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Primary Care Providers' Willingness to Recommend *BRCA1/2* Testing to Adolescents

Suzanne C. O'Neill, PhD,
Lombardi Comprehensive Cancer Center Georgetown University Medical Center

George Luta, PhD,
Lombardi Comprehensive Cancer Center Georgetown University Medical Center

Leslie R. Walker, MD,
Department of Pediatrics Seattle Children's Hospital

Beth N. Peshkin, MS,
Lombardi Comprehensive Cancer Center Georgetown University Medical Center

Anisha Abraham, MD, MPH, and
Department of Pediatrics Georgetown University Medical Center

Kenneth P. Tercyak, PhD
Lombardi Comprehensive Cancer Center Georgetown University Medical Center

Abstract

Introduction—Clinical practice guidelines discourage pediatric genetic testing for *BRCA1/2* mutations due to a lack of timely medical benefit and psychosocial risk. Yet, some high risk families approach primary care providers (PCPs) about testing adolescents, and little is known about PCPs attitudes regarding these requests.

Methods—We assessed recommendations for testing to a composite patient (a healthy 13 year-old female, mother is a *BRCA* mutation carrier) among 161 adolescent and family PCPs attending a national medical conference. Testing recommendations were measured with a multidimensional scale that assessed perspectives on informed consent, genetic counseling, and insurance coverage.

Results—PCPs expressed moderate willingness to recommend testing; surprisingly, 31% recommended adolescent testing "unconditionally." In multivariable regression modeling, recommendation was positively associated with higher clinical practice volume ($p<.05$) and greater frequency of ordering other pediatric genetic tests ($p<.01$).

Conclusion—Despite a decade of clinical practice guideline advice to the contrary, experienced PCPs may still be inclined to recommend *BRCA1/2* genetic testing to adolescents from high risk families. When paired with emerging data on the relative safety and efficacy of breast cancer genetic testing for high risk women, and the advent of direct-to-consumer marketing of *BRCA1/2* cancer genetic tests, professional societies may need to explore best practices to counsel high risk families and their PCPs about the potential risks and benefits of pediatric *BRCA1/2* testing.

Introduction

One of the main reasons why women seek *BRCA1/2* testing is to learn whether they may pass hereditary cancer risks to their children [1-4]. Despite this interest, clinical practice

Address correspondence to: Suzanne C. O'Neill, PhD, Cancer Control Program, Lombardi Comprehensive Cancer Center, 3300 Whitehaven St., NW, Suite 4100, Washington, DC 20007. sco4@georgetown.edu.

guidelines strongly discourage pediatric genetic testing for *BRCA1/2* mutations. Though some guidelines acknowledge that there may be psychological benefits to knowing risk status as a means of reducing uncertainty, the majority of guidelines that distinguish adult-onset diseases from child-onset diseases state that testing is only recommended when an established, effective, and important medical treatment can be offered during childhood or when testing prevents, delays or eases the disease itself, or its symptoms, from manifesting [5-10]. In the case of *BRCA1/2* testing, risk-reduction options are available in the form of surgery (i.e., bilateral mastectomy or oophorectomy), enhanced screening via mammography and breast MRI, or tamoxifen chemoprevention [11] and none of these options are recommended until a female mutation carrier reaches age 25 [11]. Therefore, while some parents believe that having their children tested could foster healthy behaviors and reduce uncertainty [12], and research to date on hereditary cancer testing among high-risk adults suggests that serious adverse outcomes are rare [13-16], there remains no clear medical benefit for such testing among minors.

Despite these guidelines, there are a number of reasons why their application in real-world clinical practice sometimes proves difficult. First, though legal age of majority is considered 18 in most countries, no guideline offers a lower age limit. The rationale for using an age-based guideline is to delay testing until the individual considering testing is 'old enough' to make an autonomous, informed choice. Yet, guidelines are designed with flexibility in mind to permit shared decision making between patients and primary care providers (PCPs). The development of cognitive and decision making capacity are highly variable during adolescence [17] and there has been little work into how to formally assess these [18]. Due to ethical concerns, it is also difficult to conduct research on outcomes related to offering testing to minors in clinical contexts, and this has hampered direct assessment of key outcomes, such as actual risks and benefits to testing children [19].

