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ARTICLE

Feasibility of an electronic patient-facing cancer family history tool in medically underserved populations

Heather Spencer Feigelson[1,2,*], Kathleen F. Mittendorf[3], Sonia Okuyama[4], Kathryn M. Porter[5], Joanna Bulkley[6], Elizabeth Shuster[7], Katherine P. Anderson[4], Marian J. Gilmore[6], Jamilyn M. Zepp[6], Tia L. Kauffman[7], Nangel M. Lindberg[7], Kristin R. Muessig[6], Cecelia Bellcross[8], Chinedu Ukaegbu[9], Sapna Syngal[10], Michael C. Leo[7], Benjamin S. Wilfond[5,11]; on behalf of the Cancer Health Assessments Reaching Many (CHARM) Study

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ABSTRACT

Purpose: We developed an electronic patient-facing family history collection tool including B-RST 3.0, PREMM$_5$ risk assessments and "limited family knowledge/structure" information designed for primary care settings. We evaluated the tool's performance compared with genetic-counselor-collected information for clinical risk stratification in a population with barriers to access.

Methods: English- or Spanish-speaking patients aged 18 to 49 were invited to participate. Individuals with limited family knowledge or at high or moderate risk based on their responses in the tool were offered genetic testing and counseling. We assessed overall agreement of family history collected in the tool compared with family history collected by the genetic counselors using Krippendorff's alpha (K-alpha). Multivariable logistic regression was used to assess characteristics associated with inaccuracy.

Results: Most people (94%, n = 1711) who interacted with the tool completed it. Those included in the agreement analysis (n = 604) had a median age of 36.3 years, 81.6% were female, and 44.4% were Non-Hispanic White. Both the B-RST 3.0 and PREMM$_5$ had moderate agreement: 69.9% (K-alpha = .40, 95% CI [0.32, 0.47]) and 83.9% (K-alpha = .52, 95% CI [0.43, 0.60]), respectively. Agreement was high (96%) for people with clinically significant risk for one of the hereditary cancer syndromes. For B-RST 3.0, the factors significantly associated with inaccuracy were study site, sex, and race/ethnicity. For PREMM$_5$, age, sex, and education were associated with inaccuracy. Barriers to access were not associated with inaccuracy.

Conclusion: Implementation of this tool could increase identification of individuals at risk for hereditary cancer syndromes, including those with barriers to health care access.

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*Correspondence and requests for materials should be addressed to Heather Spencer Feigelson, Kaiser Permanente Institute for Health Research, Central Support Services, 16601 East Centretech Parkway, Aurora, CO 80011. *Email address:* heather.s.feigelson@kp.org

Affiliations are at the end of the document.

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Introduction

The 2 most common hereditary cancer syndromes, hereditary breast and ovarian cancer syndrome (HBOC) and Lynch syndrome (LS), confer a high lifetime risk of cancer and affect as many as 1 in 200 individuals.[1,2] Diagnosis of these syndromes via genetic testing can reduce cancer morbidity and mortality through early detection, chemoprevention, and prophylactic surgeries. National organizations have recommended cancer family history to be collected in primary care settings to evaluate the patient risk of HBOC and LS.[3,4] Because the collection of detailed family history is time consuming and competes with other health concerns, many at-risk patients remain unidentified.[5] Individuals from underserved groups face additional barriers to hereditary cancer diagnosis; they are less likely to have family history collected or receive referral to genetic services when indicated.[6-11] To address this gap in preventive services, it is necessary to develop strategies that ease the burden on clinicians while also facilitating equitable family history collection and referral to genetics services.

Patient-facing electronic family history collection tools have been shown to improve accuracy and consistency of family history collection and recognition of at-risk patients across a variety of health settings and are acceptable to clinicians and patients.[12-15] Although these tools may reduce barriers to recognition and referral, studies have shown demographic inequities among enrolled participants in terms of completion rates, suggesting that these tools could perpetuate existing disparities.[16,17]

The Cancer Health Assessments Reaching Many (CHARM) study developed a novel, literacy-adapted electronic patient-facing family history tool in Spanish and English using 2 clinically validated clinician-facing modules.[18,19] We evaluated this tool in a population enriched for individuals with lower literacy and lower resources as part of the Clinical Sequencing Evidence-Generating Research consortium.[20] Herein, we describe the completion rate and agreement between the tool completed by participants compared with a genetic-counselor-collected standard. We also examine whether sociodemographic factors are related to inaccuracy of participant reported family history in the tool.

