

# The impact of proband mediated information dissemination in families with a *BRCA1/2* gene mutation

E Sermijn, G Goelen, E Teugels, L Kaufman, M Bonduelle, B Neyns, B Poppe, A De Paepe, J De Grève

*J Med Genet* 2004;41:e23 (<http://www.jmedgenet.com/cgi/content/full/41/3/e23>). doi: 10.1136/jmg.2003.011353

Since the identification of the *BRCA1* (17q21)<sup>1</sup> and *BRCA2* (13q12–13)<sup>2–3</sup> genes as the major predisposition genes for hereditary breast and ovarian cancer (HBOC),<sup>4</sup> genetic counselling and predictive testing has progressively been introduced and applied throughout the world. In many centres, the initial approach towards these families has been very cautious, mainly because of lack of prospective data on the effects of preventive measures to be proposed for mutation carriers and the uncertainty of the psychological impact of this information within these families. In the Familial Cancer Clinic of the Vrije Universiteit Brussel (VUB), Belgium, a multidisciplinary team adopted a protocol of ‘non-directive’ counselling based on the international guidelines used for Huntington families.<sup>5</sup> Non-directiveness is a form of counselling that includes the presentation of several options without recommending a specific choice, but in the context of this study, non-directiveness is rather focused on the way the counselling team behaves towards other family members. According to this aspect of the protocol, the proband is the major and initially unique interlocutor between the family and the familial cancer team as represented by the counsellor. The proband helps in establishing the family pedigree and is informed about the various aspects of HBOC and predictive genetic testing. After a mutation is found, the relevant information and availability of predictive testing is communicated to the remainder of the family, initially through the proband and subsequently through other family members who come forward for testing. In contrast to persons affected by Huntington’s disease, several options are available to mutation carriers, which can alter their outcome. Recently, prospective data on the effectiveness of some preventive options have emerged, including the short term protection provided by preventive mastectomy compared with preventive screening.<sup>6</sup> The availability of effective screening and prophylactic treatment makes “the right to know” a prominent issue. Therefore, critical examination of this classical counselling approach in making genetic testing available towards the *BRCA1/2* families is needed.

In this paper we report on the effectiveness of information dissemination through the proband within families with a *BRCA1/2* gene mutation that received non-directive counselling in the familial cancer clinic of our hospital. We also report on the attitudes towards predictive testing and counselling within these families.

## SUBJECTS AND METHODS

### Counselling method and mutation screening

When a proband visits our familial cancer clinic, the counsellor first explains the various aspects of HBOC, including the risks associated with being a carrier of a *BRCA1* or *BRCA2* gene mutation, the autosomal dominant pattern of these genes, and the possibility of having a predictive genetic test. The counsellor also mentions the possibility of having an inconclusive test result. Afterwards,

### Key points

- Genetic counselling for hereditary breast and/or ovarian cancer (HBOC) is usually based on a protocol of non-directive counselling from the international guidelines used for the Huntington families. In this study, non-directiveness applies to the approach of the counselling team towards family members besides the proband. When a *BRCA1/2* gene mutation is found in a family, the possibility of predictive counselling and testing is also offered to the other family members, but only through informing the proband. We examined the efficiency of information transfer from the proband to the other relatives, and compared the level of transferred information to the needs in these families.
- Fourteen families (with a *BRCA1/2* mutation) with 107 subjects participated in the study. Subjects were eligible for participating if they were first degree relatives of an affected person with breast cancer, ovarian cancer, or another primary cancer, or if they were first degree relatives of a known or probable mutation carrier. Data were collected with semi-structured interviews.
- This study clearly reveals that the transfer of information from probands to their relatives is highly defective. In contrast and surprisingly, almost all participating relatives wanted to be informed about the various aspects concerning HBOC, and even wanted to have a predictive genetic test.
- The results of this study leads to the conclusion that the current practice of counselling is inefficient in predictive genetic testing for cancer for which preventive measures are available, and that the counselling procedure should be more directive for other at risk family members. We propose to systematically inform relevant relatives of *BRCA1/2* mutation carriers with an informative letter, without revealing personal genetic test results.

the current risk reduction strategies for carriers are outlined, including regular surveillance, prophylactic mastectomy, prophylactic oophorectomy, and chemoprevention, and the risks, benefits, and limitations of each are addressed. A family tree is then designed, and families are considered eligible for mutation screening if there are two or more first

**Abbreviations:** HBOC, hereditary breast/ovarian cancer; VUB, Vrije Universiteit Brussel

degree relatives with breast cancer with one person younger than 50 years, or if there is a first degree relative affected by an ovarian cancer. If the proband definitely wants to have a predictive genetic test after the counselling session, a mutation screen is performed on leucocytes obtained from a consenting affected family member (family member with breast and/or ovarian cancer). Both *BRCA* genes are extensively screened for mutations by a protein truncation test and conformation sensitive gel electrophoresis. When a *BRCA* mutation is found, the proband is contacted and invited for a second counselling session, in which the results are discussed. During this session, the counsellor explains to the proband that they have a key role in further informing the other family members about the various aspects concerning HBOC, and subsequently invites the proband to assume this important assignment. Additionally, the availability of predictive counselling and testing for the other family members is exclusively disseminated through the proband.

### Families and subjects included in the study

A mutation in either *BRCA1* or *BRCA2* was found in 54 Belgian families screened in our centre out of an initial database of 270 families that were screened for a *BRCA1/2* germline mutation. Of these, 25 families were considered for the current study. The 25 families actually included were counselled and followed at the Familial Cancer Clinic of the VUB. The other families in which a mutation had been found were counselled in other, distant centres and were only referred to our centre for mutation analysis. Inclusion of these families in the current study was deemed logistically impossible.

