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Genetic Counseling Approaches To Moderate-Penetrance Breast Cancer

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An investigation of approaches to genetic counseling regarding moderate-penetrance breast cancer susceptibility genes

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GENETIC COUNSELING APPROACHES TO MODERATE-PENETRANCE BREAST CANCER GENES

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Abstract

ATM, *CHEK2*, and *PALB2* are considered to be moderate-penetrance breast cancer susceptibility genes (MPBCSGs). MPBCSG mutation-carriers are predicted to have a lower risk for breast cancer than carriers of mutations in genes such as *BRCA1*, *BRCA2*, and other high-penetrance breast cancer susceptibility genes. Ninety-one practicing genetic counselors were surveyed to investigate genetic counselor utilization of the NCCN guidelines and recommendations for carriers of *ATM*, *PALB2*, and *CHEK2* based on personal and family history of breast cancer. Although the majority indicated that they would follow the guidelines regardless of personal or family history of breast cancer, some genetic counselor recommendations exceeded NCCN guidelines when there was a personal and/or family history of breast cancer for an individual with a MPBCSG mutation. For counselors that said they would exceed the NCCN guidelines, additional recommendations included consideration of risk-reducing mastectomy, bilateral risk-reducing mastectomy, increased screening for relatives, a referral to a breast surgeon, and use of risk models to clarify breast MRI recommendations. Our study is the first to report trends in the field regarding approaches to providing genetic counseling regarding *ATM*, *CHEK2*, and *PALB2*. The results demonstrate that personal/family history of breast cancer is a significant predictor of genetic counselor recommendation.

Key words: *ATM*, *CHEK2*, *PALB2*, breast cancer, moderate-penetrance gene, MPBCSG, genetic counseling, NCCN

Introduction

The discovery of breast cancer susceptibility genes has had a profound impact on the field of genetic counseling since the discovery of *BRCA1* and *BRCA2* in the 1990s (Miki et al., 1994; Wooster et al., 1995; Wooster et al., 1994; Antoniou et al., 2003). Patients with family or personal medical histories suggestive of hereditary breast and ovarian cancer syndrome (HBOC) are now regularly offered genetic counseling and testing for *BRCA1* and *BRCA2* gene mutations (Economopoulou, Dimitriadis, & Psyrri, 2015). Comprehensive, evidence-based clinical practice guidelines for surveillance and management in

patients with *BRCA1/2* mutations as well as other, rarer high-penetrance breast cancer susceptibility gene mutations such as *TP53*, *PTEN*, *STK11*, and *CDH1* are regularly established and updated by the National Comprehensive Cancer Network (NCCN, 2019).

Within the past decade, next-generation sequencing platforms have facilitated the identification of novel breast cancer susceptibility genes considered to confer moderate breast cancer risk. Multi-gene panels have been updated to include moderate-penetrance breast cancer susceptibility genes (MPBCSGs), and in one study, approximately 2-5% of individuals referred for clinical genetic testing were identified to carry a MPBCSG mutation (Tung et al., 2016). While there is a significant need for further research on this subset of genes, *ATM*, *CHEK2*, and *PALB2* are among the most well-studied and commonly tested for MPBCSGs in clinical genetics settings (Broeks et al., 2000; Economopoulou, Dimitriadis, & Psyrri, 2015; Goldgar et al., 2011; Apostolou & Fostira, 2013; Cybulski et al., 2004; Bell et al., 1999; Vahteristo et al., 2001; Vahteristo et al., 2002; Cybulski et al., 2011; Xia et al., 2006; Reid et al., 2007; Rahman et al., 2007; Antoniou et al., 2014; Southey et al., 2016; Okur & Chung, 2017; Easton et al., 2015). The lifetime risk for breast cancer in a woman carrying a mutation in *ATM*, *CHEK2*, or *PALB2* is estimated to be between 20-60% depending on factors such as the gene in consideration, specific pathogenic variant identified, and family history of breast cancer (Apostolou & Fostira, 2013; Friedrichsen, Malone, Doody, Daling, and Ostrander, 2004; Iniesta et al., 2010; Kuusisto, Bebel, Vihinen, Schleutker & Sallinen, 2011; Easton et al., 2015). For example, the *CHEK2* pathogenic variant, c.110delC is considered to confer a higher risk of breast cancer (The CHEK2 Breast Cancer Case-Control Consortium, 2004; Iniesta et al., 2010; Schmidt et al., 2016).