Materials and Methods

Study setting and recruitment

The CHARM study implemented a multimodal intervention to increase access to genetics services in medically underserved populations. The study is described in detail elsewhere.[18,19] Briefly, all English- or Spanish-speaking individuals aged 18 to 49 years enrolled at Kaiser Permanente Northwest (KPNW), an integrated health care system, and Denver Health (DH), a safety-net health care system, were eligible.

To maximize enrollment of participants from medically underserved populations, we focused recruitment at KPNW on 3 clinics with the highest proportion of racial or ethnic minority patients or those living in a census tract with low socioeconomic status (approximately 38% of patients at these clinics). The DH patient population is approximately 69% racial or ethnic minorities, 81% publicly insured or uninsured, and about 21% of adult patients speak Spanish primarily or exclusively.

Informed by prior recruitment experience,[21] DH focused on in-clinic recruitment, direct outreach to patients known to be at high risk, and referrals from providers. KPNW primarily utilized remote recruitment methods (email, text message, postcard, and telephone). Informed consent was obtained electronically. The KPNW IRB approved this study, and all collaborating IRBs ceded to KPNW, except Dana Farber Cancer Institute and Columbia University, who approved the study separately.

Data collection

The family history collection tool ("tool") consisted of 3 modules: 2 validated risk assessment modules, B-RST 3.0 and $PREMM_5$, and a novel "limited family history/structure" module, which was designed in accordance with National Comprehensive Cancer Network guidelines for individuals who had little knowledge about their family history (for example, adoptees).[3,4,22-26] Only those who reported no personal or family history on initial questions or who screened as not at increased risk on the B-RST 3.0 and $PREMM_5$ modules were exposed to the limited family knowledge/structure module. Bilingual staff were available to assist participants in completing the family history assessment if needed. The tool automatically calculated risk from participant input, and all participants were immediately presented a summary of their risk assessment results and next clinical steps. Only those individuals screening at high or moderate risk on the B-RST 3.0, at clinically significant risk ($\geq$2.5%) on the $PREMM_5$, or those having limited family history or structure were invited to receive genetic testing and counseling. Participants then completed a survey of demographic characteristics and 2 validated measures: the 3-item subjective numeracy scale and the BRIEF Health Literacy survey.[27,28]

We characterized participants as having "barriers to access" if they met any of these criteria: (1) Hispanic ethnicity

or a race other than White, (2) residing in a Health Resources and Services Administration-defined medically underserved area, (3) Spanish-language preference for any study assessment, (4) less than high school graduate, (5) income <200% of the federal poverty level, (6) Medicaid insurance or uninsured, and (7) sexual orientation other than heterosexual or gender identity other than cisgender female or male.[29]

Genetic testing and counseling

Participants provided a saliva sample for clinical genomic sequencing. Most test results (91%) were disclosed by study genetic counselors over the telephone; results for a small number of participants with limited family knowledge/structure and no positive findings were returned by mail. During results disclosure phone calls, genetic counselors collected family history, which was then used to compute a second set of B-RST 3.0 and $PREMM_5$ scores for each participant; these scores were used to assess agreement with scores calculated from patient-entered data in the tool.

Statistical analysis

An automated tracking system recorded all participant interactions with the tool, including number of interactions, completion, and time spent. A total of 20 seconds were added to all participant times to account for time to input answers to the first 2 screening questions.

Agreement evaluation was limited to those participants exposed to $PREMM_5$ and B-RST 3.0 risk assessment modules. We assessed overall agreement of family history collected in the tool compared with family history collected by the genetic counselors during results disclosure using Krippendorff's alpha (K-alpha).[30] K-alpha is a measure of interrater agreement that ranges from −1 (perfect disagreement) to 1 (perfect agreement). Compared with other measures of agreement, it can handle any number of raters, missing data, any measurement level (binary, nominal, ordinal, interval, ratio, polar, and circular), and any sample size. B-RST 3.0 scores were assigned a binary categorization of "high risk" versus "not high risk" (combining "moderate" and "average" risk scores), using established criteria.[24] For $PREMM_5$, we assigned a categorical risk stratification value using a score cutoff of 2.5% (<2.5% = not clinically significant risk; ≥2.5% = clinically significant risk).[22]

