Genetics inMedicine | ORIGINAL RESEARCH ARTICLE

Challenges in managing genetic cancer risk: a long-term qualitative study of unaffected women carrying *BRCA1/BRCA2* mutations

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Purpose: Women carrying *BRCA1/BRCA2* germ-line mutations have an increased risk of developing breast/ovarian cancer. To minimize this risk, international guidelines recommend lifelong surveillance and preventive measures. This study explores the challenges that unaffected women genetically predisposed to breast/ovarian cancer face in managing their risk over time and the psychosocial processes behind these challenges.

Methods: Between 2011 and 2013, biographical qualitative interviews were conducted in Switzerland with 32 unaffected French- and Italian-speaking women carrying *BRCA1/BRCA2* mutations. Their mutation status had been known for at least 3 years (mean, 6 years). Data were analyzed through constant comparative analysis using software for qualitative analysis.

Results: From the time these women received their positive genetic test results, they were encouraged to follow medical guidelines. Meanwhile, their adherence to these guidelines was constantly questioned by their social and medical environments. As a result of these contradictory pressures, *BRCA1/BRCA2* mutation carriers experienced a sense of disorientation about the most appropriate way of dealing with genetic risk.

Conclusion: Given the contradictory attitudes of health-care professionals in caring for unaffected *BRCA1/BRCA2* mutation carriers, there is an urgent need to educate physicians in dealing with genetically at-risk women and to promote a shared representation of this condition among them.

Genet Med advance online publication 11 December 2014

Key Words: *BRCA1/BRCA2*; challenges; preventive medicine; qualitative research; risk management

INTRODUCTION

In the past two decades, genetic testing has allowed unaffected women to know whether they are predisposed to breast/ovarian cancer due to *BRCA1/BRCA2* germ-line mutations. A woman carrying a *BRCA1/BRCA2* mutation has a significant probability (as high as 75%) of developing breast or ovarian cancer within her lifetime.[1–3]

Knowledge of a genetic risk for breast/ovarian cancer implies new choices for managing health. Together with the positive genetic results, female carriers receive a check-up agenda based on international guidelines, typically requiring biannual medical consultations and screenings.[4–7] Clinical recommendations for women with *BRCA1/BRCA2*-associated hereditary breast/ovarian cancer syndrome can be summarized as follows: semi-annual clinical breast examinations starting from the age of 25 years; annual breast magnetic resonance imaging and mammograms starting from the age of 25–30 years; semi-annual transvaginal ultrasounds and blood tests (tumor marker CA125) starting from the age of 30 years; risk-reducing salpingo-oophorectomy ideally before the age of 40 years; and prophylactic bilateral mastectomy as an option to be discussed on an individual basis. Thus, at-risk women are encouraged to pursue a lifetime health program in close collaboration with several health-care professionals. These surveillance and prevention recommendations aim to minimize cancer risk and death. However, carriers' adherence is supposed to be a personal decision based on individual risk perception. Self-determination is a central concept in current human genetics,[8] as underlined by laws recently introduced in many countries.[9]

In Switzerland, the management of women with genetic breast/ovarian cancer risk is not limited to specialized institutional units: once *BRCA1/BRCA2* mutations have been identified and posttesting genetic counseling has been performed, carriers are usually referred to their gynecologists and primary-care physicians in the private health-care sector to implement long-term surveillance and prevention measures. These measures are covered by basic health-insurance policies that are mandatory for the resident population.

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Submitted 12 July 2014; accepted 11 November 2014; advance online publication 11 December 2014. doi:10.1038/gim.2014.183

The long-term effects of genetic testing have been explored by some recent studies. There is an emerging consensus that *BRCA1/BRCA2* testing is not associated with major psychological problems for unaffected women,[10–12] except if these women meet particular criteria, such as being young or having lost a relative due to breast/ovarian cancer.[13,14] Nonetheless, other studies have shown that a positive *BRCA1/BRCA2* result continues to have a significant emotional impact on carriers years after testing.[15,16] These contradictory findings may be explained by the different ways in which these studies measure the distress associated with genetic testing.[17] The existing literature has examined the impact of genetic testing through a quantitative approach by measuring specific variables and looking for correlations between them at a particular time after genetic testing.