Family history has been considered to be a significant modifier of breast cancer risk in MPBCSG mutation carriers. One study of women with truncating variants in *CHEK2* estimated the lifetime risk of breast cancer to be 20% for a woman with no affected relative, 28% for a woman with an affected second-degree relative, 34% for a woman with an affected first-degree relative, and 44% for a woman with affected first- and second-degree relatives (Cybulski et al., 2011). For *PALB2* mutation carriers, the

NCCN quotes a breast cancer risk to age 70 of 33% for individuals with no first-degree relatives with breast cancer, compared to 58% for individuals with two first-degree relatives (Antoniou et al., 2014). Another study mentioned in the NCCN guidelines demonstrated a lower 10-year survival rate associated with *PALB2* mutation carriers who have breast cancer (Cybulski et al., 2015).

In 2014, the NCCN added ATM, CHEK2, and PALB2 as new criteria for screening breast MRI (Kurian et a., 2017). The NCCN clinical practice guidelines for *ATM*, *CHEK2*, and *PALB2* mutation carriers are fewer and less detailed than the recommendations for individuals identified to carry mutations in high-penetrance breast cancer susceptibility genes. Currently, the NCCN breast cancer screening guidelines for women identified to carry a mutation include annual mammogram with consideration of tomosynthesis and breast MRI with contrast beginning at age 30 for *PALB2* mutation carriers and at age 40 for *CHEK2* and *ATM* mutation carriers. The NCCN states that evidence is insufficient to recommend risk-reducing mastectomy (RRM) and advises providers to manage risk based upon family history (NCCN, 2019).

To date, no study has investigated approaches to genetic counseling regarding moderate-penetrance breast cancer susceptibility genes. It is unknown how consistently genetic counselors follow the NCCN guidelines when discussing management recommendations with patients who test positive for MPBCSG mutations. In addition, the attitudes of genetic counselors toward providing genetic counseling regarding MPBCSGs remains unclear. In this study, we surveyed genetic counselors in order to evaluate approaches to providing genetic counseling regarding *ATM*, *CHEK2*, and *PALB2*. We specifically investigated counselor attitudes toward the NCCN guidelines and the influence of personal and family breast cancer history on the utilization of NCCN guidelines to provide genetic counseling about *ATM*, *CHEK2*, and *PALB2*. Given the increasing prevalence of the use of multi-gene panels to test for these types of mutations, it is important to evaluate trends in the field of genetic counseling regarding *ATM*, *CHEK2*, and *PALB2*.

We hypothesized that as personal and family history of breast cancer increased in severity, that participants may exceed what is recommended by the NCCN guidelines for individuals with MPBCSG mutations. We also hypothesized that because *PALB2* has been postulated as a high-penetrance breast cancer susceptibility gene, there may be an increased tendency to exceed NCCN recommendations in these cases.

Methods

Participants and Procedures

Exempt status for this study was granted by the Sarah Lawrence College Institutional Review Board. The survey was distributed via the National Society of Genetic Counselors (NSGC) email blast to an estimated 3,300 genetic counselors practicing in the United States and Canada. Board-certified genetic counselors providing cancer genetic counseling were eligible to participate in the study. A total of 103 genetic counselors consented to participate in the survey, and 93 genetic counselors completed the survey. 91 out of 93 responses were included in our data set.

Responses of individuals who did not complete the survey in full were not included in our data analysis. The additional *CHEK2* personal/family history scenario including affected first- and second-degree relatives was removed from our data set in order to be consistent in our analysis among genes and because there were no differences in responses between the two scenarios which included a family history of breast cancer. Because just 2 participants out of 91 indicated that they would recommend less than the NCCN guidelines for just 1-2 scenarios, they were removed from our data set. The data regarding the severity of gene variants was not analyzed and may be used in a future study.

Instrumentation

An online, anonymous survey was created and distributed using Survey Monkey (www.surveymonkey.com). The survey included a consent form followed by 44 questions: four multiple choice questions regarding demographics; six multiple choice questions regarding attitudes towards counseling regarding *ATM*, *CHEK2*, and *PALB2*; ten questions in which counselors indicated how they

would manage a case after reviewing a pedigree, eight multiple choice questions about perceived severity of *ATM*, *CHEK2*, and *PALB2* variants, and four spaces to provide additional comments. Pedigrees were designed with Progeny.

