Too Many Referrals of Low-Risk Women for BRCA1/2 Genetic Services by Family Physicians

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Abstract

The increasing availability and public awareness of BRCA1/2 genetic testing will increase women’s self-referrals to genetic services. The objective of this study was to examine whether patient characteristics influence the referral decisions of family physicians when a patient requests BRCA1/2 genetic testing. Family physicians (n = 284) completed a Web-based survey in 2006 to assess their attitudes and practices related to the use of genetics in their clinical practice. Using a 2 × 2 × 2 factorial design, we tested the effects of a hypothetical patient’s race, level of worry, and insurance status on the decisions of family physicians to refer her for BRCA1/2 testing. The patient was not appropriate for referral based on U.S. Preventive Services Task Force guidelines. No patient characteristics were associated with the family physicians’ referral decisions.

Introduction

The integration of genomics into clinical practice is forecast to have important benefits for health care delivery and health outcomes (1). BRCA1 and BRCA2 (BRCA1/2) testing for familial breast and ovarian cancer is an example of the kinds of testing that will be available clinically. Carriers of BRCA1/2 mutations are at substantially increased risk of breast and ovarian cancer. However, the distribution of BRCA1/2 mutations in the general population is very low, estimated at 1 in 300 to 500 (2). Additionally, hereditary breast cancers account for about 5% to 10% of all breast cancer cases, with BRCA1/2 mutations only contributing to a small fraction of these cases (3). Our study reported that within an average general practitioner’s caseload of 1,700 patients, only 140 patients would be estimated to have a family history of breast, colorectal, or breast/ovarian cancer, and 10 of these patients would be considered appropriate for referral to genetic counseling based on well-defined risk criteria (4).

Direct-to-consumer marketing of BRCA1/2 testing and the tendency among American women to overestimate their risks of breast cancer (5) create consumer demand as women “self refer” to primary care clinicians and request genetic testing (6-9). Traditionally, genetic testing is provided in the context of appropriate genetic counseling or education, yet clinical genetic services in the U.S. remain relatively scarce (10-12). The low prevalence of BRCA1/2 mutations means that in the majority of self-referral situations, primary care clinicians will be in the position of having to dissuade low-risk women from BRCA1/2 counseling and testing. This will put considerable pressure on clinicians to make appropriate referrals.

Inappropriate referral to BRCA1/2 testing also could have significant implications for health care costs and service delivery. The results of Myriad Genetics Laboratories’ direct-to-consumer marketing campaign for BRACAnalysis led to a 240% increase in the number of referrals to genetic services within managed care settings (6, 7), creating delays in patient access to these services (6). At $3,000 per test in the United States, BRCA testing and supportive genetic counseling is a significant expenditure of resources (13).

Moreover, the patient-clinician conversations required to clarify why a patient is or is not appropriate for genetic service referral may increase visit time in ways that do not directly benefit patient care. This may be particularly true in circumstances in which women present with heightened worry and misperceptions about the factors that contribute to their risk. Insurance status also may further complicate these conversations when women with health care insurance believe that they have the right to services even if they are not appropriate.
Biases such as underreferral of minority women to BRCA1/2 services also could occur in ways that exacerbate existing racial/ethnic disparities in health delivery (14-17). Patient characteristics such as age, race, and gender have been noted as reasons for patients not receiving clinically recommended services (16). Evidence to date suggests, however, that patient demands for clinical services (18, 19), including cancer susceptibility testing (20, 21), are likely to be granted even when deemed inappropriate by the physician (19, 22). The reasons for these patterns of inappropriate referral have included physician concerns about patient satisfaction and fears of malpractice (23).

To this end, the U.S. Preventive Services Task Force (USPSTF) published guidelines in late 2005 to assist clinicians in determining which patients are appropriate for referral to genetic counseling and testing for BRCA1/2 mutations (24). These guidelines recommend against routine referrals of low-risk women to BRCA1/2 genetic services. Whereas clinicians have indicated favorable attitudes toward practice guidelines (25), concerns have been raised that guidelines can be too rigid and impractical to incorporate and interfere with physician autonomy (26-28). Further, clinicians may have difficulty applying the USPSTF referral guidelines because they have low levels of confidence in their ability to calculate breast cancer risk and related counseling (4, 29, 30). Physicians also lack confidence in their ability to discuss mammography screening and to decide whether a patient should be referred for genetic counseling (4, 30).