The specificity of our study is its qualitative design, which is aimed at generating a more comprehensive understanding of the long-term impact of genetic testing. To this end, biographical, retrospective interviews were conducted between 2011 and 2013 in the French-speaking and Italian-speaking regions of Switzerland with 32 unaffected *BRCA1/BRCA2* mutation carriers who had known of their positive mutation status for at least 3 years. In particular, this study aims to explore inductively the challenges that unaffected women genetically predisposed to breast/ovarian cancer face in managing their risk over time, as well as the complex psychosocial processes behind these challenges.

MATERIALS AND METHODS

Participants were recruited through four genetic-counseling centers. After approval by local ethics committees, a letter was sent to all women who had been identified as *BRCA1/BRCA2* mutation carriers at least 3 years previously (this period was considered adequate to develop enough experience in managing genetic risk over time). Unaffected women received an invitation to be interviewed by a female sociologist regarding their past experience with genetic risk. Retrospective interviews are a good alternative to longitudinal studies because they are less time-consuming and participants do not drop out of the study.[18]

All eligible individuals ($n = 53$) were contacted between June 2011 and December 2013. Of these, 31 (58%) agreed to participate; 15 did not answer despite a reminder; 5 refused because they said they did not have time ($n = 2$), did not want to talk ($n = 1$), or had not modified their lifestyle ($n = 2$); two women could not be reached. Another woman, tested in a genetic-counseling center that did not participate in this study, contacted the principal investigator via her cousin, who was one of the participants.

The ages of the 32 participants ranged from 26 to 60 years. They were divided into three groups: early reproductive age (25–35 years) ($n = 8$), late reproductive age (36–49 years) ($n = 21$), and postreproductive age (50 years or older) ($n = 3$).

A grounded theory approach was adopted to collect and analyze the data.[19] This is typically used to describe the complex interactions between the individual and their environment, and to shed light on areas of research in which little is known. Its key features are an iterative study design and a system of analysis based on the constant comparative method.

After giving informed consent, each participant was interviewed once or twice for a total of 3 hours on average. To obtain descriptions of the participants' trajectory that were as objective as possible, we took care to ask for factual data. We verified their consistency within the narrative and cross-checked them with supplementary information (e.g., copies of letters or e-mails that the participants had exchanged with their health-care professionals). The interviews were audio-recorded and transcribed, and the participants' identities were anonymized, and pseudonyms were given to each woman.

Following the constant comparative method,[19] interviews were inductively coded; identified codes were linked and grouped into larger categories, and abstract concepts were defined to organize the different topics. Data collection and analysis continued iteratively until saturation was achieved, that is, until a consistency of responses was evident and no new ideas were introduced during subsequent interviews. Finally, all interviews were systematically coded with the support of a software program for qualitative analysis (ATLAS.ti) to verify the robustness of the findings and identify quotations for publication. These quotations were then translated into English.

The principal investigator conducted data collection and analysis, and the research team had regular discussions regarding emerging patterns to ensure analytical validity. This is because in grounded theory the point is not whether another researcher will find the same categories to interpret the data but whether a plausible interpretation of the data can be developed and accepted by those who are knowledgeable about the phenomenon under study.[19]

RESULTS

All participants had long-term experience of genetic cancer risk management with a mean time from genetic testing results of 6 years (range, 3–12 years). For 11 (34 %) women, at least 7 years had elapsed since their *BRCA1/BRCA2* testing. The characteristics of the study participants are summarized in **Table 1**. For several women, the surveillance measures and risk-reduction strategies adopted at the time of the interview were not strictly consistent with international guidelines (**Table 2**). This was the case for 3 of the 8 women belonging to the early reproductive age group, 7 of the 21 women belonging to the late reproductive age group, and 1 of the 3 women belonging to the postreproductive age group.

