ARTICLE | Genetics inMedicine

Assessing relatives' readiness for hereditary cancer cascade genetic testing

Erica M. Bednar, MS, MPH[1,2], Charlotte C. Sun, DrPH[3], Sheryl McCurdy, PhD[4] and Sally W. Vernon, PhD[4]

Purpose: To explore the readiness of living, untested first-degree relatives (FDRs) to have cascade genetic testing (CGT) for a hereditary predisposition to cancer.

Methods: Adults with a hereditary predisposition to cancer completed an anonymous, online survey about their genetic testing and their FDRs' vital status, awareness of the variant, uptake of CGT, and readiness for CGT among living, untested FDRs using transtheoretical model stages of change.

Results: One hundred fifty participants completed the survey and reported 825 FDRs. Overall, 70.3% of FDRs were reportedly aware of the variant and 30.5% had completed CGT. Siblings had higher rates of awareness and CGT than parents or children ($p < 0.001$). Relatives' sex was associated with awareness and CGT; mothers were aware and had CGT at higher rates than fathers ($p = 0.049$ and $p < 0.001$), sisters were aware and had CGT at higher rates than brothers ($p = 0.041$ and $p = 0.002$), and daughters had higher rates of awareness than sons ($p = 0.038$). Of 340 living, untested FDRs, 79.4% were in the precontemplation stage of change, with no difference by relatives' sex or relationship to the participant.

Conclusions: Most living, untested FDRs were in precontemplation stage, indicating they are not ready or planning to have CGT within the next six months.

Genetics in Medicine (2020) https://doi.org/10.1038/s41436-019-0735-3

Keywords: hereditary cancer; cascade testing; genetic testing; transtheoretical model; stage of change

INTRODUCTION

Cascade genetic testing is the systematic process of providing genetic counseling and genetic testing to at-risk blood relatives after a germline pathogenic variant is identified in a family member.[1,2] In the setting of hereditary cancer and tumor predisposition syndromes, cascade genetic testing can provide relatives with information about their variant status, the probability for their children to inherit a predisposition to cancer, estimates of risks to develop cancer or tumors, and which cancer screening and risk reduction strategies are recommended. The National Comprehensive Cancer Network, the American College of Obstetricians and Gynecologists, the Society of Gynecologic Oncology, the Evaluation of Genomic Applications in Practice and Prevention, and the National Cancer Moonshot Blue Ribbon Panel recommend cascade genetic testing for relatives after the identification of a pathogenic or likely pathogenic cancer predisposition variant in a family member.[1,3–7]

Although cascade genetic testing provides important information to relatives and several organizations recommend testing, the uptake of cascade genetic testing within families with hereditary predispositions to cancer is lacking. Most studies of cascade genetic testing for hereditary cancer predispositions have focused on families with hereditary breast and ovarian cancer (HBOC) and Lynch syndrome, which are due to germline variants in *BRCA1*, *BRCA2*, and *MLH1*, *MSH2*, *EPCAM*, *MSH6*, and *PMS2*, respectively. In families with HBOC or Lynch syndrome, relatives' awareness of the familial variant is high (60% to 90% are aware), but rates of cascade genetic testing completion are lower, with rates of testing uptake ranging from 8% to 97%, with most studies reporting rates between 30% and 60%.[8,9] Cascade genetic testing patterns in families with moderate-penetrant gene variants, increasingly identified on multigene panel genetic testing, have not been characterized.

Behavioral science theory can aid in understanding the role of determinants, barriers, and facilitators of cascade genetic testing within families. The transtheoretical model is a behavioral science theory that provides a framework for understanding how people change health behaviors over time, and includes six stages of change through which an individual may progress when changing a health behavior.[10] The stages of change include precontemplation (no intention to take ction in the next six months), contemplation (intention to act within the next six months), preparation (intention to act within the next 30 days), action (behavior changed for less

[1]Clinical Cancer Genetics, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Cancer Prevention and Control Platform, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [3]Gynecologic Oncology and Reproductive Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [4]Department of Health Promotion and Behavioral Sciences, The University of Texas Health Science Center at Houston School of Public Health, Houston, TX, USA.
Correspondence: Erica M. Bednar (embednar@mdanderson.org)