Multivariable logistic regression was used to assess whether participant characteristics were associated with inaccuracy of clinical risk stratification for each module. Characteristics of interest included study site, age, sex assigned at birth (male/female), language choice for the tool (English/Spanish), education (less that a high school graduate, high school graduate or some post-high school education, or associate degree or higher), received assistance to complete tool (yes/no), a combined race/ethnicity variable (White [non-Hispanic], Hispanic [in any race category], Black, Asian, and a collapsed variable for all other reported racial and/or ethnic identities due to small sample size ["Another reported racial and/or ethnic identity"]), personal cancer history (yes/no), health literacy score, and 3-item subjective numeracy scale score. In separate models, "barriers to access" (yes/no) was used in place of study site, language choice, education, and race/ethnicity.

All inferential tests were evaluated using a 2-tailed alpha level of .05 and were conducted using Stata 17.

Results

A total of 1814 individuals interacted with the tool; the majority (N = 1711, 94.3%) completed it (Figure 1). Of these, 245 people (13.5%) had at least 1 incomplete attempt. Most (N = 91/103, 88.3%) of the people who never completed the tool were from KPNW, and all but 1 (97.1%) used the English version. The mean completion time was 4.3 minutes (SD = 3.9 minutes, min to max: 0.4 to 53.5 minutes) and most participants (N = 1540, 90.0%) completed the tool without assistance. Of the 171 people receiving assistance, 77.2% (N = 132) used the Spanish-language version of the tool.

Based on tool results, 1252 individuals (73.2% of individuals completing the tool) were offered genetic testing and counseling. Our analysis included 604 people (48.2% of those eligible) who had results disclosed by a genetic counselor over the phone.

Table 1 displays the characteristics of participants who completed the family history tool (N = 1711), and compares participants included in the agreement analysis (N = 604) with participants not included in the agreement analysis (N = 1107). Those included in the analysis had a mean age of 36.3 years, 81.6% were assigned female at birth, 55.1% reported a race/ethnicity other than White, 51.5% reported having an associate degree or higher, 14.1% completed the tool in Spanish, 77.3% had at least 1 of the defined barriers to access, and 12.6% had a personal history of cancer. Compared with those included in the agreement analysis, those not included were more likely to be from KPNW (P < .001), less likely to be female (P < .001), complete the tool in Spanish (P < .001), and have assistance completing the tool (P < .001); most (94.6%) had no personal history of cancer. Because only those offered genetic counseling were asked to complete a survey including demographic characteristics, we know less about those not included in the agreement analysis; for example, race/ethnicity data are missing on 45.8% of these individuals, education is missing on 68.6% of these individuals, and SNS and Health Literacy scores are only available on a subset (Table 1).

As shown in Figure 2, participant scores from both modules had moderate agreement with scores generated from genetic-counselor-collected family history data: 69.9% for B-RST 3.0 (K-alpha = .40, 95% CI [0.32, 0.47]) and 83.9% for $PREMM_5$ (K-alpha = .52, 95% CI [0.43, 0.60]).