Participants described their medical trajectory in detail, particularly regarding the management of their cancer risk. They stated that in the months and years after genetic testing, they tended to experience the health program suggested by medical guidelines in two contradictory ways: as a rational and moral responsibility (i.e., as something they had no choice but to implement) and as a questionable option (i.e., as something that could be contested at any time).

The health program as a rational and moral responsibility

After the identification of *BRCA1* or *BRCA2* mutations, at-risk women were referred to their gynecologists and primary-care physicians in private practice to implement surveillance programs and further discuss risk-reduction strategies. From the moment the participants had discovered that they carried these mutations, they increasingly felt they had no alternative but to follow the international guidelines. The health program became a "must-do," a rational and moral duty. Genetically at-risk women became aware of this responsibility as a result of four factors.

Table 1 Characteristics of the study participants

Number of *BRCA1/BRCA2* mutation carriers	*N* = 32
Age	
Mean	40.6 years (range, 26–60)
Women of early reproductive age (25–35 years), *n*	8
Women of late reproductive age (36–49 years), *n*	21
Women of postreproductive age (≥50 years), *n*	3
Type of germ-line mutation	
BRCA1	18
BRCA2	14
Time since genetic testing	
Mean	6 years (range, 3–12)
Women with 3- to 6-year interval, *n*	21
Women with 7- to 12-year interval, *n*	11
Family status	
Married	26
Single	3
Divorced	2
Living with a partner	1
Children	
Yes	25[a]
No	7
Education	
Secondary level	19
University level	13
Genetic-counseling centers	
Centre Hospitalier Universitaire Vaudois, Lausanne	15
Hôpitaux Universitaires de Genève, Genève	8
Ente Ospedaliero Cantonale, Bellinzona	4
Réseau Santé Valais, Sion	4
Hôpital Neuchâtelois, La Chaux-de-Fonds	1

[a]Eleven participants gave birth after genetic testing.

The imperative to reduce the risk of cancer. Participants reported having often experienced pressure from their health-care professionals to adhere to management guidelines. In case of noncompliance, they felt that they were considered irresponsible or irrational. In some cases, physicians used soft persuasion strategies to convince women to adopt cancer risk–reduction behaviors. Sometimes, the pressure was much more firm and explicit. Attilia provided a good example of this last scenario: this 42-year-old *BRCA2* mutation carrier, despite not wanting any more children, refused to have her ovaries removed. Her gynecologist considered her choice illogical and harmful and constantly reminded her of the risk she was running:

> She [the gynecologist] always tells me: "But what are you waiting for? Is it better to go under the scalpel when you decide to do so and when you are in good health or when you get sick? If you consider the consequences of menopause or the consequences of a disease, I don't know what is better. In my opinion, menopause is better." (Attilia, 42)

The moral responsibility toward family members. Participants were also pressured to adhere to medical recommendations because of a complex sense of duty toward their kin. First, at-risk women felt a duty to remain healthy for their close relatives. The implicit or explicit pressure from family members to do everything possible to avoid getting sick reinforced this moral obligation.

Second, at-risk women felt similar obligations toward their ancestors: having access to information and health care that their parents and grandparents did not have, they considered it almost "immoral" not to use it.

Finally, this feeling of obligation was also extended to participants' descendants. Because the participants may have

Table 2 Surveillance measures and risk-reducing procedures applied at the time of interviews

	Study participants		
	Early reproductive age (25–35 years)	Late reproductive age (36–49 years)	Postreproductive age (≥50 years)
Type of management	***n* = 8**	***n* = 21**	***n* = 3**
Breast surveillance only (*n* = 1)	1 (*BRCA2*: 1)	0	0
Breast and ovarian surveillance (*n* = 9)	5 (*BRCA1*: 4; *BRCA2*: 1)	3 (*BRCA1*: 1; *BRCA2*: 2)	1 (*BRCA2*: 1)
BSO + breast surveillance (*n* = 12)	2 (*BRCA1*: 2)	8 (*BRCA1*: 5; *BRCA2*: 3)	2 (*BRCA1*: 1; *BRCA2*: 1)
Bilateral RRM + ovarian surveillance (*n* = 4)	0	4 (*BRCA1*: 3; *BRCA2*: 1)	0
BSO + bilateral RRM (*n* = 6)	0	6 (*BRCA1*: 2; *BRCA2*: 4)	0

BSO, bilateral salpingo-oophorectomy; RRM, risk-reducing mastectomy.

transmitted the cancer predisposition to their children, they considered it important to be an example of proactivity.