Submitted 10 September 2019; revised 9 December 2019; accepted: 10 December 2019
Published online: 20 December 2019

than six months), maintenance (behavior changed for more than six months), and termination (no temptation to relapse to prior behavior).[10,11] Research across a variety of health behaviors has identified that, on average, 40% of a population is in precontemplation stage, 40% are in contemplation stage, and 20% are in preparation stage of change.[10] Several studies have used the transtheoretical model to evaluate intention to have genetic counseling and genetic testing among individuals with breast cancer.[12–14] No published studies have assessed at-risk relatives' readiness, or stage of change, to undergo cascade genetic testing for hereditary cancer predisposition. In this study, we applied the transtheoretical model's stages of change to explore the readiness of living, untested first-degree relatives to undergo cascade genetic testing for a hereditary cancer predisposition variant identified in a family member.

MATERIALS AND METHODS

Approval for the conduct of the research study with a waiver of informed consent was obtained from the University of Texas Health Science Center at Houston Institutional Review Board (IRB). Data were collected using an anonymous, online Qualtrics survey. Individuals were eligible to participate if they were at least 18 years of age; resided in the United States; were able to complete a survey in English; reported having a pathogenic or suspected pathogenic variant detected in 1 of 73 autosomal dominantly inherited, adult-onset cancer predisposition genes; and could provide information about at least one blood relative. Genes were selected for inclusion in the study by review of several US laboratories' clinical genetic testing offerings in early 2018, and autosomal dominant inheritance and adult-onset cancer and tumor risks were assessed by reviewing GeneReviews and OMIM entries.[15,16] Participant recruitment occurred between 1 August 2018 and 1 March 2019. The survey opportunity was shared through a study Twitter account and through social media, newsletters, and discussion forums of various hereditary cancer patient support and advocacy organizations who agreed to distribute the research opportunity. Participants could enter a raffle for one of four $25 gift cards upon completion of the survey.

The survey collected participants' demographic information (age, biologic sex, race, ethnicity, state of residence, and if they had a cancer diagnosis), and genetic testing information (relevant gene, year of testing, health-care providers who ordered the genetic testing and who helped to explain the results, and if the variant was confirmed or suspected to be maternally or paternally inherited). Participants provided information about their first-degree relatives including the total count of each relative (parents, siblings, and children), each relative's vital status, participant report of relatives' awareness of the variant in the family, and if the relative was reported to have had cascade genetic testing. Individuals who completed cascade testing were in the "action" stage of the transtheoretical model. Participants reported their living, untested first-degree relatives' stage of change (cascade genetic testing readiness) by answering, "Which of the following best describes your [mother/father/sister/brother/son/daughter]'s readiness for genetic testing?" The available choices included "[He/She] does not plan to ever have genetic testing," "[He/She] plans to have genetic testing but not in the next 6 months," "[He/She] plans to have testing in the next 6 months," and "[He/She] plans to have genetic testing in the next month." If the relative was reported as planning to never have genetic testing, or planning to have testing but not in the next six months, they were considered to be in precontemplation stage. Relatives who were reportedly planning to have testing in the next six months were in contemplation stage, and relatives reportedly planning to have testing in the next month were in preparation stage. The time frames were selected based on the transtheoretical model's defined stages of change.[10] Participants could skip any survey question not directly tied to eligibility determination.

Descriptive statistics such as frequencies, means, and medians were used to characterize the clinical and demographic variables in the study sample. Proportions and percentages were calculated for first-degree relatives' vital status, awareness of the variant (aware, unaware), cascade genetic testing status (tested, untested), and readiness (planning: contemplation and preparation, not planning: precontemplation) for cascade genetic testing among living, untested first-degree relatives. To assess for potential differences between the relationship to the participant (parent, sibling, or child) and first-degree relatives' awareness, cascade testing status, and readiness by the relative's sex (male or female), we employed McNemar and Friedman tests for comparisons between paired or *n*-group–related samples of categorical variables, and Wilcoxon signed rank tests for comparisons involving paired samples of nonparametric continuous data. Potential associations between participant factors (including age, involvement of a genetics professional during the genetic testing process, year of genetic testing, and gene with variant) and first-degree relatives' awareness and uptake of cascade genetic testing were assessed using the Kruskal–Wallis (*n*-group comparison of nonparametric data) and Mann–Whitney tests (2-group comparison of nonparametric data). Differences in awareness among living, untested first-degree relatives by their relationship type (parent, sibling, or child) were analyzed using a Friedman test. A 2-sided p value of 0.05 was considered statistically significant. Statistical analysis was performed using IBM SPSS version 24.

