

Personal Genomic Testing for Cancer Risk: Results From the Impact of Personal Genomics Study

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A B S T R A C T

Purpose

Significant concerns exist regarding the potential for unwarranted behavior changes and the overuse of health care resources in response to direct-to-consumer personal genomic testing (PGT). However, little is known about customers' behaviors after PGT.

Methods

Longitudinal surveys were given to new customers of 23andMe (Mountain View, CA) and Pathway Genomics (San Diego, CA). Survey data were linked to individual-level PGT results through a secure data transfer process.

Results

Of the 1,042 customers who completed baseline and 6-month surveys (response rate, 71.2%), 762 had complete cancer-related data and were analyzed. Most customers reported that learning about their genetic risk of cancers was a motivation for testing (colorectal, 88%; prostate, 95%; breast, 94%). No customers tested positive for pathogenic mutations in highly penetrant cancer susceptibility genes. A minority of individuals received elevated single nucleotide polymorphism-based PGT cancer risk estimates (colorectal, 24%; prostate, 24%; breast, 12%). At 6 months, customers who received elevated PGT cancer risk estimates were not significantly more likely to change their diet, exercise, or advanced planning behaviors or engage in cancer screening, compared with individuals at average or reduced risk. Men who received elevated PGT prostate cancer risk estimates changed their vitamin and supplement use more than those at average or reduced risk (22% v 7.6%, respectively; adjusted odds ratio, 3.41; 95% CI, 1.44 to 8.18). Predictors of 6-month behavior include baseline behavior (exercise, vitamin or supplement use, and screening), worse health status (diet and vitamin or supplement use), and older age (advanced planning, screening).

Conclusion

Most adults receiving elevated direct-to-consumer PGT single nucleotide polymorphism-based cancer risk estimates did not significantly change their diet, exercise, advanced care planning, or cancer screening behaviors.

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INTRODUCTION

Although the vast majority of cancer genomic testing occurs within the health care system, direct-to-consumer (DTC) personal genomic testing (PGT) is an innovation that seeks to democratize access to genomic technologies and enhance efforts in cancer control. However, there are growing concerns about the potential for unwarranted health behavior change and the overuse of health care resources in the wake of PGT.¹ These concerns often stem from the fact that the modest increases in cancer risk associated with single nucleotide

polymorphism (SNP) based testing are not currently considered medically actionable.^{2,3} Critics of DTC-PGT have expressed concerns that customers may inappropriately alter their health behavior on the basis of highly uncertain genetic information that has little or no known clinical utility, that they may not receive proper guidance on health decisions, and that they may strain an already overburdened health care system if they pursue costly follow-up care based on PGT results.⁴⁻⁸ Early studies of PGT suggested that customers may rely on their physicians to help interpret results and recommend follow-up testing based on PGT data,⁹⁻¹¹ and recent work suggests that some customers

ASSOCIATED CONTENT



Appendix
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change health behaviors after testing.¹²⁻¹⁴ In contrast, others have found little evidence to suggest that customers significantly alter their health behaviors after PGT.¹⁵⁻¹⁸

The future of PGT remains an area of intense debate. For the time being, the US Food and Drug Administration has limited consumer access to the health component of some PGTs out of concern that such testing could have significant health consequences. In its warning letter to 23andMe (Mountain View, CA), the Food and Drug Administration expressed specific concerns about *BRCA1/2*-related cancer risk assessment given that such testing is considered a high-risk indication.¹⁹ In addition, the American Medical Association called for a ban on DTC advertising of prescription drugs and medical devices, citing concerns that DTC advertising may inflate demand.²⁰ Although policymakers are actively debating the regulation of the genomic testing industry broadly,²¹⁻²⁴ and of PGT specifically, regulatory decisions are significantly hampered by a lack of data that evaluate the effect of PGT on customer health behaviors and health care resource use.²⁵⁻²⁷

The Impact of Personal Genomics (PGen) Study is a prospective, longitudinal cohort study that was designed to examine the psychosocial, behavioral, and health outcomes related to DTC-PGT. The objective of the present analysis was to determine whether customers who received elevated SNP-based PGT cancer risk estimates were more likely to change their health-related (ie,

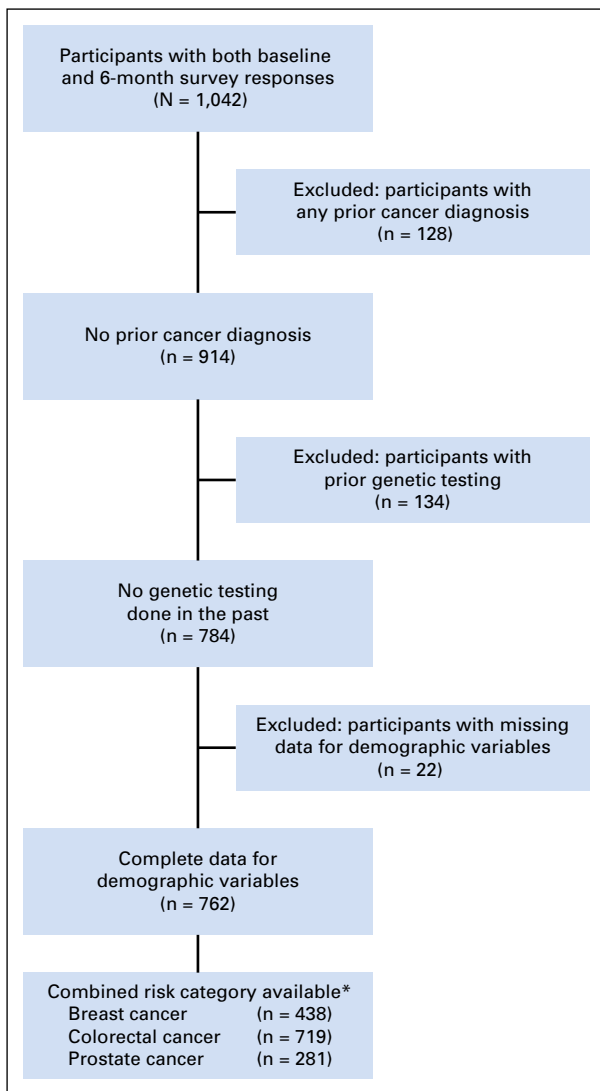


Fig 1. Study enrollment. *Individuals may have received risk information for some but not all cancers. Missing data on breast and prostate risk are out of a total of 456 women and 306 men in the sample, respectively.

