Translational Behavioral Medicine, 2022, 12, 683–687
https://doi.org/10.1093/tbm/ibac034
Advance access publication 12 May 2022
Brief Report

Assessment of melanoma precision prevention materials incorporating *MC1R* genetic risk information

John Charles A. Lacson,[1] Stephanie M. Forgas,[1] Scarlet H. Doyle,[1] Lu Qian,[2] Jocelyn Del Rio,[1] Stella Valavanis,[1] Rodrigo Carvajal,[3] Guillermo Gonzalez-Calderon,[3] Youngchul Kim,[4] Richard G. Roetzheim,[5] Susan T. Vadaparampil,[6] Peter A. Kanetsky[1]

[1]Department of Cancer Epidemiology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA
[2]SWOG Statistics and Data Management Center, Fred Hutchinson Cancer Research Center, Seattle, WA 98109, USA
[3]Biostatistics and Bioinformatics Shared Resource, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA
[4]Department of Biostatistics and Bioinformatics, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA
[5]Department of Family Medicine, Morsani College of Medicine, University of South Florida, Tampa, FL, USA
[6]Department of Health and Behavioral Outcomes, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA

Correspondence to: P A Kanetsky, Peter.Kanetsky@moffitt.org
Lacson and Forgas contributed equally to this work.

Abstract

Few studies have examined cognitive responses to mailed precision prevention materials. *MC1R* is a robust, well-described melanoma susceptibility marker. The purpose was to assess cognitive responses to generic or precision prevention materials incorporating *MC1R* genetic risk. Non-Hispanic White participants (n = 1134) enrolled in a randomized controlled trial received either precision prevention materials incorporating *MC1R* genetic risk (higher/average) or generic prevention (standard) materials. Six months after baseline, 808 (71.3%) participants reported on the amount of prevention materials read (5-point scale); believability and clarity of materials; intention to change preventive behaviors (7-point Likert scale); and recall of their *MC1R* genetic risk. Comparisons were conducted using Kruskal–Wallis and chi-squared tests. Overall, participants read most to all (Mdn = 4, IQR = 2) of the prevention materials, reported high believability (Mdn = 7, IQR = 1) and clarity (Mdn = 7, IQR = 1), and moderate intention to change preventive behaviors (Mdn = 5, IQR = 2). Higher-risk participants reported slightly less clarity (Mdn = 6, IQR = 2) than either average-risk (Mdn = 6, IQR = 1, $p = 2.50 \times 10^{-3}$) or standard participants (Mdn = 7, IQR = 1, $p = 2.30 \times 10^{-5}$); and slightly less believability (Mdn = 6, IQR = 1) than standard participants (Mdn = 7, IQR = 1, p = .005). Higher-risk participants were 2.21 times as likely (95% CI = 1.43–3.43) to misremember or forget their risk compared to average-risk participants; misremembering was observed only among higher-risk participants (14%). Mailed precision prevention information were mostly read, highly believable and clear, and resulted in moderate levels of intention to change sun protection behaviors, bolstering the feasibility of population-level precision prevention. Defensive reactions may explain lower clarity, believability, and higher incorrect risk recall among higher-risk participants.

Lay Summary

Precision prevention uses an individual's genetics, environment, and/or lifestyle to promote prevention behaviors. However, if materials incorporating precision prevention information are not easily accessible, individuals may misinterpret or distrust findings. Few studies have examined participant-reported believability and clarity of mailed precision prevention materials, how much they read, and whether they intend to change preventive behaviors. We assessed genetic risk for melanoma by determining DNA variation at the *MC1R* gene, a known melanoma risk marker. Participants were mailed either precision prevention materials conveying their *MC1R* genetic risk or generic (without genetic risk information) prevention materials. Overall, participants read most of the materials, gave high believability and clarity scores, and reported moderate levels of intention to change preventive behavior. However, participants at higher genetic risk had slightly lower believability and clarity scores than the generic group and were more likely to forget or misremember their genetic risk than participants at average genetic risk. Among participants who correctly recalled their genetic risk, differences in believability diminished, while differences in clarity remained. We conclude that precision prevention materials are highly believable and clear, but additional strategies may be necessary to maximize believability, clarity, and risk recall for individuals at a higher genetic risk.