Second, some high risk families approach PCPs about testing adolescents. Parental disclosure of test results to minor children occurs fairly frequently. Approximately one-half of parents inform their minor-age children of parents' *BRCA1/2* test results, with girls and older children more likely to be informed [3, 20-24]. Early studies found that about one-quarter of parents would allow their minor children to be tested and one-fifth wanted this testing for their children [25]. More recent reports suggest that about one-half of mothers who participate in *BRCA1/2* testing support testing of minors (48%; [12]), and 30% of parents who disclosed mutation status information to their children under age 25 (and too young to medically benefit from testing) did so in order for the child to be tested [24]. Generally, disclosure is associated with higher maternal interest in pediatric *BRCA1/2* testing [20]: mothers who more frequently talk to their children about familial cancer and are more inclined towards disclosing their results to their children are also more in favor of pediatric *BRCA1/2* testing [4].

Though there is a fairly high rate of disclosure of maternal *BRCA1/2* test results to minor children, parents perceive a balance between the risks and benefits of sharing parental mutation status with their children and of having minor children tested. On the one hand, parents report potential psychological risks and the immaturity of minors as reasons to not offer testing to this age group [12]. Indeed, many tested parents who disclose their own mutation status do not think their children appreciated the significance of the information and that disclosure resulted in negative emotional impact [24]. On the other hand, some parents also perceive a positive behavioral impact through improved lifestyle [12]. Empirical data are needed to better support parental decision making in this emerging area [26].

Disclosure of parental genetic test results to minors may impact minor children's interest in pursuing testing, and therefore, consequent discussions with PCPs. Disclosure may impact this process either directly or indirectly. Parents may share their own interests in having their children tested with these children, specifically piquing a child's interest in being tested. Knowledge of parental test results also may lead children to worry about their own future cancer risks, indirectly prompting interest in being tested [20]; adolescent girls with positive family histories of breast cancer are more interested in testing than those without this history [27], while those from high risk families express concern about their personal risks for the diseases [20, 28].

A combination of flexible guidelines and moderately high parental interest sets the stage for PCPs to encounter requests for pediatric *BRCA1/2* testing. Very little is known about how PCPs respond to such requests, and if or how they are influenced by parental preferences. In a small study of pediatricians and geneticists, a majority indicated they would provide *BRCA1/2* testing to a minor upon request, especially when coupled with patient assent and parental consent. Surprisingly, though none would offer *BRCA1/2* testing without adolescent consent, 80% would permit newborn screening for mutations in these genes [29]. In a survey of clinical geneticists practicing in Europe, 20% were willing to offer *BRCA1/2* testing to a 16 year-old patient; 71 % had provided such counseling to young patients, and 1% provided testing for these patients [30].

Overall, some parents from high risk families are inclined to want testing for their adolescents, and testing companies are making it easier for individuals to directly gain access to testing outside of standard clinical settings [6, 31, 32]. While most clinical guidelines caution against the testing of minors for susceptibility to adult-onset conditions, these guidelines are written to allow clinicians to make exceptions based on their own clinical judgment. Again, there is a dearth of information about the actual risks and benefits of testing in this population to inform these judgments, especially for adolescents who demonstrate varying levels of maturity. We need a better understanding of PCPs' willingness and inclination to provide *BRCA1/2* testing to minor children and the variables that predict this willingness so that targeted interventions can be developed around this issue. In light of this, the purpose of this study was to examine PCPs' willingness to recommend *BRCA1/2* testing to adolescents, and to identify predictors of their doing so. Predictors included both demographic and clinical practice variables, such as self-reported health and wellness screening behaviors with pediatric patients. It was hypothesized that PCPs engaged in more regular screening would be more willing to recommend pediatric *BRCA1/2* testing.

Methods

Participants and Procedure

A complete description of the study sample and data collection procedures are described elsewhere [33, 34]. Briefly, the survey was distributed in March, 2005 at the annual scientific conference of the Society for Adolescent Medicine (SAM). During this conference, trained research assistants approached conference attendees (identified by their conference badges) in the meeting registration area to complete an anonymous and confidential 10 minute survey regarding PCPs' knowledge, attitudes, beliefs, and behaviors regarding cancer control. Upon returning a completed survey during the conference (56%), respondents were offered a $5 gift certificate to a media store to acknowledge their time and effort. The study was reviewed and approved by the host institution's Institutional Review Board and by the Society for Adolescent Medicine.

BRCA1/2 hypothetical testing scenario

While the use of a hypothetical scenario comes with some disadvantages (such as not necessarily reflecting eventual behavior; [35]), this approach remains an important tool to examine social and behavioral issues related to genetic testing [36]. This is also an informative approach when exploring provider practices [37] or comparing provider behavior to well-established clinical practice guidelines [38]. Most previous studies have assessed PCPs attitudes toward genetic testing and behavioral intentions, rather than the complexities that might influence PCPs' attitudes and behaviors as confronted in a clinical encounter [33, 39, 40].

