

ELECTRONIC LETTER

Parental attitude towards genetic testing for familial hypercholesterolaemia in children

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Nationwide screening for familial hypercholesterolaemia (FH), using family investigation and molecular testing, has been operative in The Netherlands since 1994.¹ FH is a common inherited disorder of lipoprotein metabolism with a prevalence of 1 in 400 to 500 persons in western societies.² Untreated, the disorder leads to hypercholesterolaemia, premature cardiovascular disease, and untimely death.³ Consequently, the life expectancy of FH patients is reduced by 10-20 years.⁴ Unfortunately, the disorder is often diagnosed after cardiovascular symptoms become evident and precious time for reducing the cardiovascular burden by efficacious lipid lowering drug treatment is lost.^{5,6} The aim of the programme is therefore to identify presymptomatic FH patients and to initiate treatment at an early stage of the disease. Patients are diagnosed on the basis of carriership of one of the 159 different LDL receptor gene mutations causing FH that have been identified in Dutch patients to date.⁷

Currently, the benefits of screening and treatment of FH children are under debate; guidelines for genetic screening programmes in The Netherlands still exclude children under 16.⁸⁻¹⁰ The dilemmas associated with genetic testing for adult onset diseases in childhood have led experts to conclude that "not to know" should prevail and that people should only be tested when they can decide for themselves.^{11,12} However, information on the attitudes of parents is not available with regard to genetic testing for FH in their children. Gender, carrier status, educational level, and religion are known to influence the attitude towards genetic screening for other diseases in children.¹³ Psychological studies have shown four factors to be relevant in the decision making: (1) information about the disease, (2) previous experience of the disease, (3) expectations regarding treatment options and the impact on daily life, and (4) emotions such as fear, guilt, and uncertainty.^{14,15} Therefore, we chose to work with a decision model based on these four factors: information, experience, expectation, and emotion.

The aim of the present study was to assess parental attitudes towards genetic testing for FH in children and to investigate the factors that might influence their decision.

METHODS

Sample

Consecutive participants were recruited from the FH screening programme previously described in detail.¹ Adults who carried a mutation in the LDL receptor gene and their unaffected spouses were included if they had children under 16 years. The FH parent was informed about the test result two weeks to, at most, three months before the study. To avoid bias by familial conditions, only one couple per kindred was approached.

Procedure

Informed consent was obtained from each participant. The actual survey was done by telephone and each parent was

interviewed separately. First degree relatives of index cases were contacted, after written consent to contact family members had been obtained from the index case. A specialist nurse visited the relatives at home for consent, blood sampling, and collection of personal and family data. If carrier status was confirmed, the family tree was expanded with first degree relatives of this newly identified FH patient, following the same procedure (cascade principle). Throughout the years, the participation rate in the programme exceeded 90%.

The questionnaire was ordered into three segments; questions were formulated by a team of clinicians and nurses involved in the screening programme and in the treatment of FH.

(1) Demographics

Collection of demographic data included educational level, age, gender, religion, and number and age of the children. For educational level of the participant, the total number of years of education starting at primary school level was calculated. For religion, we used the method of the Dutch Social and Cultural Planning Institution, which uses a two step approach of questioning: (1) Do you consider yourself a member of a church? (2) If yes, what is your religious denomination?

(2) Importance grading and rating

Participants were asked to grade the importance of the four factors (information, experience, expectations, and emotions) on a scale of 1 to 10. Subsequently, parents were asked to rank these factors in order of importance: most important, important, less important, and least important.

(3) Attitudes

Following the decision model based on information, experience, expectation, and emotion, four statements were formulated for each factor. In the information section, attention was paid to the quantity and quality of the information. The statements regarding experience addressed the amount and intensity of experience of the participant, either through their own experience or through relatives with FH. In the expectation section, statements were formulated to assess the significance of attitudes towards perception of the future, risk reduction, treatment options, and quality of life if their child proved to be a carrier of the FH mutation. Finally, in the emotion section, participants were specifically asked about feelings of guilt, uncertainty, fear, or obligation. Participants were offered four options to express their attitude towards each statement: agree completely, agree, disagree, and disagree totally.

