Genetic testing for hereditary melanoma and pancreatic cancer: a longitudinal study of psychological outcome

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Abstract

Objective: CDKN2A/p16 mutations confer 76% lifetime risk of melanoma and up to 17% lifetime risk of pancreatic cancer. Our objective was to determine the short- and long-term impact of CDKN2A/p16 genetic counseling and test reporting on psychological distress, cancer worry, and perceived costs and benefits of testing.

Methods: Prospective changes in anxiety, depression, and cancer worry following CDKN2A/p16 counseling and test reporting were evaluated at multiple assessments over 2 years among 60 adult members of melanoma-prone families; 37 participants completed the 2-year follow-up. Quantitative and qualitative assessments of the costs and benefits of testing were carried out. Outcomes were evaluated among unaffected noncarriers (n = 27), unaffected carriers (n = 15), and affected carriers (n = 18).

Results: Reported anxiety and depression were low. For carriers and noncarriers, anxiety decreased significantly throughout the 2-year period, whereas depression and melanoma worry showed short-term decreases. Worry about pancreatic cancer was low and decreased significantly. In all groups, test-related distress and uncertainty were low, regret was absent, and positive experiences were high. All participants (>93% at each assessment) reported at least one perceived benefit of genetic testing; only 15.9% listed any negative aspect. Carriers reported increased knowledge about melanoma risk and prevention (78.3%) and increased prevention and screening behaviors for self and family (65.2%). Noncarriers reported increased knowledge (95.2%) and emotional benefits (71.4%).

Conclusion: Among US participants familiar with their hereditary melanoma risk through prior epidemiological research participation, CDKN2A/p16 genetic testing provides multiple perceived benefits to both carriers and noncarriers without inducing distress in general or worry about melanoma or pancreatic cancer.

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Keywords: cancer; oncology; melanoma; genetic testing; anxiety; pancreatic cancer

Introduction

Melanoma, the most lethal skin cancer, is now the fifth and seventh most common cancer in men and women, respectively, and approximately 70,239 persons are predicted to develop melanoma in the United States in 2011 [1]. Of all melanomas, 5% to 10% have a familial clustering, and 20% to 40% of these are associated with a pathogenic mutation in CDKN2A/p16 (or simply p16) [2,3], a tumor suppressor that regulates cell cycle and senescence. The availability of predictive genetic tests for hereditary melanoma offers the prospect of tailored medical treatment and behavioral management recommendations to decrease disease impact and/or increase life expectancy among people at familial risk.

Because p16 testing has only recently entered clinical use, there are limited data on psychological outcomes or perceived costs and benefits of p16 counseling and test reporting [4–10]. To date, psychological costs and benefits of genetic testing have been primarily examined for diseases such as hereditary breast and ovarian cancer (HBOC) [11] and colon cancer [12], for which mutation carriers must decide between prophylactic surgery or annual screening regimes to manage elevated cancer risk. In these instances, there are only limited data indicating that lifestyle factors will significantly reduce the risk for developing cancer. Hereditary melanoma susceptibility is unique because, in addition to genetic and phenotypic factors, behavioral lifestyle factors play a key role in the etiology of melanoma. The risk of melanoma among p16 mutation carriers varies geographically, with higher penetrance in areas with high ultraviolet radiation (UVR) intensity (e.g. 76% risk in the United States and 91% in Australia [13]). These findings suggest that UVR exposure significantly increases the risk...
of melanoma in p16 mutation carriers, and that photoprotection may reduce risk.

Evidence to date from our study of 60 adult members of the Utah kindreds, including 33 mutation carriers, suggests that p16 counseling and test reporting successfully promote intentions to avoid UVR exposure and increase the use of sunscreen and photoprotective clothing [8] and increase both the frequency and thoroughness of skin self-examinations [7]. However, less is known about psychological outcomes. We predict that the potential to modify risk through daily photoprotection behaviors and regular screening may result in low levels of negative psychological outcomes, such as anxiety and worry about melanoma. The present study reports both short- and long-term psychological outcomes and perceived costs and benefits of melanoma genetic counseling and test reporting in the same group of Utah counselees.

To date, only one major study has reported prospective psychological outcomes of p16 counseling and test reporting in high-risk families. In a recent Australian study in which 119 family members were offered p16 testing, 25 elected testing and 15 were mutation positive [4]. The receipt of positive p16 genetic test results was associated with short-term reductions in anxiety and depression 1 week later, and increased depression 1 year later, with no increase in melanoma-specific distress. These findings suggest that there may be psychological benefits of melanoma genetic testing, although outcomes could not be evaluated among noncarriers because of the modest sample size.

It is likely that the implications of p16 counseling and test reporting for daily behaviors may influence the perceived costs and benefits of melanoma genetic testing. However, at this early juncture, more is known about anticipated benefits associated with test uptake than about outcomes following p16 counseling and test reporting. In the aforementioned Australian study [4] and a Dutch study of 94 participants who had elected p16 testing and were awaiting their results [9], a majority of counselees reported seeking genetic testing in order to learn more about their own risk, to learn about their children’s risk, and to help scientific research (see also Ref. 10). Additionally, 77% of participants in the Australian study reported that they expected to learn about ways to reduce their own melanoma risk.

These findings suggest that members of the high-risk families anticipate multiple benefits of melanoma genetic counseling and testing, but there have been no reports on perceived costs and benefits following p16 counseling and test reporting.

In considering the potential costs and benefits of p16 test reporting, it is important to note that the p16 mutation also confers a 17% lifetime chance of developing pancreatic cancer in some families [14]. In contrast to melanoma, there are no well-established, reliable prevention or early detection measures that would reduce pancreatic cancer risk and there are few effective treatments for the disease. Current approaches being considered for pancreatic cancer screening include evaluation of tumor markers such as CA19-9 and imaging by endoscopic ultrasound and/or magnetic resonance cholangiopancreatography (MRCP) beginning at age 50 or ten years prior to the earliest diagnosis of pancreatic cancer in the family. However, there are still limited data confirming an improved outcome from screening. At-risk individuals may also benefit from smoking cessation and being alert to symptoms, such as new-onset diabetes [15,16].

The long-term psychological impact of learning about the increased pancreatic cancer risk associated with p16 mutations has yet to be examined. In the aforementioned Dutch study [9], 49% of counselees awaiting p16 test results indicated at least some degree of worry about their risk of developing pancreatic cancer. Although reported anxiety and depression were very low overall, worry about developing pancreatic cancer was a significant predictor of concurrent anxiety and depression. Further, worry about melanoma and pancreatic cancer was significantly associated with declining the test following genetic counseling. It has yet to be determined whether the receipt of positive p16 results creates sustained worry about pancreatic cancer. Of particular interest, information about pancreatic cancer risk is more likely to be novel than information about melanoma risk among family members selected for research and/or referred for clinical genetic testing and counseling because of their high rates of familial melanoma. In the Dutch study, 40% of counselees indicated that they had not expected to be informed about their risk of developing pancreatic cancer [9]. This finding underscores the importance of examining how people respond to counseling and test reporting for genetic mutations that may predispose to multiple cancer syndromes [17].