Family physicians who provide the majority of primary care in the United States (31) will be fielding the majority of self-referral for BRCA1/2 testing. Thus, the adherence of family physicians to USPSTF guidelines has significant implications for the effect of self-referral on genetic services and breast cancer screening more generally. The competence of family physicians in considering women’s concerns about breast cancer has broader implications for cancer control. For example, inappropriate referral could influence women’s adherence to screening guidelines if they misunderstand indications from their doctors that they are unlikely to have increased familial risk.

This report describes the results of an experiment where family physicians, through a Web-based survey, were presented with a hypothetical patient named “Terry” who requests genetic testing but is not appropriate for referral based on USPSTF guidelines. The experiment also tested whether varying Terry’s personal characteristics influenced the decisions of family physicians for BRCA1/2 testing.

Materials and Methods

Study Design. A cross-sectional 2 × 2 × 2 factorial design was used. All family physicians viewed a hypothetical patient named Terry who presents for her annual exam and requests genetic testing for breast cancer. The vignette describes Terry’s request as being prompted by her sister’s recent diagnosis of breast cancer at age 53 years and provided a description of Terry, including her age, health status, family history of cancer, ethnicity (not Ashkenazi Jewish), and results of the previous year’s mammography results. Physicians were randomized to see one of eight variations of the vignette based on the three experimental factors: (a) level of worry (high versus not high), (b) insurance status (insured versus not insured), and (c) race (black versus white as indicated by the picture provided with the vignette; see Fig. 1). In each vignette, Terry was not appropriate for referral to BRCA1/2 genetic services based on the USPSTF guidelines (24); the estimated prevalence of BRCA1/2 mutations in women with the same health history as Terry is 2.8% and 2.9% for Terry’s sister (32).

After reading the vignette, physicians were asked a series of questions that included their decision regarding whether or not to refer Terry to genetic services. For these questions, physicians were not allowed to scroll back to the page with the patient description. Participants who completed the follow-up survey were entered into a lottery to receive one of six iPods. The study procedures were approved by the Institutional Review Boards of the National Human Genome Research Institute and the American Academy of Family Physicians.

Sample. The sample for this report was drawn from a longitudinal survey of members of the American Academy of Family Physicians (AAFP) conducted to evaluate the AAFP’s Annual Clinical Focus on Genomics in January 2005. First, a random stratified sample of 10,000 AAFP members was drawn such that half of the sample had completed residency less than 15 years ago; a total of 1,035 family physicians completed this Web-based survey (10% response rate). Compared with the AAFP membership as a whole, family physicians who completed the first survey were significantly more likely to be working in teaching hospitals compared with the AAFP membership as a whole (18% versus 9%, respectively). At the end of this survey, family physicians who completed the survey were asked to provide personal identifiers that would enable them to be recontacted for a similar survey a year hence.

A total of 694 of the 1,035 family physicians (67%) agreed to be recontacted via e-mail to complete the follow-up survey. E-mails were sent to inform these family physicians that they could log onto a Web site, review brief consent information, and complete a follow-up survey between May 8, 2006, and June 2, 2006. Two e-mail reminders went to each participant; one at 7 days after the broadcast e-mail, and the other at 14 days after the broadcast e-mail. The final sample included the 284 physicians (27% response rate) who completed questions related to the referral of Terry to genetic services. This sample size enables us to detect the effects of the experimental manipulation that are in the small to medium range of standardized effect sizes with 80% power at the $P < 0.05$ level of significance (33). Analyses were conducted in the fall of 2006.

Measures and Survey Items

Demographics and Practice Characteristics. Gender and time out of residency were obtained from AAFP membership records. Self-identified race and practice characteristics (including approach to work, teaching/training environment, urban setting or not, the proportion of non-white residents, and residents living in poverty) were assessed in the initial Web-based survey.
Referral Decision. Family physicians were asked the following question: “How likely are you to refer Terry to the following services considering the circumstances described?” (Neither genetic testing nor genetic counseling, both genetic testing and genetic counseling, genetic testing as she requests, genetic counseling, or other).”

Attitudes about the Referral Decision. Family physicians were asked two questions: (a) “How sure are you that your decision about this referral is the best clinical decision?” and (b) “How sure are you that your decision about this referral is an optimal use of genetic services?” For each question family physicians rated their responses on a scale of 1 (not at all sure) to 7 (extremely sure).