> When I told my daughters about that [the genetic predisposition], they were upset in the sense that they said, "It could happen to us as well." But I explained them: "You are lucky. Because I will know how it works, I will be able to tell you. I will not get sick, I will do all that is needed." … My daughters are the main motivation for everything I do: I want to show them the way. (Elin, 45)

The vicarious experience of the disease. All participants experienced cancer vicariously through the illness of close family members. The more dramatic the indirect experience, the stronger the desire to do everything possible to avoid getting ill. The health program offered by the medical system was thus absolutely welcomed.

> I don't want to find myself in the same situation as my mother; I don't even want to think about that. …One day, imagining someone will tell me: "Well, you have cancer," just that … just thinking about that makes me shudder. (Paula, 42)

The emphasis on living one's own life. All participants wished to emancipate themselves from their "genetic destiny" to live their own lives. The following quotation of Anissa exemplifies this wish.

> I don't want to be a victim. I made a decision. I decided that… well, I'll block its [the gene's] path. I know that I carry the gene, OK, then I am not going to wait. No. Not this kind of fatalism. I will not end up like them [family members who died from cancer]. I'll live my own life. (Anissa, 42)

The health program as a questionable option

Although the health program was perceived as a rational and moral responsibility, data also showed that, at the same time, it was continuously questioned. Participants reported having experienced a sense of disorientation concerning the most appropriate way of dealing with genetic risk. Despite the existence of evidence-based medical guidelines, the path to follow to manage cancer risk was frequently unclear. This was particularly the case for women surrounded by a social and medical environment that had contradictory opinions regarding genetic risk and its management, and for women aged 35–45 years. The four following factors explain the participants' disorientation.

The fragmentation of the medical system. Following up women with *BRCA1/BRCA2*-associated cancer risk requires complex teamwork involving several specialists (gynecologist, radiologist, surgeon, medical geneticist), usually in collaboration with a primary-care physician. However, our data suggest that the health-care professionals in charge of the participants did not always have similar views of genetic risk and its management. Three issues can be highlighted.

First, some of the specialists were not well informed. Anouch illustrated this point when she described, with a touch of humor, the discussion with her gynecologist about how to manage her cancer risk:

> Every time I meet [the gynecologist], he asks: "And now? How do we go on?" (Anouch, 40)

Second, risk-reduction strategies were far from being accepted by all participants' physicians. Sometimes, at-risk women found themselves confronted with opposing points of view regarding the legitimacy of the genetic-risk status and its management. Fedora (58), for instance, retained her ovaries in contradiction to the medical guidelines. Yet her behavior was consistent with the advice of her gynecologist, who told her that with an ultrasound twice a year, she did not run any risk.

Finally, physicians tended to develop their own interpretation of management guidelines, especially regarding the frequency and the age at which to begin these measures. For instance, Avril's gynecologist proposed that she have only an annual breast examination because Avril found more frequent breast examinations extremely stressful. Yet her radiologist considered her surveillance program insufficient. Avril (42) was caught in the middle of these divergent medical opinions.

The fragility of the genetically at-risk status. Participants found it difficult to pursue their health program because of the fragility of their at-risk status. We use the concept of "status" in its sociological sense, as the position held by the women in the medical system. Data showed that the at-risk status had three main features that made it fragile and thus difficult to assume.