RESULTS

At the conclusion of study recruitment, 204 individuals initiated a survey, 153 were eligible to participate, and 150 (98.0%) eligible participants completed the survey and were included in analysis. Reasons for response exclusion are outlined in Table 1. Participant demographics are reported in Table 2. Participants were predominantly female (88.0%), white (93.3%), non-Hispanic (92.7%), and more than half (51.3%) reported a personal history of cancer. Nearly half of the participants (48.7%) completed genetic testing recently, between 2017 and 2019. Genes reported to have a pathogenic variant by participants were varied, with the most commonly

Table 1 Participant survey responses and reasons for ineligibility.

	Number of survey responses
Total survey responses received	204
Reasons for survey response exclusion	
No participant age provided	8
No state of residence selected	9
No genetic testing performed	16
No variant found on genetic testing	9
No gene selected	9
No family member information provided	3
Total survey responses included in analysis	150

reported genes including *CHEK2* (28.7%), *BRCA1* and *BRCA2* (23.3%), Lynch syndrome genes (16%), and *SDHB* and *SDHC* (13.3%). Six participants reported variants in genes that, to date, have been associated only with female-specific cancer risks (four *BARD1*, two *BRIP1*), with all other reported genes having cancer and tumor risk implications for men and women. Most participants (82.0%) reported the involvement of a genetics professional (genetic counselor or geneticist) during their genetic testing process (pretest, post-test, or both).

Relatives' awareness of the familial variant

Participants reported 825 first-degree relatives including 296 parents, 283 siblings, and 246 children. Overall, 580 (70.3%) first-degree relatives were reported to be aware of the participant's genetic testing results. The proportions of mothers, fathers, brothers, sisters, sons, and daughters who were reported as aware of the variant, have had cascade genetic testing, and who are living and untested are provided in Table 3. Awareness of the familial variant varied by relatives' sex, with a higher proportion of mothers aware compared with fathers ($p = 0.049$), sisters aware compared with brothers ($p = 0.041$), and daughters aware compared with sons ($p = 0.038$). Awareness also varied by the relative's relationship to the participant, with significantly higher awareness reported for siblings than for parents or children ($p < 0.001$). Relatives' awareness of the variant was not statistically significantly different based on whether the associated variant in the family was in a high penetrant, well-characterized cancer predisposition syndrome (HBOC or Lynch syndrome) or a lesser-studied, rare, or moderate-penetrant gene ($p = 0.870$). The involvement of a genetics professional during the participant's genetic testing process was not significantly associated with awareness in relatives ($p = 0.258$). The time since the participant's genetic testing (recently in 2017–2019 versus prior to 2017) was not associated with relatives' awareness of the variant ($p = 0.345$).

Table 2 Participant demographics and genetic testing characteristics.

Characteristic	*N*	%
Age (years)	Mean: 46.2	Range: 19–78
Sex		
Male	18	12.0
Female	132	88.0
Race		
White	140	93.3
Other race(s)[a]	10	6.7
Ethnicity[b]		
Non-Hispanic	139	92.7
Hispanic	10	6.7
History of cancer diagnosis		
Yes	77	51.3
US state of residence (US Census region)		
South	43	28.7
Northeast	42	28.0
Midwest	33	22.0
West	32	21.3
Gene with variant		
CHEK2	43	28.7
BRCA1	20	13.3
SDHB	16	10.7
BRCA2	15	10.0
PMS2	10	6.7
MSH6	6	4.0
PALB2	5	3.3
ATM	5	3.3
MLH1	4	2.7
MSH2	4	2.7
BARD1	4	2.7
SDHC	4	2.7
BAP1	3	2.0
PTEN	3	2.0
Other[c]	8	5.3
Year of genetic testing		
2007 and prior	5	3.3
2008–2010	10	6.7
2011–2013	14	9.3
2014–2016	48	32.0
2017–2019	73	48.7

[a]Other races included 2 Black/African American, 2 American Indian/Alaska Native, 1 Asian Indian, 1 Chinese, 4 Other.
[b]One person selected "prefer not to answer" and was not included in either Hispanic or Non-Hispanic.
[c]Other genes included 2 *BRIP1*, 2 *AXIN2*, 1 *APC*, 1 *NF1*, 1 *TP53*, and 1 *VHL*.

