboratory team. M.B. Delatycki is an NHMRC Practitioner Fellow.

References

- 1 Massie J, Olsen M, Glazner J, Robertson CF, Francis I: Newborn screening for cystic fibrosis in Victoria: 10 years' experience (1989–1998). *Med J Aust* 2000;172:584–587.
- 2 Collins V, Williamson R: Providing services for families with a genetic condition: a contrast between cystic fibrosis and Down syndrome. *Pediatrics* 2003;112:1177–1180.
- 3 Rowe SM, Miller S, Sorscher EJ: Cystic fibrosis. *New Engl J Med* 2005;352:1992–2001.
- 4 Elborn JS, Shale DJ, Britton JR: Cystic fibrosis: current survival and population estimates to the year 2000. *Thorax* 1991;46:881–885.
- 5 Boulton M, Cummings C, Williamson R: The views of general practitioners on community carrier screening for cystic fibrosis. *Br J Gen Pract* 1996;46:299–301.
- 6 Grody WW, Cutting GR, Klinger KW, Richards SC, Watson MS, Desnick RJ: Laboratory standards and guidelines for population-based cystic fibrosis carrier screening. *Genet Med* 2001;3:149–154.
- 7 Massie J, Delatycki MB, Bankier A: Screening couples for cystic fibrosis carrier status: why are we waiting? *Med J Aust* 2005;183:501–502.
- 8 Honnor M, Zubrick SR, Walpole I, Bower C, Goldblatt J: Population screening for cystic fibrosis in Western Australia: community response. *Am J Med Genet* 2000;93:198–204.
- 9 Wake SA, Rogers CJ, Colley PW, Hieatt EA, Jenner CF, Turner GM: Cystic fibrosis carrier screening in two New South Wales country towns. *Med J Aust* 1996;164:471–474.
- 10 Czaja R, Blair J: *Designing Surveys: A Guide to Decisions and Procedures*, ed 2. Thousand Oaks, Print Forge Press, 2005.
- 11 Gason AA, Metcalfe SA, Delatycki MB, Petrou V, Sheffield E, Bankier A, Aitken M: Tay Sachs disease carrier screening in schools: educational alternatives and cheekbrush sampling. *Genet Med* 2005;7:626–632.
- 12 Marteau TM, Bekker H: The development of a six-item short-form of the state scale of the Spielberger State-Trait Anxiety Inventory (STAI). *Br J Clin Psychol* 1992;31:301–306.
- 13 Clayton EW, Hannig VL, Pfothenhauer JP, Parker RA, Campbell PW 3rd, Phillips JA 3rd: Lack of interest by nonpregnant couples in population-based cystic fibrosis carrier screening. *Am J Hum Genet* 1996;58:617–627.
- 14 McClaren BJ, Delatycki MB, Collins V, Metcalfe SA, Aitken M: 'It is not in my world': an exploration of attitudes and influences associated with cystic fibrosis carrier screening. *Eur J Hum Genet* 2008;16:435–444.
- 15 Wald NJ, George L, Wald N, MacKenzie IZ: Further observations in connection with couple screening for cystic fibrosis. *Prenat Diagn* 1995;15:589–590.
- 16 Fang CY, Dunkel-Schetter C, Tatsugawa ZH, Fox MA, Bass HN, Crandall BF, Grody WW: Attitudes toward genetic carrier screening for cystic fibrosis among pregnant women: the role of health beliefs and avoidant coping style. *Womens Health* 1997;3:31–51.
- 17 Henneman L, Bramsen I, van der Ploeg HM, Ader HJ, van der Horst HE, Gille JJ, ten Kate LP: Participation in preconceptional carrier couple screening: characteristics, attitudes, and knowledge of both partners. *J Med Genet* 2001;38:695–703.
- 18 McClaren BJ, Aitken M, Massie J, Metcalfe SA, Amor DJ: Cascade carrier testing for cystic fibrosis: an Australian experience. Abstracts of the 31st European Cystic Fibrosis Conference. *J Cyst Fibros* 2008;7:S2.
- 19 Levenkron JC, Loader S, Rowley PT: Carrier screening for cystic fibrosis: test acceptance and one year follow-up. *Am J Med Genet* 1997;73:378–386.
- 20 Botkin JR, Alemagno S: Carrier screening for cystic fibrosis: a pilot study of the attitudes of pregnant women. *Am J Public Health* 1992;82:723–725.
- 21 Watson EK, Marchant J, Bush A, Williamson B: Attitudes towards prenatal diagnosis and carrier screening for cystic fibrosis among the parents of patients in a paediatric cystic fibrosis clinic. *J Med Genet* 1992;29:490–491.
- 22 Henneman L, Bramsen I, van der Ploeg HM, ten Kate LP: Preconception cystic fibrosis carrier couple screening: impact, understanding, and satisfaction. *Genet Test* 2002;6:195–203.
- 23 Ormond KE, Mills PL, Lester LA, Ross LF: Effect of family history on disclosure patterns of cystic fibrosis carrier status. *Am J Med Genet* 2003;119:70–77.