The present study
The goal of the present study was to examine both the short- and long-term impact of p16 counseling and test reporting on psychological outcomes, including anxiety, depression, and worry about both melanoma and pancreatic cancer, among unaffected carriers, affected carriers, and unaffected noncarriers. Multiple assessments were conducted over a 2-year period. Additionally, specific positive and negative responses to testing (positive experiences, uncertainty, distress) were assessed via standardized inventory at 1 and 6 months following counseling and test reporting. Finally, participants completed three open-ended qualitative assessments of the perceived benefits and costs of genetic testing in the year following test reporting.

Patients and methods
Study population and procedures
Companion test-reporting and follow-up studies were approved by the Institutional Review Board at the University of Utah (IRB #s7916 and 13816). All
participants were adult members of two large melanoma pedigrees enrolled in previous \( p16 \) identification studies who had contributed DNA samples for research genetic testing [18,19]. All of the patients enrolled in this study were participants in a minimum of two previous studies. Our participants were originally from an IRB-approved study in the late 1980s that utilized the Utah Population Database to identify pedigrees with a hereditary pattern of melanoma. No specific enrollment criteria for that study have been published, but the pedigrees utilized in this study are available [19]. In the early 2000s, every living participant in the gene identification studies was invited to participate in a longitudinal phenotyping study [2]. This study included comprehensive phenotyping and mutation testing for \( p16 \), but no \( p16 \) test results were reported to participants. Every participant in the longitudinal phenotyping study who was a member of a \( p16 \)-positive kindred was invited to participate in the present study (\( n = 77 \)).

Although all participants had received extensive prior counseling regarding their elevated melanoma risk and the corresponding necessity for consistent photoprotection and screening during in-person clinic visits as part of their participation in these two initial studies, none were aware of their genetic status or the presence of the \( p16 \) mutation in their family prior to disclosure through the present test-reporting study. None had received prior counseling regarding elevated pancreatic cancer risk.

### Participant recruitment, enrollment, and retention

Seventy-seven research participants were recontacted and offered the opportunity to receive clinically confirmed genetic test results. The predisclosure counseling and genetic test reporting sessions were offered free of charge, and participants received modest nonmonetary incentives (e.g. tote bags, book lights) for completing follow-up questionnaires.

Recruitment and retention are summarized in Figure 1. From May to November 2005, 64 (83.1%) participants completed a baseline questionnaire and a test reporting and counseling session. The baseline questionnaire was completed at the clinic visit prior to genetic counseling and test reporting. All 64 participants elected to receive results, and 62 completed an immediate post-counseling questionnaire during this initial clinic visit. Sixty-one participants were then invited to enroll in a follow-up study of psychological and behavioral responses to \( p16 \) test reporting; of these, 53 (86.9%) enrolled and 45 (73.8%) completed the 1-month, 39 (63.6%) completed the 6-month, 30 (49.2%) completed the 1-year, and 40 (65.6%) completed the 2-year questionnaire.

As shown in Figure 1, several participants missed one or more assessments, but later rejoined the study. Specifically, in addition to the baseline, 23 participants completed all five follow-up assessments in the parent study (which included a post-counseling assessment not reported in the current paper), 10 completed four follow-ups, 6 completed three follow-ups, 10 completed two follow-ups, and 11 participants completed only one follow-up assessment. Thus, for 49 of 60 participants (82%), we had at least two follow-up assessments in addition to the baseline. We retained participants for analysis if they completed at least one assessment following counseling and test reporting and if they were a member of one of the three largest participant groups defined by melanoma history and \( p16 \) mutation status. Stratification of the sample by melanoma history is important, as past research has found increased distress to be most likely among unaffected carriers [20,21]. Three participants with a melanoma history tested negative, and these participants were excluded from analyses because the small number of affected noncarriers precluded drawing conclusions and making appropriate comparisons with the other groups. Thus, the final sample for analysis consisted of 60 participants (unaffected noncarriers, \( n = 27 \); unaffected carriers, \( n = 15 \); affected carriers, \( n = 18 \)). There was no difference among the three groups in the proportion of participants completing any follow-up assessment, and there were no differences in baseline anxiety, depression, or melanoma worry between those who completed particular follow-ups and those who did not.

### Melanoma and pancreatic cancer genetics education and risk communication

Prior to being offered the option to receive genetic test results, participants received melanoma genetic counseling and education\(^2\) (see Supplementary Materials in Ref. [7] for complete protocol). The counseling protocol included presentation of basic genetics information, including the function of genes, concept of a mutation, and autosomal dominant inheritance. Participants were informed of the general population risk of melanoma and pancreatic cancer, the relative risks associated with phenotypic factors and UVR exposure, and the risks for melanoma and pancreatic cancer in \( p16 \) mutation carriers. They were informed of the likelihood that they had inherited a mutation and of the implications of receiving a positive or negative result for determining the risks for offspring. Participants were informed that a \( p16 \) mutation increased melanoma risk 35- to 70-fold above the general population risk to 50% by age 50 and 76% by age 80. While a negative test result would greatly reduce the risk of melanoma, participants were informed that they would still have a residual 1.7-fold risk of melanoma due to the possibility of there being other factors such as physical features or UVR exposure contributing to the risk in these highly penetrant families. The pancreatic cancer risk in \( p16 \) mutation carriers was described as approximately 17% by age 75. Almost all participants were from two major kindreds, and participants in one kindred (Kindred A) were informed that they had a known family history of pancreatic cancer and were thus definitely at elevated risk. Participants in Kindred B were
informed that they did not have a known family history of pancreatic cancer, but that their risk may be elevated nonetheless. Information about the costs and benefits of genetic testing was discussed on a case-by-case basis in response to participant questions (e.g. privacy, insurance discrimination, need to modify recreational activities, etc.). Following this education, all counselees elected to receive their results. The counselor reported the participant’s genetic status and then reviewed information about risks and management options specific to the participant’s genetic status. Regardless of genetic status, all participants were specifically counseled to minimize sun exposure and prevent sunburns and to perform monthly self-skin exams to maximize the opportunity for early detection. Clinical total body skin exams were recommended every 6 to 12 months for individuals testing positive or possessing other risk factors such as numerous moles. Participants testing positive were also informed that their children or future children would be at 50% risk for inheriting the mutation and that screening is recommended for at-risk children beginning at age 10. Participants testing positive were told that no effective surveillance techniques for early diagnosis of pancreatic cancer currently exist, but that new techniques to screen for pancreatic cancer were an area of active research. All carriers signed and received a copy of a disclosure concerning their elevated risk of pancreatic cancer and were referred to two University specialists to obtain additional information about endoscopic ultrasound and spiral computed tomography.