Keywords: Melanoma, MC1R, Genetic testing, Public health genomics, Precision prevention

Implications

Practice: Mailed precision melanoma prevention materials are mostly read, have high believability and clarity, and result in moderately high levels of intention to change sun protective behaviors among non-Hispanic Whites with limited melanoma risk phenotypes.
Policy: Efforts to reduce the burden of melanoma should utilize precision prevention materials that have high levels of believability and clarity and can be easily disseminated on a population level.
Research: Future research should examine strategies to further maximize believability and clarity of precision prevention materials and address the tendency to incorrectly recall genetic risk, especially among those at genetically higher risk.

Introduction

Precision prevention intervention trials aim to improve preventive behaviors among those at elevated genetic risk for disease and have provided mailed genetic testing results with prevention materials as an inexpensive and high-throughput intervention with the potential to scale to a population-level [1]. Precision prevention intervention trials for melanoma have been successful in modifying some primary preventive behaviors [2–4]; have low negative psychological or emotional impact [2, 5]; and have no increases in risky behavior among non-carriers or those with low to average genetic risk [2–4, 6]. However, recipients of genetic testing results may find materials that convey test results hard to understand or believe, which in turn may lead to misinterpretations of test findings [7]. The scientific literature examining cognitive feedback on precision prevention materials is sparse.

This study reports on participant uptake and cognitive assessment (amount of prevention materials read, believability, clarity, and intention to change preventive behavior) of melanoma precision prevention materials that incorporates risk information based on genotyping of the melanocortin-1 receptor (*MC1R*) gene. Because risk variants at *MC1R* impart relatively low to moderate melanoma risk [8], similar in magnitude to many other risk factors for melanoma [9, 10], and our precision prevention materials recommend behavioral prevention measures (i.e., primary prevention) that are within the agency of recipients and screening measures (i.e., secondary prevention) that are non-invasive, our study did not provide formal genetic counseling after receipt of precision prevention materials. We hypothesized that prevention materials would be mostly read, highly believable and clear, and would motivate individuals to change their preventive behavior, especially among those at higher genetic risk.

Materials and Methods

Participants and setting

Data were obtained from a published randomized controlled intervention trial designed to test the efficacy of precision prevention materials to improve melanoma prevention activities [4]. Briefly, participants were 18 years or older, non-Hispanic White, and had limited melanoma risk phenotypes. Participants completed a baseline questionnaire, provided a saliva sample for isolation of DNA and sequencing of *MC1R*, and were randomized within *MC1R* risk stratum (average or higher) to receive precision prevention or generic prevention materials (standard).

Prevention materials

Full details of the prevention materials are published [4]. Succinctly, generic prevention materials included publicly available prevention guidelines; and precision prevention materials conveyed participants' *MC1R* genetic risk category (average or higher) and genetics-driven preventive guidelines. Precision prevention materials were anchored in Protection Motivation Theory, minimized health literacy and numeracy demands, and were adapted from Hay and colleagues [11, 12].

Questionnaire measures

The baseline instrument collected information on demographics, health literacy [13], health numeracy [14], and family history of melanoma, skin cancer, and other cancers. Participants completed a follow-up survey at 6 months either online or via mailed hardcopy. To assess the amount of the prevention materials read, participants were asked "How much of the information would you say you read?" (all, most, some, hardly any, or none of the information). Believability of the prevention materials was measured by asking "How much do you agree or disagree that the information about *MC1R* genetic testing and prevention behaviors for melanoma and other types of skin cancer was believable?" (1 = "Strongly Disagree" to 7 = "Strongly Agree"). Clarity of the prevention materials was measured by asking "How clear do you think the information about *MC1R* genetic testing and prevention behaviors for melanoma and other types of skin cancer was?" (1 = "Not at all" to 7 = "Completely"). Intention to change sun protection behavior was assessed by asking "How much did finding out about your genetic result and prevention behaviors for melanoma and other types of skin cancer make you feel determined to change your sun protection behavior?" (1 = "Not at all" to 7 = "A great deal"). Recipients of the generic prevention materials were asked these questions with no reference to genetic risk. Recall of *MC1R* genetic risk category was assessed (precision prevention groups only—"Yes, it was average risk."; "Yes, it was high risk."; or "No, I don't recall.").

Statistical analyses

Baseline characteristics were compared across the standard, average-, and higher-risk precision prevention groups using ANOVA, Kruskal–Wallis, or chi-square tests. We compared median scores for amount read, believability, clarity, and intention to change sun protection behavior across the three groups using a Kruskal–Wallis test; a p-value < .05 indicated a statistical difference. *P*-values for pairwise differences were adjusted using Bonferroni correction to account for multiple hypotheses testing. We used a chi-square homogeneity test to assess differences in the proportion of participants who correctly recalled their *MC1R* risk category. In sensitivity analyses, we compared assessment of prevention materials across groups after excluding individuals who incorrectly recalled or forgot their *MC1R* genetic risk category.