Table 1. Sociodemographic and Risk Characteristics of Participants

Characteristic	No. of Participants (N = 762) (%)
Age, years	
Median	42
25-75th percentiles	31-57
Range	19-81
> 50	275 (36)
Race	
Nonwhite	117 (15)
Hispanic	47 (6)
Female sex	456 (60)
Education	
Less than college	151 (20)
College	253 (33)
Greater than college	358 (47)
Employment	
Full time	425 (56)
Retired	122 (16)
Other	215 (28)
Household income	
≤ \$99,999	432 (57)
\$100,000-\$199,999	236 (31)
≥ \$200,000	94 (12)
Family history of cancer	590 (77)
No health insurance	36 (5)
Health status	
Excellent	115 (15)
Very good	333 (44)
Good, fair, or poor	314 (41)
Interest in cancer genetic risk*	
Somewhat or very interested in learning about genetic risk for	
Breast cancer	429 (94)
Colorectal cancer	671 (88)
Prostate cancer	290 (95)
Perceived risk*	
Baseline perceived risk higher than average	
Breast cancer	76 (17)
Colorectal cancer	124 (16)
Prostate cancer	61 (20)
6-month perceived risk higher than average	
Breast cancer	58 (13)
Colorectal cancer	118 (16)
Prostate cancer	46 (15)
Combined risk category*	
Elevated PGT risk for	
Breast cancer	52 (12)
Colorectal cancer	171 (24)
Prostate cancer	65 (23)
Pathogenic mutations in cancer risk genes†	
<i>BRCA</i> mutations	0

NOTE. The total number of participants reported includes participants who are included in at least one screening analysis at 6 months.

Abbreviation: PGT, personal genomic testing.

*Not mutually exclusive; percentage for breast cancer was calculated among women and percentage for prostate cancer was calculated among men.

†Pathogenic mutations in cancer risk genes are only reported by one PGT company

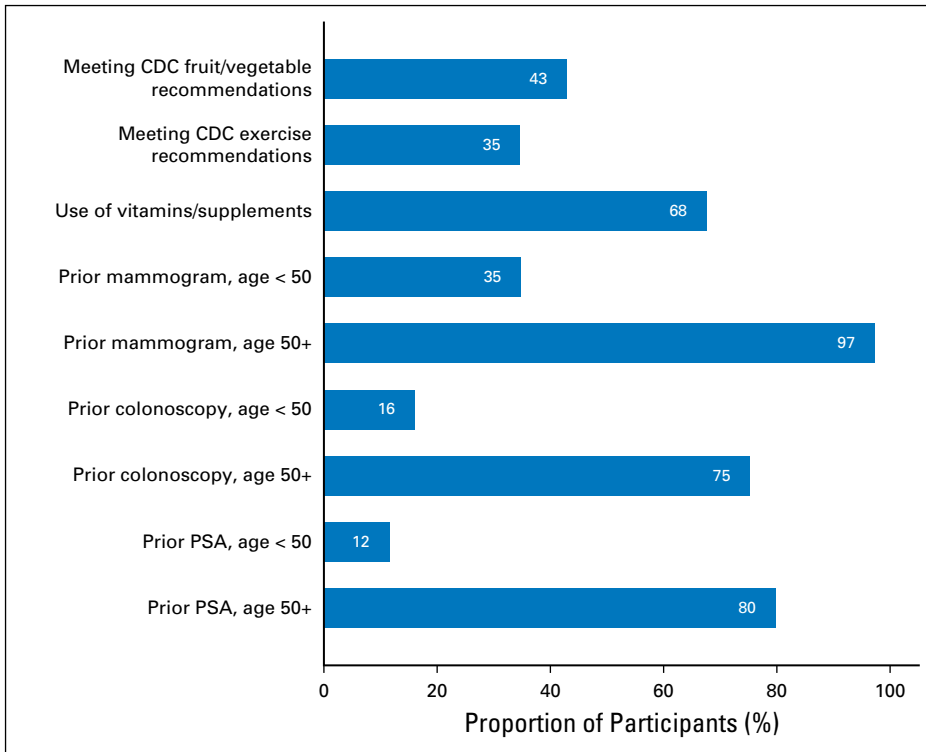


Fig 2. Baseline behaviors according to compliance with Centers for Disease Control and Prevention (CDC) recommendations, proportion using vitamins or supplements, and cancer screening by age. PSA, prostate-specific antigen.

diet, exercise, vitamin and supplement use, and advanced care planning) and cancer screening behaviors than customers who received average or reduced PGT cancer risk estimates. Because we were most interested in the use of relatively high-cost screening modalities, we evaluated mammography and colonoscopy for breast and colon cancer screening, respectively. Because imaging modalities and invasive procedures are not widely used for prostate cancer screening, we evaluated use of prostate-specific antigen (PSA) testing for prostate cancer. We hypothesized that customers who receive elevated PGT cancer risk estimates would not significantly alter their health-related behaviors but that they would be more likely to engage in cancer screening than consumers who receive average or reduced PGT cancer risk estimates. Secondary

objectives were to describe individuals' cancer-related motivations for PGT and to describe individual-level PGT cancer risk estimates.

METHODS

Study Design and Procedures

New customers of 23andMe²⁸ and Pathway Genomics (San Diego, CA)²⁹ were invited to enroll onto the PGen Study between March and July 2012. Participants were invited to complete three Web-based surveys at the following time points: at baseline (BL) before receiving results and 2 weeks and 6 months (6M) after viewing results. PGT results were returned to customers per standard company practice and then deidentified, linked to survey data, and provided to researchers. The PGen Study was approved by

Table 2. Patient-Reported Behaviors at Baseline

Behavior	Overall (N = 762)	Men (n = 306)	Women (n = 456)
Diet, No. of servings on a typical day, mean (SD)			
Fruit	2.0 (1.1)	1.8 (1.1)	2.2 (1.1)
Vegetables	2.5 (1.2)	2.4 (1.2)	2.6 (1.2)
Vitamins/herbal supplements, current use of vitamins on a regular basis or use of herbal supplements, %	68	57	75
Exercise, No. of days per week of leisure-time physical activities, mean (SD)			
Vigorous	2.4 (2.1)	2.5 (2.0)	2.3 (2.1)
Moderate	3.5 (2.3)	3.3 (2.2)	3.6 (2.3)
Strengthening	1.4 (1.8)	1.5 (1.8)	1.4 (1.8)
Cancer screening tests, %			
Colonoscopy	37	32	41
Mammogram	NA	NA	60
Prostate-specific antigen	NA	31	NA

Abbreviations: NA, not applicable; SD, standard deviation.