All participants received a letter approximately 1 month later, which reiterated their test results, the associated risks for melanoma and pancreatic cancer, and management recommendations, including the recommendation to consult with a gastroenterologist concerning pancreatic cancer screening. The letter further specified that p16 mutation carriers with a family history of pancreatic cancer should consider screening at age 50 or 10 years prior to the youngest known diagnosed case of pancreatic cancer in the family (whichever is first). Mutation carriers without a known history of pancreatic cancer in the family were advised, “Even though there may not be a known history of pancreatic cancer in your family, there may still be an increased risk for pancreatic cancer in carriers of the

Figure 1. Recruitment, retention, and attrition of noncarriers, unaffected carriers, and affected carriers in the genetic test reporting and follow-up studies, along with reasons for participant non-response to initial invitation and each subsequent assessment.

*aThe total column includes three additional participants who completed baseline and multiple follow-up assessments but were excluded from analyses because they were noncarriers with a melanoma history. One additional participant (an affected carrier) was excluded from analyses because he did not complete any post-counseling assessment.
gene mutation. All gene mutation carriers should be aware of their heightened risk for pancreatic cancer and should consider screening and medical management options’.

Measures

Demographics and melanoma history
Participants completed standard demographic questions. We confirmed the melanoma history of each participant through the pathology reports, Utah Cancer Registry (a SEER Registry), and Utah Population Database. Participants also reported any history of pancreatic and other cancers at baseline.

Genetic testing result
Sequence analysis demonstrated two pathogenic CDKN2A/p16 mutations in our study population: V126D and 5’UTR-34G > T.

Psychological distress
At baseline, 1 month, 6 months, 1 year, and 2 years, participants completed the Hospital Anxiety and Depression Scale (HADS) [22], which measures symptoms of anxiety and depression in the past month. Response options in the original HADS include four endpoints for each item, all items were scored on a scale, with different descriptors for each level for each item. To standardize the endpoints across multiple instruments in the baseline questionnaire and to reduce participant burden to read different endpoints for each item, all items were scored on a scale of 1 (strongly disagree) to 5 (strongly agree). Seven anxiety items were averaged to form an anxiety scale, \( \alpha = 0.80–0.91 \). Seven depression items were averaged to form a depression scale, \( \alpha = 0.74–0.83 \). All reported results refer to these means. The scores were later converted to HADS total scores to afford comparison to established cutoffs for mild (8–10), moderate (11–15), or severe (16–21) anxiety or depression [23].

We converted each item as follows: 1 'strongly disagree' and 2 'disagree' were recoded as 0, because both response options reflected non-endorsement of each symptom; 3 'neither agree nor disagree' was recoded as 1; 4 'agree' was recoded as 2; and 5 'strongly agree' was recoded as 3. Correlations between the original and converted HADS scales were high, ranging from 0.86 to 0.96 for anxiety and from 0.77 to 0.80 for depression.

Cancer worry
At each assessment, participants completed three items on melanoma worry [24] that assessed how often in the past month participants reported thinking about their own or family members’ chances of developing melanoma and how often these thoughts had affected their mood (1, ‘none of the time’; 5, ‘all the time’), as well as how concerned they were about the possibility of themselves or their family members developing melanoma (1, ‘not at all concerned’; 5, ‘very concerned’). These items were averaged to form a melanoma worry scale, \( \alpha = 0.62–0.67 \). Parallel items assessed pancreatic cancer worry at 1 month, 6 months, 1 year (carriers only), and 2 years, \( \alpha = 0.46–0.72 \). (We did not assess pancreatic cancer worry at baseline as participants had not yet been counseled about the pancreatic cancer risk associated with p16 mutations.)

Multidimensional Impact of Cancer Risk Assessment
The Multidimensional Impact of Cancer Risk Assessment (MICRA) [25] was administered at 1 and 6 months. Developed in a large sample of women undergoing BRCA1/2 testing, the MICRA assesses specific thoughts (e.g. worry, confusion, and uncertainty about cancer risk), feelings (e.g. upset or sad), and experiences (e.g. difficulties with family communication) following genetic test reporting (1, ‘not at all’; 5, ‘very much’). The inventory assesses both positive (positive experiences, four items) and negative outcomes (distress, six items; uncertainty, nine items). As shown in Table 1, the MICRA includes five additional individual items. Although the MICRA subscales were reliable in the original validation sample, they were less so in the present study: distress, \( \alpha = 0.61 \) and \( \alpha = 0.59 \); uncertainty, \( \alpha = 0.65 \) and \( \alpha = 0.67 \); positive experiences, \( \alpha = 0.59 \) and \( \alpha = 0.53 \). The MICRA items assess positive and negative outcomes of cancer genetic testing in general and are not specific to either melanoma or pancreatic cancer risk. To assess distress that may arise from receiving information about one’s elevated risk for an aggressive cancer for which there are no well-established prevention or early detection measures, we expanded two key items from the uncertainty index to create one set referring to melanoma and another to pancreatic cancer. Thus, participants were asked whether they were having difficulties making decisions about melanoma (pancreatic cancer) screening and prevention, and whether they were feeling frustrated that there were no definite melanoma (pancreatic cancer) prevention guidelines. To retain comparability to the established scoring procedures for the uncertainty index, we included items pertaining to melanoma risk in the scale totals, and presented items pertaining to pancreatic cancer risk separately.

Participant reports of the costs and benefits of p16 genetic test reporting
At the 1-month, 6-month, and 1-year follow-ups, participants were given several blank lines to respond to the following open-ended questions: (i) ‘Have there been any benefits or positive aspects of learning your genetic test results?’ and (ii) ‘Have there been any downsides or negative aspects of learning your genetic test results?’ A coding scheme was developed by identifying recurring themes, and two independent raters coded responses with 80% agreement prior to discussion. Disagreements were resolved through discussion. We next analyzed
pre-discussion percent agreement within the three major categories of perceived benefits: emotional benefits (77.1%), informational benefits (86.2%), and behavioral benefits (86.4%). For this analysis, we counted codes as agreeing if both raters’ codes were within the same major category. Thus, for the major categories of perceived benefits presented, acceptable agreement was obtained, and initial disagreements between coders were more likely to occur within rather than across major categories. Additionally, agreement was highest at the 6-month assessment (87.1%), intermediate at 1 year (77.6%), and lowest at 1 month (74.7%). Finally, agreement was highest among codes given to unaffected noncarriers’ statements (85.4%), intermediate among unaffected carriers (78.1%), and lowest among affected carriers (72.6%).