The current study used a hypothetical clinical scenario to examine PCPs' willingness to recommend pediatric *BRCA1/2* testing to adolescents under different circumstances, and modeled this approach after scenarios developed for other cancer-related outcomes [34]. Importantly, the scenario made clear the age of the adolescent and consideration of *BRCA1/2* testing. From the standpoint of clinical practice guidelines, this information in and of itself should have been sufficient to not recommend testing. It also provided information about hereditary cancer risks, family history, and child gender. These features were added to the scenario to highlight the potential high risk context typically encountered in clinical situations that might lend themselves more toward recommending testing. The scenario read as follows: BRCA1/2 gene mutations are associated with up to an 85% risk of breast cancer and a 40% risk of ovarian cancer in adult women. Biological children of a parent with a BRCA1/2 mutation have a 50% chance of testing positive. Assume the biological mother of your healthy 13 year-old patient Sara has tested positive.

Dependent variable—Respondents were immediately asked to complete four items that varied the circumstances under which PCPs' willingness to recommend *BRCA1/2* for Sara was queried: 1) unconditionally, 2) with parental/patient consent/assent, 3) after Sara is seen by a genetic counselor or geneticist first, 4) even if not covered by patient insurance. Responses to each item were given on a five-point Likert scale ranging from *strongly agree* to *strongly disagree*. The sum of these items served as an index of overall willingness to recommend *BRCA1/2* testing (range = 4-16; Cronbach's alpha coefficient = .76).

Independent variables

Demographics and clinical practice information: Survey respondents reported their age, gender, race, professional affiliation and training, the number of patients seen per week, percent of practice consisting of adolescent minor patients (< 18), and practice setting.

General wellness and at-risk screening behaviors: Respondents indicated how often they engaged in general wellness screening for eight well-established adolescent morbidities [41, 42] using a five-point Likert scale (1 = *never* to 5 = *always*; range 8-40): 1) eating disorders, 2) sexual activity, 3) alcohol and other drug use, 4) tobacco use, 5) physical abuse, 6) poor school performance, 7) depression and 8) suicide risk. PCPs also indicated how frequently they ordered screening tests for adolescents at-risk for high cholesterol, tuberculosis, HIV, and other STDs on a five-point Likert scale (1 = *never* to 5 = *always*; range 4-20); higher scores indicate more frequent screening behaviors.

Genetic testing behaviors: Respondents indicated how frequently they ordered or recommended four types of genetic services using a five-point Likert scale (1 = *never* to 5 = *always*). Domains included chromosome analyses, biochemical or other laboratory tests for asymptomatic patients with a positive family history of a specific condition, genetic testing for conditions occurring in childhood, and genetic testing for conditions occurring in

adulthood. Responses were summed to create a total score (range = 4-16); higher scores indicate more frequent genetic testing behaviors.

Data Analysis

Analyses were conducted in the following steps. First, descriptive statistics for all study variables were calculated, and their distributions were examined for outliers and missing data. Second, we performed bivariate analyses to identify covariates related to willingness to recommend pediatric *BRCA1/2* testing from the available study variables. Tests for correlation (based on the Pearson correlation coefficient) were used for the continuous variables and t-tests for the binary variables. Statistically significant covariates were included in the subsequent multiple linear regression model predicting willingness to recommend pediatric *BRCA1/2* testing.

Results

Demographics, Clinical Practice Information and Scenario Frequencies

Participants included 161 survey respondents whose previous clinical experience could have included ordering genetic tests (i.e., trainees and psychologists in our overall sample were excluded from analyses). Participants were mostly female (64%), physicians (85%), white (77%), and employed within academic medical settings (68%). Mean age was 45 (range = 28-64). As a group, they reported being in practice for a mean of 13.5 years, with 68% reporting having been in practice for at least six years. Respondents reported seeing, on average, 50 patients per week, with approximately half seeing at least 30 patients per week. Seventy-three percent indicated that at least half of their practice consisted of patients aged 0-17. Eight percent indicated that they had received formal training in clinical genetics.

As seen in Table 1, there were high rates of wellness screening and at-risk testing. Specifically, with the exception of abuse, participants reported performing other screening behaviors “frequently” or “always” at least 90% of the time and reported performing at-risk screening behaviors “frequently” or “always” at least 75% of the time. Participants indicated providing genetic services overall fairly often (M = 11.3, SD = 2.78), though this varied widely by the type of testing offered. For example, they reported “frequently” or “always” providing testing for childhood-onset conditions 80% of the time, but they reported “frequently” or “always” providing testing for adult-onset conditions 3% of the time. As seen in Table 2, PCPs expressed moderate overall enthusiasm for recommending *BRCA1/2* testing (Mean=12.9, SD=3.7), with 30% reporting that they would recommend this testing “unconditionally.” There was greater enthusiasm for offering this testing in other scenarios.

