Professional Challenges in Cancer Genetic Testing: Who Is the Patient?

**GAYUN CHAN-SMUTKO, DEVANSHI PATEL, KRISTEN M. SHANNON, PAULA D. RYAN**

Massachusetts General Hospital Cancer Center/Center for Cancer Risk Assessment, Boston, Massachusetts, USA

**Key Words.** Duty-to-warn • Genetic testing • Family dynamics • Patient confidentiality

**Disclosure:** No potential conflicts of interest were reported by the authors, planners, reviewers, or staff managers of this article.

**ABSTRACT**

In the genetic counseling setting, the health care provider can be challenged by opposing duties to members of the same family: protecting the privacy of the patient identified with a gene mutation and the ethical obligation to warn at-risk relatives. In a situation of nondisclosure between members of a family with a known disease-predisposing mutation, this type of dilemma can present in acute form for the provider who cares for different members of the family. This can hinder effective medical decision making. To minimize this effect, we recommend detailed pretest genetic counseling steps to empower the patient to communicate with their at-risk relatives their intent to pursue testing and willingness to share information. In addition, post-test counseling should reiterate the implications of a positive result for at-risk relatives and conclude with a written summary that patients can share with their family. *The Oncologist* 2008;13:232–238

**INTRODUCTION**

Genetic testing, by definition, involves the patient and their blood relatives. The cancer genetic counseling process records the entire family medical history, and this pedigree reveals whether the patient and family members may have an increased risk for developing certain cancers. However, shared genes do not necessarily equal shared knowledge of genetic information. We present and discuss two case vignettes, each posing different ethical and professional challenges to the health care providers involved in the case. The cases were selected because they illustrate examples of where genetic information and family dynamics intersect such that providers are presented with a dilemma in determining which individual is their primary patient and defining their professional duty to each.

**CASE 1**

A 42-year-old woman with a personal history of endometrial cancer diagnosed at age 39 is known to carry a deleterious mutation in the mutS homolog 6 gene (*MSH6*). Germline mutations in this gene are known to cause hereditary nonpolyposis colorectal cancer (HNPCC) (Table 1). At a follow-up visit with her gynecologist, the patient is encouraged to inform her at-risk family members of her mutation status (Fig. 1A). The patient replies that she will consider it. The physician documents the conversation in her visit note.
The patient’s only sister has the same gynecologist and presents to the physician’s office for follow-up after a dilation and curettage for endometrial polyps. She is a 39-year-old mother of two young children and has no personal history of cancer. She is aware that her sister has a history of endometrial cancer and is concerned about her own cancer risk. She recently learned that her maternal grandfather died of colon cancer at age 48. The unaffected sister asks the gynecologist if the two cancers could be linked.

What Is the Physician’s Duty to Each Patient?

The physician has a legal duty to the affected patient to protect her privacy. Under the Health Insurance Portability and Accountability Act Privacy Rules [1], the physician cannot disclose the affected sister’s genetic test results to another party without her written consent. The physician has documented in the affected sister’s chart that she encouraged the patient to inform her relatives.

The physician has an ethical duty to the unaffected sister to provide appropriate medical advice based on the family history. The patient needs to be informed of the appropriate cancer detection strategies as recommended by the National Comprehensive Cancer Network [2]. Care of both sisters is complicated by the fact that the physician cannot document her knowledge of the familial mutation in the unaffected sister’s chart without a release on file from the affected sister. The physician is therefore burdened with the need to rely solely on her personal knowledge of the familial mutation with no formal documentation in the unaffected sister’s chart.

The physician informs the unaffected patient that the endometrial and colon cancers are suggestive of HNPCC. The physician explains that the most informative member of the family to have genetic testing would be the affected sister. The physician asks the patient whether or not her sister has ever had genetic testing. The patient replies that she does not know, and adds that they are not on speaking terms. The physician suggests to the patient that she approach her affected sister regarding testing.