**Multiple imputation procedure**

As noted earlier, several participants missed one or more assessments but later rejoined the study. Because a listwise deletion procedure across the multiple assessments in the repeated-measures analyses (see ‘Overview of analyses’ section) would have resulted in an artificially small sample size of complete cases that may not be representative of the full population, multiple imputation was performed to generate complete data for all 60 participants [26,27]. Multiple imputation uses available nonmissing data, including data from completed assessments and ‘auxiliary variables’, such as demographic, psychosocial, and other baseline values that might either predict noncompletion of subsequent assessments or be useful in predicting subsequent assessments in multiple regression models to estimate values for missing assessments. Following standard practice, we completed 10 imputations sets using NORM [28] and then transferred the data to PASW18 for analysis. By generating multiple assessments of the missing values, multiple imputation approximates the type of measurement error that is present in real but not singly imputed data [26] and performs well with small sample sizes and large amounts of missing data, as well as when data are missing at random and often when missing not at random. For this reason, multiple imputation is preferred over listwise deletion, reweighting, or mean substitution [27]. Because the imputed values have greater variability than actual data, these values are underweighted in the analyses compared with actual data. Following standard practice, analyses were repeated with each data set, and all reported results were computed from the average of the coefficients yielded by the 10 separate data sets. The results presented below concerning general distress, specific outcomes of genetic test reporting, and melanoma worry were virtually identical with or without the multiple imputation procedure; a single exception is noted.

The multiple imputation procedure for items assessing pancreatic cancer worry was slightly different. Because we did not assess pancreatic cancer worry at baseline, values were imputed only for the 42 participants completing assessments at 1 month, with the multiple imputation procedure used to estimate values

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**Table 1. Mean distress, uncertainty, and positive experiences following CDKN2A/p16 genetic testing at 1 month and 6 months among unaffected noncarriers, unaffected carriers, and affected carriers as assessed by MICRA subscales and individual MICRA items**

<table>
<thead>
<tr>
<th>Responses to CDKN2A/p16 genetic testing</th>
<th>1 month</th>
<th>6 months</th>
<th>Main effect of group, F(2,57)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MICRA subscales</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distress</td>
<td>1.01</td>
<td>1.22</td>
<td>1.37</td>
</tr>
<tr>
<td>Uncertainty</td>
<td>1.09</td>
<td>1.25</td>
<td>1.56</td>
</tr>
<tr>
<td>Positive experiences</td>
<td>4.29</td>
<td>3.24</td>
<td>3.56</td>
</tr>
<tr>
<td>Happy about my test result</td>
<td>3.94</td>
<td>1.53</td>
<td>1.32</td>
</tr>
<tr>
<td>Relieved about my test result</td>
<td>4.01</td>
<td>2.09</td>
<td>2.83</td>
</tr>
<tr>
<td>Family supportiveness during genetic counseling and testing process</td>
<td>4.51</td>
<td>4.57</td>
<td>5.31*</td>
</tr>
<tr>
<td>Satisfaction w/ family communication about my genetic test result</td>
<td>4.70</td>
<td>4.77</td>
<td>4.76</td>
</tr>
<tr>
<td><strong>MICRA individual items</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feeling regret about getting my test result</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Having a clear understanding of my choices for cancer prevention or early detection</td>
<td>3.96</td>
<td>4.38</td>
<td>3.47</td>
</tr>
<tr>
<td>Worry about the possibility of my children getting cancerb</td>
<td>2.30</td>
<td>2.71</td>
<td>3.74</td>
</tr>
<tr>
<td>(n = 22)(n = 10)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feel guilty about possibly passing on disease risk to my children</td>
<td>1.39</td>
<td>1.63</td>
<td>1.87</td>
</tr>
<tr>
<td>Genetic test result has made it easier to cope with my cancer</td>
<td>4.01</td>
<td>4.02</td>
<td>N/A</td>
</tr>
</tbody>
</table>

*a-p < 0.01.

**p < 0.001.

The multiple imputation procedure created one mean out of range. The mean value in the original data set was 4.56.

*As per the MICRA instructions, items pertaining to children were answered only by participants with children.
for participants missing any subsequent assessments (e.g. at 6 months, 1 year, or 2 years). For pancreatic cancer worry, there were minor differences between the imputed and actual data, and these will be noted.

Results

 Participant characteristics

Of the total sample, 50% were men, the mean age was 49.56 (SD = 14.05), 77.8% were married, 83.3% had more than a high school education, and median income was $60,000–69,000. Thirty percent had a confirmed history of melanoma. Affected participants had an average of 2.2 melanomas (SD = 1.26), which were diagnosed an average of 11.06 years prior to the baseline assessment (SD = 11.52). No participant reported a diagnosis of pancreatic cancer. No significant difference was found among the three groups (unaffected noncarriers, unaffected carriers, affected carriers) on any demographic measure.

Overview of analyses

Repeated-measures analyses of variance (ANOVAs) tested prospective changes in anxiety, depression, and melanoma worry as a function of Time of Assessment (baseline, 1 month, 6 months, 1 year, 2 years) and participant Group (affected carriers, unaffected carriers, and unaffected noncarriers). Similarly, repeated-measures ANOVAs tested worry about pancreatic cancer as a function of Time of Assessment (1 month, 6 months, 2 years) and participant Group. Next, repeated-measures ANOVAs tested whether the three groups reported significant differences in test-related distress, uncertainty, or positive experiences 1 and 6 months following test reporting. Finally, percentages of carriers and noncarriers listing perceived costs and benefits of genetic testing at 1 month, 6 months, and 1 year are presented.

General psychological distress

Anxiety

The analysis of HADS anxiety ratings yielded a significant main effect of Time (F(4,54) = 4.79, p < 0.002), with both significant quadratic and cubic patterns (F(1,57) = 9.44, p < 0.003, and 7.33, p < 0.009, respectively). All mean comparisons employed two-tailed tests to allow for the possibility of either increased or decreased distress. As shown in Figure 2A, participants in all three groups reported significant decreases in anxiety from baseline to all subsequent assessments except 1 year (1 month, t(228) = 3.52, p < 0.001; 6 months, t(228) = 2.67, p < 0.008; 1 year, t(228) = 1.91, p < 0.057; and 2 years, t(228) = 2.03, p < 0.043). There were no differences among groups (F(2,57) = 0.94, p < 0.395), and there was no Group × Time interaction (F(8,108) = 1.59, p < 0.136). Further, anxiety ratings were low at all assessments; converted HADS scores ranged from 3.22 at baseline to a high of 2.98 at 6 months, well below the cutoff of 8 for mild anxiety.