The final study sample (see below) consisted of 107 subjects from 14 families. Subjects, both men and women, were eligible for participating in the study if they were first degree relatives of an affected person with breast, ovarian, or another primary cancer, or if they were first degree relatives of a known or possible mutation carrier. Subjects had to be more than 21 years old to be eligible for the study.

### Methods

The study was carried out between December 2000 and September 2002. Firstly, the proband of each family was contacted by phone. The study was explained and permission asked to contact first degree relatives in writing. In a second step, letters were mailed to all the participating probands and eligible relatives providing them with information about the purpose and modalities of the study. The study subjects were all first degree relatives of family members with breast, ovarian, or another primary cancer, or of known and probable mutation carriers for whom we could obtain the contact details. A few first degree relatives were deliberately not contacted on explicit request from the probands because they had severe medical problems or other problems such as psychological instability or pregnancy. A few first degree relatives were also not contacted because they had emigrated. In a third step, further information was provided by phone to the participating subjects who could be reached. The aim of the study was explained and the subjects were invited for a personal interview in our familial cancer clinic. If it seemed difficult for them to visit the hospital, we proposed an interview at their home. An in depth semi-structured interview was conducted with the consenting subjects. The first part consisted of preset questions examining their knowledge or awareness about the existence of HBOC in general, the prior identification of a *BRCA* mutation in their own family, the mode of inheritance of such a mutation, and the possibility of antenatal diagnosis. The second part contained questions about their knowledge concerning the cancer risks associated with a *BRCA* mutation, and the

available preventive options for mutation carriers. In the third part, we asked whether they were aware of the possibility of having a predictive genetic test, and explored their attitudes towards predictive genetic testing both generally and personally. The interviews had an average duration of 60 minutes. All the initial phone calls, subsequent interviews, and the interpretation of answers were performed by a single investigator (ES), maximising the consistency in the comparative analysis of the responses. After the interview, we counselled the subjects about the various aspects concerning HBOC of which they were unaware. The subjects also were offered the possibility of requesting a predictive genetic test. All the participating subjects actually did request and undergo a predictive genetic test after the counselling sessions.

### Qualitative data analysis and statistical analysis

The interviews that were conducted in the families with (other than the proband) only one eligible family member or only one family member for whom we could obtain contact details were eliminated in the current study, as we were mainly interested in the information transfer from the probands to the other family members, and obviously this issue can not be studied properly in the presence of information merely about the proband and one other eligible family member. The interviews with the 14 original probands also were not used for the analysis of data because they were not the targets for information transfer. Consequently, only 107 of the 131 interviews that were conducted were used for the data analysis. The answers given to the questions of the different parts of the interview were scored with a 4 point scale coded as 0 = complete unawareness, 1 = limited awareness, 2 = good awareness, and 3 = complete awareness. A coding scheme was developed specifically for each item of the interview by deciding which elements were necessary to constitute a complete answer. For the subjects' attitudes towards predictive testing and counselling, we also used a 4 point scale, this time coded as 0 = definitely did not want to have a predictive test/counselling session, 1 = probably would not want to have a predictive test/counselling session; 2 = probably would want to have a predictive test/counselling session, and 3 = definitely wanted to have a predictive test/counselling session. Afterwards the scores of 0/1 and 2/3 were amalgamated into two groups, taking into consideration the sample size of the study. Statistics for all the items were performed on both an individual and a familial basis. The purpose of the analysis on a familial basis was to equalise the weight of each proband, independent of the number of participating subjects in each family. Standard deviations on these values were calculated with a statistical analysis software program (SPSS).

The correlation between the scores on the different items and several parameters was examined with the appropriate statistical tests. The correlation with gender was calculated by means of a paired *t* test. The correlation with age and degree of relationship towards the proband was both made by a Pearson and a Spearman correlation. The scores of the different items were also compared between the probands and the non-probands with a Wilcoxon signed ranks test and a paired *t* test. All *p* values are two tailed. Statistical analyses were performed using SPSS.

## RESULTS

### Participation in the study and characteristics of the study population

Of the original 25 probands, 24 probands (96%) were reached by phone, of whom 21 (84%) agreed to participate in the study. They cooperated by bringing us into contact with relevant family members (see Methods). One proband had

moved and could not be traced. Three probands preferred not to participate in the survey for various reasons.

In the second step, letters were mailed to all 21 participating probands and their 152 relevant relatives, providing them with information about the purpose and modalities of the study. Fourteen first degree relatives were deliberately not contacted on explicit request from the probands (see Methods). Thus, 159 subjects (92%) could be reached by phone. Of these, 131 (82.4%) agreed to participate in the study. Twenty eight (17.6%) refused to participate for various reasons: distrust in medical research, feeling too young or too old to participate in a study, refusal to discuss the topic of cancer, or being too busy.

With the consenting 131 subjects, an in depth semi-structured interview was conducted. Interviews from 107 subjects belonging to 14 families were further analysed (excluding families with only one eligible subject other than the proband and interviews with probands; see Data analysis).

The characteristics of the study population and the mutations found are shown in tables 1 and 2.

### Awareness of general information concerning HBOC

The level of information was determined in all study subjects, on both an individual and a familial basis (average of results of all participating members of a single family). For each item studied and described below, the results calculated on an individual basis did not differ from the results calculated on a familial basis.

### The existence of HBOC

Fifty of the 107 participating subjects (48.9%; SD 30.6%) in the study population were not or were only slightly aware of the existence of HBOC (score 0–1). In the group that was aware of the existence of HBOC (score 2–3), only one third of the subjects had complete awareness (score 3).