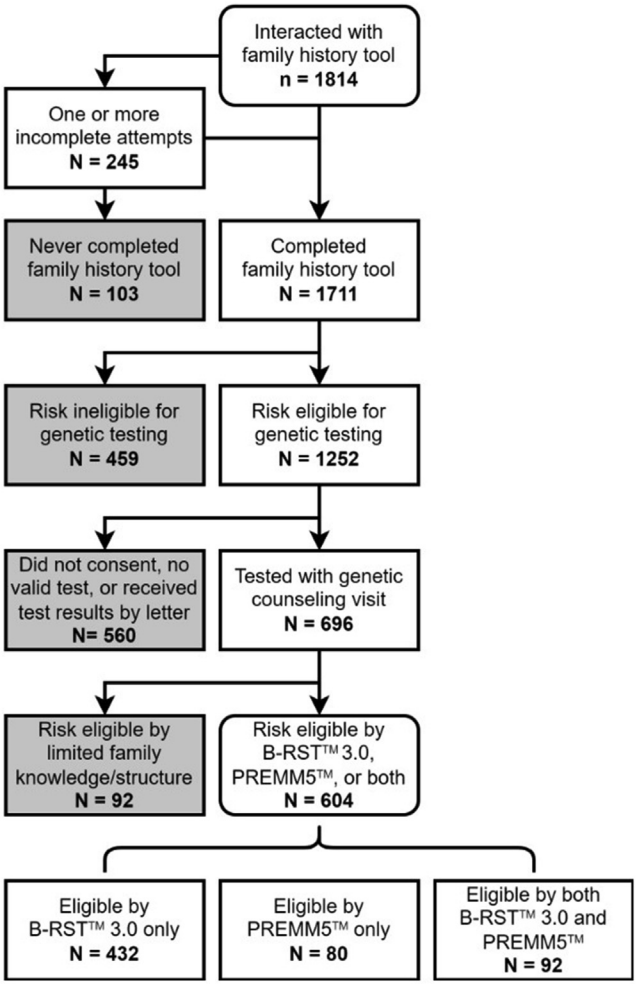

Figure 1 **Study flow diagram**.

Participants' scores from the tool tended to overestimate risk; 45% (N = 173/384) and 54% (N = 94/173), respectively, of participants who were classified at risk on the B-RST 3.0 and PREMM$_5$ modules were not at risk according to the genetic counselor's assessment. The disagreement was usually due to reporting the wrong type of cancer (such as ovarian versus uterine) or confusion about identifying first degree relatives (such as including cancer diagnosis in a cousin). For those at clinically significant risk after evaluation by a counselor, agreement between scores from the participant and the genetic counselor was much higher (211/220 = 95.9% for B-RST 3.0 and 79/82 = 96.3% for PREMM$_5$).

Factors associated with inaccuracy of clinical risk stratification are shown in Table 2. For B-RST 3.0, the factors associated with inaccuracy were study site, sex, and race/ethnicity. Participants from KPNW were more likely to be inaccurate than those from DH (OR = 0.62, 95% CI [0.39, 0.99]), and females were more likely to be inaccurate than males (OR = 2.59, 95% CI [1.45, 4.63]). The collapsed group of racial and/or ethnic identities whose individual groups were too small for independent evaluation ("Another reported racial and/or ethnic identity") were more likely to be inaccurate compared with non-Hispanic White participants (OR = 1.92, 95% CI [1.00, 3.70]); there were no significant associations with inaccuracy in any other race/ethnicity group compared with non-Hispanic White participants.

For PREMM$_5$, age, sex, and education were associated with inaccuracy. Increasing age was associated with less inaccuracy (OR = 0.83 per 5-year increase in age, 95% CI [0.71, 0.97]) as was female sex (OR = 0.42, 95% CI [0.24, 0.73]). Those with an associate degree or higher were more accurate compared with those with less education. Importantly, using the Spanish-language version of the tool, assistance completing the tool, personal history of cancer, numeracy, and health literacy were not significant predictors of inaccurate family history reporting on either module.

In multivariable models which a binary "barriers to access" variable was used in place of study site, language choice, education, and race/ethnicity, we found that having barrier(s) to access was not significantly associated with inaccuracy (OR = 1.21, 95% CI [0.76,1.94]) for B-RST 3.0, and OR = 1.43 (95% CI [0.77, 2.66]) for PREMM$_5$ (Supplemental Table 1).

Discussion

The CHARM study developed an electronic patient-facing family history collection tool to identify people at high risk for HBOC and LS. Most people completed the tool without assistance in less than 5 minutes. Although both the B-RST 3.0 and PREMM$_5$ modules had moderate agreement with a genetic-counselor-collected standard, both modules were highly accurate (96%, Figure 2) in identifying individuals who were at risk based on the genetic counselor's assessment. Our study population was diverse, and the majority had at least one barrier to health care access. Spanish-language preference, health literacy, numeracy, and safety-net health system use were not associated with inaccuracy, suggesting that this tool could be equitably implemented in a variety of health care settings, including those that provide care to underserved populations.