Data analysis

All data were analysed using SPSS software (version 9.0, SPSS, Chicago, USA). Multilevel logistic regression analysis was performed using MLWIN.¹⁶

Table 1 Demographic characteristics

Characteristics	Mothers (n=35)	Fathers (n=35)
Age in y, mean (SD)	35.9 (4.8)	37.6 (5.4)
Carrier	16 (45.7%)	19 (54.3%)
Religious*	7 (20%)	7 (20%)
Educational level*		
≤10 y	12 (34.3%)	9 (25.7%)
10 < y ≤14 y	14 (40.0%)	15 (42.9%)
≥14 y	9 (25.7%)	11 (31.4%)
Total number of children		71
Age 0–7 y		50
Age 8–15 y		21

SD: standard deviation.

*These characteristics of the study population are a reflection of the Dutch population (Data of the Dutch Central Bureau of Statistics 1999).

Importance grading and rating

For each factor following the grading method, a mean grade and a standard deviation were calculated.

Attitudes

The answers to the statements in the attitude part, agree completely, agree, disagree, and disagree totally, were ranked on a four point scale (1 to 4), so that each statement was indicative of the underlying factor. By summing the scores of the statements per factor, scale scores of each factor were obtained (Cronbach's alpha for these scales were 0.55, 0.71, 0.62, and 0.68, respectively) and used in the analyses. Variables considered as possible predictors for the decision on testing children were gender, carrier status, religion, having older children (aged >8 y), age of the parent, education, and the four factors from the decision model. Because the study population consisted of couples (dependent), a multilevel analysis was used first. The relationships between the predictor variables and the decision to test were assessed by bivariate multilevel logistic regression analyses. Chi-square statistics (Wald test) evaluated these predictors. For analyses in which there are few related studies to provide theoretical or empirical precedents, a more liberal criterion for inclusion in the multivariate analysis is suggested.¹⁷ Therefore, all predictor variables, correlated at $p \leq 0.15$ in the bivariate analyses, were entered into the multivariate logistic regression equation, using a stepwise backwards method.

RESULTS

Participants

The present study reports on 70 parents in 35 different FH kindreds. Half of these were FH carriers and the other half spouses.

During this study period, 411 participants received a test result, of whom 137 (33%) proved to be a carrier of a mutation in the LDL receptor gene causing FH. Of these, 38 couples met the inclusion criteria. Three couples refused to participate. Seventy parents (35 couples) gave consent for the study.

Table 3 Predictors of decision to test

Variable	Support for FH genetic testing in children (n=70)		Chi-square†
	Yes to testing (%)		
Gender			
Male	94.3		2.88*
Female	80.0		
Carrier status			
Carrier	88.6		0.13
Spouse	85.7		
Religious			
No	89.3		0.93
Yes	78.6		
Children aged ≥8 y			
No	92.7		2.24*
Yes	79.3		
	Mean (SD)		
Variable	Yes (testing)	No (testing)	Chi-square†
Age (y)	36.5 (5.4)	38.6 (2.5)	1.07
Education (y)	12.3 (2.6)	14.2 (2.6)	3.69*
Information	10.5 (2.0)	9.9 (2.2)	0.52
Experience	8.82 (3.3)	7.2 (3.0)	1.57
Expectation	12.8 (1.6)	11.8 (1.2)	2.44*
Emotion	12.9 (2.0)	10.6 (1.9)	7.52**

* $p \leq 0.15$, ** $p < 0.05$. †Chi-square statistics concern the Wald test of regression coefficients in separate bivariate multilevel logistic regression analysis (df=1).

These 35 couples had 71 children below the age of 16 years. Fifty children were aged 0-8 years and 21 children were aged 9-15 years. The demographic background of the participants is shown in table 1. The ages of the parents at the time of the study ranged from 26 to 48 years. Twenty percent reported a religious denomination. The educational level of the study population was similar to the educational level in the general Dutch population (Dutch Central Bureau of Statistics, 1999).

Sixty-one (87.1%) of the parents wanted their child(ren) tested, while nine parents (12.9%) rejected the possibility of genetic testing. In 28 of the 35 couples, the parents were unanimous (27 in favour, one against testing) and in seven cases the parents disagreed.