### The risks related with being a carrier of a *BRCA1/2* mutation

Sixty three of the 107 participating subjects (57.4%; SD 31.8%) in the study population were not or only slightly

**Table 1** Description of the study population

Number of participating families/subjects	14/107
Males/females	44/63
Minimum/maximum age of the subjects	21 years/83 years
Relationship to the proband	1st–4th degree (largest group 1st–3rd)
Families with a <i>BRCA1/BRCA2</i> mutation*	7/7
No. of carriers of a <i>BRCA1/BRCA2</i> mutation†	23/22
No. of non-carriers of a <i>BRCA1/2</i> mutation†	62
Percentage of subjects with:	
no breast or ovarian cancer ‡	85.9%
breast cancer‡	10.3% (1.7% bilateral BC)
ovarian cancer‡	3.7%
breast and ovarian cancer‡	0.9%

BC, breast cancer

\*For specific mutations see table 2.

†At the initiation of the study, the carrier status was known in 31 of the participating subjects. During the study all included subjects wanted to have a predictive genetic *BRCA* test, so that in the end we knew the carrier status of all participating subjects.

‡These statistics do not represent the actual cancer incidence, as only living individuals are included in this study. The *BRCA1* mutation was carried by 36% of the subjects, *BRCA2* by 46%, and 18% did not carry the familial *BRCA1/2* mutation and were considered to be sporadic cancers. Of the subjects with ovarian cancer, 75% carried a *BRCA1* mutation, and 25% a *BRCA2* mutation. The only subject with breast and ovarian cancer carried a *BRCA2* mutation. Of the subjects without breast or ovarian cancer, 19% carried a *BRCA1* mutation, 19% had a *BRCA2* mutation, and 62% did not carry a *BRCA1/2* mutation.

**Table 2** Specific *BRCA1/2* gene mutations in the 14 participating families

Family	Mutated gene	Specific mutation
1	<i>BRCA1</i>	5382insC
2	<i>BRCA2</i>	6672delTATT
3	<i>BRCA2</i>	6498delTA
4	<i>BRCA2</i>	6503delTT
5	<i>BRCA1</i>	3668AG→T
6	<i>BRCA1</i>	IVS22+5G→A
7	<i>BRCA1</i>	3780G→T
8	<i>BRCA2</i>	384insAlu
9	<i>BRCA1</i>	IVS5+3A→G
10	<i>BRCA1</i>	5382insC
11	<i>BRCA2</i>	5163delA
12	<i>BRCA1</i>	2312del5
13	<i>BRCA2</i>	1898T→G
14	<i>BRCA2</i>	6503delTT

aware of the risks associated with being a carrier of a *BRCA1/2* mutation (score 0–1). In the group of subjects that was aware of the risks (score 2 and 3), only 8.3% was completely aware (score 3).

### Preventive options available to carriers of a *BRCA1/2* mutation

Sixty eight of the 107 participating subjects (63%; SD 35.4%) in the study population were not or only slightly aware of the different preventive options available to carriers of a *BRCA1/2* mutation (score 0–1). In the group of subjects that was aware (score 2–3), only a quarter had complete awareness (score 3).

### The possibility of predictive genetic *BRCA1/2* testing

Fifty six of the 107 participating subjects (55%; SD 35.4%) in the study population were not or only slightly aware of the possibility of having a predictive genetic test for a *BRCA1/2* mutation (score 0–1). In the group of subjects aware of the possibility (score 2–3), almost everyone (95%) was completely aware (score 3) (fig 1).

### The autosomal dominant pattern of inheritance of a *BRCA1/2* mutation

The majority of the subjects (84 of 107) (85.4%; SD 18.0%) in the study population was not aware of the autosomal dominant pattern of inheritance of a *BRCA1/2* mutation (score 0–1).

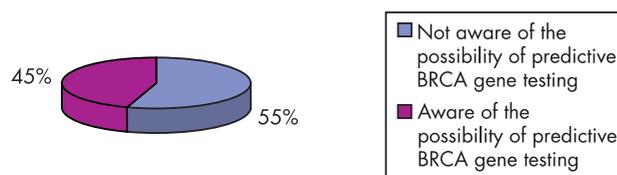
### The possibility of antenatal diagnosis for a *BRCA1/2* mutation in the reproductive subgroup of the study population

Almost all subjects (96.1%) in the reproductive subgroup of the study population (women < 50 years and all men) were unaware of the possibility of antenatal diagnosis for a *BRCA1/2* mutation (score 0–1).

### Awareness of family specific information concerning HBOC

#### The familial pattern of breast/ovarian cancer in the subjects' own family

Sixty one of the 107 participating subjects (63.4%; SD 29.2%) in the study population were aware of a familial pattern of breast/ovarian cancer in their own family (score 2–3); a significant minority (36.6%) was not or was only slightly aware (score 0–1). In the group that was aware, about half of the subjects was completely aware (48.6%) (score 3).



**Figure 1** Awareness of the possibility of predictive *BRCA* gene testing

### The existence of a *BRCA1/2* mutation in the subjects' own family

Fifty-six of the 107 participating subjects (54.3%; SD 34.1%) in the study population were not or only slightly aware of the existence of a *BRCA1/2* mutation in their own family (score 0–1) and half were aware (score 2–3) (fig 2).

### Attitudes towards predictive genetic counselling and testing

#### Willingness to be informed by a physician about HBOC, family mutation status, and predictive genetic testing

Almost all subjects (97.8%; SD 4.9%) in the study population wanted to be informed by a physician about HBOC, their family mutation status, and the possibility of predictive genetic testing (score 2–3). Only a minority did not want to be informed (2.2%) (score 0–1) (fig 3).

#### Willingness to have a predictive genetic test

Almost all subjects (96.6%; SD 6.2%) in the study population wanted to have a predictive genetic test for a *BRCA1/2* mutation (score 2–3) after counselling. Only five of the participating subjects did not want the test (score 0–1) (fig 4).