A description of the ten questions in which counselors indicated how they would manage a case regarding *ATM*, *CHEK2*, and *PALB2* is displayed in Table 1. For each of these questions, there were three personal/family history scenarios: 1) no family history of breast cancer, 2) personal history of breast cancer only, and 3) personal and family history of breast cancer. For the personal and family history scenario, the affected relative was a 68-year-old mother with breast cancer diagnosed at age 52. For all pedigrees, the proband was a 40-year-old woman with a mutation in either *ATM*, *CHEK2*, or *PALB2*.For *CHEK2*, the personal/family history scenarios were expanded to include an additional scenario including a personal history of breast cancer and a family history of breast cancer in a first degree relative and a second degree relative. The second degree relative was a maternal aunt in her 60s diagnosed with breast cancer at age 60. None of the relatives in any scenario had genetic testing results. For all questions of this type, genetic counselors were able to review the NCCN guidelines (NCCN Clinical Practice Guidelines in Oncology: Genetic/Familial High-Risk Assessment: Breast and Ovarian) for an individual with the gene mutation in consideration and had three answer choices: 1) I would recommend less than what is recommended by the NCCN. 2) I would follow the NCCN guidelines. 3) I would recommend more than what is recommended by the NCCN. Participants were asked to comment to provide detail if they said they would recommend less or recommend more.

Table 1. Descriptions of survey questions in which participants were asked to analyze pedigrees and provide information about how they would manage each case.

Question	Gene mutation in proband	NCCN Guideline (v.2.2019)	Personal/family history scenario	Answer choices
1	*ATM*	*Screening:* Annual mammogram with consideration of tomosynthesis and consider breast MRI with contrast starting at **age 40.** *Risk-reducing mastectomy*: Evidence insufficient, manage based on family history.	No family history	1. I would recommend less than what is recommended by the NCCN (Please comment). 2. I would follow the NCCN guidelines. 3. I would recommend more than what is recommended by the NCCN (Please comment).
2			Personal history only	
3			Personal and family history	
4	*PALB2*	*Screening:* Annual mammogram with consideration of tomosynthesis and consider breast MRI with contrast starting at **age 30.** *Risk-reducing mastectomy*: Evidence insufficient, manage based on family history.	No family history	
5			Personal history only	
6			Personal and family history	
7	*CHEK2* truncating /frameshift	*Screening:* Annual mammogram with consideration of tomosynthesis and consider breast MRI with contrast starting at **age 40.** *Risk-reducing mastectomy*: Evidence insufficient, manage based on family history.	No family history	
8			Personal history only	
9			Personal and family history (1 FDR*)	
10			Personal and family history (1 FDRand1 SDR)	

*FDR = first-degree relative, SDR = second-degree relative

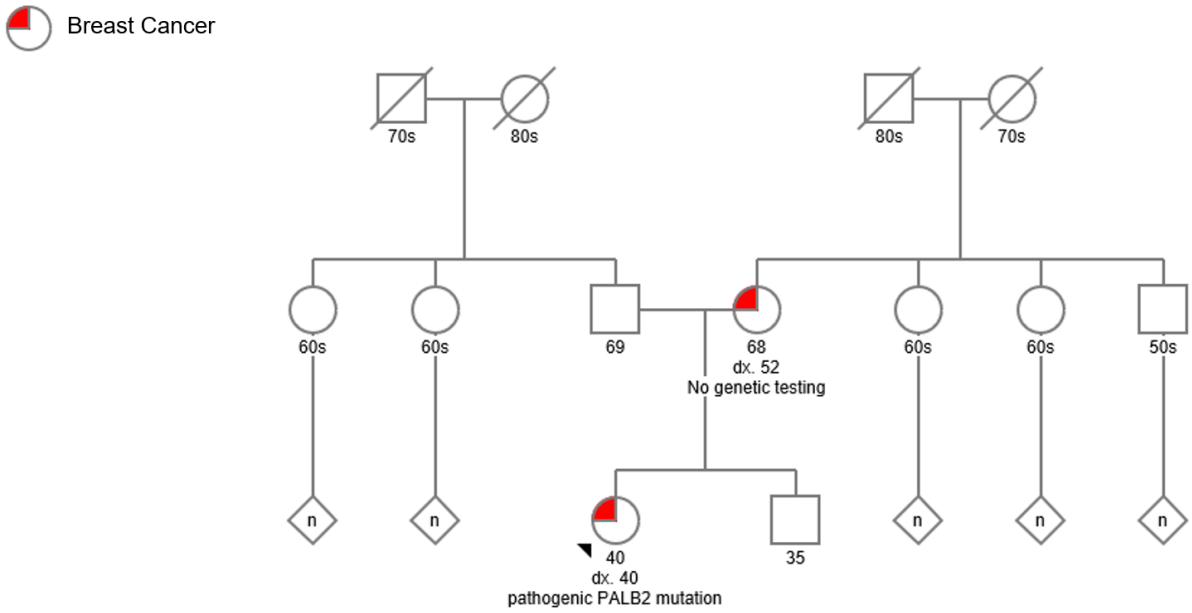

Figure 1. A sample pedigree utilized for the survey. Genetic counselors were asked to review the NCCN guidelines for an individual with a *PALB2* mutation, in this case, and decide whether they would recommend less than the guidelines, follow the guidelines, or recommend more than the guidelines.