Table 3. Unadjusted Associations Between Genetic Risk Scores and Participants' Diet at 6 Months, Overall and Separately by Behavior at Baseline

PGT Cancer Risk	Overall			Not Meeting CDC Recommendations for Fruit and Vegetables at Baseline			Meeting CDC Recommendations for Fruit and Vegetables at Baseline		
	No.	Changed Diet, %	P	No.	Changed Diet, %	P	No.	Changed Diet, %	P
Breast cancer risk			.50			.82			.30
Not elevated	375	34.7		180	30.6		195	38.5	
Elevated	44	29.5		27	33.3		17	23.5	
Colorectal cancer risk			.73			.90			.56
Not elevated	524	30.3		294	27.9		230	33.5	
Elevated	166	28.9		97	28.9		69	29.0	
Prostate cancer risk			.70			.24			.23
Not elevated	207	24.2		137	23.4		70	25.7	
Elevated	64	26.6		46	32.6		18	11.1	

Abbreviations: CDC, Centers for Disease Control and Prevention; PGT, personal genomic testing.

the Partners Human Research Committee and the University of Michigan Institutional Review Board. The study design^{30,31} and other findings have been reported previously.³²⁻³⁷

Study Measures

Participants from both companies received a single genetic risk estimate based on genotyping of multiple SNPs for breast (women only), prostate (men only), and colorectal cancer. Consistent with prior analyses of PGen data, a threshold relative risk (RR) level was selected to distinguish between elevated and nonelevated genetic risk, with results dichotomized into the following two categories: average or reduced genetic risk (23andMe RR < 1.2; two lowest Pathway categories) and elevated genetic risk (23andMe RR ≥ 1.2; three highest Pathway categories).³⁵ The survey also queried participants about their interest in learning their cancer genetic risk and about BL cancer risk perceptions.³⁸ At 6M, participants were asked about changes in their diet and exercise behaviors and use of vitamins and herbal supplements that were specifically motivated by their PGT results and about changes, or plans to make any changes, to advanced care planning (eg, creating a will, advance directives) as a result of learning their genetic information.³⁹ Mammography, colonoscopy, and PSA testing were measured at BL and 6M.⁴⁰ Additional details on the study measures are included in the Appendix (online only).

Statistical Analyses

Data from the BL and 6M surveys were analyzed. Participants were excluded if they reported any prior cancer diagnosis, reported prior genetic testing, and/or had missing data on demographic characteristics or PGT cancer risk estimates. We estimated whether participants' BL health

behaviors met published standards by comparing participants' self-reported dietary and exercise behaviors with recommendations from the Centers for Disease Control and Prevention (CDC) and examined screening behaviors for participants younger and older than age 50 years (Appendix). We reported BL vitamin and/or supplement use as a dichotomous response (any use v no use).

Separate analyses were conducted for each behavioral outcome. Participants who affirmatively answered that they had made changes in their health behavior (eg, diet, exercise) that were specifically motivated by their PGT results were compared with those who did not make changes. We examined univariable associations between PGT risk estimates for each cancer and behaviors at 6M using the χ^2 and Fisher's exact tests. We examined unadjusted associations between participants' genetic risk scores and their 6M behaviors according to whether the participant was above or below the recommended behavior level (or used vitamins or supplements) at BL. We then fit multivariable logistic regression models to examine the same associations, adjusting for all covariates of interest (ie, age, race, ethnicity, sex, education, employment, income, family history of cancer, insurance status, and health status) plus the BL behavior specific to the behavioral outcome (eg, BL fruit and vegetable consumption for 6M changes in diet, BL mammography for 6M mammography use) regardless of statistical significance. Additionally, because health-related behaviors may be influenced by the risk of developing diseases other than cancer, for these outcomes, we adjusted for participants' PGT risks for type 2 diabetes, obesity, and heart disease. Finally, because interest in cancer risk information and cancer risk perception can be predictors of screening, we adjusted for these items in the models for the screening outcomes. In exploratory analyses, we evaluated the associations between genetic risk scores and screening at 6M for participants younger than age 50 years and in those age 50 years or older.

Table 4. Unadjusted Associations Between Genetic Risk Scores and Participants' Exercise Behavior at 6 Months, Overall and Separately by Behavior at Baseline

PGT Cancer Risk	Overall			Not Meeting CDC Recommendations for Exercise at Baseline			Meeting CDC Recommendations for Exercise at Baseline		
	No.	Changed Exercise, %	P	No.	Changed Exercise, %	P	No.	Changed Exercise, %	P
Breast cancer risk			.57			.83			.53
Not elevated	375	27.7		254	28.3		135	26.4	
Elevated	44	31.8		30	30.0		14	35.7	
Colorectal cancer risk			.27			.24			.87
Not elevated	524	24.0		346	23.7		178	24.7	
Elevated	166	28.3		104	29.8		62	25.8	
Prostate cancer risk			.052			.12			.25
Not elevated	207	18.4		120	16.7		87	20.7	
Elevated	64	29.7		43	27.9		21	33.3	

Abbreviations: CDC, Centers for Disease Control and Prevention; PGT, personal genomic testing.

Table 5. Unadjusted Associations Between Genetic Risk Scores and Participants' Use of Vitamins or Herbal Supplements at 6 Months, Overall and Separately by Use at Baseline

PGT Cancer Risk	Overall			Not Using Vitamins or Herbal Supplements at Baseline			Using Vitamins or Herbal Supplements at Baseline		
	No.	Changed Use of Vitamins/Herbal Supplements, %	P	No.	Changed Use of Vitamins/Herbal Supplements, %	P	No.	Changed Use of Vitamins/Herbal Supplements, %	P
Breast cancer risk			.79			.99			.99
Not elevated	375	24.5		96	14.6		279	28.0	
Elevated	44	22.7		11	9.1		33	27.3	
Colorectal cancer risk			.53			.42			.39
Not elevated	524	19.5		177	10.7		347	23.9	
Elevated	166	21.7		49	6.1		117	28.2	
Prostate cancer risk			.008			.68			.001
Not elevated	207	11.6		89	7.9		118	14.4	
Elevated	64	25.0		28	3.6		36	41.7	

Abbreviation: PGT, personal genomic testing.