The majority (73%) of people who completed the family history tool were eligible for genetic testing. This is likely a reflection of our recruitment methods, as well as the "limited family history" module in the tool. Although any health plan member between the ages of 18 to 49 (who spoke English or Spanish) were eligible to interact with the tool, it is likely that people who were concerned about their risk, either from a personal history of cancer, or cancer in their family, were more likely to use the tool than those with no such history. Further, people who did not know their family history (such as someone who was adopted or estranged from their family) were offered genetic testing and counseling. This "self-selection" into the study likely results in bias. However, if this tool were adopted widely, our study population reflects

Table 1 Characteristics of study population

Characteristic	Completed Family History Assessment (N = 1711)	Included in Agreement Analysis (N = 604)	Not Included in Agreement Analysis (N = 1107)	P Value[a]
	N, %	N, %	N, %	
Study Site				<.001
Kaiser Permanente	1347 (78.7%)	387 (64.1%)	960 (86.7%)	
Denver Health	364 (21.3%)	217 (35.9%)	147 (13.3%)	
Age (mean, SD)	36.1 (8.3)	36.3 (8.2)	35.9 (8.3)	.35
Sex assigned at birth				<.001
Female	1312 (76.7%)	493 (81.6%)	819 (74.0%)	
Male	399 (23.3%)	111 (18.4%)	288 (26.0%)	
Race/ethnicity				<.001
White	527 (30.8%)	268 (44.4%)	259 (23.4%)	
Hispanic/Hispanic multiracial	424 (24.8%)	225 (37.3%)	199 (18.0%)	
Black	81 (4.7%)	31 (5.1%)	50 (4.5%)	
Asian	81 (4.7%)	24 (4.0%)	57 (5.2%)	
Another reported racial and/or ethnic identity[b]	88 (5.1%)	53 (8.8%)	35 (3.2%)	
Unknown	510 (29.8%)	3 (0.5%)	507 (45.8%)	
Education				.23
Less than high school/some high school	105 (6.1%)	70 (11.6%)	35 (3.2%)	
HS graduate/some post-high school training	300 (17.5%)	174 (28.8%)	126 (11.4%)	
Associate degree/bachelor's degree/ grad or professional degree	498 (29.1%)	311 (51.5%)	348 (31.4%)	
Unknown	808 (47.2%)	49 (8.1%)	759 (68.6%)	
Completed tool in Spanish				<.001
Y	161 (9.4%)	85 (14.1%)	76 (6.9%)	
N	1550 (90.6%)	519 (85.9%)	1031 (93.1%)	
Had assistance completing tool				<.001
Y	171 (10.0%)	92 (15.2%)	79 (7.1%)	
N	1540 (90.0%)	512 (84.8%)	1028 (92.9%)	
Barriers to access				.55
Y	1017 (59.4%)	467 (77.3%)	550 (49.7%)	
N	285 (16.7%)	137 (22.7%)	148 (13.4%)	
U	409 (23.9%)	0 (0.0%)	409 (37.0%)	
Personal History of cancer				<.001
Y	136 (8.0%)	76 (12.6%)	60 (5.4%)	
N	1575 (92%)	528 (87.4%)	1047 (94.6%)	
U	0 (0.0%)	0 (0.0%)	0 (0.0%)	
SNS (mean, [SD]), n	12.9 (4.0) n = 835	12.9 (3.9) n = 555	12.9 (4.2) n = 280	.84
Health Literacy (mean, [SD]), n	18.1 (2.6) n = 854	18.0 (2.8) n = 558	18.3 (2.3) n = 296	.04

[a]Difference between those included and not included in agreement analysis.

[b]Another reported racial and/or ethnic identity: this group was collapsed because sample sizes of individual categories were too small for independent evaluation. Reported racial and/or ethnic identities included in this collapsed group: Native American, Hawaiian/Pacific Islander, and Middle Eastern.

the types of individuals who genetic counseling and testing may benefit the most.

Some of our predictors of accuracy warrant further discussion. For both B-RST 3.0 and PREMM$_5$, the DH population was more accurate than KPNW. This may reflect differences in the recruitment methods at each study site. KPNW primarily utilized remote recruitment methods (email, text message, postcard, and telephone), whereas DH primarily used direct outreach to patients known to be at high risk (including those with a personal history of cancer) and referrals from providers. Individuals who already know that they are at high risk may have a better understanding of their family history and thus are able to report it more accurately. Further, although only 15% of people had assistance completing the tool, most of them were from DH (data not shown). We did not expect to see that females were more likely to be inaccurate on B-RST 3.0, but men were more likely to be inaccurate for PREMM$_5$. Prior studies have shown that females report more family history than men[31]; however, accuracy was not assessed. It is possible that women have more knowledge about people who have been diagnosed with cancer in the family, especially "female cancers," but they may not have accurate information on the cancer