Factors Important in Referral Decision. Family physicians were asked to rate the importance of patient characteristics (e.g., Terry’s race, age, sister’s age at diagnosis) in their referral decision on a scale of 1 (not at all important) to 7 (extremely important). Family physicians were also asked the extent to which they agreed or disagreed with the following: “If you refuse to refer Terry for genetic counseling or testing, it will harm your relationship with her.” Family physicians rated their agreement using a 5-point Likert scale (strongly disagree, disagree, neither agree nor disagree, agree, strongly agree). Family physicians’ opinions about Terry’s level of risk for breast cancer were assessed with the following two questions: (a) “What do you think is the likelihood that Terry has a genetic mutation that increases her risk for breast cancer?” and (b) “How would you rate Terry’s level of breast cancer risk?” Family physicians responded on a scale of 1 (very low) to 7 (very high).

Value of Referral to Genetic Services. Family physicians were asked a series of questions to assess their opinions on the value of referring Terry to genetic counseling (e.g., “Terry could get needed reassurance from your referral for genetic counseling even if she isn’t appropriate for testing”) and for genetic testing (e.g., “There’s no harm in referring Terry for genetic testing even if she isn’t really appropriate for testing”). Family physicians rated their responses using a 5-point Likert scale (strongly disagree, disagree, neither agree nor disagree, agree, strongly agree).

Statistical Analyses. Means and proportions were computed to describe the distribution of survey items. Contingency tables were used to examine the bivariate relationships among the three experimental factors: (a) level of worry (high versus not high), (b) insurance status (insured versus not insured), and (c) race (black picture versus white picture) and outcome variable of interest (i.e., family physician’s referral decision). Multivariable polytomous logistic regression models were used to test the association of the three experimental dichotomous factors on family physician’s referral decision. Throughout this report P < 0.05 is used as the criterion for statistical significance.
Results

Sample Characteristics. Family physicians who completed the follow-up survey were predominantly non-Hispanic white physicians (87%) and male (71%); most practiced in urban areas (65%), half were more than 15 years out of residency, and one third were currently working in a teaching or training environment. About half reported practicing in a clinic where more than 15% were minority patients, and 43% practiced in a clinic where more than 10% of residents lived in poverty. Family physicians who completed the first and second surveys were demographically similar (e.g., male: 67% and 71%, respectively; preferred innovative practice: 61% and 66%, respectively; and practiced in a teaching environment: 30% and 35%, respectively).

Experiment Outcomes. The referral decisions of family physicians were not associated with Terry’s level of worry ($P = 0.89$), insurance status ($P = 0.99$), or race ($P = 0.65$). Although Terry was not appropriate for referral to BRCA1/2 genetic services, only 8% of family physicians made a decision against referral (see Fig. 2). Thus, 92% of family physicians made a referral decision inconsistent with the USPSTF guidelines. Half reported they would refer Terry for genetic counseling only, 23% said they would refer her to both genetic testing and counseling, 13% would refer Terry directly to genetic testing as requested, and 6% of participants noted they would make a decision other than those presented, such as asking to have Terry’s sister tested for BRCA1/2.

Manipulation checks on the experimental factors showed that family physicians accurately recalled the details of Terry’s age, race, and emotional status. Fifty nine percent of family physicians accurately recalled that Terry’s age was below 50 years, 94% of family physicians who saw a white Terry identified her race as white, and 70% who saw a black Terry indicated that she was black. Family physicians who saw the High Worry Terry rated her as significantly more nervous ($P < 0.001$) and afraid ($P < 0.001$), than those for whom Terry presented without mention of worry.

Explanations for Non-Guideline Recommended Referral Decisions. To better understand the factors that might underlie the referral decisions of the 260 family physicians who indicated a decision inconsistent with referral guidelines, we explored the family physicians’ beliefs about the appropriateness of their referral decision (see Table 1). Family physicians perceived Terry’s risk of breast cancer to be moderate (mean, 4.2; SD, 1.1); but regarded her risk of having a genetic mutation as relatively low (mean, 2.8; SD, 1.4). Family physicians reported being relatively sure that their referral decision was the best clinical decision (mean, 4.8; SD, 1.4) and an optimal use of genetic services (mean, 4.5; SD, 1.5). Family physicians rated Terry’s level of emotional distress (mean, 5.5; SD, 1.2; scale 1-7) and her sister’s age at diagnosis (mean 5.1; SD, 1.5; scale 1-7) as important factors in their referral decision. Terry’s race (mean, 3.2; SD, 1.7) and insurance status (mean, 3.4; SD, 1.9) were less important factors in their decision.