Relatives' uptake of cascade genetic testing

Of the 825 reported first-degree relatives, 252 (30.5%) were reported to have completed cascade genetic testing. Participants' reported completion of cascade genetic testing varied by relatives' sex for parents and siblings, with a higher proportion of mothers tested compared with fathers ($p < 0.001$) and sisters tested compared with brothers ($p = 0.002$).

Table 3 Relatives' awareness and uptake of cascade genetic testing.

Relation to participant	Total number	Aware of familial variant		Completed cascade genetic testing		Alive, untested	
		n	%	*n*	%	*n*	%
Father	146	77	52.7	17	11.6	55	37.7
Mother	150	93	62.0	48	32.0	39	26.0
Brother	167	120	71.9	46	27.5	67	40.1
Sister	116	107	92.2	76	65.5	27	23.3
Son	132	93	70.5	32	24.2	78	59.1
Daughter	114	90	78.9	33	28.9	74	64.9
Total	825	580	70.3	252	30.5	340	41.2

However, there was no significant difference in cascade genetic testing in daughters compared with sons ($p = 0.178$). Cascade genetic testing also varied by relationship to the participant: siblings had significantly higher rates of cascade genetic testing than parents or children ($p < 0.001$). Cascade genetic testing reported by study participants for their first-degree relatives was higher when participants completed genetic testing prior to 2017 (mean testing rate of 42.5%) compared with those with more recent testing (mean testing rate of 24.3%) ($p = 0.003$). First-degree relatives' cascade genetic testing rates were not significantly different based on the cancer predisposition syndrome (HBOC and Lynch syndrome versus all other genes) ($p = 0.376$), or based on the involvement of a genetics professional in the participant's genetic testing process ($p = 0.751$).

Relatives' readiness for cascade genetic testing

Of the total 340 first-degree relatives who were living and untested, the majority (270, 79.4%), were reported by the study participant to be in the precontemplation stage of change, and were either planning to never have cascade genetic testing or were not planning to have cascade genetic testing in the next six months. Only 23 (6.8%) first-degree relatives were reported to be in the contemplation stage and planning to have cascade genetic testing in the next six months, and 15 (4.4%) were reported to be in the preparation stage and planning to have cascade genetic testing in the next month. The remaining 32 living, untested first-degree relatives had no status reported by the study participant. The distribution of living, untested relatives by their reported stage of change status are found in Table 4.

Unlike awareness and cascade genetic testing status, there were no statistically significant differences in readiness for cascade genetic testing by sex among living, untested relatives when comparing male first-degree relatives with female first-degree relatives ($p = 0.892$), or when comparing mothers and fathers ($p = 0.317$), brothers and sisters ($p = 0.655$), or sons and daughters ($p = 0.180$). There was also no statistically significant difference in readiness by the relatives' relationship to the participant: living, untested parents, siblings, and children were all primarily in the precontemplation stage ($p = 0.646$).

Living, untested children in the precontemplation stage were often categorized as planning to pursue cascade genetic testing but not within the next six months (61.2%), whereas most parents and siblings in the precontemplation stage were planning to never have cascade genetic testing (78.7% and 50.0%, respectively). One potential reason for this difference could be relatives' age, since the age of a child is a relevant consideration in the recommendation of cascade genetic testing for adult-onset cancer predisposition. We evaluated this consideration from the perspective of participant age, and found that participants who were under age 50 had more untested children compared with participants age 50 or older ($p = 0.007$), which suggests that younger participants may have young children who may not be old enough to be recommended to pursue cascade genetic testing.

The readiness of participants' parents to undergo cascade genetic testing may also depend on whether the variant is maternally or paternally inherited. In some families, the inheritance of a variant is confirmed by the results of cascade genetic testing in a parent or a more distant (second or third degree) relative, the inheritance may be suspected based on family history of cancer, or the inheritance may be unknown due to lack of family history of cancer and lack of cascade genetic testing. Evaluating the relationship between inheritance and the readiness of parents to have cascade genetic testing was complicated by the significantly higher rates of cascade genetic testing among mothers, and the high proportion of living, untested parents in the precontemplation stage in all inheritance scenarios. Among participants who reported that the gene variant was confirmed or likely maternally inherited, 3 of 3 (100%) living and untested mothers, and 26 of 29 (90.0%) living and untested fathers were in the precontemplation stage. Participants who reported that the variant was confirmed or likely paternally inherited had 19 of 20 (95%) living, untested mothers and 10 of 11 (91.0%) living, untested fathers in the precontemplation stage.

