Social and ethical implications of BRCA testing

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Oncologists are asked with increasing frequency to counsel their patients with respect to the medical, psychological and social repercussions of genetic testing for cancer susceptibility that may have been prescribed by physicians or carried out through direct-to-consumer tests. This article critically reviews the main ethical and social implications of BRCA testing, focusing on genetic responsibility and genetic discrimination. Genetic responsibility toward oneself and others is a highly debated implication of genetic testing for cancer predisposition that requires broad considerations of the boundaries between individual and community rights and a reappraisal of the notion of autonomy as relational. Physicians’ duty to warn ‘at risk’ relatives can be an ethical quandary, yet confidentiality is key to the patient–doctor relationship. Mutation carriers may be subject to different forms and degrees of genetic discrimination and many individuals at risk have forgone BRCA testing to avoid potential discrimination. The scientific and medical community, together with patients and the public, has actively engaged against genetic discrimination. The legislation in many countries now protects against genetic discrimination by insurance companies and employers. Legal and regulatory issues are not the final answer to discrimination and profound cultural changes are required to create understanding and acceptance of all differences.

introduction

Breast cancer is highly prevalent and is the second cause of cancer death in women. In the USA, ~180 000 American women were diagnosed with invasive breast cancer in 2007 and another 62 000 with in situ or non-invasive breast cancer, while >40 000 women were expected to die from breast cancer in the same year [1]. In 2007, 22 500 women were diagnosed with ovarian cancer, accounting for 3% of all cancers among women, and 15 280 women were projected to die from ovarian cancer [1]. Only 10% of all breast cancer is hereditary, and <1% of the general population is estimated to carry a mutation in BRCA1 or BRCA2. BRCA mutations are associated with a relative increased lifetime risk of breast cancer of 2.7–6.4 times, and a relative lifetime risk of ovarian cancer of 9.3–35.3 times greater than average risk women [2, 3].

Women who carry a BRCA mutation are given options of early and intensive surveillance, chemoprevention and prophylactic surgery. Oncologists and geneticists help women understand the risk their BRCA status represents for them and their relatives. They also identify and address biopsychosocial factors that may foster women’s adherence to preventive and/or risk-reducing strategies, in order to reduce the morbidity and mortality associated with hereditary or familial cancers [4, 5]. Available risk reduction options in the past 15 years seem to have significantly lowered the chance that high-risk women develop the breast and ovarian cancers [6, 7].

Since the initial application of BRCA testing in research first, and subsequently also in oncology practices, scientists, physicians and bioethicists have consistently cared about the medical and psychosocial well-being of mutation carriers, and have cautioned the public about the limited predictive power of genetic testing, especially outside high-risk families, due to the relatively low gene penetrance, the possibility of new mutations with different significance that are still to be identified, and the role of environmental factors in cancerogenesis and tumor progression. Furthermore, preventive and interventional measures are still being developed and genetic testing carries potentially negative psychosocial repercussions for individual carriers and their families [8, 9].

The identification of DNA mutations predisposing to cancer susceptibility is now expanding to include whole-genome profiling for personalized approaches to cancer patients and direct-to-consumer (DTC) genetic testing. Knowledge about the ethical and juridical implications of genetic testing is becoming essential for oncologists, who are being asked with increasing frequency to counsel their patients with respect to the medical, psychological and social repercussions of genetic information, even when obtained outside the context of an established patient–doctor relationship. Many articles and reviews have addressed the main ethical and social implications of BRCA testing [10–18], including informed consent, privacy and confidentiality, a person’s right to know or not to know their genetic information, carriers’ responsibility to share
is genetic information different from other medical information?

Genetic information refers to genetic testing for patients and/or for family members up to fourth-degree relatives. A genetic test is any analysis to detect genotypes, genetic mutations or chromosomal changes, not including analysis of proteins or metabolites directly related to a manifested disease. Genetic information also refers to any manifestation of disease or disorder in a family member, and/or to the participation of a person or family member in research that involves genetic testing, counseling or education. Genetic information thus has unique aspects with respect to other medical information, as it carries potential value, but also danger, for individuals other than the person tested [21, 22].

This and other unique aspects of genetic knowledge have led to ‘genetic exceptionalism’, the separate treatment of the ethical and legal implications of genetic testing. Genetic exceptionalism is a dangerous ethical position that can lead to segregation of a group of persons at risk [22]. The application of the ethical principles and methodologies used to analyze and resolve ethical quandaries in medicine in general can be applied to the complex questions of autonomy, privacy and responsibility raised by genetic knowledge, as well as to the potential legal conflicts surrounding genetic testing [8, 10, 14, 22].

