Intention to Obtain Genetic Testing for Melanoma among Individuals at Low to Moderate Risk for Hereditary Melanoma

Susan T. Vadaparampil, Lora Azzarello, Jennifer Pickard, and Paul B. Jacobsen

BACKGROUND

An estimated 5-10% of all melanoma occurs in patients with a family history of the disease. Several inherited germline mutations have been linked to hereditary melanoma, including CDK2NA (a.k.a. INK4a, MSTI, or P16), CDK4, and P14ARF. Of these mutations, CDK2NA is the most clinically relevant and accounts for approximately 20-40% of hereditary cases of melanoma. Individuals carrying this mutation have a lifetime risk of developing melanoma of up to 76%. The likelihood of finding a mutation in CDK2NA increases with the number of family members affected with melanoma. The mutation detection rate increases from approximately 5% in families with 2 cases of melanoma to approximately 20-40% in families with 3 or more cases.

Commercially available genetic CDK2NA testing for melanoma is now available. Although there has been discussion of the potential utility of genetic testing for hereditary melanoma (GTHM) in clinical settings, the Melanoma Genetics Consortium (MGC) does not currently recommend GTHM outside of research protocols due to several limitations. These limitations include (a) the low likelihood of finding mutations in known melanoma susceptibility genes, even in 60% of melanoma-prone families, (b) the large variability in estimates of prevalence and penetrance of identified mutations, (c) a possible false sense of reassurance among those who test negative despite a higher incidence of melanoma among non-mutation-carriers in CDKN2A families when compared to the general population.

Despite recommendations against clinical use of GTHM and direct-to-consumer advertising of genetic testing, GTHM is being directly marketed to consumers. According to reports from the

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MGC and others, there is a rise in patient demand for information about and/or access to GTHM.\textsuperscript{1,3-5} The MGC contends that this interest and/or demand is likely based on unrealistic expectations about the definitiveness, sensitivity, and specificity of GTHM.\textsuperscript{14} As shown in previous studies of other hereditary cancers, those at low objective risk, particularly those with a family history of cancer, may still be interested in pursuing genetic testing.\textsuperscript{25} However, to our knowledge there are no published reports of awareness about and attitudes toward GTHM among low-to-moderate-risk individuals, defined as those with 0 or fewer first-degree relatives (FDRs) with melanoma. Thus, little empirical research exists on what factors should be addressed when educating low-to-moderate-risk relatives of melanoma patients about GTHM. Toward that end, the primary aim of this study is to identify demographic, clinical, attitudinal, and health belief factors associated with intention to obtain GTHM among low-to-moderate-risk FDRs of melanoma patients.

**METHODS**

**Subject Recruitment and Data Collection**

Upon approval of the University of South Florida Institutional Review Board, the current study was conducted as part of a larger study that examined skin cancer detection and sun protection behaviors among FDRs of melanoma patients. Patients (index cases) with a confirmed diagnosis of melanoma within the previous five years being followed at the H. Lee Moffitt Cancer Center (Tampa, FL) were approached in person during routine clinic visits or contacted by telephone following a recent clinic visit and asked to nominate FDRs of melanoma aside from family history (i.e., hair color, freckling, actinic keratosis, blistering sunburns before the age of 20), and whether they had ever had a skin exam (defined as going to a physician or other health care professional for a thorough and complete examination of the skin). The risk factor questions were derived from previous research on risk factors for melanoma.\textsuperscript{18-22} The skin exam item was developed after review of the literature on skin cancer detection behaviors.\textsuperscript{22,21,22}

Attitudinal Variables: Nine items were developed to measure interest in genetic testing. Items were based on previous studies of attitudes toward genetic testing for hereditary breast, ovarian, colorectal, and prostate cancer.\textsuperscript{23-26} Four items assessed positive attitudes toward GTHM (e.g., “I would be likely to have the genetic test if it helped me make health care choices”), and five items assessed negative attitudes toward GTHM (e.g., “I would not have the genetic test because I am concerned that this information could interfere with my getting insurance”). Respondents were asked to rate their responses to this question using a Likert-type response format (1=strongly agree, 2=agree, 3=don’t know, 4=disagree, 5=strongly disagree). For analysis, responses were collapsed into 2 categories: (1) those who responded “strongly agree” or “agree,” and (2) those who responded “strongly disagree,” “disagree,” or “don’t know.”