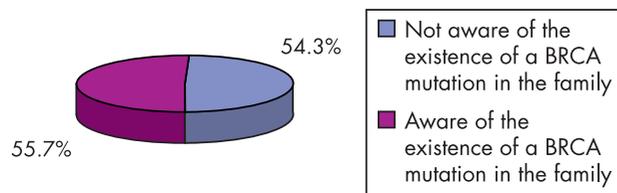
### Correlation between the results of the interviews and the gender, age, and degree of relationship of the subjects to the proband

#### Gender

Women were generally better informed and have a better awareness than men of the existence of HBOC ( $p = 0.03$ ), of the risks related with being a carrier of a *BRCA1/2* mutation ( $p = 0.01$ ), of the different preventive options available for carriers ( $p < 0.001$ ), of a familial pattern of breast/ovarian cancer in their own family ( $p = 0.031$ ), and of the existence of a *BRCA1/2* mutation in their own family ( $p = 0.034$ ). They did not have a better awareness of the possibility of predictive genetic testing for a *BRCA1/2* mutation and of the autosomal dominant pattern of inheritance. There was no statistically significant difference between men and women concerning their attitude towards predictive counselling and predictive testing for a *BRCA1/2* gene mutation.

#### Age of the subjects

The age of the subjects was inversely proportional to the awareness of the different items of the interview. Younger subjects (minimum age 21 years) had a better awareness of the existence of HBOC ( $p < 0.001$ ), of the risks associated with



**Figure 2** Awareness of the existence of a *BRCA* mutation in the subject's own family.

carrier status for a *BRCA1/2* mutation ( $p = 0.004$ ), of the different preventive options available for carriers ( $p = 0.016$ ), of the possibility of predictive genetic testing ( $p = 0.003$ ), of the autosomal dominant pattern of inheritance ( $p < 0.001$ ), of a familial pattern of breast/ovarian cancer in their own family ( $p < 0.001$ ), and of the existence of a *BRCA1/2* mutation in their own family ( $p = 0.003$ ). Younger subjects also have a more positive attitude towards predictive counselling ( $p = 0.011$ ) and predictive gene testing ( $p = 0.006$ ) than elderly subjects.

### Proximity of relationship of the subjects towards the proband

The subjects who were closer in degree of relationship towards the proband had a better awareness of the existence of HBOC ( $p < 0.001$ ), of the risks associated with being a carrier ( $p < 0.001$ ), of the different preventive options available for carriers ( $p < 0.001$ ), of the possibility of predictive genetic testing ( $P < 0.001$ ), of the autosomal dominant pattern of inheritance ( $p = 0.001$ ), of a familial pattern of breast/ovarian cancer in their own family ( $p < 0.001$ ), and of the existence of a *BRCA1/2* mutation in their own family ( $p < 0.001$ ). There was no significant difference between the subjects who are closer or further in degree of relationship towards the proband concerning their attitude towards predictive counselling and predictive gene testing.

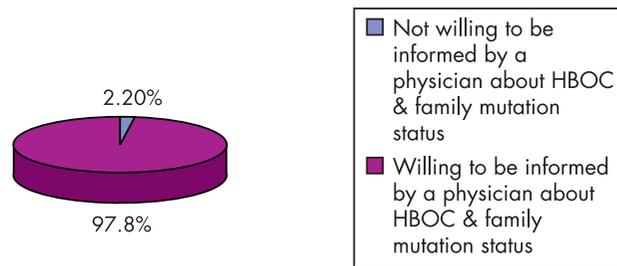
### Comparison of probands with the other family members

The original 14 probands had a significantly better awareness of the existence of HBOC ( $p = 0.003$ ), of the risks associated with being a carrier ( $p = 0.011$ ), of the different preventive options available for carriers ( $p = 0.002$ ), of the possibility of predictive genetic testing ( $p = 0.002$ ), of a familial pattern of breast/ovarian cancer in their own family ( $p = 0.01$ ), and of the existence of a *BRCA1/2* mutation in their own family ( $p = 0.005$ ). There was no statistical difference between the awareness of the original 14 probands and the 107 subjects of the study population concerning the autosomal dominant pattern of inheritance of a *BRCA1/2* mutation and their attitude towards predictive testing and counselling.

## DISCUSSION

The proportion of breast cancers directly attributable to hereditary factors has been estimated at 5–10%. Since the identification of the two *BRCA1-3* genes as the major predisposition genes for familial breast and ovarian cancer,<sup>4</sup> genetic counselling and predictive testing has become available and applied in many centres throughout the world. Initially the psychological implications of predictive testing, as well as the medical and psychological consequences of preventive options, including preventive surgery, were ill defined. The only information available came from retrospective studies on preventive actions in high risk individuals.<sup>7</sup> In most centres a prudent protocol of 'non-directive' counselling was initially used, based on the international guidelines for genetic counselling in Huntington families.<sup>5</sup>

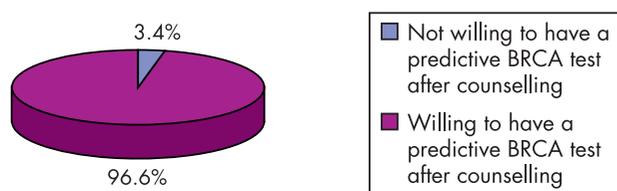
In the Familial Cancer Clinic of the VUB, a multi-disciplinary team has also worked according to a protocol of 'non-directive' counselling.<sup>8-9</sup> In the context of this study non-directiveness is focused on the way the counselling team behaves towards other family members. When a *BRCA1/2* gene mutation is found, the possibility of predictive counselling and testing is offered to the other family members only through the informed proband, subsequently cascading through the other relatives who come forward for counselling and testing. Besides the proband, no other family members are contacted directly by our team. It has previously been reported that in Huntington families the information transmitted by family members towards relatives is likely to