Table 1. Beliefs about the appropriateness of referral decision among physicians who reported non-guideline recommended referral decisions for Terry ($n = 260$)

<table>
<thead>
<tr>
<th>Item</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Terry’s level of risk*</td>
<td>4.2 (1.1)</td>
</tr>
<tr>
<td>Likelihood Terry has genetic mutation</td>
<td>2.8 (1.4)</td>
</tr>
<tr>
<td>Beliefs about referral decision †</td>
<td></td>
</tr>
<tr>
<td>Best clinical decision</td>
<td>4.8 (1.4)</td>
</tr>
<tr>
<td>Optimal use of genetic services</td>
<td>4.5 (1.5)</td>
</tr>
<tr>
<td>Factors important in the referral decision †</td>
<td></td>
</tr>
<tr>
<td>Terry’s level of emotional distress</td>
<td>5.5 (1.2)</td>
</tr>
<tr>
<td>Her sister’s age at diagnosis of breast cancer</td>
<td>5.1 (1.5)</td>
</tr>
<tr>
<td>Her having daughters</td>
<td>4.7 (1.5)</td>
</tr>
<tr>
<td>Terry’s age</td>
<td>4.3 (1.6)</td>
</tr>
<tr>
<td>Her mammography results from last year</td>
<td>3.8 (1.8)</td>
</tr>
<tr>
<td>What she told you about her insurance status</td>
<td>3.4 (1.9)</td>
</tr>
<tr>
<td>Her race</td>
<td>3.2 (1.7)</td>
</tr>
<tr>
<td>Her aunt’s age at diagnosis of lung cancer</td>
<td>2.9 (1.7)</td>
</tr>
<tr>
<td>That she is not Ashkenazi Jewish</td>
<td>2.9 (1.7)</td>
</tr>
</tbody>
</table>

* Seven-point scale: 1, very low; 7, very high.
† Seven-point scale: 1, not at all sure; 7, extremely sure.
‡ Seven-point scale: 1, not at all important; 7, extremely important.
We also explored family physicians’ beliefs about the costs and benefits of their referral decisions (see Table 2). The majority of family physicians agreed that Terry would be likely to benefit from genetic counseling, could get needed reassurance from the referral to genetic counseling even if she was not appropriate for testing, and that there was no harm in referring Terry for genetic counseling even if she was not appropriate for testing. Reponses to the likelihood of benefit from referral to genetic counseling and benefit from referral to genetic testing were significantly associated ($\chi^2 = 7.45; df = 1; P = 0.01$). Those who indicated Terry could benefit from testing were significantly more likely to say she would benefit from counseling as well, whereas the reverse was not the case. Most respondents (65%) believed that refusing Terry’s request might harm their relationship with her. Family physicians who decided to refer Terry were more likely to agree that refusal to refer Terry would harm the relationship than those who did not refer Terry on for genetic services.

### Discussion

The USPSTF guidelines recommend against routine referrals of low-risk women for BRCA1/2 genetic services (24). The patient in this report, did not meet the guidelines for referral. Nonetheless, 92% of family physicians chose to refer her to genetic services. No presenting characteristics (e.g., level of worry, insurance status, race) were associated with the referral decision.

Most family physicians believed that the decision to refer was an optimal use of genetic services, suggesting that they may underestimate the “costs” of referral. Indeed, although Myriad’s direct-to-consumer marketing campaign increased referrals to genetic services by 240%, the majority of physicians in the market area perceived that the campaign had no effect on clinical practice (6, 7). Moreover, the majority of women referred by physicians reported having delays of more than 6 months to access genetic services (6). Referral of low-risk women could create a bottleneck in getting services to high-risk women who stand to benefit most.

Our results also suggest that family physicians made referral decisions, in part, to preserve their relationship with the patient. Similarly, previous research suggests that cancer susceptibility testing is more likely to be ordered when directly requested by patients (20, 21). Moreover, direct-to-consumer advertising consistently has been associated with increased patient demand in the form of more requests for prescriptions (34) and other clinical services (22). The fact that these requests frequently are granted even when clinicians deem them to be clinically inappropriate suggests that physicians may need additional support in declining patient requests (19, 22).

In the case of Terry, family physicians may have struck the balance between Terry’s request for genetic services and their belief that Terry was unlikely to have a BRCA1/2 mutation by referring her to genetic counseling rather than genetic testing. For example, the challenge of helping women discriminate genetic risk from other risk factors such as age may have seemed more suited to a genetic counseling session than the primary care visit.