Health Belief Variables: Perceived risk and perceived severity of melanoma were assessed at the time of recruitment via scales developed specifically for this study. Perceived risk was assessed with three items derived from previous research examining perceived risk of developing breast cancer.\textsuperscript{27} Perceived absolute, conditional, and relative risk were measured using the following items: (1) perceived lifetime risk of developing melanoma on an 11-point scale (0=0% to 10=100%); (2) perceived lifetime risk of
developing melanoma if they did not engage in sun protective behaviors (i.e., never use sunscreen, never wear protective clothing) on an 11-point scale (0=much lower to 10=much higher). The three items were converted to a standard metric and combined to create a total score for perceived risk, with possible scores ranging from 0 to 120 (Cronbach's alpha=.80). Items measuring perceived severity were modified from Jackson and Aiken's measure assessing perceived severity of skin cancer.21 Perceived severity was measured with 5 items (e.g., "I think that people who develop melanoma can still live a long time"), using a 6-point response format (1=strongly agree to 6=strongly disagree) with possible scores ranging from 5 to 30 (Cronbach's alpha=.59). Higher scores on each of the health belief variables reflected higher levels of the belief.

Awareness of and Intention to Obtain GTHM. Similar to previous studies assessing interest in genetic testing,28 we used a multicomponent assessment of intention to obtain genetic testing that included supplementary information.29 The questions were preceded with the following brief description of GTHM: "Among men and women with a strong family history of certain cancers such as colon, breast, and ovarian cancer, genetic testing has become available to identify those at higher risk of developing cancer. A similar test has recently been developed for identifying those at higher risk for certain types of skin cancer such as melanoma." This description was followed by a question asking whether the participant had heard of such a test. Twenty-one percent (n=43) reported ever having a skin cancer screening exam by a health care professional.

Of the 92 respondents, 11% had heard of GTHM prior to the study. Since such a test was described, 48% (n=44) reported intention to obtain GTHM, and 52% (n=48) reported no intention to obtain, or being unsure about, obtaining GTHM (Table 2). The vast majority of respondents (>90%) endorsed provider recommendation and helping family members to make genetic testing or health care decisions as good reasons for undergoing GTHM. Conversely, less than half the sample (45%) responded that they would be likely to obtain genetic testing if it would help them make personal health care decisions. The most commonly cited reason against genetic testing was fear of insurance discrimination (15%). Fewer respondents cited cost of testing (8%), fear of job discrimination (3%), lack of preventive treatments available for melanoma (3%), and pain associated with getting the test (1%) as reasons against genetic testing.

Overall, respondents were far more likely to endorse positive attitudes toward genetic testing than negative attitudes (3:1). Additionally, participants had moderate levels of perceived severity of melanoma (15.5±4.4; possible range 6-30) and perceived risk of melanoma (76.8±30.1; possible range 0-120).

Results of unadjusted analyses comparing those who intended versus those who did not intend to obtain or were unsure about obtaining a genetic test for hereditary melanoma are also shown in Tables 1 and 2. With regard to demographic and clinical variables, results indicated that older participants (p=.04) and those who were mar-
ried (p=.02) were more likely to express an intention to undergo genetic testing. There appeared to be no difference between the two groups regarding other variables: gender, race, education, income, employment, relationship of FDR to index patient, having additional risk factors for melanoma, or ever having a skin cancer screening by a health care provider (p>.05). With regard to attitudinal factors, physician recommendation (p=.01) and helping family members make health care choices (p=.03) were associated with intention to undergo genetic testing. However, helping in personal health care choices, helping family members make decisions about genetic testing, as well as negative attitudinal factors and health beliefs were not significantly different between the two groups (p>.05).

Multivariate logistic regression analysis (presented in Table 3) showed that among those factors demonstrating significant univariate relationships with intention to obtain GTHM, the following were independent predictors: being married (OR=6.27; 95% CI 1.56-25.21), having a doctor recommend testing (OR=3.80; 95% CI 1.29-11.21), and helping family members make health care decisions (OR =3.15; 95% CI 1.23-8.07).

**DISCUSSION**

In general, GTHM is not currently recommended outside the context of research protocols. However, direct-to-consumer advertising of GTHM and increased patient demand for GTHM have been reported, and GTHM is being considered as a clinical option. To our knowledge, this is the first study to provide information about awareness of GTHM as well as demographic, attitudinal, and health care factors associated with intention to obtain GTHM among individuals at low to moderate risk of hereditary melanoma.