**Figure 3** Willingness to be informed by a physician about HBOC, family mutation status, and the possibility of predictive genetic testing

be inadequate.<sup>10</sup> Likewise, Ayme *et al* found that a significant proportion of patients do not share the genetic information they receive with all their relatives. They also showed that patients communicate the news in such a way that their relatives do not understand the necessity of exploring genetic testing.<sup>11</sup> A recent small study in five HNPCC families showed that all participating probands shared information about the HNPCC mutation in their family with their relatives, but all probands were cancer survivors themselves, which may have facilitated the motivation to share information. Furthermore, the study supported a tendency for individuals not to discuss genetic information beyond their first degree relatives.<sup>12</sup> The efficiency of information transmission in families with a known *BRCA1/2* gene mutation using a derived counselling procedure has not been well documented. Only a limited number of studies has reported data on a group of affected and unaffected individuals with regard to post-test communication of genetic test results.<sup>13–17</sup> These studies focused on communication to close relatives and overall have shown that in most cases there is a willingness to share information with first degree relatives, but difficulties in further family communication were reported. One recently published study also focused on communication to more distant relatives and found that information dissemination was more problematic.<sup>18</sup> In our experience only a minority of the other family members besides the proband actually visited the Familial Cancer Clinic for predictive counselling and testing.<sup>9</sup> Many factors could be involved, the two most important being a lack of interest in counselling or a deficit in information transmission.

In this study we examined the efficiency and accuracy of information transfer from the proband to other family members, and compared this with the actual needs of these individuals by examining their attitudes towards genetic counselling and predictive testing. In particular, we focused on first degree relatives of mutation carriers or probable mutation carriers, those being the family members for whom this information is likely to be the most relevant. The study was performed with in depth semi-structured interviews with specific items to be covered instead of questionnaires. Interpretation of responses to a questionnaire in such a sensitive matter as predictive genetic testing was anticipated to be difficult. Narrative texts generated by semi-structured open ended interviews are a known form of qualitative data



**Figure 4** Willingness to have a predictive *BRCA* test after counselling.

that provide useful insights that are otherwise overlooked by more structured designs such as questionnaires.<sup>19</sup>

Our results show that the initial probands, who were already informed about HBOC by previous counselling sessions, were sufficiently provided with information about the various aspects concerning HBOC, with exception of the understanding of the autosomal dominant pattern of inheritance of a *BRCA1/2* gene mutation and the possibility of antenatal diagnosis. This is not surprising as these items require some biological knowledge that may be absent in the general public. There is evidence from other studies that genetic advice is often poorly understood and remembered.<sup>20–22</sup> Thus, the low understanding of the autosomal dominant pattern of inheritance among the probands is understandable, and does not correlate with their intellectual or social abilities. We can conclude from these results that the predictive counselling sessions that were given to the probands were quite complete and rather well assimilated.

Our study also reveals that women were generally better informed than men, consistent with findings of another recent study.<sup>12</sup> This could be due to various factors, such as women being more interested in health matters and communicating more easily than men. Women have been described as playing a larger role in communicating about inherited cancers, particularly breast cancer, compared with men.<sup>12</sup> Julian-Reynier *et al* also found that women visiting a familial cancer clinic because of HBOC stated that they would be informing their at risk female relatives much more frequently than their at risk male relatives if they were carrier of a *BRCA* gene mutation.<sup>23</sup> However, women were not better informed about more technical aspects of the disease such as the autosomal dominant pattern of inheritance. The results also demonstrate that the age of the subjects was inversely proportional to the level of awareness about the different aspects of HBOC. These results are also consistent with other recent findings.<sup>12</sup> Younger generations are generally more educated about health in general, and are more familiar with health and cancer prevention. The actual reporting of health matters in the media (such as television and the internet) also plays an important role in informing the younger generation about health issues.

Owing to the probands' high awareness of the various aspects of HBOC, we would have expected that the other family members would have been well informed by the probands, but our results show that the transfer of general information from probands to family members for whom this information can be of great importance is highly defective. Less than half of all potentially interested subjects knew about the existence of HBOC, the availability of predictive gene testing, and the cancer risk incurred by mutation carriers. Even for most of these subjects, the information was incomplete. Only one third knew about potential preventive implications, while only a small minority manifested any understanding of the dominant inheritance mechanism. Only a couple of individuals were aware of the possibility of antenatal diagnosis. Of those who were informed about these items, an even smaller proportion could be considered adequately informed. A similar picture emerged with regard to the flow of family specific data. Therefore, we concluded that information transmission following the Huntington protocol is incomplete both quantitatively and qualitatively in the context of counselling for families with a *BRCA1/2* gene mutation, consistent with recent findings of another group.<sup>22</sup> Various reasons, at both the proband and family level, could be the cause of this observation. The task for the proband is difficult, both intellectually and emotionally. Probands may have intellectual problems in understanding and transmitting the information, or may be unwilling to share information with all or parts of the family for personal reasons.<sup>24</sup>

However, we found a progressive decline in the level of information with growing distance of the relationship of the subjects from the probands. This indicates that the dynamics of family communication play an additional important role. Another recently published study showed that most of the probands shared information and disclosed genetic test results with their relatives. That study had a smaller scope and considered only the adult children and siblings of the probands.<sup>16</sup> The results were, however, consistent with our finding that the level of relationship of the subjects to the proband is important for family communication. Probands also face a difficult task at communicating such sensitive information, even if supported by a counselling team. In a family the “messenger” is often particularly vulnerable.<sup>25</sup> One study clearly showed that some probands would have preferred their relatives to be notified of their cancer risk directly by the counsellor conducting the study.<sup>26</sup> Another study showed that probands with positive genetic test results more often had difficulty in explaining their results to their relatives.<sup>12</sup> Other studies of knowledge about HBOC also demonstrated in general a lack of basic knowledge about cancer genetics both in the general population and in patients with breast and ovarian cancer.<sup>27–28</sup> The defective communication that we have identified is of great concern. In contrast to Huntington disease, interventions that could alter the outcome for carriers of *BRCA1/2* mutations do exist, such as clinical surveillance, prophylactic oophorectomy, and prophylactic mastectomy, with proven important risk reduction.<sup>6, 29–31</sup> It therefore seems important that the right to know be respected with regard to this vital information, and that a different approach towards counselling is warranted in *BRCA1/2* families.