Data Analysis

Statistical analyses were completed using SPSS version 1.0.0.1131. We conducted 1) a paired t-test to determine differences in recommendation by gene (*ATM*, *CHEK2*, and *PALB2*) and 2) a paired t-test to determine differences in recommendation by family history (no family history, personal history only, and personal and family history).

We analyzed differences in genetic counseling among the three MPBCSGs and among the three personal/family history scenarios separately. An example of how responses were scored is displayed in Table 2 and Table 3. To analyze differences in genetic counselor recommendations among genes, each participant was given a score across their responses for each gene. They were given a 1 if they ever recommend more than the NCCN guidelines in any scenario for each gene, and they were given a 0 if

they always indicated that they would follow the NCCN guidelines across all scenarios. To analyze differences in genetic counselor recommendations among personal/family history scenarios, participants were scored the same way, but across their responses for each personal/family history scenario.

Table 2. Sample of scoring system used to determine differences in genetic counseling recommendations among genes for one participant's responses.

ATM	No family history	(Follow guidelines)
	Personal history only	(Follow guidelines)
	Personal and family history	(Follow guidelines)
	Summary score	**0**
PALB2	No family history	(Follow guidelines)
	Personal history only	(Follow guidelines)
	Personal and family history	(Recommend more)
	Summary score	**1**
CHEK2	No family history	(Follow guidelines)
	Personal history only	(Recommend more)
	Personal and family history	(Recommend more)
	Summary score	**1**

Table 3. Sample of scoring system used to determine differences in genetic counseling recommendations among personal/family history scenarios for one participant's responses.

No family history	*ATM*	(Follow guidelines)
	CHEK2	(Follow guidelines)
	PALB2	(Follow guidelines)
	Summary score	**0**
Personal history only	*ATM*	(Follow guidelines)
	CHEK2	(Recommend more)
	PALB2	(Follow guidelines)
	Summary score	**1**
Personal and family history	*ATM*	(Recommend more)
	CHEK2	(Recommend more)
	PALB2	(Recommend more)
	Summary score	**1**

Results

Sample Demographics

Participant demographics are reported in Table 4. The majority of genetic counselors who participated in the survey were cancer genetic counselors with less than 6 years of experience. The demographics of the study participants are different from the demographics of the genetic counseling field as a whole based on the 2019 Professional Status Survey (PSS) (www.nsgc.org). The sample population had more respondents who worked in the cancer specialty than is reported in the PSS, as these individuals were part of the target population. In contrast, NSGC region demographics were largely representative of data from the PSS.

Table 4. Participant demographics.

		Survey respondents *n* (%)
Primary specialty	Cancer genetics	86.02
	Prenatal genetics	6.45
	Pediatric genetics	2.15
	Other[a]	5.38
Years practicing	0-3 years	48.39
	3-6 years	23.66
	6-9 years	11.83
	9+ years	16.13
Years of experience in cancer genetic counseling specialty	None	1.08
	0-3 years	55.91
	3-6 years	17.20
	6-9 years	15.05
	9+ years	10.75
NSGC Region	Region 1 (CT, MA, ME, NH, RI, VT, CN Maritime Provinces)	9.68
	Region 2 (DC, DE, MD, NJ, NY, PA, VA, WV, PR, VI, Quebec)	27.96
	Region 3 (AL, FL, GA, KY, LA, MS, NC, SC, TN)	10.75
	Region 4 (AR, IA, IL, IN, KS, MI, MN, MO, ND, NE, OH, OK, SD, WI, Ontario)	24.73
	Region 5 (AZ, CO, MT, NM, TX, UT, WY, Alberta, Manitoba, Saskatchewan)	13.98
	Region 6 (AK, CA, HI, ID, NV, OR, WA, British Columbia, Yukon)	12.90

[a]Other included cardiovascular, administrative, education, and general specialties

Genetic Counselor Attitudes

The majority of genetic counselors reported that they were comfortable to very comfortable providing genetic counseling regarding *ATM*, *CHEK2*, and *PALB2* (Figure 2). Almost all participants (98.91%) reported that they frequently or always utilize the NCCN guidelines, and 100% of participants reported that the NCCN guidelines are at least somewhat helpful when providing genetic counseling regarding *ATM*, *CHEK2*, and *PALB2.* When asked about the extent to which they felt the NCCN guidelines for *ATM*, *CHEK2*, and *PALB2* should be changed, 26.88% of participants reported that no edits were necessary in their opinion, while 73.12% of participants indicated that they felt the guidelines should be edited to contain more information and be more specific.