Depression

The analysis of HADS depression ratings yielded similarly low reports of depressive symptoms at all assessments, as well as a significant main effect of Time (F(4,54) = 4.82, p < 0.002) and a significant Group × Time interaction (F(8,108) = 2.32, p < 0.025). As shown in Figure 2B, depression showed a significant curvilinear pattern (F(1,57) = 8.20, p < 0.006), with significant decreases from baseline to 1 month (t(228) = 2.39, p < 0.018) and 6 months (t(228) = 3.26, p < 0.002) and a return to baseline at 1 year (t(228) = 1.12, p < 0.116) and 2 years (t(228) = 1.01, p < 0.314). As was the case for anxiety, converted scores fell far below the cutoff of 8 for mild depression, ranging from 1.50 at baseline to 1.74 at 1 year.

Cancer-specific distress

Melanoma worry

Results for melanoma worry revealed significant main effects of both Group (F(2,57) = 7.32, p < 0.01) and Time (F(4,54) = 6.19, p < 0.01). As shown in Figure 2C, affected carriers reported greater melanoma worry than either of the two unaffected groups at all assessments; however, reported worry was significantly below the midpoint of the scale at all assessments except at 1 month. The main effect of Time was significantly cubic (F(1,57) = 5.97, p < 0.02), such that melanoma worry significantly decreased in all groups from baseline to 6 months (t(228) = 2.22, p < 0.027) and from 1 month to 6 months (t(228) = 3.73, p < 0.001); however, there were no other significant changes from one assessment to the next. Last, the Group × Time interaction was not significant (F(8,108) = 0.64, p < 0.75), indicating that melanoma worry was not exacerbated by a positive test result in either carrier group.

Pancreatic cancer worry

Pancreatic cancer worry was low and significantly below the scale midpoint at each assessment for all groups, including p16 mutation carriers (1 month, M = 1.41, SD = 0.47; 6 months, M = 1.52, SD = 0.55; 1 year, M = 1.26, SD = 0.48; 2 years, M = 1.23, SD = 0.37). Because the kindreds differed in whether there was a known history of pancreatic cancer in the extended family and were counseled accordingly, we included Kindred as a factor in the analysis. A repeated-measures Kindred × Group ANOVA with Time of Assessment (1 month, 6 months, 2 years) as a within-subjects factor yielded a significant Kindred × Group interaction (F(2,36) = 3.41, p < 0.044), a marginally significant main effect of Group (F(2,36) = 3.20, p < 0.053), and a significant main effect of Time (F(2,72) = 7.39, p < 0.001). As shown in Figure 2D, pancreatic cancer worry at 1 month was greatest among affected carriers in both kindreds and unaffected carriers from Kindred A, the kindred with a known history of pancreatic cancer. From 1 month to 2 years, unaffected carriers in Kindred A consistently
reported higher levels of pancreatic cancer worry ($M = 1.56$) than unaffected carriers in Kindred B ($M = 1.03$; $F(1,36) = 7.15$, $p < 0.011$). Finally, the significant main effect of Time showed a curvilinear pattern such that pancreatic cancer worry increased slightly from 1 month ($M = 1.43$) to 6 months ($M = 1.54$) and then decreased significantly from 6 months to 2 years ($M = 1.24$; $t(72) = 2.29$, $p < 0.001$), yielding a significant net decrease from 1 month to 2 years ($t(72) = 3.47$, $p < 0.025$). No other main effects or interactions were significant. Thus, although affected carriers in both kindreds and unaffected carriers in Kindred A consistently reported greater worry about pancreatic cancer than other participants, reported worry was consistently below the scale midpoint and decreased over time.

**Testing-specific outcomes**

As shown in Table 1, the three MICRA subscales and the two individual items pertaining to concerns about children’s cancer risk all showed significant main effects of Group, with no significant main effect of Time or Group × Time interaction on any measure.

**MICRA distress and uncertainty**

Reported distress and uncertainty in response to learning one’s test result were low in all three groups both 1 and 6 months after test reporting. As shown in Table 1, affected carriers reported greater distress than unaffected noncarriers ($t(43) = 4.52$, $p < 0.001$), whereas unaffected carriers reported intermediate levels of distress that were marginally higher than noncarriers ($t(40) = 1.75$, $p < 0.088$). Affected carriers reported greater levels of uncertainty than both unaffected noncarriers ($t(43) = 4.43$, $p < 0.001$) and unaffected carriers ($t(31) = 3.16$, $p < 0.004$).
assessments, especially among unaffected noncarriers. As shown in Table 1, unaffected noncarriers reported more favorable experiences overall than both unaffected carriers \((t(40) = 3.90, p = 0.001)\) and affected carriers \((t(43) = 3.56, p < 0.001)\). As shown in Table 1, these group differences were obtained for reported happiness and relief, but not for family supportiveness and satisfaction with family communication about the genetic test result.

MICRA individual items
As shown in Table 1, no participant in any group reported any regret about getting test results at either assessment. Additionally, participants in all groups reported a high degree of understanding of their choices for cancer prevention or early detection. Among respondents with children (75%), affected carriers reported greater worry about their children getting cancer \((t(43) = 3.20, p = 0.003)\) than did unaffected noncarriers, whereas unaffected carriers’ reports were intermediate to and not significantly different from either group. Reported feelings of guilt about potentially passing cancer risk on to one’s children were low, with affected carriers’ feelings of guilt significantly greater than those of unaffected noncarriers \((t(43) = 3.08, p = 0.004)\) and marginally greater than those of unaffected carriers \((t(31) = 1.81, p = 0.080)\). Finally, affected carriers reported that receiving their genetic test results had made it easier to cope with their cancer.

MICRA pancreatic cancer items
At both 1 month and 6 months, participants in all groups reported low levels of difficulty making decisions about pancreatic cancer screening or prevention (means in all groups were below 1.5 at both assessments), with no significant effects involving Kindred, Group, or Time of Assessment. For frustration about the lack of pancreatic cancer prevention guidelines, there was a marginally significant Kindred \(\times\) Group interaction \((F(2,36) = 2.99, p < 0.063)\), which suggested a similar pattern to pancreatic cancer worry in that unaffected carriers in Kindred A reported greater frustration about the lack of pancreatic cancer prevention guidelines than unaffected carriers in Kindred B, although the means for all groups were lower than 2 (‘a little’) at both assessments. There were no other significant main effects or interactions for this item.