The unaffected sister calls the physician a few weeks later. She called her father to see if he knew whether or not the affected sister ever had genetic testing. The father did not know. The patient still refuses to call her sister, and remains eager to pursue genetic testing.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Genes</th>
<th>Families are characterized by</th>
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<tbody>
<tr>
<td>HNPCC</td>
<td>MLH1, MSH2, MSH6, PMS2,ab PMS1ab</td>
<td>Colorectal and endometrial cancer, age of onset &lt;50 May observe extracolonic cancers such as stomach, small bowel, ureter or renal-pelvis, ovary, brain, sebaceous skin tumors Autosomal dominant transmission: multiple cases of HNPCC-related tumors in paternal or maternal lineage, and in more than one generation</td>
</tr>
<tr>
<td>HBOCS</td>
<td>BRCA1, BRCA2</td>
<td>Breast cancer, age at onset &lt;50 Nonmucinous epithelial ovarian cancer Autosomal dominant transmission: multiple cases of breast and/or ovarian cancer in paternal or maternal lineage, and in more than one generation</td>
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- Clinical testing not available.
- Accounts for <5% of HNPCC mutation–positive families.

Abbreviations: HBOCS, hereditary breast and ovarian cancer; HNPCC, hereditary nonpolyposis colorectal cancer.

Figure 1. Pedigrees. (A) and (B) correspond to the pedigrees from cases 1 and 2, respectively. The number preceding yrs refers to current age. Cancer diagnoses are abbreviated and followed by the age at diagnosis. + indicates a mutation carrier. Abbreviations: BR, breast cancer; CO, colorectal cancer; d, death; ENDO, endometrial cancer; PPT, primary peritoneal carcinoma.

The physician asks the patient whether or not her sister has ever had genetic testing. The patient replies that she does not know, and adds that they are not on speaking terms. The physician suggests to the patient that she approach her affected sister regarding testing.

The unaffected sister calls the physician a few weeks later. She called her father to see if he knew whether or not the affected sister ever had genetic testing. The father did not know. The patient still refuses to call her sister, and remains eager to pursue genetic testing.
Medical Management Dilemma

In the absence of genetic testing, the physician is faced with a dilemma in providing appropriate care to the unaffected patient. Table 2 represents how clinical management for this patient would be affected with the knowledge of her genetic status.

The physician decides that a discussion of genetic testing is the pressing issue for the patient and offers her a genetic counseling referral.

The genetic counselor reviews the records prior to the consult. A three-generation family medical history is obtained, and the paternal family history is noncontributory. The patient reports that her mother died at age 65 from cardiac arrest, and had a total abdominal hysterectomy at age 43 for abnormal uterine bleeding. As far as she could recall, her mother “hated going to the doctor” and never had a screening colonoscopy.

The genetic counselor discusses the natural history of HNPCC and recommends that her affected sister pursue genetic testing. The patient reveals that she and her sister had a “falling out” 2 years ago after her divorce and that they have not spoken to each other since then.

The genetic counselor explains that the patient has the option of pursuing genetic testing with the caveat that a negative test result would not be meaningful in the absence of knowing whether an affected family member has a mutation. If she elects this option, she will need to undergo comprehensive mutation screening of all three DNA mismatch-repair genes associated with HNPCC (MLH1, MSH2, and MSH6) for which clinical testing is available. The patient feels that, in the event she is mutation positive, she would be able to plan a risk-reducing hysterectomy and bilateral salpingo-oophorectomy, and if she is negative, she will deal with that later.

The patient elects to pursue the full screen but learns that her insurance plan will not cover comprehensive mutation screening because she is unaffected. The out-of-pocket cost of comprehensive testing is beyond her financial means (~$3,000 for all three genes). The genetic counselor encourages her again to contact her sister and broach the subject of genetic testing. If her sister’s test reveals a mutation, the out-of-pocket cost for a single-site mutation analysis would be significantly lower for the patient.