Given our sample size, the observed proportion of participants with elevated risk, and a one-sided type I error rate of 0.05, our study had power of 80% to detect absolute differences in excess of 20%, 12%, and 20% for changes motivated by being at elevated risk for breast, colorectal, or prostate cancer, respectively. No variable had $\geq 10\%$ missing data. All statistical analyses were conducted using Stata version 13.1 (StataCorp, College Station, TX).

RESULTS

Participant Characteristics, PGT Results, and BL Behaviors

An enrollment summary is shown in Figure 1. Demographic and health characteristics and PGT risk estimates for the 762 participants included in at least one cancer screening behavior analysis are listed in Table 1. Self-reported BL behaviors are shown in Figure 2 and Table 2. At BL, 68% of participants used vitamins or supplements, 43% met CDC dietary recommendations, and 35% met CDC exercise recommendations. At BL, participants age 50 years and older reported high rates of past screening (mammogram, 97%; colonoscopy, 75%; PSA, 80%).

Table 6. Unadjusted Associations Between Genetic Risk Scores and Participants' Advance Planning at 6 Months

PGT Cancer Risk	Overall		
	No.	Changed Advanced Planning, %	P
Breast cancer risk			.16
Not elevated	374	9.6	
Elevated	43	2.3	
Colorectal cancer risk			.09
Not elevated	522	7.3	
Elevated	166	3.6	
Prostate cancer risk			.45
Not elevated	207	2.9	
Elevated	64	4.7	

NOTE. Details about advanced planning were not asked on the baseline survey. Abbreviation: PGT, personal genomic testing.

Health-Related Behaviors and Cancer Screening at 6M

At 6M, a minority of participants made changes in their diet (31%), exercise behavior (26%), advanced care planning behavior (6%), or use of vitamins/herbal supplements (21%) in response to PGT. Overall, screening since receiving PGT test results, as reported on the 6M survey, was 26% for mammography, 7% for colonoscopy, and 19% for PSA testing. Across all three cancers, participants who reported screening in the year before ordering PGT were the most likely to report screening at 6M. This trend was maintained after stratification by age ($< v \geq 50$ years), with the exception of prostate cancer, where frequency counts were small. A small percentage of participants who reported no prior history of screening at BL reported screening at the 6M follow-up (mammography, 0.6%; colonoscopy, 2.0%; PSA, 2.5%) with slightly higher reported rates of colonoscopy (6.5%) and PSA testing (7.1%) in participants age 50 and older.

Associations Between Genetic Risk and Behavior at 6M

Results of univariable analyses between PGT risk scores and outcomes are listed in Tables 3-7. Six-month vitamin or supplement use significantly changed among men who were vitamin or supplement users at BL, and the use of PSA testing went up among men who had not reported PSA testing at BL.

Figure 3 and Appendix Tables A1 and A2 (online only) present the multivariable logistic regression model results for 6M behaviors. Individuals with elevated cancer genetic risk scores were not significantly more likely to change their diet, exercise, use of vitamins or herbal supplements, or cancer screening behavior or engage in more advanced care planning than individuals who received average or reduced risk estimates, with one exception; men who had elevated PGT prostate cancer risk estimates were more likely to change their vitamin or herbal supplement use (22% of participants at elevated risk v 8% not at elevated risk; adjusted odds ratio, 3.43; 95% CI, 1.44 to 8.18). Other significant predictors of behavior change at 6M include BL behavior (eg, vigorous exercise; vitamin/supplement use; mammography, colonoscopy, and PSA testing), worse health status (for diet and vitamin or supplement use), and older age (for advanced planning and for mammography, PSA and colonoscopy). Finally, higher incomes

Table 7. Unadjusted Associations Between Genetic Risk Scores and Participants' Cancer-Specific Screening at 6 Months, Overall and Separately by Prior Screening

PGT Cancer Risk	Overall			No Prior Cancer-Specific Screening			Prior Cancer-Specific Screening		
	No.	Screened, %	<i>P</i>	No.	Screened, %	<i>P</i>	No.	Screened, %	<i>P</i>
Breast cancer risk			.22			.99			.25
Not elevated	386	27.2		155	0.6		231	45.0	
Elevated	52	19.2		22	0.0		30	33.3	
Colorectal cancer risk			.52			.99			.41
Not elevated	548	6.2		342	2.0		206	13.1	
Elevated	171	7.6		108	1.9		63	17.5	
Prostate cancer risk			.048			.007			.99
Not elevated	216	16.7		151	0.7		65	53.8	
Elevated	65	27.7		40	10.0		65	56.0	

Abbreviation: PGT, personal genomic testing.

were inversely associated with 6M changes in exercise, and women were more likely to report 6M changes in advanced care planning. Participants' perception of elevated cancer risk at BL was a significant predictor only of colonoscopy use. Finally, we found no significant associations between elevated risk scores and 6M screening in participants younger than age 50 or age 50 and older (Appendix Table A3, online only).

DISCUSSION

This study uses a longitudinal design to examine the impact of return of DTC-PGT cancer risk test results from two prominent PGT companies on study participants' cancer-related behaviors. Consistent with our hypothesis, most PGT customers did not alter their health-related behaviors in the wake of PGT cancer results, with one exception; men who received elevated PGT prostate cancer risk estimates were significantly more likely to change their vitamin or supplement use than men who received average or reduced risk estimates. Counter to our hypothesis, however, we found that individuals who received elevated PGT cancer risk estimates did not have higher cancer screening rates at 6 months than individuals who received average or reduced PGT cancer risk estimates. It should be noted that our ability to detect changes in cancer screening in our sample of PGT customers was limited, particularly for those older than age 50 years, because customers tended to be high users of cancer screening at BL. In contrast, our ability to detect changes in dietary and exercise behavior was greater given that only 35% to 45% of participants reported BL behaviors that were consistent with CDC recommendations.