Importance ratings

In table 2, the grading and ranking of the four factors in the decision model are shown. When the parents were asked which factor of the decision model was most important, 44.3% of parents pointed to information, 17.1% to experience, 18.6% to expectation, and 20.0% to emotion. Parents were asked to grade the importance of each factor on a scale from 1 to 10. Information with 7.9 (SD 1.6) was most important, followed by expectation with 7.3 (SD 1.4), emotion with 7.0 (SD 1.6), and experience with 6.9 (SD 1.3). Women graded experience higher than men (mean 7.2 (SD 1.1) versus 6.6 (SD 1.4), $p < 0.05$), carriers found experience more important than the spouses (mean 7.2 (SD 1.1) versus 6.6 (SD 1.3), $p < 0.05$) and graded emotion higher (mean 7.4 (SD 1.5) versus 6.6 (SD 1.5),

Table 2 Parental grading and ranking of the four factors in decision making on genetic testing in childhood (n=70).

Factor	Most important (%)	Important (%)	Less important (%)	Least important (%)	Mean grade (SD)
Information	44.3	24.3	12.9	18.6	7.9 (1.6)
Experience	17.1	28.6	31.4	22.9	6.9 (1.3)
Expectation	18.6	35.7	30.0	15.7	7.3 (1.4)
Emotion	20.0	11.4	25.7	42.9	7.0 (1.6)

Grading was done on a scale from 1 to 10.

Table 4 Logistic regression analyses predicting support for genetic testing in childhood

Variable	B	SE	p
Gender	-2.16	1.03	0.037
Education	+0.41	0.20	0.038
Emotion	-0.64	0.24	0.007

B=regression coefficient. SE=standard error.

The negative coefficient for gender means males are more likely to say yes than females, the positive coefficient for education means that a higher degree of education yields a higher likelihood of saying yes to testing and the negative coefficient for the factor emotion reflects that those with a higher score for emotion were more likely to support genetic testing of their children.

$p < 0.05$). Further analysis showed no significant differences for gender or carrier status.

Attitudes

As indicated in table 3, male sex and not having children between 8-16 years were associated with a positive decision for genetic testing ($p \leq 0.15$). Younger age ($p \leq 0.15$) and lower educational level ($p < 0.05$) of the parent were also associated with a positive attitude towards testing. From the decision model, the factors expectation ($p \leq 0.15$) and emotion ($p < 0.05$) were also associated with a positive attitude. When these variables were entered in a multivariate logistic regression, male gender and lower educational level predicted genetic testing for children under 16 ($p < 0.05$, table 4), similarly for the factor emotion. The other predictor variables were not significantly related to the decision favouring genetic testing.

DISCUSSION

Our study shows that 87.1% of parents from FH families wanted their children to undergo a genetic test. This is in contrast to the opinion of ethical experts that children should not be included in genetic screening programmes. Obviously, parents from families with FH assume an advantage in having their children tested for carrier status. Earlier studies on genetic testing in childhood have focused on the severe and untreatable adult onset diseases, such as Huntington's disease and inherited cancers.^{18, 19} However, in the case of FH, a typical adult onset disease, effective treatment is widely available. Our findings are in line with those of Tonstadt *et al*,^{20, 21} who showed that FH families did not consider FH to be a major psychosocial burden and that most parents actually wanted cholesterol screening for their children. In our study, based on genetic testing, parental attitude towards screening for FH in childhood was also positive. As we have shown before, screening for FH by genetic testing is highly sensitive compared to cholesterol measurement.¹

Since the study population consisted of people who had just made the decision to participate in the screening themselves or were involved in the decision of the spouse, selection might have had an influence on the positive attitude towards testing for their children. However, the primary participation rate in the national screening programme for FH in The Netherlands of over 90% reflects that the group targeted readily accepted the genetic testing procedure. Other genetic screening programmes yield significantly lower rates, such as 38% for breast cancer and 19% for Huntington's disease, probably because treatment options are unattractive or non-existent.^{22, 23}

The parental attitude in FH families is in striking contrast to the situation for other disorders.^{24, 25} Among adults tested for the mutations predisposing to inherited breast cancer, only 26.1% supported screening in childhood.¹³ Men and spouses were more likely to consent to testing for minors. Our results

also show that male gender and those with a lower educational level were more likely to favour genetic testing of children.

Most parents found information the most important factor in the decision making process. However, in the multivariate analysis it became evident that emotion was actually the only predictive factor and that factors information, experience, and expectation did not show a significant relationship with the decision to test. These data indicate that the decision is based less on rationality than parents wish to believe.

As genetic testing for a variety of disorders is becoming more frequent in a clinical setting, the number of test requests for minors will undoubtedly increase. Further studies are needed to focus in depth on the decision making process to optimise and individualise the counselling of families with children at risk. Most FH families do wish their children to be tested.

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