Beyond the ethical and legal implications of genetic testing, experts and the public have expressed different views on the value of BRCA testing, from stressing the importance of genetic knowledge for high-risk women as a means to enhance control of their lives, to worrying about the potentially negative repercussions of genetic information [10, 22].

geneic discrimination and legislative efforts

Genetic discrimination against asymptomatic individuals or their relatives on the basis of actual or presumed genetic differences or characteristics has been a concern among women with strong family histories of breast or ovarian cancer and their oncologists, since genetic discrimination has occurred in the past for non-oncologic diseases [23–26]. BRCA mutation carriers may also be subject to overt discrimination or to more subtle forms of estrangement and rejection by their families or communities, as being regarded as less-than-ideal partners or parents [10, 15]. Many high-risk women refrain from being tested, due to fear of discrimination by health insurance or by actual or potential employers, or fearing discrimination against their children [27]. Similar concerns have also been reported among genetic experts and oncologists [28].

People who refrain from being tested out of fears of discrimination from insurers or employers may suffer damage to their health due to forgoing preventative care measures, monitoring, and/or other interventions that might follow from testing. Health care delivery has been affected by fear of genetic discrimination, as patients have sometimes paid out of pocket, or used false names, or may have asked their doctors to omit genetic information from their medical records. The threat of genetic discrimination may have also hindered medical research aimed at developing personalized medicine and new treatment modalities for genetic diseases [29, 30].

Although documenting the exact magnitude of genetic discrimination is an arduous task, cases have been reported in the USA with regard to life and health insurance, the employment market, and in access to higher education and adoption [23, 26, 28, 31]. While some authors have pointed out that society’s concern for genetic discrimination may have been excessive, the active engagement of medical and patient organizations has positively influenced the recent development of national and international efforts by legislators to regulate the collection and use of genetic information and the enactment of anti-discrimination legislation in the USA and other countries [32–34].

Various countries now have legislation and regulations to protect against discrimination by insurance companies and in the workplace. Belgium passed a genetic non-discrimination law in 1990; other European nations followed suit [35, 36]. The Biomedicine Convention of the Council of Europe and UNESCO based their legislative efforts on considering individual patients as the only subject of genetic information and on ‘explicitly recognizing the right not to know’ [35].

In 2008, the US Congress passed the Genetic Information Nondiscrimination Act (GINA) to protect individuals against discrimination by health insurers and employers on the basis of genetic information [37–42]. GINA prohibits insurance companies from taking into account genetic conditions or family history when determining risk assessment, thus protecting mutation carriers from paying higher insurance premiums or being denied health coverage. GINA also prohibits employers from making employment and promotional decisions based on genetic information, imposing fines of up to $300,000 per violation.

GINA is, in large part, the result of the anticipatory work of researchers and clinicians involved in the development of the Human Genome Project, who raised concerns about the risk of genetic discrimination at the outset of the project [38]. Among common genetic tests protected by GINA are tests for BRCA1 and BRCA2 mutations and HNPCC mutations that predispose to breast, ovarian, colon and other cancers, as well as tests that help classify the genetic profile of an existing cancer. GINA thus protects mutation carriers and facilitates research on the biology and treatment of cancers associated with specific genetic mutations [37, 38].

GINA does not regulate insurance underwriting based on a person’s current health status, does not mandate coverage for any particular test or treatment, does not cover life, disability or long-term care insurance and does not interfere with health professionals’ recommendations for genetic testing to their patients [37]. GINA does, however, substantially lower patients’
risk of genetic discrimination. As of writing, one claim of genetic discrimination has been filed since GINA was approved, by a BRCA-positive woman who allegedly lost her position at work after undergoing bilateral prophylactic mastectomy [43].

Genetic non-discrimination legislation is based on the fact that individuals have no control over their genes. While also persons with low or unknown genetic risk share the increased health-care cost for carriers of genetic mutations, such legislation may lead to decreased overall long-term health-care costs, if prevention or early interventions prove to be cost-effective. Given the lack of a clear definition of genetic test and genetic data in the laws, however, and of a clear distinction between genetic and non-genetic data in insurance practices, the efficacy of genetic non-discrimination laws may not be as complete as anticipated [44, 45]. It has been reported, for example, that in European countries the enactment of genetic non-discrimination legislation may have been less effective than expected in regard to insurance practice, due to lack of clear definitions of terms and boundaries between genetic and non-genetic tests and data, thus providing 'only the illusion of protection' [36]. In addition, legislation may unintentionally have fostered increased discrimination against patients whose illnesses are related to lifestyle risks that are assumed to be under the control of the individual [7, 46]. As the interaction of genetic and environmental factors is not yet fully understood for many pathologic entities, increasing the burden of personal responsibility for high-risk takers may represent a shifting of discriminatory attitudes from one group of potential patients to another [36]. The ultimate response to discrimination involves deep cultural changes, beyond legal and regulatory issues, to foster a non-discriminatory approach to all illnesses and disabilities [26, 47–49]. As Billings wrote in 2008, 'antidiscrimination laws are only effective as guideposts to better understanding and tolerance’ [50].