Results

Participant characteristics

Of the 1,134 participants in our intervention trial, 566 (50%) were in the standard group, 226 (20%) were in the average-risk precision prevention group, and 342 (30%) were in the higher-risk precision prevention group. The 6-month follow-up questionnaire was completed by 398 (70%), 170 (75%), and 240 (70%) of participants in the standard, average-risk, and higher-risk groups, respectively. Patient characteristics are summarized in Table 1. There was a statistically significant difference in median education level across the three groups (p = .046), and pairwise comparisons showed greater median education level in the higher-risk group compared to the average-risk group (p = .039).

Assessment of prevention materials

Overall, individuals from all three groups reported reading most to all (Mdn = 4, IQR = 2) of the prevention materials, very high believability (Mdn = 7, IQR = 1), very high

Table 1 | Baseline characteristics of participants who completed the 6-month follow-up

Variable	Standard, *n* (%)	Average risk, *n* (%)	Higher risk, *n* (%)	*P*-value[a]
	(*n* = 398)	(*n* = 170)	(*n* =240)	
Education				0.046
Less than high school or GED	9 (2.3%)	8 (4.7%)	5 (2.1%)	
High school or GED	62 (15.6%)	29 (17.1%)	30 (12.5%)	
Some college[b]	62 (15.6%)	35 (20.6%)	34 (14.2%)	
Four-year college degree	120 (30.2%)	47 (27.6%)	88 (36.7%)	
Graduate degree or higher	143 (35.9%)	51 (30.0%)	83 (34.6%)	
Marital status				0.37
Single or never married	87 (21.9%)	45 (26.5%)	61 (25.4%)	
Married, domestic partnership, or civil union	262 (65.8%)	99 (58.2%)	144 (60.0%)	
Divorced, separated, or widowed	47 (11.8%)	26 (15.3%)	35 (14.6%)	
Age (mean, SD)	48.5 (16.2)	47.9 (16.5)	48.1 (15.5)	0.90
Sex				0.80
Female	208 (52.3%)	91 (53.5%)	132 (55.0%)	
Family history of cancer				
Melanoma	71 (17.8%)	36 (21.2%)	46 (19.2%)	0.67
Non-melanoma skin cancer	125 (31.4%)	49 (28.8%)	75 (31.3%)	0.83
Other cancer	244(61.3%)	109 (64.1%)	162 (67.5%)	0.30
Health literacy				0.74
Extremely confident	282 (70.9%)	118 (69.4%)	165 (68.8%)	
Quite a bit confident	91 (22.9%)	32 (18.8%)	58 (24.2%)	
Not at all, a little bit, somewhat confident	24 (6.0%)	19 (11.2%)	17 (7.1%)	
Health numeracy				0.09
Very easy	198 (49.7%)	70 (41.2%)	103 (42.9%)	
Easy	178 (44.7%)	84 (49.4%)	126 (52.5%)	
Hard or very hard	21 (5.3%)	15 (8.8%)	10 (4.2%)	

[a]*P*-values are from ANOVA, Kruskal–Wallis, or chi-squared tests comparing across the standard, average-, and higher-risk groups.
[b]Participants who indicated they received their education outside of the USA were assigned to the median value (some college).

clarity (Mdn = 7, IQR = 1), and moderately high intention to change sun protection behaviors (Mdn = 5, IQR = 2, Fig. 1A–D). Detailed breakdown of responses to each outcome is tabulated in Supplementary Table S1. There was a significant difference in median scores for believability (p = .0065) and clarity ($p = 9.0 \times 10^{-6}$) across all groups. The standard group reported slightly higher believability (Mdn = 7, IQR=1) than the higher-risk precision prevention group (Mdn = 6, IQR = 1, p = .005), and reported slightly higher clarity (Mdn = 7, IQR = 1) than those in either the average-risk (Mdn = 6, IQR = 1, p = .0025) or higher-risk (Mdn = 6, IQR = 2, $p = 2.3 \times 10^{-5}$) precision prevention groups. No other differences were statistically significant.