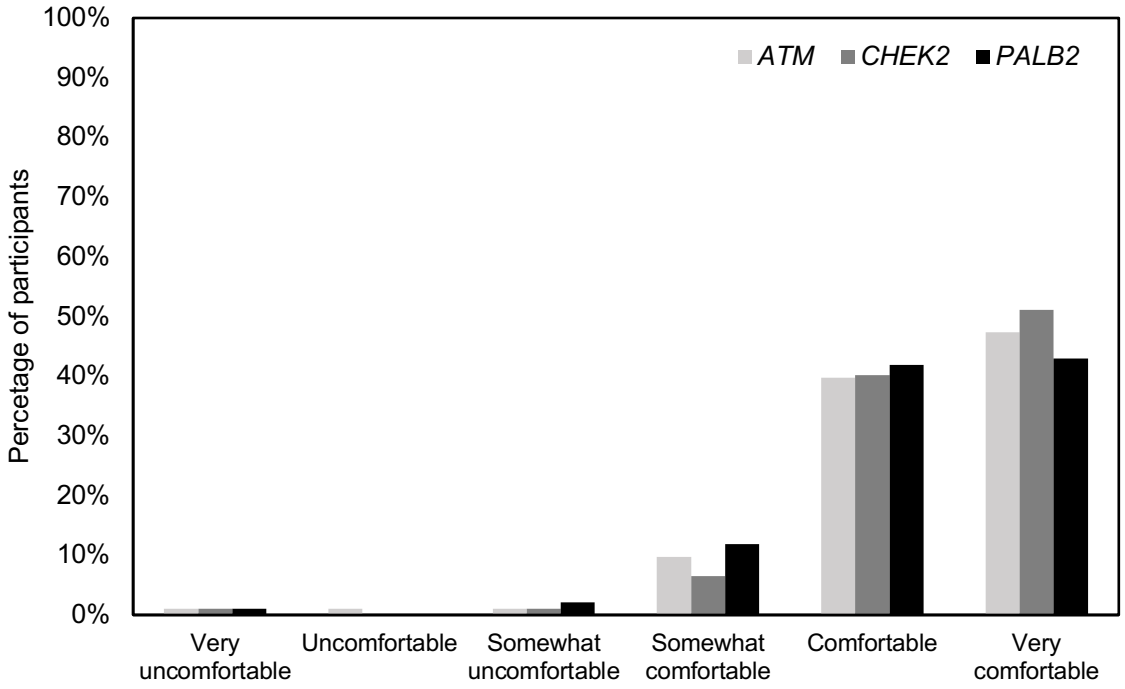

Figure 2. Participant comfortability with providing genetic counseling regarding *ATM*, *CHEK2*, and *PALB2*.

Genetic Counselor Recommendations

Personal/family history was found to be a significant predictor of genetic counselor recommendations regarding *ATM*, *PALB2*, and *CHEK2*, as more genetic counselors tended to indicate that they would recommend more than the guidelines as personal/family history severity increased (Figure 3A). There was a significant difference in the recommendations for no family history and personal history only ($M=-0.21978$, $SD=0.41639$, $t=-5.035$, $p<0.001$) as well as for no family history and personal and family history ($M=-0.24176$, $SD=0.45560$, $t=-5.062$, $p<0.001$). There was no significant difference between personal history only and personal and family history ($M=-0.02198$, $SD=0.20966$, $t=-1.000$, $p=0.320$). The gene in which the proband had a mutation was not found to be a significant predictor of genetic counselor recommendation (Figure 3B). There were no significant differences between *ATM* and *PALB2* ($M=-0.03297$, $SD=0.31449$, $t=-1.000$, $p=0.320$), *CHEK2* and *PALB2* ($M=-0.04396$, $SD=0.29485$, $t=-1.422$, $p=0.158$), or *ATM* and *CHEK2* ($M=0.01099$, $SD=0.018224$, $t=0.575$, $p=0.567$). Despite these findings, the majority of genetic counselors indicated that they would follow the NCCN guidelines across all scenarios.

For those who recommended more than the guidelines for individuals with no family history who tested positive for a MPBCSG mutation, many felt that it was reasonable to recommend increased screening (i.e., tomosynthesis and breast MRI with contrast) along with risk-reducing mastectomy or bilateral mastectomy even though the NCCN guidelines state that evidence is insufficient. Others said that they would discuss the increased screening and option of risk-reducing mastectomy with the patient even though they personally felt that the NCCN guidelines for management were unnecessary or unjustifiable. Also, many participants said that they would engage the patient in a discussion about the difference in evidence for risk-reducing mastectomy between individuals with high-penetrance breast cancer susceptibility gene mutations (i.e., *BRCA1/2*) and individuals with mutations in MPBCSGs. Additionally, some participants said that they would utilize risk models (i.e., BOADICEA, etc.) to help assess risk and

recommendations for breast MRI. Others said they would refer the patient to a breast surgeon to discuss options for surgical management.