The patient calls her affected sister, who shares her MSH6 mutation status. She has testing for the familial MSH6 mutation and is found to be negative.

Case Discussion

Cancer predisposition genetic testing often reveals risk information for both the patient and their family. As part of the informed consent process, a genetic counselor will inform the patient of the implications of their genetic test result for their family members prior to undergoing testing. The American Medical Association and American Society of Clinical Oncology (ASCO) have both tackled the dilemma and provided their memberships with professional guidelines on the “duty to warn” family members in the specific context of genetic diseases. In their respective position statements, both societies encourage their members to delineate circumstances to their patients under which the physician expects the patient to notify at-risk family members of the availability of information related to the risk of developing a disease [3, 4].

In 1998, the American Society of Human Genetics (ASHG) published its policy statement on professional disclosure of familial genetic information. The position of the ASHG Social Issues Subcommittee on Familial Disclosure is that, in exceptional cases, “disclosure should be permissible where attempts to encourage disclosure on the part of the patient have failed; where the harm is highly likely to occur and is serious and foreseeable; where the at-risk relative(s) is identifiable; and where either the disease is preventable/treatable or medically accepted standards indicate that early monitoring will reduced the genetic risk.” Furthermore, the harm from failing to disclose should outweigh the harm from disclosure [5].

Table 2. Clinical management and genetic status

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<th>Genetic testing status</th>
<th>Endometrial cancer</th>
<th>Colonoscopy</th>
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<tr>
<td>No testing information (family history alone) or uninformative negative test result</td>
<td>Endometrial biopsies and transvaginal ultrasound every year</td>
<td>Every 1–3 years</td>
</tr>
<tr>
<td>Positive for mutation</td>
<td>Endometrial biopsies and transvaginal ultrasound annually; consideration of prophylactic hysterectomy, oophorectomy</td>
<td>Annually</td>
</tr>
<tr>
<td>Negative for familial mutation</td>
<td>None</td>
<td>Every 5 years starting at age 50</td>
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In this vignette, the physician’s challenging dilemma is that she is the health care provider of both siblings. The exceptional conditions set forth by the ASHG are met in this case, such that the physician could act upon her discretionary privilege to disclose the mutation information to the unaffected patient. It is important to note, however, that the definition of “serious” is subjective, and in the realm of HNPPC, “foreseeable” is a relative notion given that genetic testing can never be predictive of developing disease.

In a survey of ASHG and American College of Medical Genetics members published in 2003 by Falk et. al [6], over half of the respondents reported having been faced with a situation in which the patient refused to notify at-risk relatives. One-fourth of the respondents reporting this dilemma seriously considered disclosure without patient consent. Clearly the dilemma described in case 1 is not unique to the field of genetics professionals who have a wealth of experience in dealing with families and genetic diseases. For a medical oncologist who sees fewer patients with hereditary disease, the dilemma can be more difficult because he/she does not have as much experience to rely on. It can be learned from the Falk et. al [6] study that most of the genetics professionals who seriously considered disclosure without patient consent ultimately did not release the information. They cited the sanctity of the physician–patient relationship, eventual case resolution by other means, and legal liability as the top three reasons.

A practical solution to minimize the chance of being faced with this dilemma is for the provider to raise the issue during a pretest discussion of sharing genetic information with family members. During the results disclosure visit the provider should also remind the patient of the carrier risk for family members. Genetic counselors will often offer patients practical advice on ways to disseminate the information effectively, such as standardized letters [7]. However, in our experience, the best outcome is often achieved when family disclosure is discussed with the patient at the pretest counseling encounter. By doing so, the patient has an opportunity to think about the potential impact their result may have on family members and how each family member may react to the information. This dialogue allows the provider to help the patient devise effective strategies ahead of time.

This case illustrates the importance of family communication and the great impact genetic testing information (or lack thereof) can have on the clinical management of the patient. If the patient had undergone genetic testing without any knowledge of the familial MSH6 mutation, she would still need to be screened aggressively (Table 2) despite her negative test result. Because there was a resolution to the family communication problem, she now can avoid unnecessary screening procedures.