Bivariate Analyses

We assessed bivariate relationships between willingness to offer *BRCA1/2* testing and demographic and practice-related variables. PCPs’ willingness to offer *BRCA1/2* testing to adolescents was related to how frequently they had ordered other types of genetic testing in the past as quantified by the score for genetic testing behavior ($r = .24$, $p<.01$) and practice volume ($r = .18$, $p<.05$), such that PCPs who had more experience with providing other genetic services and those who saw 30 or more patients per week were more likely to order *BRCA1/2* tests than other PCPs. Other covariates considered, including age, gender, race, professional training and affiliation, formal genetics training, and wellness and at-risk screening behaviors, did not reach statistical significance and were not considered further.

Multivariate Analyses

Linear regression analyses were performed in order to determine predictors of overall willingness to offer *BRCA1/2* testing to the 13 year-old patient described in our scenario. As

seen in Table 3, PCPs who had more experience with providing genetic services ($p<.01$) and who saw more patients per week ($p<.05$) were significantly more willing to offer *BRCA1/2* testing to this patient.

Discussion

The purpose of this analog study was to determine PCPs attitudes about willingness to offer *BRCA1/2* testing to a 13 year-old daughter of a mutation carrier, as well as predictors of willingness. The results suggest that, overall, PCPs are somewhat willing to offer this service and that the majority would offer this service if both patient and parent provide assent/consent or if the patient was seen by a genetics provider first. PCPs who offer other genetic services in their practice and those who see more patients are more willing to offer this testing as compared to other PCPs. Previous experience in offering genetic services may reflect a number of factors, including experience and comfort with providing these services and an appreciation for the definite benefits offered by genetic information in certain circumstances. The fact that PCPs who see more patients were more willing to offer this service is more curious. Given that other setting-related variables, such as practice in an academic medical setting or age of patients seen, were not predictive of willingness to offer testing, suggests that perhaps these PCPs would be more willing to offer testing to their patients due to the demand of practice volume [38].

We examined a number of variables that were not predictive of willingness to offer *BRCA1/2* testing. The fact that general wellness practices did not predict willingness to offer testing suggests that PCPs view the ordering of these tests as a special circumstance and not part of routine preventive care in this population. Given that ordering and recommending of other genetic services was a predictor in our study, it is notable that previous training in genetics was not a predictor. Indeed, frequency of offering of genetic services and previous training were not significantly related ($r = -.09$, $p = .28$). Communicating genetic information and facilitating informed decision making by patients is an essential provider skill, but many PCPs lack sufficient training in this area [42]. Continuing education and research in the areas of provider-patient communication, patient education and genetic risk assessment would facilitate the development of the skills to provide care that balances the often competing implications of practice guidelines, risk management, patient preferences and healthcare costs [34, 38]. For example, it is possible that, after a more thorough discussion with the parents about the potential risks and benefits of testing minor children, testing could be deferred until the child is older. Counseling also could address a number of ongoing issues, ranging from a parent's anxiety about not knowing a child's risk, a child's anxiety about developing cancer or dying from the disease, and interest in modifying risk through diet and physical activity. Testing may not resolve these issues. PCPs could also assist parents in how to communicate with their children about disease risk. Sharing genetic risk information with children is a gradual process, with unique challenges at each phase [44]. Providing relevant information, ensuring understanding, and managing emotional responses are integral in guiding children through this process, but many parents report difficulty in one or more of these areas [45]. Thorough assessment and follow-up by a multidisciplinary team, including psychologists, physicians, and genetic counselors, throughout this process helps to facilitate family adjustment.

This study has several limitations. The sample was relatively small. The overall response rate of the survey was less than 60%, which we further limited to providers whose practice could have included offering testing. However, this response rate is similar to other studies that have recruited at professional conferences and the demographics with regard to gender, age and practice setting are similar to those applying for board certification in adolescent medicine in 2005, the year the study was conducted [46]. Likewise, our method limits the

generalizability of our results. Our use of hypothetical scenarios to assess practice likely does not reflect actual test uptake [47] and certain important factors that would impact actual clinical care, such as the parents' attitudes towards testing and the adolescent patient's capacity to make an informed choice, were not included. Finally, the responses of the participants in our study also may not reflect those of other SAM members or other PCPs, as most of our respondents were either physicians or worked in academic medical settings. Specifically, given that SAM conference attendees may be particularly sensitive to adolescents' developmental differences, willingness to offer testing in other samples might have been higher.