Although it is not possible to generalize the results of this study to all Americans, it is important to study early adopters of PGT as a first step in understanding how direct access to genetics may or may not affect health-related behaviors and health care use. Our data advance the field by addressing the questions of whether customers will change their health-related behaviors or use cancer screening after receiving PGT results. The provision of DTC-PGT SNP risk estimates to consumers remains controversial because the clinical implications of low effect size risk variants are uncertain and the use of SNP data to independently predict cancer risk is limited.^{2,3,41,42} Other studies have found that participants report visiting providers and altering their health behaviors in the wake of testing¹²⁻¹⁴;

however, recent review articles suggest that the effect of PGT on personal health behaviors is minimal.^{4,27,43} Our data confirm and extend the cancer-related findings from the Scripps study,^{15,16} in that neither that study nor ours found significant associations between the return of individuals' condition-specific genetic risk estimates and health-related behaviors or cancer-related screening. Our data also contribute to the evolving body of literature that indicates that individuals infrequently alter their risk behaviors after the receipt of genetic risk estimates. Recent meta-analyses of studies investigating DNA-based risk estimate testing find no changes in physical activity, smoking, diet, medication or supplement use, or other unintended adverse effects of testing.^{44,45}

The association between the receipt of elevated PGT prostate cancer risk estimates and the use of dietary supplements among men is notable given the conflicting data about the relative benefits and harms of vitamin and supplement use for prostate cancer prevention and management.⁴⁶⁻⁵¹ In fact, the American College of Preventive Medicine recently recommended against the use of supplements (ie, multivitamins, vitamin E, and β-carotene) for cancer prevention.⁵² Our findings are also consistent with data from the Risk Evaluation and Education for Alzheimer's Disease (REVEAL) study in which investigators found that 16% of participants reported a change in dietary supplement use (eg, vitamins E, ginkgo biloba) after undergoing genetic risk assessment for Alzheimer disease.⁵³ Notably, individuals who had at least one copy of the allele that confers an elevated risk of Alzheimer disease (ie, apolipoprotein E ε4) had an odds of supplement use 4.75 times the odds of individuals without the elevated risk allele. However, given that our survey asked specifically about changes in vitamin or supplement use related to PGT testing, we are unable to determine whether vitamin or supplement use increased or decreased. Additionally, customers tended to be high vitamin and supplement users at BL, and the changes in vitamin and supplement use after PGT tended to be greatest among BL users. Given the growing nutraceutical industry in the United States and the paucity of regulation of dietary supplements, findings such as these raise questions about how PGT and clinic-based genetic testing might be contributing to the growth of this industry and highlight the need for studies that specifically focus on the use of nutraceuticals after genomic testing.

Variation across studies in regard to the effect of PGT on health-related behavior may be attributed to multiple factors. Changes in screening behaviors in the wake of PGT may be less common than lifestyle changes given that providers often play

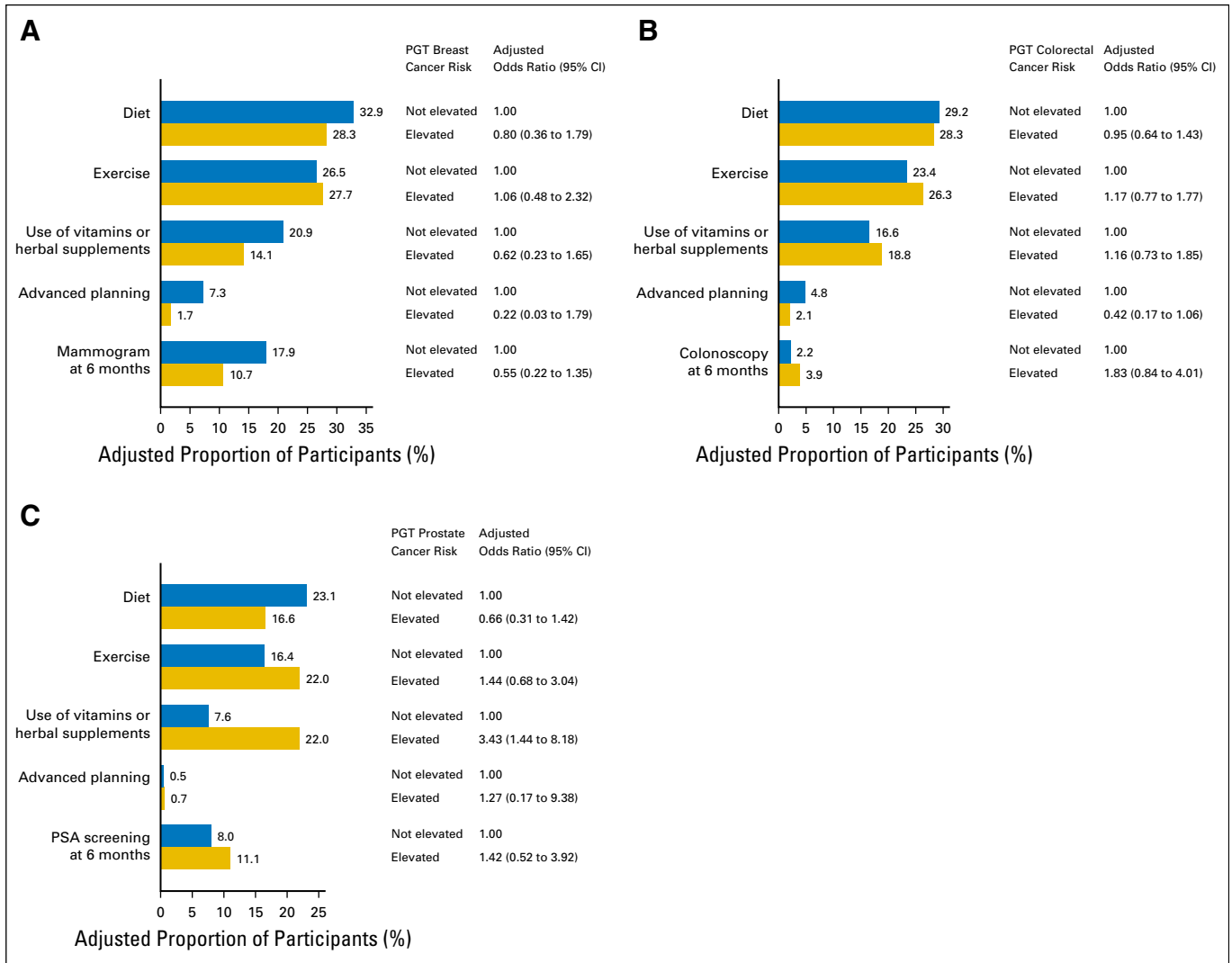


Fig 3. Behavioral and cancer screening changes specifically motivated by personal genomic testing (PGT) risk for (A) breast cancer, (B) colorectal cancer, and (C) prostate cancer. Adjusted proportions and odds ratios from multivariable logistic regression are shown. All models are adjusted for age, race, ethnicity, sex, education, employment, household income, family history of cancer, health insurance, health status, and baseline behavior. Baseline behavior was defined by participant reports of fruit and vegetable consumption (diet); number of days of leisure-time physical activity (exercise); use of vitamins or herbal supplements; and mammography, colonoscopy, or prostate-specific antigen (PSA) testing within the year before testing. Of note, there was no baseline item that specifically pertained to advanced planning. All models except for the mammography, colonoscopy, or PSA outcome are adjusted further for PGT risk for type 2 diabetes, obesity, and coronary heart disease. The model for the mammography outcome is adjusted further for interest in genetic risk for breast cancer and baseline perceived risk for breast cancer. The model for the colonoscopy outcome is adjusted further for interest in genetic risk for colorectal cancer and baseline perceived risk for colorectal cancer. The model for the PSA outcome is adjusted further for interest in genetic risk for prostate cancer and baseline perceived risk for prostate cancer.