**CASE 2**

A 35-year-old woman presents to a high-risk breast cancer center to meet with a genetic counselor for genetic testing. Her father was found to be a carrier of a deleterious BRCA2 mutation and the patient is interested in learning her carrier status.

The genetic counselor elicits the personal and family history (Fig. 1B). The patient is in good health and her ovaries and uterus are intact. Her 60-year-old paternal aunt was diagnosed with primary peritoneal cancer at age 59 and is a carrier of the 6174delT BRCA2 mutation, which is one of the three Ashkenazi Jewish (AJ) founder mutations in BRCA1 and BRCA2 [8]. Her father, age 62, is unaffected but is a known 6174delT carrier. Her unaffected mother is 59 years old and her ovaries and uterus are intact. The patient’s maternal aunt died at age 38 from breast cancer diagnosed at age 35. The patient has no maternal cousins. Her maternal grandmother died in her 20s in childbirth, and her maternal grandfather died at age 78. Both of the patient’s parents are of AJ descent.

**BRCA1/2 Ashkenazi Jewish Founder Mutations**

An estimated 1 in 40 (2.5%) Ashkenazi Jewish individuals carries one of the three founder mutations in BRCA1 or BRCA2. The frequency of the two mutations in the BRCA1 gene (187delAG and 5385insC) and one mutation in the BRCA2 gene (6174delT) are 1.5%, 0.15%, and 1.0%, respectively [8]. If there is a personal and/or family history of breast and/or ovarian cancer, the chance that the cancer could be a result of one of these mutations is significantly greater.

After obtaining the family history, the genetic counselor reviews the benefits and limitations of genetic testing for the familial BRCA2 mutation and the possible implications of test results on clinical management. The genetic counselor also explains that, along with testing for the paternal mutation, it would be important to investigate the maternal family history of cancer. The genetic counselor recommends that the patient’s mother pursue genetic testing for the AJ BRCA1 and BRCA2 founder mutations because of the maternal aunt’s history of early-onset breast cancer.

The genetic counselor asks the patient if she would consider informing her mother of this risk and the recommendation for testing. The patient states that they have discussed it before and her mother refuses to pursue testing. The genetic counselor explains that it is standard practice to recommend testing for all three founder mutations for individuals of AJ descent, even in the presence of a known mutation on one side of the family [9]. Should the patient pursue testing, the genetic counselor cautions, there is a reasonable probability that she will test positive for a gene mu-
tation from her maternal lineage and her mother would be an obligate mutation carrier.

After the discussion, the patient opts to pursue genetic testing for the AJ BRCA1 and BRCA2 founder mutations.

**Should the Patient Be Tested for Only the Known BRCA2 Mutation in the Family?**

Typically, when a non-AJ patient presents for genetic testing with a known mutation in the family, a complete family history—including detailed information on the other lineage—is obtained. If there is no significant family history of breast and/or ovarian cancer, the likelihood of a BRCA1 or BRCA2 mutation on this side of the family is very low. The person is then tested only for the known familial mutation [9].

If the patient presenting with a known familial mutation is of AJ descent, however, the testing strategy is a bit different. Again, the full family history is obtained. If the other lineage is also of AJ background, then the risk for carrying one of the AJ founder mutations is not insignificant (2.5%)—even if there is no history of breast or ovarian cancer. In this instance, it is recommended that the full AJ panel of mutations be examined to account for this possibility [9].

In a few weeks the results are available. The patient is found to be negative for the paternal BRCA2 mutation but is positive for the BRCA1 mutation 187delAG. This is presumed to be coming from the maternal lineage and her mother’s carrier status is now known.

During the results disclosure, the genetic counselor stresses the importance of providing this information to the patient’s mother as it will greatly impact her medical care. The patient refuses and asks the genetic counselor to call her mother with this information. The genetic counselor explains that she is not able to call the mother, as the mother is not a patient of the genetic counselor. The patient interjects and states that she recently found out from her father that her mother is actually a past patient of the genetic counselor.