Risk recall

Similar proportions of participants in the average-risk (n = 114, 72%) and higher-risk (n = 150, 70%) precision prevention groups reported recalling their melanoma risk associated with *MC1R* genotype. No individuals in the average-risk group incorrectly recalled their risk, whereas 14% (n = 34) of those in the higher-risk precision prevention group incorrectly recalled their risk as average risk. Higher-risk participants were over 2-fold as likely (odds ratio = 2.21; 95% CI = 1.43–3.43) to incorrectly recall or not recall their risk compared to average-risk participants. After excluding participants who forgot or incorrectly recalled their *MC1R* risk category, there was a significant difference in the median scores for amount read across the three groups ($p = 9.2 \times 10^{-5}$, Fig. 1E). The standard prevention group read the least (Mdn = 4, IQR = 2) compared to the average-risk (Mdn = 5, IQR = 1, p = .0004) and higher-risk (Mdn = 5, IQR = 1, p = 0.02) precision prevention groups. The difference in median scores for believability (p = .43) was no longer significant across the three groups, but the difference in median scores for clarity across the groups remained statistically significant (p = .024), driven by a small difference between the standard (Mdn = 7, IQR = 1) and higher-risk precision prevention groups (Mdn = 6.5, IQR = 1, p = .03, Fig. 1F and G). No other differences were statistically significant. Detailed breakdown of responses to each outcome are tabulated in Supplementary Table S1.

Discussion

Our study found that individuals who were mailed melanoma prevention information read most or all the prevention materials, rated the materials with a high level of believability and clarity, and conveyed moderately high levels of intention to change sun protection behaviors in reaction to the materials. We noted that participants in the standard prevention group found their materials slightly more believable than the those in the higher-risk precision prevention group and found their materials slightly clearer than those in either the average- or higher-risk precision prevention group. As anticipated, our results are similar to those reported by Kaphingst et al. [5] since our precision prevention materials were adapted from those used in their study.

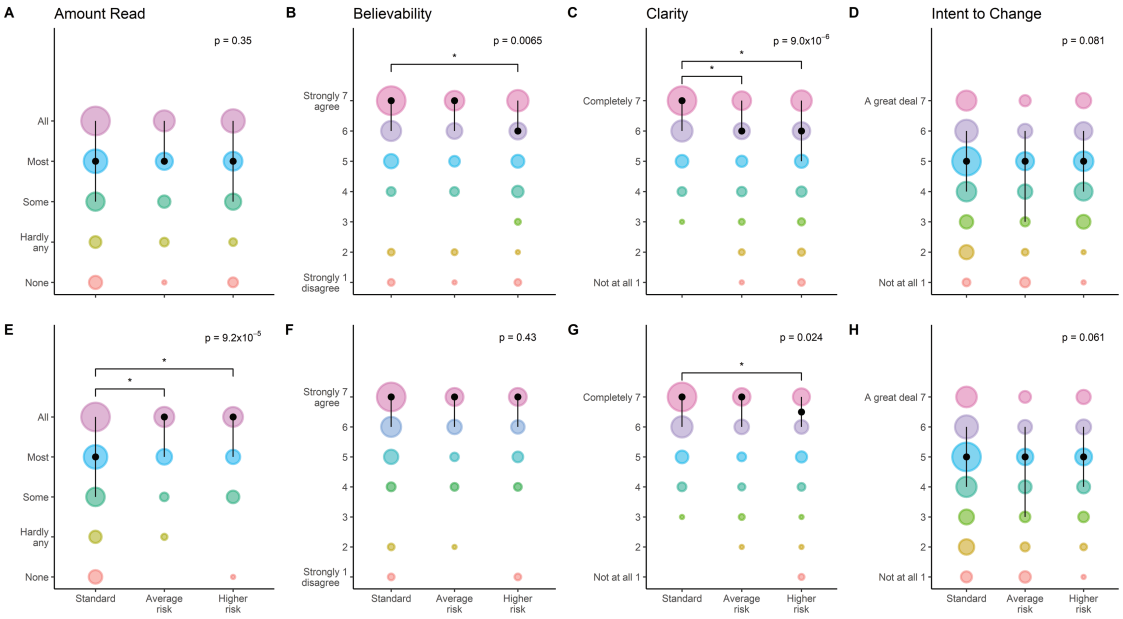

Fig. 1 | Bubble plots show the distribution of amount of intervention materials read (A, E), believability (B, F), clarity (C, G), and intention to change preventive behaviors (D, H) by standard, average- and higher-risk precision prevention groups among all study participants (A-D) and among those who correctly recalled their *MC1R* risk category (E-H). Median values for each group are represented as black dots, with black lines showing the interquartile range. *P*-values in the upper right-hand corner of each plot are global *p*-values from Kruskal–Wallis tests. Starred brackets indicate pairwise comparisons that were statistically significant at alpha = 0.05 after Bonferroni correction. The diameter of each circle is proportional to the number of participants who reported that score, which is reported in Supplementary Table S1.