Reported costs and benefits of receiving \(p16\) genetic test results
We identified three major categories of perceived benefits: emotional benefits, such as relief and decreased distress; informational benefits, such as increased knowledge about personal and familial risk and other topics; and behavioral benefits, such as increased health behaviors or plans with respect to photoprotection and/or screening. The frequency with which carriers and noncarriers listed perceived costs and benefits at each of the three follow-up assessments is summarized in Table 2. Nearly 95% of participants at each assessment listed one or more positive aspects of learning their genetic test results, whereas only 15.9% overall (11.9% at 1 month, 8.1% at 6 months, and 3.3% at 1 year) listed a negative aspect at any assessment.

We next examined the proportion of respondents who listed specific perceived benefits at any of the three follow-up assessments. As shown in Figure 3, significantly more unaffected noncarriers (71.4%) than carriers (26.1%) reported at least one emotional benefit of test reporting \((\chi^2(1) = 9.05, p < 0.003)\). For example, one unaffected noncarrier wrote, ‘I am more at ease about my genetic propensity of getting a melanoma. Also, I am more at ease for my children’s sake’, and an unaffected carrier wrote, ‘I feel that there are choices and options for the better about taking steps to prevent melanoma. It is not hopeless’. Importantly, for participants with a melanoma history, distress reduction did not refer to reduced risk of melanoma, but rather to having an explanation for prior melanomas (e.g. ‘I don’t feel quite so guilty about having had melanoma, as I did when I thought it was all due to my sun exposure’).

The perceived informational benefit of increased knowledge about melanoma risk and its management was frequently reported by both groups (95.2% of noncarriers, 78.3% of carriers; \(\chi^2(1) = 2.69, p < 0.101)\). For example, one unaffected noncarrier wrote, ‘I now have more accurate (and readily available) information on melanoma. It was good to know that the \(p16\) gene does not do a generation so I cannot pass it on to my grandchildren’. An affected carrier wrote, ‘The more information the better. The more I know, the more I’ll be able to take precautionary measures and get skin check-ups’.

Finally, the perceived behavioral benefits of improved health behaviors or plans to increase the practice of photoprotection and screening were reported by 65.2% of carriers and 38.1% of noncarriers \((\chi^2(1) = 3.24, p < 0.072)\). One affected carrier wrote, ‘Having the test results be positive has increased my vigilance’, while another wrote, ‘I’m glad to know my standing, it will be helpful as I plan for summer, future appointments and with my family’. Similarly, an unaffected carrier wrote, ‘I think more about what I’m doing in the sun and take more measures to protect myself and my family’.

Negative aspects
Of the 44 respondents who completed at least one of the three qualitative assessments, four carriers and three unaffected noncarriers mentioned a cost of genetic testing. Of these, four participants (9.1%) mentioned being discouraged or distressed by their results. For example, one affected carrier wrote, ‘A little discouraging, but I would rather know’, while one unaffected carrier expressed frustration: ‘Just that there is no genetic way
of fixing it yet—it ticks me off’. One affected carrier cited insurance concerns. Only one participant, an unaffected noncarrier, reported a negative impact on his or her practice of photoprotection and screening behaviors (‘less diligence’) at 1 year. Two carriers expressed a desire to know more about pancreatic cancer causes, including how melanoma risk and pancreatic cancer risk were connected. Of these, one expressed mixed feelings about the information: ‘Positive that it was brought up and negative that they don’t know anything about it’. Finally, all respondents who listed a negative aspect of genetic test reporting also listed at least one positive aspect.

### Discussion

Across multiple measures of psychological distress over a 2-year period, there was no evidence that any group of respondents reported either short- or long-term increases in anxiety, depression, or worry about melanoma or pancreatic cancer following receipt of CDKN2A/p16 genetic test results. Reported anxiety decreased significantly from baseline over the 2-year period following test reporting and counseling, and reported depression and melanoma worry both showed short-term decreases. Following counseling and test reporting, mutation carriers did not report high or even moderate levels of worry about pancreatic cancer. With the exception of concern about children’s cancer risk, respondents reported uniformly low levels of test-related distress and uncertainty 1 and 6 months following test reporting. Although noncarriers reported greater happiness and relief, carriers and noncarriers reported equivalently high levels of positive experiences involving family support and communication. No respondent in any group reported any degree of regret about receiving test results. Finally, qualitative reports of the costs and benefits of melanoma genetic testing assessed three times in the following year indicated that all respondents noted at least one perceived emotional, informational, or behavioral benefit of p16 testing, with only a small minority listing any cost. These findings suggest that p16 genetic test reporting does not result in psychological distress and

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**Table 2.** The proportion of respondents reporting perceived costs and specific emotional, informational, and behavioral benefits of CDKN2A/p16 genetic testing at 1 month, 6 months, and 1 year, stratified by p16 mutation status

<table>
<thead>
<tr>
<th></th>
<th>1 month</th>
<th>6 months</th>
<th>1 year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Carriers, n = 22</td>
<td>Noncarriers, n = 20</td>
<td>Carriers, n = 19</td>
</tr>
<tr>
<td>Any positive aspect (%)</td>
<td>95.5</td>
<td>95.0</td>
<td>89.5</td>
</tr>
<tr>
<td>Any negative aspect</td>
<td>18.2</td>
<td>5.0</td>
<td>10.5</td>
</tr>
<tr>
<td>Emotional benefits</td>
<td>18.2</td>
<td>50.0</td>
<td>15.8</td>
</tr>
<tr>
<td>Decreased distress or worry for self</td>
<td>0</td>
<td>40.0</td>
<td>10.5</td>
</tr>
<tr>
<td>Decreased distress or worry for family/kids</td>
<td>0</td>
<td>15.0</td>
<td>0</td>
</tr>
<tr>
<td>Decreased guilt or fatalism</td>
<td>13.6</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>Increased hope or happiness</td>
<td>4.6</td>
<td>5.0</td>
<td>10.5</td>
</tr>
<tr>
<td>Increased knowledge</td>
<td>63.6</td>
<td>60.0</td>
<td>42.1</td>
</tr>
<tr>
<td>Increased health behaviors or plans</td>
<td>50.0</td>
<td>20.0</td>
<td>42.1</td>
</tr>
<tr>
<td>Prevention for self</td>
<td>22.7</td>
<td>5.0</td>
<td>15.8</td>
</tr>
<tr>
<td>Prevention for kids/family</td>
<td>9.1</td>
<td>0</td>
<td>10.5</td>
</tr>
<tr>
<td>Screening for self</td>
<td>13.6</td>
<td>100</td>
<td>21.1</td>
</tr>
<tr>
<td>Screening for kids/family</td>
<td>0</td>
<td>0</td>
<td>5.3</td>
</tr>
<tr>
<td>Unspecified health behavior for self</td>
<td>18.2</td>
<td>10.0</td>
<td>5.3</td>
</tr>
<tr>
<td>Unspecified health behavior for kids/family</td>
<td>4.6</td>
<td>5.0</td>
<td>15.8</td>
</tr>
</tbody>
</table>

The total percentages for each major category of benefits (emotional benefits, increased knowledge, increased health behaviors or plans) reflect the proportion of respondents who mentioned one or more subcategories of each respective benefit. A respondent who mentioned multiple benefits or costs within a category or subcategory is counted only once in the bold summary row.