Awareness of the variant could affect relatives' readiness for cascade genetic testing; however, most (79.7%) living, untested first-degree relatives were reportedly aware of the variant in the family, which did not vary by relationship (parent, sibling, or child) to the participant ($p = 0.368$). This finding suggests that awareness of the variant was not a major

Table 4 Relatives' readiness to undergo cascade genetic testing.

Relation to participant	Total alive, untested	Transtheoretical model stage of change									
		Precontemplation				Contemplation		Preparation		Not reported	
		Does not plan to ever have testing		Plans to have testing but not in the next 6 months		Plans to have testing in the next 6 months		Plans to have testing in the next month			
		n	%	*n*	%	*n*	%	*n*	%	*n*	%
Father	55	44	80.0	4	7.3	3	5.5	1	1.8	3	5.5
Mother	39	30	76.9	6	15.4	3	7.7	0	0.0	0	0.0
Brother	67	38	56.7	18	26.9	4	6.0	2	3.0	5	7.5
Sister	27	9	33.3	11	40.7	2	7.4	2	7.4	3	11.1
Son	78	10	12.8	44	56.4	2	2.6	6	7.7	16	20.5
Daughter	74	7	9.5	49	66.2	9	12.2	4	5.4	5	6.8
Total	340	138	40.6	132	38.8	23	6.8	15	4.4	32	9.4

factor contributing to the lack of readiness to pursue cascade genetic testing among living, untested relatives.

DISCUSSION

Consistent with prior studies, 70.3% of first-degree relatives were reported to be aware of the hereditary risk for cancer in their family, but only 30.5% were reported to have had completed cascade genetic testing. Also consistent with prior studies, these rates varied by relatives' sex, with female relatives having higher rates of awareness and cascade genetic testing compared with male relatives. There was no statistical difference in first-degree relatives' awareness of the variant based on how recently the participant completed genetic testing, which aligns with studies reporting that individuals communicate their results to close relatives within 48 hours, and up to one month, after receipt of a positive test result.[17,18]

We found that only 11.2% of first-degree relatives who had not completed cascade genetic testing were reported by their family member to be ready and planning to have testing in the next one to six months. Most first-degree relatives were reported to be in the precontemplation stage of change for cascade genetic testing—the transtheoretical model stage of change with the least readiness for action or behavior change. The majority of living, untested first-degree relatives were reported to be aware of the variant, suggesting that this was not a likely cause for the lack of cascade testing readiness. Notably, readiness of relatives to undergo cascade genetic testing did not vary by the relatives' sex or relationship to the participant (parent, sibling, or child).

Lack of cascade genetic testing for hereditary predispositions to cancer among at-risk relatives is a concern among scientists, clinicians, and patient advocates, primarily due to the missed opportunity to reduce cancer incidence and mortality through recommended cancer screening, risk reduction, and use of targeted cancer therapies. Interventions to increase communication of risk information within families and to improve access to genetic testing have had limited or no effects on cascade genetic testing outcomes, have focused predominantly on well-characterized hereditary cancer syndromes (HBOC and Lynch syndrome), and may not translate across settings due to differences in country and state laws, health-care policies, and care delivery infrastructure.[2,19–28] Although environmental barriers to cascade genetic testing in the United States have changed, leading to increased access to genetic counseling and testing, decreased genetic testing costs, improved protections against genetic discrimination through the Genetic Information Nondiscrimination Act, and increased rates of health insurance coverage secondary to the Affordable Care Act, cascade genetic testing rates have not noticeably increased.

The results of this study may guide future efforts to increase rates of cascade genetic testing by encouraging greater consideration of the stages and processes of behavior change and identifying family members who may benefit from cascade genetic testing interventions. For example, sharing of genetic test results and awareness of a variant in a family

occur relatively frequently, and represent an important precursor to cascade genetic testing. However, rates of awareness are consistently lower among male relatives, suggesting that efforts to improve communication within families may not be reaching male relatives effectively, and that communication-focused interventions alone may not significantly influence the cascade genetic testing decision-making and behavior change processes of relatives. Similarly, interventions that provide more accessible genetic counseling and genetic testing to at-risk relatives may benefit the relatives actively seeking cascade genetic testing in the contemplation and preparation stages, which represent only 11% of living, untested relatives in our study. Focusing on increasing accessibility of genetic testing may be unlikely to address the needs of at-risk relatives in the precontemplation stage. Comprehensive, theoretically grounded, and tailored approaches in cascade genetic testing intervention and research program design are needed.