Overall, our study found that while the majority of respondents were unaware of GTHM, once such a test was described, approximately half reported they would have GTHM in the next six months if it were available to them. In other studies of FDRs of cancer patients, the range of participants stating that they would have or were interested in genetic testing was 75-82% for hereditary breast or ovarian cancer, 26-92% for hereditary colon cancer, and 68-84% for hereditary prostate cancer. With the exception of one colon cancer study where interest in genetic testing was low (26%), our respondents had lower rates of interest in genetic testing than participants in all of the studies just cited. One possible explanation may be that many of these studies were conducted earlier in the development of genetic testing for inherited cancer susceptibility. At that time, the public may have based their intentions on overly simplified representations by the popular media of new genetic discoveries that provided little information about the limitations of genetic testing. As the public has become more aware of the real or perceived limitations of genetic testing, they may have also expressed less interest in GTHM.

GTHM was associated with two factors that may represent the desire to have testing to help family members. First, married respondents were more likely to express intention to obtain GTHM. Although not

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**Table 1. Demographic Characteristics and Medical Characteristics of First-Degree Relatives of Melanoma Patients**

<table>
<thead>
<tr>
<th>Total* n (%)</th>
<th>Intent to obtain genetic testing in next 6 months b</th>
<th>Do not intend to obtain genetic testing in next 6 months c</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (√±SD)</td>
<td>45.7 (12.8)</td>
<td>48.6 (11.4)</td>
<td>43.1 (13.6)</td>
</tr>
<tr>
<td>Females</td>
<td>54 (58.7)</td>
<td>26 (59.1)</td>
<td>28 (58.3)</td>
</tr>
<tr>
<td>Married</td>
<td>74 (80.3)</td>
<td>40 (90.9)</td>
<td>34 (70.8)</td>
</tr>
<tr>
<td>Caucasian</td>
<td>90 (97.8)</td>
<td>43 (97.7)</td>
<td>47 (97.9)</td>
</tr>
<tr>
<td>Education≥college</td>
<td>48 (52.2)</td>
<td>21 (47.7)</td>
<td>27 (56.3)</td>
</tr>
<tr>
<td>Income&gt;$40,000</td>
<td>69 (77.5)</td>
<td>36 (81.8)</td>
<td>33 (73.3)</td>
</tr>
<tr>
<td>Employed</td>
<td>70 (76.1)</td>
<td>35 (79.6)</td>
<td>35 (72.9)</td>
</tr>
<tr>
<td>Parent with melanoma</td>
<td>57 (62.6)</td>
<td>24 (54.6)</td>
<td>33 (70.2)</td>
</tr>
<tr>
<td>≥2 additional risk factors for melanoma (other than family history)</td>
<td>37 (40.2)</td>
<td>19 (43.2)</td>
<td>18 (37.5)</td>
</tr>
<tr>
<td>Ever had skin cancer screening by a health care provider</td>
<td>43 (47.7)</td>
<td>25 (56.8)</td>
<td>18 (37.5)</td>
</tr>
</tbody>
</table>

Note: For dichotomous variables, X² test of heterogeneity used to compare groups; for continuous variables, independent samples t-test used to compare groups; Fisher’s Exact Test used in variables with <5 in each cell; *=significant at p<0.05

*an=92
bn=44
cn=48
assessed in the present survey, marital status may be an indicator of having children. Second, those who endorsed the importance of helping family members make health care decisions were more likely to express intention to obtain genetic testing. These findings are consistent with previous studies in which providing information to family members, particularly children, was found to be one of the most important predictors of interest in and/or intention to obtain genetic testing for a variety of hereditary cancers.23,30,37

Another key finding was the influence of physician recommendation on intention to obtain GTHM. However, genetic testing for inherited cancer susceptibility represents one area where many physicians may have lower levels of awareness and knowledge about appropriate clinical utilization of testing.38 In a national study of 1,251 U.S. physicians, less than 40% were aware of paternal inheritance of BRCA1/2 mutations, the frequency of BRCA1/2 mutations in breast cancer patients, or BRCA1/2 gene penetrance.39 In the same sample, only one-third of physicians correctly estimated the penetrance of mutations associated with hereditary nonpolyposis colorectal cancer (HNPCC). The importance of physician recommendation in our study further underscores the need for providing physicians with education about hereditary cancers, guidelines for identifying and referring high-risk patients, as well as the skills needed to reassure low-to-moderate-risk patients.