First, the at-risk status was qualified as "self-confronting." Because the woman is not really sick, she is responsible for her risk management: it is up to her to organize medical examinations and make the final decision regarding how to proceed. This way of doing things reflects the principle of self-determination that is central in current human genetics.[8] However, participants would have liked to be oriented more in their decision-making process. Elin, for instance, spent a lot of time collecting information, but in the end she was still uncertain about whether to undergo preventive mastectomy. She asked her physician for an opinion, but he did not offer her one, stating instead that she had to follow her deepest feelings. This attitude left Elin feeling helpless:

> He said that I had to follow my deepest feelings, my instinct, and then he would adapt to my own conclusions. "We [physicians] propose [the options], you dispose," he said. … I would have liked him to stick his neck out a bit more. He was in a good position to offer … a kind of "synthesis." That is: "based on your situation and on what I have heard from you, this is what I would suggest." (Elin, 45)

Second, the at-risk status was qualified as "solitary." Participants usually expressed their difficulty in identifying with other genetically at-risk women. This population is quite rare. Moreover, participants considered genetic risk of breast/ovarian cancer a private issue because it involves intimate parts of the body. Given the difficulty of developing a sense of belonging to a peer group, the participants lacked the strength of a collective identity.

Finally, the at-risk status was qualified as "secondary." Because at-risk women were not really sick, health-care professionals tended to classify them as "not urgent cases" for appointments or feedback on screening results. Many participants reported having been hurt by this "lack of consideration."

The contradiction between the health program and other life projects. Unlike most sick people, the participants were not relieved from common social duties and responsibilities, but instead were expected to continue living normally while working on their health program. This situation could pull them in conflicting directions, in particular regarding family planning. Judith provided an illustration of the existential conflict she faced. This 30-year-old *BRCA1* mutation carrier was found to have several fibromas in her breasts. She was recommended to have a prophylactic mastectomy because of the difficulty of implementing effective surveillance measures in her case. She refused, but not without some worry.

> From the time I turned 25, the physicians suggest and insist that I have my breasts removed. But I resist. …In the future, I think I will undergo prophylactic mastectomy, but not now. Never mind, I'll take the risk. There are things that are too important for me. … I really want to breastfeed. … Well, sometimes, I get worried: if I get sick, will I be able to forgive myself? (Judith, 30)

Judith's desire to breast-feed clashed with her health program, but her decision not to have the mastectomy, for the time being at least, did not completely solve her dilemma about the most appropriate way to act.

We observed that the contradiction between the health program and other life projects tended to be particularly strong when women were between 35 and 45 years of age: medical guidelines for this age range were very demanding (e.g., evidence-based recommendation for risk-reduction salpingo-oophorectomy), but at the same time other issues (e.g., maternity) were still at the forefront of women's concerns.

The potential illegitimacy of any action toward dealing with risk. Even if the health program was constantly questioned, it is worth noting that all risk-management strategies were subject to the same fate: surveillance, prophylactic surgery, and even inaction could be contested. This was due to the uncertainty of the concept of risk: because one did not know whether the disease would actually develop one day, surveillance and prevention could be considered unnecessary; because one did not know how serious the illness would be if it developed, surveillance could be seen as insufficient and prevention excessive; and because one could not exclude that the illness would develop, inaction could be considered fatal. Study participants provided several examples of people expressing doubts about their risk-management behaviors. In short, given the uncertain nature of risk, no risk-management behavior was universally considered legitimate.

DISCUSSION

This study has highlighted the challenges that genetically at-risk women face in managing their risk of breast/ovarian cancer over time. Prior studies of the long-term effects of genetic testing have generally used a quantitative design.[10–16] In contrast, our study adopted an explorative, qualitative approach to investigate the experience of unaffected at-risk women from their own perspective.[19]

This study showed that over time, genetically at-risk women were encouraged—and sometimes sternly pushed—to take responsibility for their health and adhere to medical guidelines to minimize their cancer risk. Meanwhile, women's adherence to these guidelines was strongly questioned by the social and medical environment, thus creating a sense of disorientation concerning the most appropriate way of coping with genetic risk.