How does this lack of information compare with the actual needs of the subjects? This aspect has, to our knowledge, never been investigated previously in the specific context of whole families with a *BRCA1/2* gene mutation. Surprisingly, our results indicate that almost all individuals who agreed to participate in the study wanted to be informed about the different aspects of HBOC and about the availability of predictive gene testing. Many even expressed regrets about not being informed earlier. The large majority of the subjects also wanted to have a predictive genetic test after counselling, and actually underwent a predictive genetic test during the study. However, in interpreting the results of our study, some limitations should be considered. Firstly, the study is of a partially selected population, because we only interviewed the family members that were already interested in participating in the survey, and secondly, testing was free of charge within the framework of the study (although the test is relatively cheap; normally only €10 for the person being tested), which may have introduced a positive selection bias. However, more than 80% of the subjects that were contacted participated in the study, and therefore our results seem to be highly relevant to the whole population of *BRCA1/2* families. As a consequence, we can conclude that the majority of all family members within a family with a *BRCA1/2* gene mutation is clearly interested in receiving information about the various aspects of HBOC, and even in having a predictive genetic test. This finding is generally consistent with several other studies of interest in cancer susceptibility gene testing, which have found 80% or more of high risk first degree relatives and of random patients affected with breast and/or ovarian cancer to be interested in testing for *BRCA1* and *BRCA2* gene mutations.<sup>28, 32–34</sup>

By performing the interviews we also established that the way in which information is provided is very important, because understanding all the aspects of a genetic syndrome is very difficult for people who are not educated in medical science. The information should be given in different

counselling sessions (multi-visit protocol), and the hallmark of the counselling sessions should be the communication of genetic information in a comprehensible and emotionally acceptable way. The counselling sessions should be headed by a multidisciplinary team (including medical oncology, medical genetics, and psychology).

In summary, we state that on the one hand family members from distinct Belgian families with a *BRCA1/2* gene mutation are not well informed about HBOC using the current procedure of “non-directive” counselling, while on the other hand the large majority of these family members actually wants to receive all available information and even to have a predictive genetic test after being informed. These findings should have a direct impact on the counselling management. In Belgium, as in most other European countries, medical confidentiality does not allow genetic counsellors to directly approach relatives of a tested individual if they have no personal request for counselling. However, taking into consideration the results of this study and the knowledge that preventive options do exist for HBOC, it is our opinion that counselling with a more directive protocol in cancer predictive genetic testing is warranted. There are different possible approaches. A protocol could be developed in which probands are educated to communicate genetic test information in a more effective way to their relatives. Daly *et al* have described a six step communication strategy to provide the proband with skills for more easily communicating genetic test results to family members, based on their relationship to each other.<sup>35</sup> However, with this type of approach, the proband is still left with the responsibility of communicating genetic test results. Another approach could be to ask the proband for permission to mail an informative letter to the other family members, so that the proband is no longer the only “messenger”. This letter would provide information about the hereditary nature of breast/ovarian cancer in their family (without revealing personal genetic test results or the identity of the proband), about the consequences of HBOC, and about the possibility of having a predictive genetic test. The letter would also provide a phone number to enable an appointment to be made with the familial cancer clinic if desired. If the proband refuses to grant permission to send these letters, the motivations behind the refusal should be addressed and evaluated. The opinion of the proband should be taken into consideration if the underlying reasons are deemed to be justified, such as the presence in the family of psychologically fragile family members. However, if the refusal of the proband is based, for example, on problematic or distant family relationships, the need and obligation to inform the other relatives should over-rule the opinion of the proband. At that moment, there could be a conflict between the wishes of the proband (confidentiality) and a duty to warn at risk relatives. The American Society of Human Genetics guidelines outline some circumstances in which breach of confidentiality may be allowed, such as a relatively high risk of disease for a relative, the availability of risk reduction by early monitoring, or the disease being preventable and treatable; in our opinion, these elements are clearly present in families with HBOC.<sup>36</sup> This more directive protocol will eventually lead to a better awareness of the various aspects of HBOC and to a better knowledge of family mutation status, which better fits the needs of these families. With such an approach, one might be concerned about the right not to know. There is indeed a small hazard of giving undesired information to individuals who may be psychologically hurt as a consequence. However, even the Huntington protocol does not avoid these possible undesirable effects. We believe that quantitatively, this is likely to be a minor issue as almost all subjects actually requested information and even predictive testing.

Moreover, even a first step of informing family members with a well designed letter still allows for a staged approach in which the flow of information to specific individuals can be halted at any time.

Members of families with a *BRCA1/2* gene mutation have “the right to know”. Educating them about genetic risks and providing other relevant information about genetic testing would increase their ability to make informed decisions, which are essential for their health. In the near future, this should lead to better prevention strategies and to fewer fatal breast/ovarian cancers within these families.

## ACKNOWLEDGEMENTS

We acknowledge the financial support from the Wetenschappelijk Fonds W Gepts of the AZ-VUB, the Voorzorgskas voor Geneesheren (VKG), and the Rik and Nel Wouters Stichting. We are grateful to I Pauwels for assistance in performing the interviews, and we thank all the families and individuals that participated in the study.