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instead is seen as a welcome and useful tool in managing familial melanoma risk.

Overall, these results suggest that, despite the many possible sources of distress among people learning genetic test results for familial melanoma susceptibility (e.g., high lifetime possibility of developing the disease, poor prognosis for melanoma if not detected early, need to make lifestyle changes to reduce UVR exposure, increased pancreatic cancer risk, and potential survivor guilt for unaffected noncarriers with carrier family members), participants in our study did not report elevated levels of distress, uncertainty, or cancer-related worry related to receiving their test results. The only item on which affected carriers reported elevated cancer worry was the individual MICRA item pertaining to concern about children’s cancer risk. In this context, it is important to note that members of these high-risk families expressed considerable interest in genetic testing for their minor children [29], and their reported improvements in photoprotection and screening frequently included their children.

These findings are strikingly consistent with those of Kasparian et al.’s [5] interview study in which participants reported expecting to calmly accept positive p16 test results. Indeed, members of this cohort who later underwent genetic testing and received their results reported reduced depression in the year following testing [4]. Our findings suggest that these benefits may persist over a longer follow-up interval of 2 years and extend to reported (rather than anticipated) costs and benefits.

These findings are also consistent with multiple reviews of the psychological impact of cancer genetic testing for other cancer syndromes, such as HBOC and hereditary nonpolyposis colorectal cancer, which find little evidence for sustained increases in distress after receiving a positive genetic test result up to 3 years after genetic testing [11,12,20,30,31]. The findings concerning perceived benefits are also consistent with recent studies in which nearly all women who underwent HBOC genetic testing retrospectively reported at least one advantage (or some degree of positive life change) [32], whereas only a minority stated any disadvantage [33,34]. In one study, nearly 75% of carriers reported the benefits of increased knowledge about their risk and increased access to screening and surgical options [34], whereas in another, carriers reported ‘instrumental advantages’ of perceived control and knowledge about health behavior options [33]. Similar to our findings, noncarriers reported peace of mind and relief as major advantages, whereas reduction of uncertainty was mentioned by both carriers and noncarriers [33,34].

As suggested by Shiloh and colleagues [35], who found decreased distress following a positive genetic test result for colorectal cancer, this lack of negative outcomes among carriers may be a result of increased confidence in screening measures, or it may be a consequence of extended counseling rather than a specific test result. Likewise, the low general psychological distress and melanoma worry reported by carriers in our sample may be due to the availability of preventive measures, such as wearing sunscreen and protective clothing, to reduce melanoma risk. Notably, the majority of participants (86.4%) mentioned increased knowledge about melanoma risks and prevention behaviors as a benefit of receiving genetic counseling and test reporting. Further, more than half, including 65.2% of mutation carriers, reported improved health behaviors and plans in the year following test reporting. In considering these reported improvements, it is important to note that many of our affected respondents reported being highly adherent at baseline and thus were unlikely to report increased vigilance following test reporting [7,8]; for unaffected family members, however, these perceived benefits may represent meaningful improvements in these key behaviors.

Finally, although we have focused on perceived informational and behavioral benefits of p16 genetic test reporting, the emotional benefits reported by our respondents on both the MICRA and the qualitative items are considerable. A 31-year-old participant wrote, ‘I grew up thinking I was doomed to get melanoma. Knowing that I am negative for the p16 gene has brought me much relief’. Although emotional benefits were more frequent among noncarriers, it is important to note that carriers also reported such benefits, particularly decreased fatalism and guilt.

Understanding the impact of p16 counseling and test reporting on pancreatic cancer worry

These results also provide new information about the impact of p16 test reporting and counseling on worry about pancreatic cancer, at least in this US sample. Although the news that the p16 mutation conferred up to 17% lifetime risk of pancreatic cancer was likely novel to participants, they reported low levels of worry from 1 month to 2 years following risk counseling and low levels of frustration or confusion concerning pancreatic cancer screening. It may be the case that counselees were more focused on parts of the counseling session that pertained to melanoma risk or that the 17% lifetime risk of pancreatic cancer seemed less impactful when presented in conjunction with the 76% lifetime risk of melanoma. Additionally, although all participants received in-person counseling and written follow-up information concerning the risk of pancreatic cancer for all p16 mutation carriers, participants who may have been doubtful about whether pancreatic cancer ran in their families may have perceived the risk as less real or applicable to them. For example, an unaffected carrier from Kindred B noted, ‘The history of melanoma in my family is high but pancreatic cancer has yet to make any type of appearance… I believe that the question of connection between p16 and pancreatic cancer versus melanoma still needs to be confidently established via more study’. Such sentiments may account for the differences found between the two kindreds in this study, such that unaffected carrier members of Kindred A with a known family history of pancreatic
cancer reported consistently greater (but still low absolute) levels of worry about pancreatic cancer and frustration concerning the lack of pancreatic cancer prevention guidelines than their counterparts in Kindred B without such a family history.

Future research should address these and other possibilities concerning how members of high-risk families respond to information about elevated risk for multiple cancer syndromes, as well as take into account other important differences between melanoma and pancreatic cancer, such as age of onset and availability of effective prevention, screening, and treatment options, which may influence responses to counseling and test reporting. Finally, as more studies of p16 counseling and test reporting in different countries are conducted, further research is needed to determine if there are genotype–phenotype or genotype–environment interactions that contribute to differences in pancreatic cancer penetrance estimates.

Limitations
First, these findings await replication in a larger and more diverse sample and among participants less experienced with melanoma research. The present sample was drawn from two large and relatively homogenous kindreds of affluent educated adults from Utah. As is the case with other p16 testing and counseling studies [9], participants were drawn from families with extensive history of research participation. Our participants had received counseling about their familial melanoma risk through their participation in prior melanoma genetics research; therefore, respondents may have been better prepared to cope with news of their elevated risk status. Nonetheless, despite prior counseling, a large majority of carriers reported such benefits as increased knowledge about melanoma risk and increased awareness and adoption of photoprotection and screening measures. Finally, our findings concerning low reported anxiety and depression both prior to and following p16 counseling and test reporting are similar to those obtained in the Netherlands [9] and Australia [4].