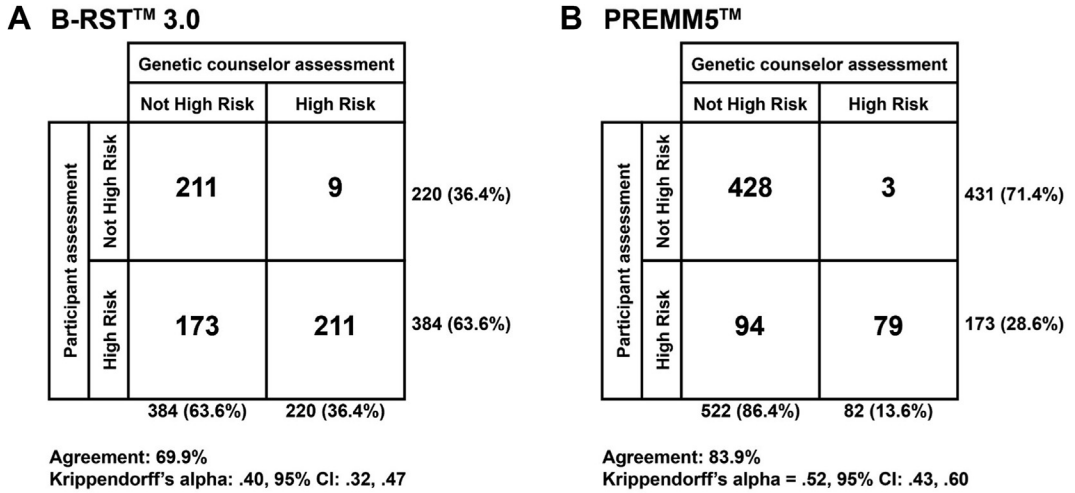

Figure 2 Results of agreement analysis. A. B-RST 3.0 module matrix showing agreement between the genetic counselor's assessment of familial risk after risk counseling compared with the participant's self-assessment of familial risk. B. $PREMM_5$ module matrix showing agreement between the genetic counselor's assessment of familial risk after risk counseling compared with the participant's self-assessment of familial risk. Both panels include only those eligible for genetic counseling and testing based on family history assessment ($N = 604$).

site. This is supported by our observation that study participants' scores from the tool tended to overestimate risk, and the disagreement between the scores from the participant compared with the genetic counselor were usually due to reporting the wrong type of cancer or confusion about who is a first degree relative (eg, listing a cousin as a first degree

Table 2 Factors associated with inaccuracy of clinical risk stratification for B-RST and $PREMM_5$

Risk Assessment Module	B-RST 3.0 ($n = 540$)[a]			$PREMM_5$ ($n = 540$)[a]		
Characteristic	OR	95% CI	*P* Value	OR	95% CI	*P* Value
Study Site						
Kaiser Permanente	ref			ref		
Denver Health	0.62	[0.39, 0.99]	.05	0.63	[0.34, 1.17]	.14
Age, per 5 year increase	1.01	[0.89, 1.14]	.94	0.83	[0.71, 0.97]	.02
Sex assigned at birth						
Female	2.59	[1.45, 4.63]	.001	0.42	[0.24, 0.73]	.002
Male	ref			ref		
Race/ethnicity						.96
White	ref			ref		
Hispanic/Hispanic multiracial	1.50	[0.91, 2.48]	.12	1.25	[0.66, 2.36]	.49
Black	1.55	[0.62, 3.87]	.35	1.33	[0.40, 4.40]	.65
Asian	0.98	[0.36, 2.69]	.97	1.19	[0.32, 4.42]	.79
Another reported racial and/or ethnic identity[b]	1.92	[1.00, 3.70]	.05	1.03	[0.42, 2.48]	.96
Education						
Less than high school/some high school	0.91	[0.39, 2.12]	.83	1.60	[0.52, 4.93]	.42
HS graduate/some post-high school training	0.86	[0.54, 1.36]	.51	2.06	[1.17, 3.64]	.01
Associate degree/bachelor's degree/grad or professional degree	ref			ref		
Completed Family History tool in Spanish						
No	ref			ref		
Yes	1.18	[0.41, 3.40]	.76	1.88	[0.51, 6.96]	.34
Had assistance completing tool						
No	ref			ref		
Yes	0.72	[0.28, 1.87]	.51	0.40	[0.11, 1.40]	.15
Personal History of cancer						
No	ref			ref		
Yes	1.09	[0.60, 1.97]	.79	0.68	[0.27, 1.73]	.42
SNS	0.99	[0.94, 1.05]	.77	1.00	[0.93, 1.08]	.95
Health Literacy	1.03	[0.95, 1.12]	.42	0.97	[0.88, 1.07]	.57

[a]Those with missing values for any covariate were excluded from the multivariable analysis.