These findings are consistent with the sociological literature regarding genetic testing. The constraining effect of genetic knowledge has already been reported,[20–22] as have the difficulties that genetically at-risk women face in making decisions.[23,24] Our contribution to this field lies in the comprehensive illustration of the sense of disorientation and in the description of the complex psychosocial processes that underlie it. Particularly, we have clarified that the contradictory attitudes of health-care professionals are one of the factors that generate or reinforce this sense of disorientation.

Of note, however, not all participants experienced a similar degree of disorientation, especially not at all moments of their lives. As we have shown, disorientation was more or less pronounced based on two factors: the social and medical environment and the life period. Participants who were surrounded by social and medical environments that did not share the same perspectives regarding the understanding and management of genetic risk were particularly prone to disorientation. Regarding life periods, disorientation was particularly strong for at-risk women between the ages of 35 and 45 years because of important conflicts that could arise between the health program and other life projects (e.g., maternity).

The sense of disorientation experienced by the participants may partially explain differences in their ways of managing their cancer risk. Participants' behaviors were not necessarily consistent with evidence-based medical guidelines (**Table 2**).

We conducted this study in two regions of a small country (Switzerland) in which the number of *BRCA1*/*BRCA2* mutation carriers is small and the issue of genetic cancer risk remains confidential, particularly in the private health-care

sector.[25,26] The Swiss medical system is fragmented in terms of cancer-risk management. However, the scientific literature suggests that the management of genetically at-risk individuals may be inconsistent in most countries. According to authors of several studies conducted in the United States, Canada, and Europe, health-care professionals are not always well-informed or trained to manage at-risk individuals.[27–31] Additionally, preventive medicine is far from being accepted by all members of the medical community.[32] Finally, physicians tend to develop their own interpretation of international guidelines.[33] Löwy and Gaudillère[34] argued that a given mutation in the *BRCA1/BRCA2* genes is identical everywhere, but its meaning depends on the local context. Thus, "hereditary risk" does not necessarily mean the same thing to a gynecologist, an oncologist, or a medical geneticist. As a consequence, a certain level of inconsistency between health-care professionals is likely to exist, except, maybe, when the management of genetically at-risk individuals is strictly centralized in defined institutions.

This study has some limitations. Although the size of the sample is appropriate for a qualitative study,[19] we were not able to achieve a balanced distribution of the participants in the three age groups. Additionally, the sample may be biased toward those women who were willing and able to share their experiences. Finally, it is unclear how the results of the present investigation could be extended to genetically at-risk women who are followed up by multidisciplinary teams working in centralized institutions, such as hereditary cancer clinics.

Despite these limitations, this study revealed some potentially crucial implications of *BRCA1/BRCA2* genetic testing. The contradictory attitudes of health-care professionals in caring for at-risk women underline the urgent need to promote a greater understanding and awareness of the genetically at-risk status and of the care for this condition within the health-care system. Evidence-based guidelines exist, but they do not always seem to be known or applied. Additionally, a concerted approach should be encouraged to improve communication and consistency among the health-care professionals involved. Finally, updated and continuous education should provide concerned health-care professionals with the necessary scientific knowledge, relational skills, and ethical attitude to efficiently support genetically at-risk individuals throughout their complex trajectory, particularly during its most delicate phase (age 35–45 years). For all these reasons, we believe that multidisciplinary hereditary cancer clinics would be particularly appropriate for regular follow-up of *BRCA1*/*BRCA2* mutation carriers. Other interventions may also be addressed with unaffected women to empower them to reduce uncertainty and/or decisional conflicts. For instance, women may benefit from traditional and/or Web-based support groups. These interventions have been found to help *BRCA1/BRCA2*-positive women in terms of risk management, because they provide information, emotional support, and specific experiential knowledge from women with similar medical conditions.[35,36]

In conclusion, this qualitative study provides new insights into the experience of unaffected women carrying *BRCA1/BRCA2* mutations. These women are exposed to contradictory pressures from the social and medical systems and are thus prone to develop a sense of disorientation regarding the most appropriate way of coping with cancer risk. The contradictory attitudes of health-care professionals are one of the factors that generate and/or reinforce this sense of disorientation. In the future, more qualitative studies are needed to explore the experience of the health-care professionals who are involved in the long-term care of carriers of genetic predispositions to cancer and, following Löwy and Gaudillère,[34] to explore their understanding of "hereditary risk" and its consequences for their way of managing these individuals.