a gatekeeping role when it comes to accessing medical technologies. Differences in cancer risk perception may be another factor, because multiple studies have shown that perceived risk is often predictive of cancer screening behavior.⁵⁴ Kaufman et al¹² found that PGT customers who considered themselves to be at high risk for colon cancer were more likely to discuss PGT results with a physician, change their diet, and increase their physical activity. Carere et al³⁵ evaluated perceived cancer risk among the broader PGen Study cohort and found that, with the exception of perceptions for lung cancer risk, consumers who received an elevated PGT risk result had modest mean positive changes in their risk perception. Among our participants, colon cancer risk perception before testing was an independent predictor of colonoscopy use

after PGT. Another factor that may contribute to variation in customer behavior after testing is customer PGT result comprehension. A separate PGen Study analysis found that customers generally interpreted PGT risk estimates correctly; however, cancer risk estimates were not specifically evaluated.³³ Kaufman et al¹² found that the majority of PGT customers interpret test results correctly when presented with hypothetical scenarios, and the Multiplex Initiative found that most individuals who received testing recalled what had been reported.¹⁸ Other studies demonstrate that individuals in the general population often misinterpret PGT test results when presented with hypothetical scenarios.⁵⁵ Finally, heterogeneity in study populations may influence PGT use and post-PGT behavior. Early adopter populations

(such as those explored in our study and others^{12,15}) may be higher health care users in general, especially compared with a more diverse sample such as the Multiplex population.¹⁸ Additional research is needed to determine whether there are specific customer populations that will be more likely to alter their behavior or use more health resources after PGT.

Our findings should be interpreted in the context of a few limitations. First, although we specifically intended to study current PGT users and the PGen Study sample is demographically representative of the DTC-PGT user population,³¹ our sample is not representative of the general population. Unlike the general population, a large proportion of participants had previously received cancer screening, with 91% of participants older than age 50 years reporting having been screened in the past (mammography, 97%; colonoscopy, 76%; PSA, 79%). For comparison, in 2010, the national estimate of adults age 50 to 75 years receiving a colonoscopy was 54.9%.⁵⁶ It is unclear how PGT would influence the cancer screening behaviors of those who do not meet the recommended rates of screening. Second, the study included 6 months of follow-up, but observing behavior changes may take longer, especially for screening behaviors that require a provider order and behaviors that are recommended on an annual or less frequent basis. Third, only limited clinical data were collected. For instance, clinical factors that may be associated with screening recommendations (eg, having received radiation) were not captured. Additionally, the survey did not ask about cancer screening through other modalities, such as flexible sigmoidoscopy, or other potential confounders (eg, physician ambivalence toward PGT test results). Finally, we had limited power to detect greater behavior change among participants at elevated risk compared with participants at average or reduced risk for some outcomes. Nonetheless, our findings may not have differed substantially had we had greater power; among our participants, for example, mammography use was actually lower among the elevated risk group.

In summary, our study found that adults receiving elevated SNP-based cancer risk estimates from PGT did not significantly alter their diet, exercise, or advanced care planning behavior and were not more likely to engage in cancer screening than adults receiving average or reduced risk estimates. Given the fact that SNP-based risk estimates have limited clinical use, patients need to be prepared for the ambiguities inherent in PGT, and providers need to be prepared to counsel patients about such testing. If PGT expands to additional clinical settings and larger populations, future research will need to assess its association with cancer-related behaviors in broader populations and health care resource use that may or may not accrue as a result.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at ascopubs.org/journal/jco.

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Appendix

Supplemental Methods

Study Measures

Genetic risk estimates. Participants from both companies received a single genetic risk estimate based on genotyping of multiple single nucleotide polymorphisms for breast (women only), prostate (men only), and colorectal cancer. 23andMe (Mountain View, CA) customers were presented with a relative risk (RR) for each cancer, whereas Pathway Genomics (San Diego, CA) customers received results on a five-category scale corresponding to increasing RR of cancer (eg, Learn More). To harmonize genetic risk information across companies, a threshold RR level was selected to distinguish elevated from nonelevated genetic risk, and results were dichotomized into the following two categories: average or reduced genetic risk (23andMe RR < 1.2; two lowest Pathway categories) and elevated genetic risk (23andMe RR ≥ 1.2; three highest Pathway categories).

Interest in learning cancer genetic risk. Interest in learning cancer genetic risk was assessed using a single item (three categories from “not at all interested” to “very interested”).

Cancer risk perceptions. At baseline, participants were asked to rate their chances of developing breast cancer (women only), prostate cancer (men only), and colorectal cancer “compared to the average [man or woman] of [the same] age.” Responses were recorded on a five-point scale ranging from “much lower than average” to “much higher than average”;³⁴ alternatively, participants could select “I have been diagnosed with this condition.”

Lifestyle behavior, supplement use, advanced care planning behaviors. At 6 months, participants were asked about changes in their diet and exercise and use of vitamins or herbal supplements that were specifically motivated by their personal genomic testing results and about changes, or plans to make any changes, to advanced care planning (eg, creating a will, advance directives) as a result of learning their genetic information.³⁵

Screening behaviors. Mammography, colonoscopy, and prostate-specific antigen testing were measured at baseline and 6 months using questions from the 2011 Behavioral Risk Factor Surveillance System Questionnaire,³⁶ modified to reflect a 6-month window of interest.

Use of vitamins and herbal supplements. At baseline, participants were asked “Are you currently taking any vitamins on a regular basis (most days)?” and “Are you currently taking any herbal supplements?” Response options were “yes” or “no.”