## Authors' affiliations

**E Sermijn, G Goelen, E Teugels, M Bonduelle, B Neyns, J De Grève**, Family Cancer Clinic, AZ-VUB, Vrije Universiteit Brussel, Laarbeeklaan 101, B-1090 Jette, Belgium  
**E Sermijn, B Neyns, J De Grève**, Department of Medical Oncology, AZ-VUB, Vrije Universiteit Brussel, Belgium  
**G Goelen, J De Grève**, Department of Cancer Prevention, AZ-VUB, Vrije Universiteit Brussel, Belgium  
**E Teugels, B Neyns, J De Grève**, Department of Molecular Oncology, AZ-VUB, Vrije Universiteit Brussel, Belgium  
**L Kaufman**, Department of Medical Statistics, AZ-VUB, Vrije Universiteit Brussel, Belgium  
**M Bonduelle**, Department of Medical Genetics, AZ-VUB, Vrije Universiteit Brussel, Belgium  
**B Poppe, A De Paep**, Centre for Medical Genetics, University Hospital of Ghent, Belgium

Correspondence to: Prof Dr J De Grève, Department of Medical Oncology, Oncologisch Centrum, AZ-VUB, Laarbeeklaan 101 1090 Jette, Belgium; jacques.degreve@az.vub.ac.be

Received 6 August 2003  
 Accepted 14 August 2003

## REFERENCES

- Miki Y, Swensen J, Shattuck-Eidens D, Futreal PA, Harshman K, Tavtigian S, Liu Q, Cochran C, Bennett LM, Ding W, Bell R, Rosenthal J, Hussey C, Tran T, McClure M, Frye C, Hattier T, Phelps R, Haugen-Strano A, Katcher H, Yakumo K, Gholami Z, Shaffer D, Stone S, Bayer S, Wray C, Bogden R, Dayananth P, Ward J, Tonin P, Narod S, Bristow PK, Norris FH, Helvering L, Morrison P, Rostek P, Lai M, Barrett JC, Lewis S, Neuhausen S, Cannon-Albright L, Goldgar D, Wiseman R, Kamb A, Skolnick MH. A strong candidate for the breast and ovarian susceptibility gene *BRCA1*. *Science* 1994;**216**:66–71.
- Wooster R, Bignell G, Lancaster J, Swift S, Seal S, Mangion J, Collins N, Gregory S, Gumbs C, Micklem G. Identification of the breast cancer susceptibility gene *BRCA2*. *Nature* 1995;**378**:789–92.
- Tavtigian SV, Simard J, Rommens J, Couch F, Shattuck-Eidens D, Neuhausen S, Merajver S, Thorlacius S, Offit K, Stoppa-Lyonnet D, Belanger C, Bell R, Berry S, Bogden R, Chen Q, Davis T, Dumont M, Frye C, Hattier T, Jammulapati S, Janecki T, Jiang P, Kehrer R, Leblanc JF, Mitchell T, McArthur-Morrison J, Nguyen K, Peng Y, Samson C, Schroeder M, Snyder SC, Steele L, Stringfellow M, Stroup C, Swedlund B, Swensen J, Teng D, Thomas A, Tran T, Tran T, Tranchant M, Wever-Feldhaus J, Wong AKC, Shizuya H, Eyfjord JE, Cannon-Albright L, Labrie F, Skolnick MH, Weber B, Kamb A, Goldgar DE. The complete *BRCA2* gene and mutations in chromosome 13q-linked kindreds. *Nat Genet* 1996;**12**:233–7.
- Ford D, Easton DF, Peto J. Estimates of the gene frequency of *BRCA1* and its contribution to breast and ovarian cancer incidence. *Am J Hum Genet* 1995;**57**:1457–62.
- Craufurd D, Tyler A. Predictive testing for Huntington's disease: protocol of the UK Huntington's Prediction Consortium. *J Med Genet* 1992;**29**:915–18.
- Meijers-Heijboer H, van Geel B, van Putten HL, Henzen-Logmans SC, Seynaeve C, Menke-Pluyms MB, Bartels CC, Verhoog LC, Verhoog LC, van den Ouweland AM, Niermeijer MF, Brekelmans CT, Klijn JG. Breast cancer after prophylactic bilateral mastectomy in women with a *BRCA1* or *BRCA2* mutation. *N Engl J Med* 2001;**345**:159–64.
- Blanchard DK, Hartmann LC. Prophylactic surgery for women at high risk for breast cancer. *Clin Breast Cancer* 2000;**1**:127–34, discussion 135.