For those who recommended more than the NCCN for individuals with a personal history of breast cancer who tested positive for a MPBCSG mutation, many said that they would recommend risk-reducing mastectomy or bilateral risk-reducing mastectomy, particularly in individuals with a *PALB2* mutation due to increased risk of contralateral breast cancer. The patient's age of diagnosis was particularly concerning to participants who said they would recommend risk-reducing mastectomy. Many also said that they would recommend screening for breast cancer 5-10 years earlier than the age of diagnosis of the proband for female family members. A few participants noted the importance of assessing patient mental health while discussing the option of risk-reducing mastectomy. Others indicated that they understood that the patient may already have had surgeries and treatments for breast cancer and would leave the discussion of management recommendations up to the patient's doctors. Still, some said that they would discuss the difference in evidence for risk-reducing mastectomy between individuals with high-penetrance breast cancer susceptibility gene mutations (i.e., *BRCA1/2*) and individuals with mutations in MPBCSGs. Furthermore, others said that they would prepare the patient for a discussion about risk-reducing mastectomy with a breast surgeon, but highlight that evidence is insufficient for risk-reducing mastectomy according to the NCCN guidelines.

For those who recommended more than the NCCN for individuals with a personal history and family history of breast cancer who tested positive for a MPBCSG mutation, the reasons for recommending more were the same as in the situation where the individual had only a personal history of breast cancer. In addition to those recommendations, some participants said that they would offer genetic testing for the affected relative. Others said they would discuss the option of pancreatic cancer screening in individuals with a *PALB2* mutation.