**DTC genetic testing: reviving the ethical debate.**

Cancer risk genomic profiling and DTC genetic testing raise many of the same ethical concerns that were already addressed above with regard to testing for genes and other tests of genetic cancer predisposition. Additional concerns in DTC genetic testing involve the major impact of economic factors that drive individuals to be tested without proper understanding of the meaning of genetic testing and its potential repercussions on them and their family members [19, 20, 51–53]. In addition, the long-term psychological ramifications of genetic knowledge not accompanied by proper counseling and medical follow-up are still unknown, and patients’ privacy and confidentiality about their genetic information will be difficult to safeguard against potential exploitation by individuals and corporations. Even with genetic non-discrimination legislation, mutation carriers may find themselves ineligible for life insurance and/or other long-term agreements. Other ethical and social concerns regard the additional health-care costs associated with carrying out the tests and dealing with the consequences of their findings [19, 20, 50–53].

According to the American College of Medical Genetics, genetic testing should be provided to the public only through the services of an appropriately qualified health-care professional, who should be responsible for both ordering and interpreting the test, as well as for pre- and post-test counseling and follow-up, as needed [19]. Thus, while individuals have rights to undergo genetic testing, they should be fully informed of its inherent risks and entitled to the confidentiality of the testing and its results [53–55]. Unfortunately, DTC genetic testing is not accompanied by proper counseling, and advertisements for DTC genetic testing are not subject to the same degree of federal oversight as those for prescription drugs, thus increasing the possibility of misleading the public and physicians in the interest of profit [55].

DTC advertisements for genetic testing, based on the obvious public fear of cancer, seem highly inappropriate, given the public’s limited understanding of genetics and the lack of comprehensive oversight of the educational value of advertisements regarding genetic testing [56]. A campaign to increase awareness among consumers and physicians about inherited susceptibility for breast and ovarian cancer, and about the availability of genetic testing for these conditions could be beneficial. As a consequence of insufficient clinician and/or patient knowledge or understanding, in fact, inappropriate referrals and misinterpretation of test results may occur, as well as inappropriate medical decision making for the patient and the entire family, including unnecessary health-care expenditure, unneeded prophylactic surgery, or false reassurance and less surveillance in women who are found not to carry a BRCA mutation. Even well-meaning health-care providers without specific training in genetics or genetic counseling may also be manipulated into ordering genetic testing or making inappropriate referrals [56].

DTC genetic testing may also include still unproven genetic markers for common multifactorial diseases, such as breast cancer. An important ethical issue is that some techniques may identify, not diagnostic genetic variants, but surrogate genetic markers, known as single-nucleotide polymorphisms (SNPs), which are associated with a very small increased risk of disease [57]. With regard to breast cancer, for example, the tests that can be used to identify SNPs in the FGFR2 gene have been associated with only a 1.2-fold increase in the risk of developing breast cancer [52]. Among other pressing ethical questions are: who should have their genome sequenced? who should prescribe the test? who should provide pre- and post-test counseling? who should have access to an individual’s genetic information? and what liability may physicians incur especially when treating more members of one family? [20, 58]. Ensuring proper continuing education for health-care professionals and implementing public education policies are needed, along with standards for accurate marketing of DTC genetic testing [20, 58–60].

**individual genetic responsibility and professionals’ duty to warn: where do we stand?**

Two of the most controversial ethical issues surrounding genetic testing for cancer predisposition are: (i) whether or not
individuals have a responsibility to acquire genetic knowledge and to share positive results with family or community members at risk [61]; (ii) whether or not health professionals have a responsibility to disclose relevant genetic information to their patients’ relatives; and (iii) how they should best counsel those mutation carriers who may decide not to share genetic information [62–65].

Genetic responsibility toward oneself and others is a highly debated implication of genetic testing for cancer predisposition. Genetic links in high-risk families would appear to be associated with moral obligations that go beyond those related to individual autonomy [61, 66]. In addition, the questions of whether and when to share genetic information requires broad consideration of the boundaries between individual and community rights and a reappraisal of the notion of autonomy as relational [66, 67]. Understanding autonomy in a relational way entails recognizing the internal and external factors that shape our decision making and the responsibilities that arise from our connections to others, as well as acknowledging the cultural, socio-economic and contextual aspects of patients’ decision making [66–68]. Yet it seems medically premature to consider genetic testing as a necessary step for people to take in regard to their future health status [69]. In addition, the psychological and social ramifications of genetic testing are so complex that questions about whether and when to be tested are legitimate ones [69].