The genetic counselor later reviews the mother’s medical record and indeed there is a consult note that documents that genetic testing for the AJ founder mutations was offered, and the mother declined testing. The mother stated that she psychologically would not be able to handle this information.

**Is the Mother Still the Genetic Counselor’s Patient?**

In general, the genetic counseling process involves a limited number of contacts with the genetic counselor. The genetic counselor typically meets with the individual, assesses the risk of carrying a genetic mutation, and discusses genetic testing options. If genetic testing is performed, the genetic counselor provides results and offers support. It is not uncommon for a genetic counselor, however, to reinitiate dialogue with the patient subsequent to test results disclosure. If the patient is known to carry a mutation, a longer relationship may result for psychological/emotional support reasons or in order that the patient be kept abreast of the most recent medical information regarding the syndrome or mutation. If the patient undergoes testing and is an uninformative negative, the genetic counselor will recontact the patient with information regarding updates in the genetic testing field (e.g., the availability of new tests).

In this case, however, the patient declined testing and thus no formal follow-up plan was discussed. The genetic counselor assured the patient that she was available to the patient should she decide to revisit the option of genetic testing at a later date. Typically in these cases, the genetic counselor will await contact from the patient to avoid the perception of “pressuring” the patient into genetic testing.

In this case, the mother has clearly declined genetic testing and cited reasons for not wanting the information. It would be unusual in this instance for the genetic counselor to reinstate the dialogue without initiation from the mother.

In the end, the genetic counselor was able to work with the patient and set up a plan of action. The genetic counselor provided the patient with a detailed letter summarizing the implications of her result and suggested that she share the letter with her mother. The patient revealed the presence of the BRCA1 mutation to her mother, and encouraged her mother to follow up with the genetic counselor. The mother was initially anxious about the information, but with the help of her genetic counselor and her family and friends was able to cope adequately with the information. She subsequently underwent prophylactic bilateral salpingo-oophorectomy and is undergoing intensive screening for breast cancer.

**Case Discussion**

Through genetic testing for the three AJ founder mutations, the patient learned that she did not carry her father’s 6174delT BRCA2 mutation, but carried the 187delAG mutation in BRCA1. The genetic counselor now has important information about the mother’s risk for developing cancer and can offer her important screening/prevention options that would clearly be of benefit. Does the genetic counselor have a duty to warn the mother of potential harm had the daughter refused to tell her mother? This is complicated by the fact that there is a question as to whether or not the mother remains a “patient” of the genetic counselor.
Consistent with the guideline set forth by the ASHG (discussed in case 1), the genetic counselor deemed it was appropriate to encourage the daughter to share the information with her mother. Recognizing that the mother did not want the information because of the potential psychological implications, it was important for the genetic counselor to emphasize to the daughter that she was also available to her mother for support. The daughter was able to relay this to her mother, thereby reopening an opportunity for the mother to contact the genetic counselor.

The additional ethical question illustrated in this case is whether testing for the AJ founder mutations is akin to “population screening” (i.e., testing the Jewish population at large without regard to family history of disease). The discipline of genetics is not unfamiliar with the issue of population screening for genetic disorders. Pregnant women over the age of 35 (population) are routinely offered prenatal testing by amniocentesis given the increased risk of a chromosomal abnormality in the fetus. Individuals of African ancestry are offered carrier screening for sickle-cell anemia, an autosomal recessive disorder that is more common to this population. Individuals of Caucasian background are routinely offered carrier screening for another autosomal recessive condition, cystic fibrosis (CF), given the frequency of CFTR gene mutations in this population [10]. In each of these instances (and many more), the genetic screen/test needs to be useful and helpful to the individual undergoing the test. For example, CF screening for a 90-year-old Caucasian woman is unlikely to be helpful as she is not going to reproduce.