Comparisons of Participants' Self-Reported Behaviors With Published Standards

Dietary recommendations. To estimate whether participants' baseline dietary behaviors met published standards, we compared their self-reported behaviors with 2010 recommendations from the Centers for Disease Control and Prevention (<http://www.choosemyplate.gov/fruit> and <http://www.choosemyplate.gov/vegetables>). For diet, we equated a serving (the unit of measurement included in the survey items) with 1 cup and rounded up where necessary. For example, if the recommendation was 1.5 cups per day, then we required the participant to report having two or more servings per day.

- Recommendations for fruit intake by age and sex
 - Women age 19 to 30 years = 2 cups per day
 - Women older than age 30 years = 1.5 cups per day (round up to two servings)
 - Men = 2 cups per day
- Recommendations for vegetable intake by age and sex
 - Women age 19 to 50 years = 2.5 cups per day (round up to three servings)
 - Women older than age 50 years = 2 cups per day

- Men = 3 or 2.5 cups per day, depending on age (round up to three servings)

Exercise recommendations. To estimate whether participants' baseline exercise behaviors met published standards, we compared their self-reported behaviors with 2008 recommendations from the Centers for Disease Control and Prevention (<http://www.cdc.gov/physicalactivity/basics/index.htm>). For exercise, we calculated an equivalent mix of moderate and vigorous activity as ($2 \times$ vigorous + moderate) exceeding the threshold set for moderate activity. Recommendations for exercise by age were as follows:

- Age 18 to 64 years (1 or 2 or 3)
 1. 150 minutes per week of moderate-intensity aerobic activity plus muscle-strengthening activities on 2 or more days per week
 2. 75 minutes per week of vigorous-intensity aerobic activity plus muscle-strengthening activities on 2 or more days per week
 3. An equivalent mix of moderate- and vigorous-intensity aerobic activity plus muscle-strengthening activities on 2 or more days per week
- Age 65 years or older (1 or 2 or 3)
 1. 300 minutes per week of moderate-intensity aerobic activity plus muscle-strengthening activities on 2 or more days per week
 2. 150 minutes a week of vigorous-intensity aerobic activity plus muscle-strengthening activities on 2 or more days per week
 3. An equivalent mix of moderate- and vigorous-intensity aerobic activity plus muscle-strengthening activities on 2 or more days per week

Table A1. Adjusted Association Between PGT Cancer Risk and Health-Related and Advanced Planning Changes, by Multivariable Logistic Regression

Factor	Changes Specifically Motivated by Results*											
	Diet			Exercise			Use of Vitamins/Herbal Supplements			Advanced Planning		
	Odds Ratio	95% CI	P	Odds Ratio	95% CI	P	Odds Ratio	95% CI	P	Odds Ratio	95% CI	P
No. of elevated cancer risks†			.45			.27			.43			.29
0	1.00			1.00			1.00			1.00		1.00
1	0.79	0.55 to 1.15		1.19	0.81 to 1.76		1.06	0.69 to 1.64		0.67	0.34 to 1.35	
2 or more	0.96	0.58 to 1.59		1.52	0.91 to 2.55		1.46	0.82 to 2.61		0.42	0.12 to 1.51	
Age (per year)	1.01	1.00 to 1.03	.12	1.00	0.98 to 1.01	.90	1.00	0.98 to 1.02	.97	1.04	1.01 to 1.07	.01
Race												
Nonwhite	1.09	0.66 to 1.80	.75	1.51	0.91 to 2.51	.11	1.17	0.66 to 2.08	.60	1.81	0.77 to 4.25	.18
Hispanic	1.50	0.68 to 3.28	.32	1.69	0.77 to 3.72	.19	2.30	0.98 to 5.38	.06	3.28	1.00 to 10.8	.05
Female sex	1.43	0.99 to 2.06	.06	1.40	0.95 to 2.05	.09	1.44	0.93 to 2.24	.10	2.80	1.26 to 6.19	.01
Education			.33			.75			.30			.59
Less than college degree	1.00			1.00			1.00			1.00		
College degree	0.93	0.58 to 1.50		1.22	0.72 to 2.05		1.25	0.72 to 2.18		0.86	0.33 to 2.27	
Greater than college degree	0.74	0.47 to 1.17	.65	1.17	0.72 to 1.90	.70	0.87	0.51 to 1.49	.30	1.29	0.56 to 2.96	.81
Employment												
Full time	1.00			1.00			1.00			1.00		
Retired	0.87	0.49 to 1.55		1.06	0.57 to 1.97		1.63	0.84 to 3.17		1.36	0.52 to 3.58	
Other	0.83	0.55 to 1.25		0.85	0.55 to 1.30		0.95	0.59 to 1.55		1.19	0.52 to 2.73	
Household income			.10			.04			.75			.46
≤ \$99,999	1.00			1.00			1.00			1.00		
\$100,000-\$199,999	0.64	0.43 to 0.97		0.57	0.37 to 0.88		0.85	0.53 to 1.35		0.87	0.40 to 1.90	
≥ \$200,000	0.85	0.49 to 1.47		0.81	0.45 to 1.45		0.85	0.42 to 1.70		0.45	0.12 to 1.61	
Family history of cancer	0.83	0.55 to 1.25	.38	1.11	0.72 to 1.72	.64	1.04	0.63 to 1.71	.88	1.10	0.49 to 2.51	.81
Not insured‡	2.11	0.98 to 4.55	.06	0.95	0.40 to 2.25	.91	3.25	1.45 to 7.30	< .01			.07
Health status			.02			.11			< .01			
Excellent	1.00			1.00			1.00			1.00		
Very good	1.71	0.98 to 2.98		1.64	0.92 to 2.92		1.23	0.62 to 2.46		0.47	0.17 to 1.29	
Good, fair, or poor	2.22	1.25 to 3.93		1.91	1.04 to 3.50		2.31	1.16 to 4.58		1.10	0.43 to 2.85	
Elevated PGT risk for type 2 diabetes	1.09	0.68 to 1.76	.73	1.32	0.80 to 2.17	.27	0.96	0.54 to 1.73	.9	0.79	0.31 to 2.06	.63
Elevated PGT risk for obesity	0.85	0.50 to 1.45	.55	0.77	0.43 to 1.38	.39	1.61	0.91 to 2.85	.1	0.94	0.30 to 2.93	.92
Elevated PGT risk for coronary heart disease	1.05	0.69 to 1.60	.81	1.11	0.71 to 1.72	.65	0.87	0.53 to 1.42	.57	0.33	0.11 to 0.98	.05
Diet												
No. of servings of fruit per day	1.07	0.89 to 1.28	.49									
No. of servings of vegetables per day	1.09	0.93 to 1.29	.29									
Baseline use of vitamins or herbal supplements							2.86	1.71 to 4.80	< .01			
Exercise												
Days per week of vigorous exercise				1.13	1.03 to 1.25	.01						
Days per week of moderate exercise				1.00	0.92 to 1.08	.97						
Days per week of strengthening exercise				0.97	0.86 to 1.09	.60						

Abbreviation: PGT, personal genomic testing.