Further, the family physicians’ instinct to refer Terry to genetic counseling may have been an appropriate response to their lack of confidence in their abilities to do genetic risk assessment or their concerns about the time it would take to adequately assess risk and provide related counseling. In this circumstance, referral to genetic counseling may have been viewed by the family physician as the only feasible alternative. This dilemma suggests the need to provide providers and patients with educational tools and decision aids on the appropriate-ness of BRCA1/2 testing. For example, an interactive computer-based decision aid designed to educate women about breast cancer genetic services has been shown to be beneficial in increasing breast cancer and genetic testing knowledge and in reducing intentions to test and risk perception among low-risk women (35). Additionally, hotlines have also been used to this end. The National Cancer Institute’s Atlantic Region Cancer Information Service implemented an educational intervention using the 1-800-4-CANCER line (36). Results at 6 months indicated that average-risk women reported decreased intentions to test and high-risk women reported increased intentions to test. Hence, additional research is needed to evaluate these services in supporting physicians and patients to make decisions about BRCA1/2 testing.

Additionally, physicians need to gain greater familiarity and understanding of what risk factors deem women to be at high genetic risk of breast cancer. Family physicians reported the age of Terry’s sister at diagnosis

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Table 2. Beliefs about the costs and benefits of referral decisions among physicians who reported non-guideline recommended referral decisions for Terry (n = 260)

<table>
<thead>
<tr>
<th>Item</th>
<th>%/%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agree harm to relationship if refuse to refer Terry</td>
<td>65</td>
</tr>
<tr>
<td>Poor use of resources to refer Terry for genetic counseling</td>
<td>84</td>
</tr>
<tr>
<td>Terry could get needed reassurance from your referral to genetic testing</td>
<td>92</td>
</tr>
<tr>
<td>No harm to refer to genetic counseling if not appropriate for testing</td>
<td>61</td>
</tr>
<tr>
<td>Values of referral to genetic testing</td>
<td>31</td>
</tr>
<tr>
<td>In the end, Terry’s insurance would probably not pay for genetic testing</td>
<td>54</td>
</tr>
<tr>
<td>No harm to refer to genetic testing if not appropriate for genetic testing</td>
<td>46</td>
</tr>
</tbody>
</table>

NOTE: Numbers are missing on some items.
*Percentage of respondents answering agree or strongly agree.
as one of the most important factors in their decision to refer Terry to genetic services. Terry’s sister’s age was not consistent with USPSTF referral guidelines (i.e., 50 years at age of diagnosis). Previous research also has noted the lack of physician knowledge about factors important in risk assessment and appropriate referrals for BRCA1/2 testing (8, 9, 29, 37) and cancer susceptibility testing in general (20, 21). Additionally, patients could also benefit from education on familial breast and ovarian cancer and related genetic testing to further enhance appropriate requests and referrals to genetic services. The services described above could be useful in raising such awareness.

Several limitations of the study must be considered in interpreting these results. Data are cross-sectional and the direction of the associations cannot be established. The response rate to the initial survey was relatively low, although the initial and follow-up survey participants seemed to well represent the larger AAFP membership (38). However, this self-selected sample of family physicians who participated was inclined toward innovation and thus may have included those who were most likely to be knowledgeable of and receptive to genetic innovations in clinical care. Thus these results may overestimate the readiness to refer.

Additionally, the USPSTF guidelines for referral to BRCA1/2 genetic services were published less than one year before the follow-up survey (24). More than 90% of family physicians in this sample reported having heard of USPSTF, but we did not assess whether family physicians were aware of the new guidelines specific for BRCA1/2 referral. Future studies should assess the awareness of the guidelines to help differentiate whether physicians are making referral decisions despite knowing practice guidelines. Further, more research is needed to assess how the letter grades used to define USPSTF guidelines may influence clinician referral behaviors. Adherence to guidelines may be influenced by physicians’ perceptions about the validity of the data used to devise the guidelines. Family physicians’ responses also were based on a hypothetical scenario and may not accurately reflect how they actually would respond in a clinical setting. Prospective studies with real patients that incorporate medical chart reviews are needed to increase the validity of physician responses and more accurately assess referrals rates.

When considering whether genomic medicine has the potential to improve health care delivery and patient health outcomes, it will be important to understand how factors such as patient characteristics, direct-to-consumer advertising, physicians’ knowledge of genetics, and adherence to guidelines might influence health care delivery and health disparities. Inappropriate referrals of patients at low risk of carrying genetic mutations to limited genetic professional services could hinder access to these services by high-risk patients and increase out-of-pocket costs to patients. This is especially true for the future of cancer prevention and control as we move toward the dissemination of genetic susceptibility testing not only for rare, hereditary cancers but also for more common “sporadic” cancers that contribute to a greater public health burden (39-41). To maximize appropriate referral for genetic services, research should focus on the role of clinician-patient relationships in referrals, patient education, and clinician training in genetic risk assessment and counseling skills.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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