Population screening for genetic susceptibility to cancer has not met the rigorous standards that these other tests have. The ASCO recommends that genetic testing be offered when (a) the individual has personal or family history features suggestive of a genetic cancer susceptibility condition, (b) the test can be adequately interpreted, and (c) the results will aid in diagnosis or influence the medical or surgical management of the patient or family members at hereditary risk for cancer [4].

In the non-AJ population, the carrier frequency of mutations in BRCA1 or BRCA2, for example, is estimated to be very small, and the cost of BRCA1 and BRCA2 testing is very high (~$3,100). It is therefore cost prohibitive to offer testing to the general population and ASCO recommendation 1 is not met. For individuals of AJ descent (with no family history of cancer), ASCO recommendation 1 is not fulfilled as well. In the AJ population, however, the carrier frequency is higher (2.5%). It could be argued that the carrier frequency alone in the AJ population is enough to be “suggestive of a genetic cancer susceptibility condition.” Unfortunately, there is currently no published position statement specific to genetic testing in this instance. And there is no formal guideline to address whether all individuals of AJ descent should be routinely tested for the founder mutations—regardless of personal or family history. In general practice, however, it is discouraged.

Case 2 is different from straightforward population screening. The individual is presenting for genetic testing specific to her family history. By taking into account the maternal and paternal family history, the genetic counselor is offering the patient the most comprehensive test available to ensure that her results are an accurate representation of her hereditary breast and ovarian cancer risk. While this rationale is reminiscent of population screening (when we solely consider the maternal side of the family with the unknown mutation status), it does not follow the exact definition of true population screening.

**TAKE-HOME POINTS**

- During pretest genetic counseling, the implications of the patient’s genetic test result for at-risk members, including dissemination of the results, should be discussed.
- The genetic counselor is experienced in helping patients explore practical ways of informing family members of genetic test results. An effective strategy is to suggest that, during the waiting period for results, the patient inform relatives that he/she is undergoing genetic testing and invite the family member to contact the patient to learn the result. In this manner, the burden of disseminating information is somewhat eased for the patient, and each family member can decide whether to learn the result (i.e., the family member can exert their right to know and right not to know).
- Individuals of AJ descent should be tested for all three founder mutations if they are of AJ descent on both sides of the family, even if there is a known founder mutation on one side of the family. Pretest genetic counseling must include full discussion of the possibility that information may be obtained on the other side of the family.
- It is important to provide the patient with written information detailing the implications of their test results in plain language that the patient can share with family members.
- Seek a consult with the hospital ethics board for recommendations on ways to resolve a professional and/or ethical dilemma.

**SUMMARY**

The two cases presented here illustrate a number of professional and ethical conflicts for which the boundaries
between the provider–patient and the provider–family relationships are not clear. By definition, any genetic test might carry implications for both the individual patient and his or her family. This concept may not always be readily apparent to every patient, particularly during the distressing time period surrounding genetic testing. The role of the provider is to introduce this concept and pave the way for the patient to inform their relatives when they are ready.

Even when a patient has full comprehension of what a positive result would mean to their at-risk family members, patients may ultimately choose not to share genetic test information. As we have discussed in cases 1 and 2, the duty-to-warn criteria set forth by the ASHG may not provide a clear definition of the provider’s professional obligation in every patient encounter.

Genetic counselors are well equipped and uniquely trained to help the patient, and their family members, understand the significance of genetic information. They are also an important resource to other health care providers involved in the genetic testing process.

**AUTHOR CONTRIBUTIONS**

Conception/design: Gayun Chan-Smutko, Devanshi Patel, Kristen M. Shannon, Paula D. Ryan

Manuscript writing: Gayun Chan-Smutko, Devanshi Patel, Kristen M. Shannon

Final approval of manuscript: Gayun Chan-Smutko, Devanshi Patel, Kristen M. Shannon, Paula D. Ryan

**REFERENCES**