[b]Another reported racial and/or ethnic identity: this group was collapsed because sample sizes of individual categories were too small for independent evaluation. Reported racial and/or ethnic identities included in this collapsed group: Native American, Hawaiian/Pacific Islander, and Middle Eastern.

relative). It is also possible that our relatively small number of men (18.4% of the agreement analysis population) represent a group of men who had a family or personal history of cancer and thus could more accurately report it.

A strength of our study is that we assessed our tool using an established framework for family history tool evaluation[32,33]; the literature suggests that few of the existing family history tools have been similarly evaluated.[32,34] Prior work has established that family history tools should ideally be (1) patient self-administered, (2) electronic, (3) easy to use, (4) EHR-integrated, and (5) dynamic (family history can be updated over time); tools should also be able to (6) draw pedigrees, (7) calculate a risk assessment, and (8) deliver tailored, evidence-based recommendations.[32,35] By design, our tool meets several of these criteria: it is patient-facing, electronic, automatically calculates risk assessment, delivers tailored recommendations, and is easy to use. With respect to ease of use, most individuals completed the tool independently and under 5 minutes, considerably faster than reported time-to-completion for similar tools.[32,36] Completion rates for our tool were also higher than in previous reports.[36] In a qualitative study of CHARM participants, those with inaccurate family history report, incomplete tool attempts, and/or more time spent on the tool still endorsed the tool as easy to use.[37]

Our cancer family history tool was designed in an iterative process collaborating directly with patient stakeholders with barriers to health care access.[18,19] This approach resulted in successful implementations in 2 very different clinical populations: an integrated health care system serving a predominately White, insured patient population, and a safety-net health care system serving primarily uninsured or publicly insured racial and ethnic minority populations. Study enrollment was reflective of the diversity of these health systems. Recently, the MeTree family history tool was implemented and evaluated in diverse health care systems.[17,38] Although MeTree was effectively implemented in these systems, the study population was 88% White and did not reflect the diversity of the eligible population. The CHARM population was considerably younger and more diverse than the MeTree population: the mean age was 36.3 years, 55.1% reported a race/ethnicity other than White, and 77.3% had at least one of the defined barriers to access. Our results suggest that the CHARM family history collection tool could facilitate early identification of hereditary cancer risk and thus early intervention and risk reduction in patients from diverse backgrounds.

Limitations and future research

Our study design likely missed high-risk individuals who did not accurately report their family history in the tool. Such individuals were not offered genetic testing and therefore were not included in our analysis. Further, our genetic-counselor-collected standard—although reflective of most clinical practice—was not further validated against the medical records and tumor registries of participant relatives, as some have recommended.[33] As such, our standard, although carefully adjudicated by a genetic counselor, could also be subject to patient reporting errors. We were unable to calculate the sensitivity and specificity of our tool because of these missing data elements and thus reported agreement between the genetic counselor and study participant. In the traditional clinical setting, high-risk individuals who do not accurately report (or do not know) their family history would similarly be classified as low risk. Another limitation of our analysis is that we did not correct for multiple comparisons.

Participants with inaccurate family history report tended to overreport familial cancers. If this tool is implemented in clinical practice, it may require clinician time to adjudicate "false-positive" family history reports. Future studies may be able to improve accuracy through simple design changes[37] or develop processes to reduce health system burden. To promote even greater inclusion, future studies could evaluate alternative solutions for individuals who prefer more interpersonal interaction. Finally, the study was not designed to recruit a random sample of health plan members; thus, our results may not be representative of our entire health plan population nor generalizable to other clinic populations.

Despite these limitations, our tool successfully identified primarily unaffected individuals who benefitted from genetic testing and counseling. As we have previously published, 5% of study participants had a pathogenic or likely pathogenic variant discovered, and 1% had a secondary finding.[39]

Conclusion

The implementation of this family history tool could increase identification of individuals at risk of hereditary cancer syndromes while reducing the burden on primary care providers. Our results suggest that the tool is accurate for a broad patient population, including Spanish speakers and those with barriers to access to health care.