Despite no differences in education, health literacy, or health numeracy between the higher-risk precision prevention and standard groups, higher-risk participants had slightly lower believability and clarity scores. Multivariate analyses using aligned rank transformation [15] confirmed that differences remained statistically significant after adjusting for these variables (data not shown). Higher-risk participants were also more likely to incorrectly recall their genetic risk category than average-risk participants, a finding that may be explained by defensive reactions. Recipients of threatening health-promoting information may react defensively by rating their information as less accurate, lowering their personal risk estimates, and spending less time reading about the threat [16].

Removing participants who incorrectly recalled or forgot their *MC1R* risk category resulted in statistically significantly higher amount read among the two precision prevention groups compared to the standard group and eliminated previously observed significant differences in believability. Thus, correct recall of *MC1R* risk category may be a proxy for higher motivation to engage with the study. Since long-term improvements in preventive behavior would confer the most benefit in melanoma prevention, more research is warranted to explore participant characteristics associated with forgetting or misremembering genetic risk and to identify measures reinforcing genetic risk messaging and precision prevention.

At the 6-month assessment, we did not find a difference in intention to change behavior across standard, average-, and higher-risk participants. That higher-risk participants were not dissimilar from the other two groups on intention is interesting given results from our primary efficacy analyses over the 12-month study period that showed improvements in some melanoma preventive behaviors among *MC1R* higher-risk participants who received precision prevention materials compared to *MC1R* higher-risk participants who received generic prevention materials, a finding absent among *MC1R* average-risk participants [4].

Participants in our study had high levels of education, health literacy, and health numeracy, likely because study recruitment occurred within an academic healthcare system. Despite education being statistically significantly different across our three groups, only 18% of participants reported receiving no more than a high school education, making stratified analyses suboptimal. Although prevention materials were designed to minimize health literacy and numeracy demands, the study may have limited generalizability among individuals with lower educational attainment, health literacy, and health numeracy.

MC1R is a susceptibility gene that imparts low to moderate melanoma risk [8], and the prevention materials recommend changes in prevention behavior that are within the agency of recipients and screening measures that are non-invasive. Thus, we speculate that intervention trials that incorporate susceptibility markers for other diseases with similar effects on risk and recommend actionable preventive behaviors and non-invasive screening would have similar participant-reported assessments.

We demonstrate that mailed precision prevention information was mostly read, highly believable and clear, and resulted in moderate levels of intention to change preventive behavior. These strong metrics, taken together with the success of recent intervention trials in improving sun-related behavior and screening [2–4], strengthen the possibility of implementing precision prevention at the population level. Future interventions may want to focus on optimizing believability, clarity, and correct genetic risk recall and overcome defensive reactions among those with higher risk.

Supplementary Material

Supplementary material is available at *Translational Behavioral Medicine* online.

Acknowledgments

This work was supported in part by the Biostatistics and Bioinformatics Shared Resource, Molecular Genomics Core, and Tissue Core, at the H. Lee Moffitt Cancer Center and Research Institute, a comprehensive cancer center designated by the National Cancer Institute and funded in part by Moffitt's Cancer Center Support Grant (P30 CA076292). We acknowledge the patients, physicians, and staff at the USF Morsani Family Medicine and General Internal Medicine Clinics.

Funding

This study was funded by American Cancer Society (grant number RSG-14-162-01-CPHPS).

Compliance with Ethical Standards

Conflicts of Interest: Authors John Charles A. Lacson, Stephanie M. Forgas, Scarlet H. Doyle, Lu Qian, Jocelyn Del Rio, Stella Valavanis, Rodrigo Carvajal, Guillermo Gonzalez-Calderon, Youngchul Kim, Richard G. Roetzheim, Susan T. Vadaparampil, and Peter A. Kanetsky declare no conflict of interest.

Ethical Approval: All procedures were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study was approved by the Institutional Review Board of the University of South Florida (protocol code Pro00020044, approved on 2 February 2015). This study did not include any animal studies.

Informed Consent: Written informed consent was obtained from all subjects involved in the study.

Study Registration: Registered on clinicaltrials.gov (NCT03509467) after its initiation.

Analytic plan pre-registration: The analysis plan for this article was not pre-registered.