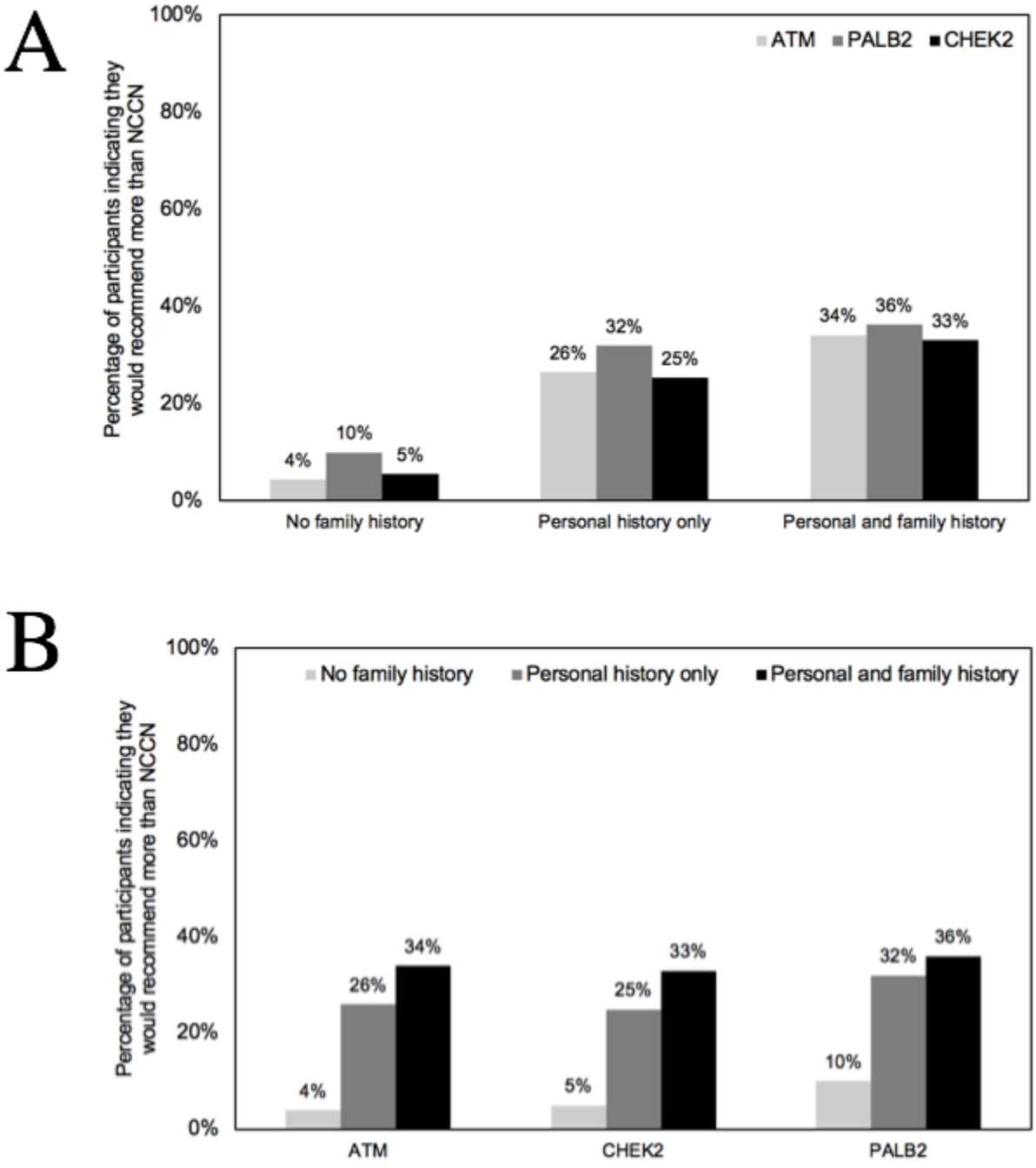

Figure 3. Percentage of participants indicating that they would recommend more than the NCCN guidelines. (A) Differences among personal/family history scenarios for each gene. (B) Differences among genes for each personal/family history scenario.

Discussion

Findings

Our study aim was to investigate genetic counseling approaches to moderate-penetrance breast cancer susceptibility genes (MPBCSGs). Overall, our study elucidated important trends in the field. The majority of participants indicated that they would follow the guidelines independently of gene mutation and/or personal and family history of breast cancer. However, a number of participants exceeded NCCN recommendations in cases where a patient with a MPBCSG mutation had a personal and/or personal and family history of breast cancer.

Participants reported a high level of comfort with providing genetic counseling services regarding *ATM*, *CHEK2*, and *PALB2*. All participants indicated a high level of usage of the NCCN guidelines, and almost all participants said that the guidelines were at least somewhat helpful when providing genetic counseling regarding MPBCSGs. Despite these findings, the majority of participants reported that they felt the NCCN guidelines for *ATM*, *PALB2*, and *CHEK2* should be edited to contain more information and be more specific.

Despite that the majority of participants indicated that they would follow the NCCN guidelines across scenarios, the data indicate that personal/family history of breast cancer is a significant predictor of whether genetic counselors will recommend more than what is recommended by the NCCN guidelines when providing genetic counseling regarding *ATM*, *PALB2*, and *CHEK2*. In contrast, the specific gene in consideration was not a significant predictor of genetic counseling recommendations. The results demonstrate that participants did not consider the gene in question as highly as the personal/family history scenario in question (Figure 3A). For counselors that said they would recommend more than the NCCN guidelines, additional recommendations included consideration of risk-reducing mastectomy, bilateral risk-reducing mastectomy, increased screening for relatives, a referral to a breast surgeon, and use of risk models to clarify breast MRI recommendations.

We hypothesized that as personal and family history of breast cancer increased in severity, that participants may include recommendations that exceed the NCCN guidelines for individuals with MPBCSG mutations. This hypothesis was support by our data. We also hypothesized that because *PALB2* has been postulated as a high-penetrance breast cancer susceptibility gene, there would be an increased tendency to exceed NCCN recommendations in these cases (Southey et al., 2016; Easton et al., 2015; Antoniou et al., 2014). While it seemed that more genetic counselors tended to say they would strongly recommend consideration of bilateral risk-reducing mastectomy for individuals with *PALB2* mutations rather than for individuals with other gene mutations, the difference in genetic counseling recommendation among genes was not statistically significant.

While the small sample size may affect the ability to detect significance, these results demonstrate that genetic counselors weigh personal and family history of breast cancer more heavily than the specific gene in question when making recommendations for carriers of *ATM*, *PALB2*, and *CHEK2* mutations. Furthermore, our data illustrate that genetic counselors rely on the NCCN guidelines to a great extent when counseling about MPBCSGs, but that in a number of cases, exceed NCCN recommendations. Overall, our study shows that there is a high level of ambiguity regarding MPBCSG cases.

Practice Implications

The study illustrates the current trends in risk counseling regarding *ATM*, *CHEK2*, and *PALB2*. The study demonstrated that with an increase in personal and family history of breast cancer, many genetic counselors exceed NCCN guidelines, which involves discussion and recommendation about risk-reducing mastectomy and other interventions. However, we did observe a difference in recommendations among our respondents. In the future, this research may provoke the formation of a focus group in which genetic counselors may engage with each other and have conversations about risk assessment for MPBCSGs on a larger platform.