Data Availability

Data used in this investigation that can be deidentified are available from the authors upon request.

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Author Contributions

Conceptualization: H.S.F., K.F.M., S.O., K.M.P., K.P.A., T.L.K., S.S., M.C.L., B.S.W.; Data Curation: K.F.M., E.S.; Formal Analysis: E.S., M.C.L.; Funding Acquisition: B.S.W.; Investigation (data collection): K.F.M., M.J.G., J.M.Z., N.M.L.; Methodology: H.S.F., K.F.M., S.O., K.M.P., K.P.A., T.L.K., N.M.L., S.S., M.C.L., B.S.W.; Project Administration: J.B., T.L.K., K.R.M.; Software: K.F.M., E.S., C.B., C.U., S.S.; Supervision: S.O., K.M.P., S.S., M.C.L., B.S.W.; Validation: M.J.G., J.M.Z.; Writing-original draft: H.S.F., K.F.M.; Writing-reviewing and editing: H.S.F., K.F.M., S.O., K.M.P., J.B., E.S., K.P.A., M.J.G., J.M.Z., T.L.K., N.M.L., K.R.M., C.B., C.U., S.S., M.C.L., B.S.W.

ORCID

Heather Spencer Feigelson: http://orcid.org/0000-0001-6691-3740

Conflict of Interest

PREMM and all associated logos are trademarks or registered trademarks of Dana Farber Cancer Institute, Inc. Dr Syngal has rights to an inventor portion of the licensing revenue from $PREMM_5$. Dr Bellcross has rights to inventor portion of the licensing revenue of the B-RST model.

Additional Information

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Nonauthor contributors

Jake Allen, Laura M. Amendola, Frank Angelo, Briana L. Arnold, Tiffany Bendelow, Barbara B. Biesecker,Kristina F Booker, Kristin D. Breslin, Mikaella Caruncho, James V. Davis, Sonia Deutsch, Beth Devine, Michael O. Dorschner, Devan M. Duenas, Donna J. Eubanks, Amanda S. Freed, Katrina A. B. Goddard, Inga Gruß, Claudia Guerra, Boya Guo, Joan Holup, Jessica Ezzell Hunter, Chalinya L. Ingphakorn, Paige Jackson, Gail P. Jarvik, Charisma L. Jenkins, Galen Joseph, Leah S. Karliner, Erin Keast, Sarah Knerr, Alyssa H. Koomas, Stephanie A. Kraft, Mi H. Lee, Robin Lee, Sandra Soo-Jin Lee, Hannah S. Lewis, Elizabeth G. Liles, Frances Lynch, Carmit K. McMullen, Elizabeth Medina, Angela R. Paolucci, C. Samuel Peterson, Chelese L. Ransom, Ana Reyes, Leslie S. Riddle, Sperry Robinson, Bradley A. Rolf, Alan F. Rope, Emily Schield, Kelly J. Shipman, Brian H. Shirts, Britta N. Torgrimson-Ojerio, Meredith L. Vandermeer, Alexandra M. Varga, David L. Veenstra, Larissa Lee White, W. Chris Whitebirch

Affiliations

[1]Institute for Health Research, Kaiser Permanente, Denver, CO; [2]Bernard J Tyson Kaiser Permanente School of Medicine, Pasadena, CA; [3]Vanderbilt-Ingram Cancer Center, Vanderbilt University Medical Center, Nashville, TN; [4]Denver Health and Hospital Authority, Denver Health, Denver, CO; [5]Treuman Katz Center for Pediatric Bioethics, Seattle Children's Research Institute, Seattle, WA; [6]Department of Translational and Applied Genomics, Kaiser Permanente Center for Health Research, Portland, OR; [7]Kaiser Permanente Center for Health Research, Portland, OR; [8]Department of Human Genetics, Emory University School of Medicine, Atlanta, GA; [9]Division of Population Sciences, Dana Farber Cancer Institute, Boston, MA; [10]Divisions of Population Sciences and Cancer Genetics and Prevention, Dana-Farber Cancer Institute and Harvard Medical School, Boston, MA; [11]Division of Bioethics and Palliative Care, Department of Pediatrics, University of Washington School of Medicine, Seattle, WA

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