In the ethical and medical literature, there is general agreement that genetic information, by virtue of its potential repercussions on the health of an entire family or community, reminds us of the ties we have with each other. Thus there is a compelling moral argument for affirming the importance of sharing genetic information with relatives who may potentially be at risk [61]. Most clinicians also support the view that individuals have a ‘right not to know’ and that this right is a correlate of the ‘right to know’, in regard to both policy making and genetic counseling. They thus believe that they must continue to respect patient’s autonomy and confidentiality, in order to establish and maintain the trust between clinicians and patients that is key to the therapeutic relationship [8, 10, 69–72]. Some authors, however, have argued that the ‘right not to know’ (or not to share) genetic information is equivalent to an irresponsible ‘right to ignorance’ that may lead to imprudent decisions and cause harm to oneself and others [61, 71]. Others have appealed to legal cases, such as the Tarasoff precedent, to advocate for physicians’ duty to warn families about genetic risks, stirring an intense debate about the application of legal precedents to genetic testing for cancer predisposition [18, 70, 73].

In the USA, the Health Insurance Portability and Accountability Act (HIPPA) reinforces the ethical and legal value of confidentiality. In addition, most medical associations agree that while physicians have a duty to advise patients of the relevance that genetic information can have to their relatives, and therefore of the importance to share such information, they do not have a duty to breach patient confidentiality and warn their patients’ relatives directly [62].

Studies have shown that some mutation carriers prefer not to share their genetic knowledge with family members due to estranged relationships, unresolved conflicts or uncertainties about whether relatives would wish to be informed [72, 74–76]. Personal or gender differences in communication preferences and styles can contribute to patients’ initial decisions not to share genetic information with others, and cross-cultural differences in ethical norms and legal requirements may influence public attitudes and decisions to disclose [76–81]. At the individual level, personal context, perception of personal risk, perceived or actual vulnerability and receptivity of relatives, content and timing of communication and personal feelings all shape individual response to whether and when to share genetic information with at-risk relatives. At the familial level, proximity of relationship to one’s relatives, family structure and interpersonal dynamics and prior familial experiences with cancer account for great variability in disclosure preference. At the community level, cultural context and roles, as well as gender and age, play an important role in communication patterns [76].

As progress is being made in our ability to prevent or ameliorate with medical or life-style interventions the many pathologic conditions that can be revealed through genetic testing, the number of relatives who would wish to be informed is growing in many countries. Physicians thus increasingly face the challenge of making judgments about when it may be appropriate to breach confidentiality on the basis of knowledge about risks and risk-reduction measures [82]. Health professionals will also require training and support in discussing genetic risks with their patients and the importance of sharing results with at-risk family members, as well as in responding to relatives’ questions with respect for the complexity of intrafamilial communication dynamics [76].

In the UK, the General Medical Council has issued guidelines urging physicians to judge ‘whether their duty to make the care of the patients their first concern is greater than their duty to help protect the other person from serious harm’ [58, 83]. This quandary may be exacerbated when physicians are caring for different members of the same family. Most international medical organizations and professional ethics codes support the notion that health professionals’ obligation is toward the patient, unless there is a risk of serious harm to others [8, 35, 62, 65]. If interventions could prevent potentially serious medical conditions, however, physicians may have to consider overriding confidentiality, and must also reflect on their potential future liability in regard to those family members [58]. It has been suggested that certain genetic information may be seen not only as the result of an individual’s test subject to full confidentiality, but also as part of a ‘familial joint account’ open to being used in guiding treatment or testing for the benefits of other family members, even when not meeting the seriousness criterion [84]. The recent presentation and discussion of two clinical cases by Parker and Lucassen powerfully illustrates a contemporary diagnostic dilemma, in which the gene penetrance and the interaction of genetic and environmental factors on the one hand, and the magnitude of risk reduction with available interventions on the other, are difficult to assess in many cases of positive genetic testing [58].

Difficult decision making on how to manage genetic information in patients and their relatives is bound to increase for all physicians and for clinical oncologists in particular. The first and essential step is to explain to patients the nature of the
genetic information and its potential relevance to their families, while refraining from being judgmental about some patients’ preferences not to know or not to disclose genetic information [8, 74]. Over time, physicians may explore with their patients their motivations related to the nature, meaning and relevance of a positive genetic test and communication of test results to family members. Through repeat encounters and through proper counseling referrals, often patients reach a deeper understanding of the implications of genetic testing and come to the decision to share relevant information with other family members. This, however, may not be the case when patients and families belong to cultures in which cancer is still a metaphor of death or of shame and guilt. In such instances, oncologists should work as part of a team in trying to convey to their patients a more realistic view of cancer as a potentially curable or chronic illness, worth preventing or treating as early as possible [80, 81].

**disclosures**

The author declares no conflict of interest.

**references**

5. Patrick-Miller L, Bradbury AR, Terry MB. Controversies in communication of genetic screening results for cancer: A Report from the American Society of Preventive Oncology’s Screening Special Interest Group. ASPO’s 33rd Annual Meeting, March 2009, Tampa, FL, USA.