Data availability: De-identified datasets can be made available upon reasonable request to the corresponding author.

Analytic code availability: Analytic code can be made available upon reasonable request to the corresponding author.

Materials availability: Materials used to conduct the study are not publicly available.

References

1. Frieser MJ, Wilson S, Vrieze S. Behavioral impact of return of genetic test results for complex disease: systematic review and meta-analysis. *Health Psychol.* 2018;37(12):1134–1144. doi:10.1037/hea0000683.
2. Smit AK, Allen M, Beswick B, et al. Impact of personal genomic risk information on melanoma prevention behaviors and psychological outcomes: a randomized controlled trial. *Genet Med.* 2021;(23):2394–2403. doi:10.1038/s41436-021-01292-w.
3. Lacson JCA, Doyle SH, Del Rio J, et al. A randomized clinical trial of precision prevention materials incorporating MC1R genetic risk to improve skin cancer prevention activities among Hispanics. *Cancer Res Commun.* 2022;2(1):28–38. doi:10.1158/2767-9764.Crc-21-0114.
4. Lacson JCA, Doyle SH, Qian L, et al. A randomized trial of precision prevention materials to improve primary and secondary melanoma prevention activities among individuals with limited melanoma risk phenotypes. *Cancers (Basel)* 2021;13(13):3143. doi:10.3390/cancers13133143.
5. Kaphingst KA, Khan E, White KM, et al. Effects of health literacy skills, educational attainment, and level of melanoma risk on responses to personalized genomic testing. *Patient Educ Couns.* 2021;104(1):12–19. doi:10.1016/j.pec.2020.07.019.
6. Glanz K, Volpicelli K, Kanetsky PA, et al. Melanoma genetic testing, counseling, and adherence to skin cancer prevention and detection behaviors. *Cancer Epidemiol Biomarkers Prev.* 2013;22(4):607–614. doi:10.1158/1055-9965.EPI-12-1174.
7. Hock KT, Christensen KD, Yashar BM, Roberts JS, Gollust SE, Uhlmann WR. Direct-to-consumer genetic testing: an assessment of genetic counselors' knowledge and beliefs. *Genet Med.* 2011;13(4):325–332. doi:10.1097/GIM.0b013e3182011636.
8. Williams PF, Olsen CM, Hayward NK, Whiteman DC. Melanocortin 1 receptor and risk of cutaneous melanoma: a meta-analysis and estimates of population burden. *Int J Cancer.* 2011;129(7):1730–1740. doi:10.1002/ijc.25804.
9. Gandini S, Sera F, Cattaruzza MS, et al. Meta-analysis of risk factors for cutaneous melanoma. III. Family history, actinic damage and phenotypic factors. *Eur J Cancer.* 2005;41(14):2040–2059. doi:10.1016/j.ejca.2005.03.034.
10. Gandini S, Sera F, Cattaruzza MS, et al. Meta-analysis of risk factors for cutaneous melanoma. I. Common and atypical naevi. *Eur J Cancer.* 2005; 41(1):28–44. doi:10.1016/j.ejca.2004.10.015.
11. Hay JL, Berwick M, Zielaskowski K, et al. Implementing an internet-delivered skin cancer genetic testing intervention to improve sun protection behavior in a diverse population: protocol for a randomized controlled trial. *JMIR Res Protoc.* 2017;6(4):e52. doi:10.2196/resprot.7158.
12. Rodriguez VM, Robers E, Zielaskowski K, et al. Translation and adaptation of skin cancer genomic risk education materials for implementation in primary care. *J Community Genet.* 2017;8(1):53–63. doi:10.1007/s12687-016-0287-z.
13. Chew LD, Bradley KA, Boyko EJ. Brief questions to identify patients with inadequate health literacy. *Fam Med.* 2004;36(8):588–594.
14. Chen Y, Feeley TH. Numeracy, information seeking, and self-efficacy in managing health: an analysis using the 2007 Health Information National Trends Survey (HINTS). *Health Commun.* 2014;29(9):843–853. doi:10.1080/10410236.2013.807904.
15. Higgins JJ, Blair RC, Tashtoush S. The aligned rank transform procedure. *Conf Appl Stat Agric.* 1990; doi:10.4148/2475-7772.1443.
16. van 't Riet J, Ruiter RAC. Defensive reactions to health-promoting information: an overview and implications for future research. *Health Psychol Rev.* 2013;7(sup1):S104–S136. doi:10.1080/17437199.2011.606782.