Although our study provides some insights into intention to obtain GTHM among FDRs of patients with melanoma, the results should be considered in light of

<p>| Table 2. Attitudes toward Genetic Testing for Hereditary Melanoma and Health Beliefs about Melanoma among First-Degree Relatives of Melanoma Patients |
|-------------------------------------------------|----------------|----------------|----------------|</p>
<table>
<thead>
<tr>
<th>Aware of GTHM</th>
<th>Totaln (%)</th>
<th>Intend to obtain genetic testing in next 6 months</th>
<th>Do not intend to obtain genetic testing in next 6 months</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aware of GTHM</td>
<td>10 (10.9)</td>
<td>2 (4.6)</td>
<td>8 (16.7)</td>
<td>0.09</td>
</tr>
</tbody>
</table>

Positive Attitudes: I would be likely to have the genetic test if the test:

<table>
<thead>
<tr>
<th>Positive Attitudes</th>
<th>Totaln (%)</th>
<th>Intend to obtain genetic testing in next 6 months</th>
<th>Do not intend to obtain genetic testing in next 6 months</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Was recommended by my doctor</td>
<td>85 (92.4)</td>
<td>44 (100.0)</td>
<td>41 (85.4)</td>
<td>0.01*</td>
</tr>
<tr>
<td>Helped me make health care choices</td>
<td>41 (44.6)</td>
<td>18 (40.9)</td>
<td>23 (47.9)</td>
<td>0.50</td>
</tr>
<tr>
<td>Helped my family make health care choices</td>
<td>86 (93.5)</td>
<td>44 (100.0)</td>
<td>42 (87.5)</td>
<td>0.03*</td>
</tr>
<tr>
<td>Helped my family make decisions about genetic testing</td>
<td>84 (91.3)</td>
<td>43 (97.7)</td>
<td>41 (85.4)</td>
<td>0.06</td>
</tr>
</tbody>
</table>

Negative Attitudes: I would not have genetic testing because:

<table>
<thead>
<tr>
<th>Negative Attitudes</th>
<th>Totaln (%)</th>
<th>Intend to obtain genetic testing in next 6 months</th>
<th>Do not intend to obtain genetic testing in next 6 months</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Results could interfere with my getting insurance</td>
<td>14 (15.2)</td>
<td>7 (15.9)</td>
<td>7 (14.6)</td>
<td>0.86</td>
</tr>
<tr>
<td>Results could interfere with my getting a job</td>
<td>3 (3.3)</td>
<td>1 (2.3)</td>
<td>2 (4.2)</td>
<td>1.00</td>
</tr>
<tr>
<td>The test is too painful</td>
<td>1 (1.1)</td>
<td>1 (2.3)</td>
<td>0 (0.0)</td>
<td>0.47</td>
</tr>
<tr>
<td>The test would cost too much</td>
<td>7 (7.7)</td>
<td>3 (7.0)</td>
<td>4 (8.3)</td>
<td>1.00</td>
</tr>
<tr>
<td>There are no treatments that would prevent my family from getting melanoma</td>
<td>3 (3.3)</td>
<td>0 (0.0)</td>
<td>3 (6.3)</td>
<td>0.24</td>
</tr>
</tbody>
</table>

Health Beliefs

<table>
<thead>
<tr>
<th>Health Beliefs</th>
<th>Totaln (%)</th>
<th>Intend to obtain genetic testing in next 6 months</th>
<th>Do not intend to obtain genetic testing in next 6 months</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perceived severity (±SD)</td>
<td>15.5 (4.4)</td>
<td>15.1 (3.9)</td>
<td>16.0 (3.3)</td>
<td>0.33</td>
</tr>
<tr>
<td>Perceived risk (±SD)</td>
<td>65.9 (25.7)</td>
<td>63.8 (25.4)</td>
<td>68.1 (26.2)</td>
<td>0.43</td>
</tr>
</tbody>
</table>

Note: For dichotomous variables, X² test of heterogeneity used to compare groups; for continuous variables, independent samples t-test used to compare groups; Fisher’s Exact Test used in variables with <5 in each cell; * = significant at p<.05

m = 92
n = 44
p = 48
certain limitations. Our response rate for index patients providing contact information was 43%. Thus the generalizability of our findings to all FDRs of melanoma patients is limited. The respondents may have been biased toward patients who are more interested in melanoma and family history, and thus may have been more likely to provide contact information for their relatives. In addition, among those patients who provided contact information for FDRs, approximately one quarter (51 out of 189) provided incorrect mailing information. Thus, it is possible that families who kept in closer contact with their FDRs (as indicated by having current mailing addresses) may be overrepresented in our sample. However, it is also possible that patients may have found it difficult to recall accurate mailing addresses for their FDRs on the spot (particularly those that were approached in person during a clinic visit). Similarly, given the prevalence of email and phone communication, persons may be less likely to regularly update family members’ mailing addresses. It is also possible that patients may have intentionally given incorrect information about family members, rather than refusing to participate outright. While this is possible, patients who are approached about a research study are informed of their right to refuse participation without affecting the quality of medical care they receive at our institution. It appears that this message was clear to patients, as several (43%) chose to decline participation.