A significant barrier to having consistent recommendations is the unavailability of risk data for MPBCSGs. One of the ways to overcome this challenge is for clinics and laboratories to share cancer

phenotypes seen in patients and their families for particular variants in MPBCSGs. This will consequently help clinical genetic counselors provide consistent risk counseling and we will hopefully have clearer risk-management guidelines for MPBCSGs in future.

Study Limitations

This study is limited by the fact that the survey was conducted only among genetic counselors who are members of the NSGC and does not include other non-NSGC member genetic counselors, making the results non-generalizable. Although the survey was aimed at all genetic counselors who are members of the National Society of Genetic Counselors, the response rate was low (2.82%, 93 out of approximately 3,300 genetic counselors). We also observed a high number of participants who had between 0 and 6 years of experience, which may not reflect the demographics of the field and may have skewed our data set.

Additionally, our survey does not take into account that patients with a personal history of breast cancer may have had a risk-reducing mastectomy already or may have been currently receiving treatment; in these cases, it may be inappropriate for a genetic counselor to make management recommendations based on the NCCN guidelines. Furthermore, the language for certain questions asked in the survey could have been more descriptive. For example, using the phrase “pathogenic variant” instead of “mutation” may have clarified our questions. We took note that a few of our respondents had difficulty grasping what “more than what is recommended by the NCCN” implied. This might have affected the readability and consequently the choice of answer by some participants.

Furthermore, our data analysis was limited by the use of the SPSS software and the way in which we asked our questions. Because we always asked genetic counselors what they would do in the context of each gene and each personal/family history scenario, there was no way to decouple the two predictors. Furthermore, in order to analyze data across genes, we had to remove the fourth personal/family history scenario from the *CHEK2* questions. However, there were no participants who had a different response for the third personal/family history scenario (personal and family history of breast cancer in a first-

degree relative) than for the fourth scenario (personal and family history of breast cancer in one first-degree relative and one second-degree relative). Because we needed to transform our data into a binomial response data set in order to work with SPSS, we were unable to analyze differences in the number of scenarios in which a participant stated that they would recommend more than the guidelines. If they ever recommended more in any scenario, they were assigned a 1, and if they always followed the guidelines, they were assigned a 0 (Table 2, Table 3). If we were instead able to give scores for each time a participant recommended more, (i.e., a score of 2 if the participant recommended more in both the personal history only scenario and the personal and family history scenario), then we would have been able to enhance the depth of our analysis.

Research Recommendations

In this study, we sought to identify the extent to which genetic counselors follow the NCCN guidelines in counseling patients that are positive for a known pathogenic variant in *ATM*, *CHEK2*, or *PALB2*. Future research could include a larger sample population that provides a more generalizable representation from the majority of genetic counseling community. The data could also be used to infer if the counseling recommendation is dependent on the years of experience in cancer genetic counseling practice.

Furthermore, our pedigree questions included patients that were either negative for or positive for a personal history of breast cancer. It might be more beneficial to understand the approach of counseling towards an unaffected patient with an affected first-degree relative, both carrying a pathogenic variant in a MPBCSG.

Currently, the NCCN guidelines state that genetic counselors should manage individuals who test positive for mutations in MPBCSGs based on family history (NCCN, 2019). Given the plethora of variability in family history, it may be helpful to include specific recommendations based on degrees of relationship, number of family members affected with cancer, cancer diagnoses and ages at diagnosis, etc. in order to better provide counseling regarding surgical intervention.

Finally, this research survey included questions about genetic counselors' risk-assessment for specific known pathogenic variants in the MPBCSGs, which were not included in the final results. As new data about these variants emerges, it will be useful to study if genetic counselors base their risk assessment and recommendations on specific variants within MPBCSGs.

Conclusions

Our study is the first to report trends in the field regarding approaches to providing genetic counseling regarding *ATM*, *CHEK2*, and *PALB2*. The results demonstrate that personal/family history of breast cancer is a significant predictor of genetic counselor recommendation. A number of genetic counselors' recommendations exceeded NCCN guidelines in cases where a person with a mutation had a personal history or personal and family history of breast cancer. The moderate-penetrance gene in question was not a significant predictor of genetic counseling recommendation. Despite these findings, the majority of participants indicated that they would follow the NCCN guidelines in across scenarios. Overall, the study highlights the ambiguity in genetic counseling regarding *ATM*, *CHEK2*, and *PALB2* and suggests that it may be helpful for the NCCN to provide more direction for genetic counseling in these types of cases.

Acknowledgments

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in2000 (5). Informed consent was obtained from all patients for being included in the study.

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