ACKNOWLEDGMENTS

This work was supported by the Swiss National Science Foundation, Switzerland (grant number PZ00P1_132633/1). We are deeply grateful to all participants for sharing their experiences with us.

DISCLOSURE

The authors declare no conflict of interest.

REFERENCES

1. Antoniou A, Pharoah PD, Narod S, et al. Average risks of breast and ovarian cancer associated with *BRCA1 or BRCA2* mutations detected in case series unselected for family history: a combined analysis of 22 studies. *Am J Hum Genet* 2003;72:1117–1130.
2. Chen S, Parmigiani G. Meta-analysis of BRCA1 and BRCA2 penetrance. *J Clin Oncol* 2007;25:1329–1333.
3. Mavaddat N, Peock S, Frost D, et al.; EMBRACE. Cancer risks for BRCA1 and BRCA2 mutation carriers: results from prospective analysis of EMBRACE. *J Natl Cancer Inst* 2013;105:812–822.
4. American College of Obstetricians and Gynecologists Committee. ACOG practice bulletin no. 103: hereditary breast and ovarian cancer syndrome. *Obstet Gynecol* 2009;113:957–966.
5. Daly MB, Axilbund JE, Buys S, et al.; National Comprehensive Cancer Network. Genetic/familial high-risk assessment: breast and ovarian. *J Natl Compr Canc Netw* 2010;8:562–594.
6. Balmaña J, Díez O, Rubio IT, Cardoso F; ESMO Guidelines Working Group. BRCA in breast cancer: ESMO clinical practice guidelines. *Ann Oncol* 2011;22(suppl 6):vi31–vi34.
7. Evans DG, Graham J, O'Connell S, Arnold S, Fitzsimmons D. Familial breast cancer: summary of updated NICE guidance. *BMJ* 2013;346:f3829.
8. Clarke A. The process of genetic counselling. In: Harper P, Clarke A, (eds). *Genetics, Society and Clinical Practice*. BIOS Scientific Publishers: Oxford, UK, 1997:179–200.
9. Lemke T, ed. *Perspectives on Genetic Discrimination*. Taylor & Francis: New York, 2013.
10. Meiser B. Psychological impact of genetic testing for cancer susceptibility: an update of the literature. *Psychooncology* 2005;14:1060–1074.
11. Halbert CH, Stopfer JE, McDonald J, et al. Long-term reactions to genetic testing for BRCA1 and BRCA2 mutations: does time heal women's concerns? *J Clin Oncol* 2011;29:4302–4306.
12. Metcalfe KA, Mian N, Enmore M, et al. Long-term follow-up of Jewish women with a BRCA1 and BRCA2 mutation who underwent population genetic screening. *Breast Cancer Res Treat* 2012;133:735–740.
13. van Oostrom I, Meijers-Heijboer H, Lodder LN, et al. Long-term psychological impact of carrying a BRCA1/2 mutation and prophylactic surgery: a 5-year follow-up study. *J Clin Oncol* 2003;21:3867–3874.
14. Watson M, Foster C, Eeles R, et al.; Psychosocial Study Collaborators. Psychosocial impact of breast/ovarian (BRCA1/2) cancer-predictive genetic testing in a UK multi-centre clinical cohort. *Br J Cancer* 2004;91:1787–1794.
15. Dagan E, Shochat T. Quality of life in asymptomatic BRCA1/2 mutation carriers. *Prev Med* 2009;48:193–196.