The majority of our sample was Caucasian, limiting applicability to other racial/ethnic groups. However, Caucasians are the racial group most likely to be affected by hereditary melanoma. We also used an oversimplified description of GTHM that did not include the criteria for or limitations of testing. However, this simplistic approach to describing testing may be similar to that taken by commercial companies wishing to increase testing use. In addition, all but one of our respondents (data not shown) had only one FDR with melanoma. To date, GTHM has most commonly been used in families with multiple affected relatives. However, based on the level of interest and overwhelmingly positive attitudes toward GTHM among our respondents, low-to-moderate-risk individuals may benefit from education about the limitations of GTHM. Our study population was also of relatively high socioeconomic status, making findings less applicable to individuals of lower socioeconomic status. Additionally, intention to undergo rather than actual uptake of GTHM was assessed. Earlier studies have found that intention to engage in genetic testing for hereditary cancer is generally higher than actual test uptake. This may be due to patients recognizing the risk criteria for testing or the complexity of testing and results that generally occurs with additional education from a health care professional. Although this study was subject to certain limitations, the recent discussions recommending incorporating GTHM into clinical practice under certain circumstances provide important information to consider about educating and reassuring those at low to moderate risk about who truly may benefit from testing.

Translation to Health Education Practice

Genetic testing for hereditary cancer generally benefits a specific segment of the population, namely those with a personal or family history that includes: several relatives in more than one generation with a particular cancer or group of cancers; early age of cancer diagnosis; and multiple primary tumors. National data suggest that the general population is unaware of genetic testing for inherited cancer susceptibility, and to date there has been no national public education campaign related to genetic testing for adult onset conditions such as cancer. As such, it is possible that the public’s first exposure to the availability of such testing may be through direct-to-consumer advertisements, which have been criticized for their exaggeration of benefits to clinical care. These advertisements fail to distinguish between a test that is widely used and accepted by medical professionals (e.g., cystic fibrosis testing) and those that may benefit only a distinct group of people with very specific medical characteristics (e.g., GTHM). The public may also lack the knowledge to make risk-appropriate decisions about whether to get tested or how to interpret results, leading to consumer demand for testing with little medical benefit.

The National Office of Public Health Genomics at the Centers for Disease Control and Prevention has developed genomic competencies for public health education professionals that may facilitate public education about genetic counseling and testing. Based on these competencies, health educators would be charged with taking relatively complex issues related to hereditary aspects of melanoma and GTHM and educating the public in a culturally and linguistically appropriate manner. Health educators who focus on cancer may work toward integrating information about the role of genetics (relative to other causes) into their cancer education programs. As genetic testing for chronic conditions including cancer becomes more widely available and integrated into clinical practice, and as direct-to-consumer advertising

<table>
<thead>
<tr>
<th>Table 3. Logistic Regression Model of Predictors of Intention to Undergo Genetic Testing for Hereditary Melanoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Married</td>
</tr>
<tr>
<td>Doctor recommendation to obtain genetic testing</td>
</tr>
<tr>
<td>Help family with health care choices</td>
</tr>
</tbody>
</table>

*significant at p<.05
continues, public demand for information about genetic testing will also increase. There is currently a documented shortage of genetic counselors; as of 2005, there were 2,035 certified genetic counselors in the United States. Therefore, other health professionals, such as health educators, will be instrumental in meeting the increased demand for information about genetic testing and ensuring that those at low risk are appropriately informed and reassured, while those at high risk are referred to a genetic professional.

In the case of GTHM, only a small proportion of individuals with a significant family history of melanoma would benefit from genetic testing. However, our study shows that many more individuals at lower risk also appear to be interested in testing. Health educators are often on the front lines of community-based education about a variety of chronic diseases such as cancer. By understanding what factors may motivate an individual to pursue genetic testing despite having a relatively low risk, health educators can directly address those issues to promote risk-appropriate use of testing. Given the current limitations associated with GTHM, there is a need to educate those low-to-moderate-risk individuals who are motivated to undergo GTHM, helping them understand that such testing is unlikely to be recommended by their physician based on current clinical guidelines, and that test results are unlikely to benefit their family in making health care decisions.

REFERENCES

32. Petersen GM et al. Attitudes toward colon


38. Stephenson J. As discoveries unfold, a new urgency to bring genetic literacy to physicians. JAMA. 1997;278:1225-1226.