A benefit of using the transtheoretical model to study behavior change is that it incorporates the stage-matched processes of change, the constructs of self-efficacy (the confidence to make a behavior change), and decisional balance (perceived pros and cons of behavior change) throughout an individual's behavior change process.[10] Prior studies of psychosocial factors involved in genetic testing decision-making have consistently identified decisional balance (perceived benefits and perceived barriers and risks) as an important determinant of genetic testing.[29] The transtheoretical model processes of change associated with moving individuals from the precontemplation stage toward the contemplation stage include consciousness raising, environmental reevaluation, and dramatic relief.[10] Consciousness raising includes activities that increase an individual's awareness of the health problem (hereditary cancer predisposition) and the health behavior (cascade genetic testing), the causes of the health problem, the consequences of performing the health behavior, and the treatments and risk reduction options for those with a hereditary cancer predisposition.[10] We found that first-degree relatives have high rates of awareness of the variant in the family; however, it is unknown whether relatives are equally aware of the consequences of cascade genetic testing, treatment and management options for hereditary predisposition to cancer, and other implications of cascade genetic testing for themselves and their family. A second process, environmental reevaluation, includes both cognitive and affective self-assessments about how an individual's behavior impacts others, and how the individual may serve as a role model for others through their behavior and actions.[10] For cascade genetic testing, environmental reevaluation-based interventions may include guided discussion and reflection on family dynamics and support systems, assessing the impact of not having cascade genetic testing on their current or future children, or considering how relatives who have tested positive for the variant or who are undergoing cancer treatment may perceive family members' disinterest in cascade testing. Sharing stories of other families facing similar hereditary cancer predispositions and cascade genetic testing decisions, and how cascade genetic testing has affected relationships between relatives, spouses, and other members of their social network could support the environmental reevaluation process. Finally, dramatic relief is a process to increase emotional experiences associated with behavior change.[10] Interventions using dramatic relief to promote readiness for cascade genetic testing could include personal testimonies or family stories about the emotional benefits (relief of knowing, empowerment to manage one's health, decreased uncertainty) of learning one's variant status and taking action to prevent cancer in themselves and their family. These transtheoretical model constructs and processes of change can be used to design and measure the effect of interventions to promote cascade genetic testing behavior within families, especially among relatives in the precontemplation stage.

Study limitations

To minimize data entry burden and to maintain participant anonymity, the survey was limited in the types and quantity of data collected about participants and relatives. Because the study was anonymous, we were unable to verify the genetic testing results of participants. Additionally, participant demographics included select data points (sex, age, race and ethnicity, US state of residence), and additional characterization of the population (such as education, income, urban or rural location) were not evaluated. The participants in our study may not be representative of families with hereditary cancer predisposition, in part due to the study recruitment strategy that relied on social media platforms, and hereditary cancer awareness and advocacy organizations, that may serve specific populations of individuals with hereditary predisposition to cancer. Recruitment via social media platforms limited the ability to determine the total number of potentially eligible participants approached to participate in the study, because social media activity may reach audiences beyond those of interest to the study.

For relatives, the survey did not collect ages or cancer histories for, evaluate determinants of cascade genetic testing in, or assess whether multiple participants were from the same family. Participants may have erroneously or accidentally misreported information about their relatives' awareness, testing, or readiness status. Family communication patterns, such as the quantity of information shared and the comprehension of information by relatives about the genetic testing result, and measurement of transtheoretical model constructs of self-efficacy and decisional balance, which interact with an individual's movement to different stages of change, were not assessed in this study. Future studies may consider collecting additional data about at-risk relatives, and may investigate pathways for relatives to self-report their own information to ensure greater accuracy of cascade genetic testing status and readiness. However a variety of ethical, legal, and logistical barriers exist that make direct contact with

living, untested at-risk relatives for the purpose of studying determinants and cascade genetic testing status challenging, especially among relatives who are not aware of the hereditary cancer predisposition in the family or those who decline participation in research.[8,28]

Future studies of cascade genetic testing should incorporate behavioral science theories and frameworks to evaluate the interaction of relevant psychosocial constructs, such as decisional balance, self-efficacy, and stage of change over time. Validated instruments exist for the measurement of these variables; however, these instruments have not been adapted and validated in populations with hereditary cancer syndromes, representing an opportunity for collaboration between behavioral scientists and genetics professionals. Future programs seeking to impact cascade genetic testing behaviors should incorporate behavioral science theories and apply frameworks such as intervention mapping in the development of programs.[30] Intervention mapping can help link hypothesized determinants and psychosocial factors to the development of evidence-based interventions and measurement of outcomes.