16. Graves KD, Vegella P, Poggi EA, et al. Long-term psychosocial outcomes of BRCA1/BRCA2 testing: differences across affected status and risk-reducing surgery choice. *Cancer Epidemiol Biomarkers Prev* 2012;21:445–455.
17. Claes E, Denayer L, Evers-Kiebooms G, Boogaerts A, Legius E. Predictive testing for hereditary non-polyposis colorectal cancer: motivation, illness representations and short-term psychological impact. *Patient Educ Couns* 2004;55:265–274.
18. Bertaux D. *Biography and Society: The Life History Approach in the Social Sciences*. Sage: London, 1981.
19. Strauss A, Corbin J, eds. *Basics of Qualitative Research: Grounded Theory Procedures and Techniques*. Sage: Newbury Park, CA, 1990.
20. Kenen RH. The at-risk health status and technology: a diagnostic invitation and the 'gift' of knowing. *Soc Sci Med* 1996;42:1545–1553.
21. d'Agincourt-Canning L. Experiences of genetic risk: disclosure and the gendering of responsibility. *Bioethics* 2001;15:231–247.
22. Lau Y, Jaye C. The 'obligation' to screen and its effect on autonomy. *J Bioeth Inq* 2009;6:495–505.
23. Ferrell BR, Smith SL, Ervin KS, Itano J, Melancon C. A qualitative analysis of social concerns of women with ovarian cancer. *Psychooncology* 2003;12:647–663.
24. Hamilton R, Williams JK, Bowers BJ, Calzone K. Life trajectories, genetic testing, and risk reduction decisions in 18-39 year old women at risk for hereditary breast and ovarian cancer. *J Genet Couns* 2009;18:147–159.
25. Escher M, Sappino AP. Primary care physicians' knowledge and attitudes towards genetic testing for breast-ovarian cancer predisposition. *Ann Oncol* 2000;11:1131–1135.
26. Pichert G, Dietrich D, Moosmann P, Zwahlen M, Stahel RA, Sappino AP. Swiss primary care physicians' knowledge, attitudes and perception towards genetic testing for hereditary breast cancer. *Fam Cancer* 2003;2:153–158.
27. Bellcross CA, Kolor K, Goddard KA, Coates RJ, Reyes M, Khoury MJ. Awareness and utilization of BRCA1/2 testing among U.S. primary care physicians. *Am J Prev Med* 2011;40:61–66.
28. Feero WG, Green ED. Genomics education for health care professionals in the 21st century. *JAMA* 2011;306:989–990.
29. Nippert I, Harris HJ, Julian-Reynier C, et al. Confidence of primary care physicians in their ability to carry out basic medical genetic tasks—a European survey in five countries-Part 1. *J Community Genet* 2011;2:1–11.
30. Trivers KF, Baldwin LM, Miller JW, et al. Reported referral for genetic counseling or BRCA 1/2 testing among United States physicians: a vignette-based study. *Cancer* 2011;117:5334–5343.
31. Weitzel JN, Blazer KR, Macdonald DJ, Culver JO, Offit K. Genetics, genomics, and cancer risk assessment: state of the art and future directions in the era of personalized medicine. *CA Cancer J Clin* 2011;61:327–359.
32. Godlee F. Preventive medicine makes us miserable. *BMJ* 2005;330:7497.
33. Cabana MD, Rand CS, Powe NR, et al. Why don't physicians follow clinical practice guidelines? A framework for improvement. *JAMA* 1999;282: 1458–1465.
34. Löwy I, Gaudillière JP. Localizing the global. Testing for hereditary risk for breast cancer. *Sci Technol Human Values* 2008;33:299–325.
35. Kenen RH, Shapiro PJ, Friedman S, Coyne JC. Peer-support in coping with medical uncertainty: discussion of oophorectomy and hormone replacement therapy on a web-based message board. *Psychooncology* 2007;16: 763–771.
36. Hughes L, Phelps C. "The bigger the network the bigger the bowl of cherries…": exploring the acceptability of, and preferences for, an ongoing support network for known BRCA 1 and BRCA 2 mutation carriers. *J Genet Couns* 2010;19: 487–496.