- Goelen G, Rigo A, Teugels E, Neyns B, Bonduelle M, De Greve J. Ethical issues in breast and ovarian cancer genetic counselling. *J Genet Couns* 1997;**6**:497–8.
- Goelen G, Rigo A, Bonduelle M, De Greve J. Moral concerns of different types of patients in clinical *BRCA1/2* gene mutation testing. *J Clin Oncol* May, 1999;**17**:1595–600.
- Tyler A, Harper PS. Attitudes of subjects at risk and their relatives towards genetic counselling in Huntington's chorea. *J Med Genet* 1983;**20**:179–88.
- Ayme S, Macquart-Moulin G, Julian-Reynier C, Chabal F, Giraud F. Diffusion of information about genetic risk within families. *Neuromusc Disord* 1993;**3**:571–4.
- Peterson SK, Watts BG, Koehly LM, Vernon SW, Baile WF, Kohlmann WK, Gritz ER. How families communicate about HNPCC genetic testing: findings from a qualitative study. *Am J Med Genet* 2003;**119C**:78–86.
- Lerman C, Peshkin BN, Hughes C, Isaacs C. Family disclosure in genetic testing for cancer susceptibility: Determinants and consequences. *J Health Care Law Policy* 1998;**1**:353–72.
- Hughes CH, Lynch H, Durham C, Snyder C, Lemon S, Narod S, Fulmore C, Main D, Lerman C. Communication of *BRCA1/2* test results in hereditary breast cancer families. *Cancer Res Ther Control* 1999;**8**:51–9.
- Tercyak KP, Hughes C, Main D, Snyder C, Lynch JF, Lynch HT, Lerman C. Parental communication of *BRCA1/2* genetic test results to children. *Patient Educ Couns* 2001;**42**:213–24.
- Costalas JW, Itzen M, Malick J, Babb JS, Bove B, Godwin AK, Daly MB. Communication of *BRCA1* and *BRCA2* results to at-risk relatives: a cancer risk assessment program's experience. *Am J Med Genet* 2003;**119C**:11–18.
- Hughes C, Lerman C, Schwartz M, Peshkin BN, Wenzel L, Narod S, Corio C, Tercyak KP, Hanna D, Isaacs C, Main D. All in the family: evaluation of the process and content of sisters communication about *BRCA1* and *BRCA2* genetic test results. *Am J Med Genet* 2002;**107**:143–50.
- Claes E, Evers-Kiebooms G, Boogaerts A, Decruyenaere M, Denayer L, Legius E. Communication with close and distant relatives in the context of genetic testing for hereditary breast and ovarian cancer in cancer patients. *Am J Med Genet* 2003;**116A**:11–19.
- Crabtree BF, Miller WL. A qualitative approach to primary care research: the long interview. *Fam Med* Feb 1991;**23**:145–51.
- Tyler A, Harper PS. Attitudes of subjects at risk and their relatives towards genetic counseling in Huntington's chorea. *J Med Genet* Jun 1983;**20**:179–88.
- Sibinga MS, Friedman CJ. Complexities of parental understanding of phenylketonuria. *Pediatrics* 1971;**48**:216–24.
- Leonard CO, Chase GA, Childs B. Genetic counseling. A consumer's view. *N Engl J Med* 1972;**287**:433–9.
- Julian-Reynier C, Eisinger F, Chabal F, Lasset C, Nogues C, Stoppa-Lyonnet D, Vennin P, Sobol H. Disclosure to the family of breast/ovarian cancer genetic test results: patient's willingness and associated factors. *Am J Med Genet* 2000;**94**:13–18.
- Green J, Richards M, Murton F, Statham H, Halowell N. Family communication and genetic counselling: The case of hereditary breast and ovarian cancer. *J Genet Couns* 1997;**6**:45–60.
- DudokdeWit AC, Tibben A, Frets PG, MeijersHeijboer EJ, Devilee P, Klijn JGM, Oosterwijk JC, Niermeijer MF. *BRCA1*. in the family: A case description of the psychological implications. *Am J Med Genet* 1997;**71**:36–71.
- Julian-Reynier C, Eisinger F, Vennin P, Chabal F, Aurran Y, Nogues C, Bignon YJ, Machelard-Roumagnac M, Maugard-Louboutin C, Serin D, Blanc B, Orsoni P, Sobol H. Attitudes towards cancer predictive testing and transmission of information to the family. *J Med Genet* 1996;**33**:731–6.
- Mogilner A, Otten M, Cunningham JD, Brower ST. Awareness and attitudes concerning *BRCA* gene testing. *Ann Surg Oncol* Oct–Nov 1998;**5**:607–12.
- Bluman LG, Rimer BK, Berry DA, Borstelmann, Iglehart JD, Regan K, Schildkraut J, Winer EP. Attitudes, knowledge and risk perceptions of women with breast and/or ovarian cancer considering testing for *BRCA1* and *BRCA2*. *J Clin Oncol* Mar 1999;**17**:1040–4.
- Hartmann LC, Sellers TA, Schaid DJ, Frank TS, Soderberg CL, Sitta DL, Frost MH, Grant CS, Donohue JH, Woods JE, McDonnell SK, Vockley CW, Deffenbaugh A, Couch FJ, Jenkins RB. Efficacy of bilateral prophylactic mastectomy in *BRCA1* and *BRCA2* gene mutation carriers. *J Natl Cancer Inst* 2001;**93**:1633–7.
- Kauff ND, Satagopan JM, Robson ME, Scheuer L, Hensley M, Hudis CA, Ellis NA, Boyd J, Borgen PI, Barakat RR, Norton L, Castiel M, Nafa K, Offit K. Risk-reducing salpingo-oophorectomy in women with a *BRCA1* or *BRCA2* mutation. *N Engl J Med* May 232002;**346**:1609–15.
- Rebbeck TR, Lynch HT, Neuhausen SL, Narod SA, Van't Veer L, Garber JE, Evans G, Isaacs C, Daly MB, Matloff E, Olopade OI, Weber BL. Prophylactic oophorectomy in carriers of *BRCA1* or *BRCA2* mutations. *N Engl J Med* May 232002;**346**:1616–22.
- Lerman C, Daly M, Masney A, Balshem A. Attitudes about genetic testing for breast-ovarian cancer susceptibility. *J Clin Oncol* 1994;**12**:843–50.
- Lerman C, Seay J, Balshem A, Audrain J. Interest in genetic testing among first-degree relatives of breast cancer patients. *Am J Med Genet* 1995;**57**:358–92.
- Struewing JP, Lerman C, Kase RG, Giambarrresi TR, Tucker MA. Anticipated uptake and impact of genetic testing in hereditary breast and ovarian cancer families. *Cancer Epidemiol Biomarkers Prev* 1995;**4**:169–73.
- Daly BM, Barsevick A, Miller MS, Buckman R, Costalas J, Montgomery S, Bingle R. Communicating genetic test results to the family: a six step, skills-building strategy. *Fam Community Health* 2001;**24**:13–26.
- Knoppers BM, Strom C, Clayton Wright E, Murray T, Fibison W, Luther L. Professional disclosure of familial genetic information. *Am J Hum Genet* 1998;**62**:474–83.