Second, the present study provides no data concerning anxiety or depression among the small minority of family members who declined to learn their test results. To date, studies have yielded inconsistent findings concerning levels of distress among decliners versus acceptors. Dutch respondents who chose to undergo p16 genetic testing had lower anxiety than those who declined [9; see also 6], whereas Australian respondents who underwent testing reported greater perceived risk and greater melanoma-specific distress (but lower fatalism about melanoma) than those who declined [4]. Thus, individuals who decline testing may not necessarily be more anxious or depressed than those who accept, although of course, little is known about members of high-risk families who decline study participation of any kind.

Third, because our respondents reported uniformly low levels of anxiety and depression, we were unable to test whether melanoma genetic testing differentially affected participants high in baseline anxiety or depression. For the same reason, we were unable to test whether demographic factors such as age, gender, or education moderated psychological outcomes. An important goal for future research on p16 testing and counseling will be to identify vulnerable participants who may require additional support to manage the emotional consequences of a positive test result and to implement corresponding recommendations for photoprotection and screening for both melanoma and pancreatic cancer.

Finally, several methodological issues warrant comment. Although there was some attrition over the 2-year period, multiple imputation procedures were used to retain participants who missed one or more assessments, including several who rejoined the study. There were no systematic differences identified between those who completed all assessments and those who dropped out, and results were highly consistent between the imputed and original data. Additionally, it should be acknowledged that our modification of the response options for the HADS scale reduced comparability with previous studies. Further, it is unknown whether the low reliabilities of the MICRA subscales are due to the smaller sample size, the inclusion of men and affected respondents, differences in responses to genetic testing for melanoma versus breast cancer, or the potential multifactorial nature of the subscales. Last, because this study did not include a control group receiving counseling alone, these results do not conclusively establish that genetic test reporting is necessary for the perceived emotional, informational, and behavioral benefits reported here.

Conclusion
Although these results await confirmation in a larger sample of high-risk family members with less experience with research participation and risk counseling, the present findings suggest that among US patients highly familiar with their hereditary risk of melanoma, p16 genetic counseling and testing appear to confer little risk of either short- or long-term adverse psychological outcomes, while providing multiple perceived emotional, informational, and behavioral benefits for both carriers and noncarriers.

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Conflict of interest

The authors declare no conflict of interest.

Notes

1. One elderly participant became fatigued during the baseline assessment and withdrew from the study prior to the completion of the post-counseling assessment. Two participants who completed the baseline assessment, genetic counseling session, and post-counseling assessment were not invited to the follow-up study for the following reasons: one participant was adopted (given the focus on family communication and other familial issues in the parent study, it was decided that this participant’s experience with genetic counseling and test reporting would be substantially different from the experiences of the other participants), and the other began study participation past the cutoff date, which was selected to ensure that the majority of respondents would be completing the parent study’s behavioral assessment of photoprotection in the same season.

2. The genetic counseling team that performed the study counseling services is involved in both clinical and research activities. For this study, they had been enlisted to both develop and enact the counseling protocol. The participants understood that they were being counseled as part of a study, but this session was performed in the same way that clinical counseling services are provided at our institution. Neither counselor is an author on this paper, but were included as authors on other papers describing counseling outcomes.

3. Because the low reliability of the worry scales suggested that the items might be examining more than one aspect of worry (i.e. frequency versus impact on mood; cf. Lerman et al. [24]), we examined reported worry in the three participant groups for each individual item. Across all assessments (including baseline), participants provided higher ratings of their concern about developing melanoma (M = 3.82 for affected carriers, M = 2.72 for unaffected carriers, and M = 2.63 for noncarriers) than either their frequency of thinking about melanoma (M = 2.53 for affected carriers, M = 2.05 for unaffected carriers, and M = 1.95 for noncarriers), or how often thinking about melanoma affected their mood (M = 1.46 for affected carriers, M = 1.21 for unaffected carriers, and M = 1.26 for noncarriers). These results suggest that although participants, especially affected carriers, reported concern about developing melanoma, reports of mood disturbance were rare throughout the study. These results also suggest that the very low endorsement of impact on mood compared with concern about melanoma or frequency of thinking about melanoma is the source of the low reliability. The corresponding analyses for pancreatic cancer worry revealed low reports of worry on all three items at all assessments: concern about developing pancreatic cancer (M = 1.88 for affected carriers, M = 1.27 for unaffected carriers, and M = 1.53 for noncarriers); how often thought about pancreatic cancer (M = 1.68 for affected carriers, M = 1.33 for unaffected carriers, and M = 1.21 for noncarriers); and how often thoughts about pancreatic cancer affected mood (M = 1.08 for affected carriers, M = 1.16 for unaffected carriers, and M = 1.05 for noncarriers). Because the individual items showed the same pattern of differences among groups as the composite scores for both melanoma and pancreatic cancer, we present the results for the composite worry scales in the main text.

4. Although the significant curvilinear effect of Time was obtained in the original data prior to the use of multiple imputation procedures, the Group × Time interaction was not. Therefore, we will not discuss this interaction effect further.

5. Because pancreatic cancer worry items were administered only to mutation carriers at 1 year, data from 1 year were not included in the repeated-measures analysis.

6. Reports of pancreatic cancer worry were similarly low across all assessments in the original data set prior to the use of multiple imputation procedures. Although the pattern of reported pancreatic cancer worry as a function of Kindred and Group was highly similar in the original data, the Kindred × Group interaction was not significant (F(2,21) = 0.83, p < 0.448), likely due to the smaller sample size of unaffected carriers resulting from listwise deletion. Thus, the pattern reported in Figure 2D awaits confirmation in a larger sample. The analysis of the original data yielded a marginally significant main effect of Group (F(2,21) = 2.72, p < 0.089) and a significant Main effect of Time (F(2,42) = 4.11, p < 0.023) that were virtually identical to the results obtained with the imputed data sets. Specifically, affected carriers reported significantly higher levels of pancreatic cancer worry than either unaffected carriers or unaffected noncarriers, and pancreatic cancer worry decreased significantly over time for all groups.

7. Reports of frustration and difficulty were similarly low in the original data. Prior to multiple imputation, a significant main effect of Group


36. Chu D, Kohlmann W, Adler DG. Identification and screening of individuals at increased risk for pancreatic cancer with