In conclusion, existing professional guidelines discourage genetic susceptibility testing of minors for adult-onset conditions [5-9]. In practice, offers and implementation of genetic susceptibility testing for *BRCA1/2* are often left to the PCPs' discretion and many parents are interested in this testing for their children once a deleterious mutation is found to be segregating in the family [12]. Our results forecast that despite a decade of clinical practice guideline advice to the contrary, experienced PCPs may be inclined to recommend *BRCA1/2* genetic testing for their minor patients. When paired with emerging data on the relative safety and efficacy of breast cancer genetic testing for high-risk women [1, 13-16, 48], the advent of direct-to-consumer marketing and offers of cancer genetic tests via mailed DNA samples [6, 31, 32], professional societies may need to revisit the issue of predictive genetic testing of adolescents for adult-onset cancers. Perhaps current guidelines should address varying developmental capacities of adolescents more fully, in conjunction with more research in this area. In the interim, efforts to better engage PCPs in the dialogue about the risks and benefits of *BRCA1/2* testing of minors are important. In addition, before such testing diffuses further into clinical care, it is important that genetics professionals team with PCPs to assist families in making informed decisions about genetic testing, and that research addresses the short and long term outcomes of genetic counseling and testing in minors.

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Table 1

Respondents Practice Behaviors and Scenario Responses (n = 161)

	%	M	SD
Wellness screening		36.5	3.8
Eating disorders			
Never/rarely/sometimes	3.8		
Frequently/always	96.2		
Sexual activity			
Never/rarely/sometimes	1.9		
Frequently/always	98.1		
Alcohol and other drug use			
Never/rarely/sometimes	0.6		
Frequently/always	99.3		
Tobacco use			
Never/rarely/sometimes	3.1		
Frequently/always	96.9		
Abuse			
Never/rarely/sometimes	13.8		
Frequently/always	86.2		
School performance			
Never/rarely/sometimes	6.8		
Frequently/always	93.2		
Depression			
Never/rarely/sometimes	8.7		
Frequently/always	91.3		
Risk for suicide			
Never/rarely/sometimes	8.7		
Frequently/always	91.3		
At-risk screening		16.9	2.7
High cholesterol			
Never/rarely/sometimes	17.5		
Frequently/always	82.5		
Tuberculosis			
Never/rarely/sometimes	25.2		
Frequently/always	74.8		
Chlamydia, gonorrhea, syphilis, and HPV			
Never/rarely/sometimes	4.4		
Frequently/always	95.6		
Human immunodeficiency virus			
Never/rarely/sometimes	20.1		
Frequently/always	79.9		
Previous genetic testing behaviors[1]		11.3	2.8

	%	M	SD
Karyotyping for abnormal features or developmental delay			
Never/rarely/sometimes	60.0		
Frequently/always	40.0		
Biochemical tests for asymptomatic patient with family history			
Never/rarely/sometimes	27.5		
Frequently/always	72.5		
Testing for childhood-onset conditions			
Never/rarely/sometimes	19.7		
Frequently/always	80.3		
Testing for adult-onset conditions			
Never/rarely/sometimes	96.9		
Frequently/always	3.1		

1 range = 4-16

Table 2

Respondents Practice Behaviors and Scenario Responses (n = 161)

	%	M	SD
Willingness to offer *BRCA1/2* testing[1]		12.9	3.7
Unconditionally			
Strongly disagree	21.9		
Disagree	23.1		
Neutral	25.0		
Agree	23.1		
Strongly agree	6.9		
With consent/asset			
Strongly disagree	7.5		
Disagree	10.1		
Neutral	20.8		
Agree	40.9		
Strongly agree	20.8		
After genetic counseling			
Strongly disagree	5.7		
Disagree	11.4		
Neutral	20.3		
Agree	43.7		
Strongly agree	19.0		
If not covered by insurance			
Strongly disagree	10.2		
Disagree	15.3		
Neutral	34.4		
Agree	33.1		
Strongly agree	7.0		

[1] range =4-16

Table 3

Linear Regression Analyses Predicting Willingness to offer BRCA1/2 Testing

Predictor	t	β
Genetic services experience	2.95	.24**
Patients seen per week (≥30)	2.21	.18*

* $p < .05$.

** $p < .01$.