Given the large proportion of living, untested relatives reported to be in precontemplation stage in our study, future studies should further evaluate the factors involved in the decision to forgo or postpone cascade genetic testing, relatives' perceived importance of each factor in the decision-making process, and the potential for misinformation to influence an individual's decision about cascade genetic testing. Assessment of the information and counseling needs of relatives in the precontemplation stage may aid in the development of appropriate interventions and genetic counseling tools for families to support informed decision-making processes.

ACKNOWLEDGEMENTS

The authors thank all of the individuals who participated in the study by completing a survey. The authors thank Claire Singletary and Georgia Hurst for advising on study feasibility and recruitment approaches, and Gary Chisholm for advising on statistical methods. We thank the following organizations and individuals who agreed to share the research opportunity with their members and social media followers: Minnesota Ovarian Cancer Alliance (MOCA), SHARE, Facing Our Risk of Cancer Empowered (FORCE), OneInForty, Male Breast Cancer Coalition, Triple-Negative Breast Cancer Foundation, Young Previvors, Pheo Para Alliance, the F.A.P. (Familial Adenomatous Polyposis) Facebook group, Christina Lizaso, Georgia Hurst, and followers of the @CascadeStudy on Twitter. This work was supported by National Institutes of Health/National Cancer Institute (NIH/NCI) award number P30CA016672 (Biostatistics Resource Group), and was completed in fulfillment of an MPH thesis (author E.M.B.). The results of this study are not published or currently under consideration for publication anywhere else. The authors affirm that this manuscript is an honest, accurate, and transparent account of the study and that no important aspects of the study have been omitted. All authors contributed substantially to the study concept, data collection, analysis, writing, and approval of the manuscript. The methods and data collection described in this article were approved by the University of Texas Health Science Center at Houston IRB. A waiver of informed consent was granted by the IRB, given the anonymous data collection strategy.

DISCLOSURE

The authors declare no conflicts of interest.

REFERENCES

1. American College of Obstetricians and Gynecologists. Cascade testing: testing women for known hereditary genetic mutations associated with cancer. ACOG Committee Opinion No. 727. Obstet Gynecol. 2018;131:31–34.
2. Caswell-Jin JL, Zimmer AD, Stedden W, et al. Cascade genetic testing of relatives for hereditary cancer risk: results of an online initiative. J Natl Cancer Inst. 2019;111:95–98.
3. National Comprehensive Cancer Network. Clinical practice guidelines in oncology. Genetic/familial high-risk assessment: breast and ovarian. 2018. http://www.nccn.org.
4. National Comprehensive Cancer Network. Clinical practice guidelines in oncology. Genetic/familial high-risk assessment: colorectal. 2018. http://www.nccn.org.
5. Jacks T, Jaffee E, Singer D. Cancer Moonshot Blue Ribbon Panel report. 2016. https://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative/blue-ribbon-panel/blue-ribbon-panel-report-2016.pdf.
6. EGAPP Working Group. Recommendations from the EGAPP Working Group: genetic testing strategies in newly diagnosed individuals with colorectal cancer aimed at reducing morbidity and mortality from Lynch syndrome in relatives. Genet Med. 2009;11:35.
7. Lancaster JM, Powell CB, Chen LM, Richardson DL, Committee SGOCP. Society of Gynecologic Oncology statement on risk assessment for inherited gynecologic cancer predispositions. Gynecol Oncol. 2015;136:3–7.
8. Menko FH, ter Stage JA, van der Kolk LE, et al. The uptake of presymptomatic genetic testing in hereditary breast-ovarian cancer and Lynch syndrome: a systematic review of the literature and implications for clinical practice. Fam Cancer. 2019;18:127–135.
9. Gaff CL, Clarke AJ, Atkinson P, et al. Process and outcome in communication of genetic information within families: a systematic review. Eur J Hum Genet. 2007;15:999.
10. Prochaska JO, Velicer WF. The transtheoretical model of health behavior change. Am J Health Promot. 1997;12:38–48.
11. Prochaska JO, ReddingCA. Evers KE. The transtheoretical model and stages of change. In: Glanz B, Rimer BK, Viswanath K, editors. Health behavior: theory, research, and practice. 5th edition. San Francisco, CA: Jossey-Bass; 2015. p. 125.
12. O'Neill SM, Peters JA, Vogel VG, Feingold E, Rubinstein WS. Referral to cancer genetic counseling: are there stages of readiness? Am J Med Genet C Semin Med Genet. 2006;142C:221–231.
13. Jacobsen PB, Valdimarsdottir HB, Brown KL, Offit K. Decision-making about genetic testing among women at familial risk for breast cancer. Psychosom Med. 1997;59:459–466.
14. Kasting ML, Conley CC, Hoogland AI. et al. A randomized controlled intervention to promote readiness to genetic counseling for breast cancer survivors. Psychooncology. 2019;28:980–988.
15. Adam MP, Ardinger HH, Pagon RA, et al. (eds.) GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993–2019. https://www.ncbi.nlm.nih.gov/books/NBK1116/.
16. Online Mendelian Inheritance in Man (OMIM). Baltimore, MD: Johns Hopkins University; 1998–2019. https://www.ncbi.nlm.nih.gov/omim.
17. Bradbury AR, Patrick-Miller L, Egleston BL, et al. When parents disclose BRCA1/2 test results: their communication and perceptions of offspring response. Cancer. 2012;118:3417–3425.