*Separate models were fit for each specification of PGT cancer risk.

†Includes breast, colorectal, prostate, and lung cancer and melanoma. Thirteen participants had three elevated cancer risks, and one participant had four elevated cancer risks.

‡Insurance status was not included in the model for changes for advanced planning, because no one who was not insured made a change in advanced planning.

Personal Genomic Testing for Cancer Risk

Table A2. Participant Characteristics Associated With Cancer Screening at 6 Months: Multivariable Logistic Regression

Characteristic	Outcome: Mammography (n = 438)			Outcome: Colonoscopy (n = 717)			Outcome: PSA Testing (n = 280)		
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
Age (per year)	1.07	1.04 to 1.10	< .001	1.04	1.00 to 1.07	.03	1.08	1.04 to 1.13	< .001
Race									
Nonwhite	0.63	0.27 to 1.49	.29	0.48	0.10 to 2.32	.36	0.59	0.09 to 3.82	.58
Hispanic	3.62	0.94 to 13.92	.06	0.33	0.03 to 4.43	.41	4.17	0.60 to 28.7	.15
Female				0.60	0.29 to 1.24	.17			
Education			.70			.46			.62
Less than college degree	1.00			1.00			1.00		
College degree	0.74	0.36 to 1.52		0.93	0.38 to 2.26		0.74	0.20 to 2.71	
Greater than college degree	0.88	0.45 to 1.72		0.61	0.26 to 1.44		0.55	0.16 to 1.87	
Employment			.90			.16			.39
Full time	1.00			1.00			1.00		
Retired	1.01	0.46 to 2.22		2.59	0.97 to 6.92		1.64	0.47 to 5.76	
Other	1.16	0.60 to 2.25		1.33	0.52 to 3.43		2.23	0.66 to 7.53	
Household income			.39			.56			.63
≤ \$99,999	1.00			1.00			1.00		
\$100,000-\$199,999	1.54	0.83 to 2.86		0.78	0.33 to 1.85		0.91	0.33 to 2.48	
≥ \$200,000	1.25	0.50 to 3.14		1.49	0.52 to 4.27		0.55	0.16 to 1.93	
Family history of cancer	0.71	0.34 to 1.47	.35	0.76	0.32 to 1.80	.53	0.68	0.26 to 1.82	.44
Not insured	0.74	0.15 to 3.59	.71	1.60	0.31 to 8.22	.57	1.45	0.18 to 11.7	.73
Health status			.75			.045			.63
Excellent	1.00			1.00			1.00		
Very good	1.37	0.59 to 3.15		5.03	0.99 to 25.7		1.77	0.49 to 6.38	
Good, fair, or poor	1.20	0.53 to 2.76		7.41	1.47 to 37.5		1.90	0.48 to 7.59	
Interested in genetic risk for cancer*	1.75	0.61 to 5.07	.3	1.62	0.46 to 5.70	.45	2.77	0.37 to 20.9	.32
Screened within year before testing†	5.77	3.24 to 10.3	< .001	8.17	3.89 to 17.2	< .001	7.64	2.92 to 20.01	< .001
Baseline perceived elevated cancer risk*	1.24	0.57 to 2.69	.58	3.30	1.53 to 7.11	.002	1.37	0.46 to 4.07	.57
PGT elevated cancer risk*	0.55	0.22 to 1.35	.19	1.83	0.84 to 4.01	.13	1.42	0.52 to 3.92	.50

Abbreviations: OR, odds ratio; PGT, personal genomic testing; PSA, prostate-specific antigen.

*Corresponding to cancer associated with specific screening outcome. For example, for the outcome of mammography, interested in genetic risk for cancer indicates interest in genetic risk for breast cancer and PGT elevated cancer risk indicates elevated risk for breast cancer.

†Corresponding to specific screening outcome. For example, for the outcome of mammography, this variable indicates whether the participant received a mammography within the year before testing. Patients who reported “don’t know or not sure” are included in the group of patients who were not screened in the year before testing.

Table A3. Unadjusted Associations Between Genetic Risk Scores and Participants’ Screening Behaviors at 6 Months by Age Group

Cancer Risk	Cancer Screening Behaviors at 6 Months for Participants Age < 50 Years				Cancer Screening Behaviors at 6 Months for Participants Age ≥ 50 Years			
	Total No.	Screened		Fisher’s Exact P	Total No.	Screened		Fisher’s Exact P
		No.	%			No.	%	
Breast cancer				.41				.07
Not elevated	226	30	12		160	79	49	
Elevated*	36	6	17		16	4	25	
Colorectal cancer				.51				.84
Not elevated	354	9	2.5		194	25	13	
Elevated†	105	4	3.8		66	9	14	
Prostate cancer				.25				.99
Not elevated	158	8	5		58	28	48	
Elevated‡	37	4	11		28	14	50	

*Among the six women younger than age 50 years with elevated risk and with a mammogram at 6 months, all six had prior screening (four within the past year and two > 1 year ago). Among the four women age ≥ 50 years with elevated risk and with a mammogram at 6 months, all four had prior screening (three within the past year and one > 1 year ago).

†Among the four participants younger than age 50 years with elevated risk and with a colonoscopy at 6 months, three had prior screening (two within the past year and one > 1 year ago). Among the nine participants age ≥ 50 years with elevated risk and with a colonoscopy at 6 months, eight had prior screening (four within the past year and four > 1 year ago).

‡Among the four participants younger than age 50 years with elevated risk and with a prostate-specific antigen test at 6 months, one had prior screening (within the past year). Among the 14 participants age ≥ 50 years with elevated risk and with a prostate-specific antigen test at 6 months, 13 had prior screening (12 within the past year and one > 1 year ago).