18. Gaff CL, Collins V, Symes T, Halliday J. Facilitating family communication about predictive genetic testing: probands' perceptions. J Genet Couns. 2005;14:133–140.
19. Montgomery SV, Barsevick AM, Egleston BL, et al. Preparing individuals to communicate genetic test results to their relatives: report of a randomized control trial. Fam Cancer. 2013;12:537–546.
20. Daly MB, Montgomery S, Bingler R, Ruth K. Communicating genetic test results within the family: is it lost in translation? A survey of relatives in the randomized six-step study. Fam Cancer. 2016;15: 697–706.
21. Suthers GK, Armstrong J, McCormack J, Trott D. Letting the family know: balancing ethics and effectiveness when notifying relatives about genetic testing for a familial disorder. J Med Genet. 2006;43:665–670.
22. Hodgson J, Metcalfe S, Gaff C, et al. Outcomes of a randomised controlled trial of a complex genetic counselling intervention to improve family communication. Eur J Hum Genet. 2016;24:356–360.
23. Forrest LE, Burke J, Bacic S, Amor DJ. Increased genetic counseling support improves communication of genetic information in families. Genet Med. 2008;10:167.
24. Kardashian A, Fehniger J, Creasman J, Cheung E, Beattie MS. A pilot study of the Sharing Risk Information Tool (ShaRIT) for families with hereditary breast and ovarian cancer syndrome. Hereditary cancer in clinical practice. 2012;10:4–4.
25. Aktan-Collan K, Haukkala A, Pylvänäinen K, et al. Direct contact in inviting high-risk members of hereditary colon cancer families to genetic counselling and DNA testing. J Med Genet. 2007;44:732–738.
26. McKinnon W, Naud S, Ashikaga T, Colletti R, Wood M. Results of an intervention for individuals and families with BRCA mutations: a model for providing medical updates and psychosocial support following genetic testing. J Genet Couns. 2007;16:433–456.
27. de Geus E, Eijzenga W, Menko FH, et al. Design and feasibility of an intervention to support cancer genetic counselees in informing their at-risk relatives. J Genet Couns. 2016;25:1179–1187.
28. Roberts MC, Dotson WD, DeVore CS, et al. Delivery of cascade screening for hereditary conditions: a scoping review of the literature. Health Affairs. 2018;37:801–808.
29. Sweeny K, Ghane A, Legg AM, Huynh HP, Andrews SE. Predictors of genetic testing decisions: a systematic review and critique of the literature. J Genet Couns. 2014;23:263–288.
30. Bartholomew Eldredge LK, Markham CM, Ruiter RAC, Fernandez ME, Kok G, Parcel GS. Planning health promotion programs: an intervention mapping approach. 4th ed. San Francisco, CA: Jossey-Bass; 2016.