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ARTICLE

Preferences for a polygenic test to estimate cancer risk in a general Australian population

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ABSTRACT

Purpose: There is significant interest in the use of polygenic risk score (PRS) tests to improve cancer risk assessment and stratified prevention. Our current understanding of preferences regarding different aspects of this novel testing approach is limited. This study examined which attributes of a PRS test most influence the likelihood of testing.

Methods: A discrete choice experiment was developed to elicit preferences for different aspects of a PRS test by surveying an online sample of the Australian population. Preferences were assessed using mixed logistic regression, latent class analysis, and marginal willingness to pay.

Results: The 1002 surveyed respondents were more likely to choose a PRS test that was more accurate, tested for multiple cancer types, and enabled cancer risk reduction through lifestyle modification, screening, or medication. There was also a preference for testing through a primary care physician rather than online or through a genetic specialist. A test that did not impact life insurance eligibility or premiums was preferred over the one that did.

Conclusion: This study found that the Australian population prefer a PRS test that is highly accurate, tests for multiple cancers, has noninvasive risk reduction measures, and is performed through primary care.

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Introduction

Polygenic risk scores (PRSs) can provide individuals with their risk of developing a particular condition. There is much interest in the potential role of PRSs to improve cancer risk assessment for risk-based prevention and screening.[1-3] Evidence of their clinical utility is growing but gaps remain in understanding how members of the public might engage with this novel testing approach.

One of the possible clinical benefits of PRSs relates to the early detection of cancer by providing individualized risk information to stratify cancer screening programs. Incorporating PRSs alongside traditional risk factors can improve risk discrimination for multiple cancer types.[4] When applied

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to cancer screening, it may impact the age at which someone commences screening, screening intervals, and the type of test used.[5-7] Focusing screening on those most at risk may be more cost-effective and avoid the potential sequelae of false positives and overdiagnosis for individuals who fall into lower-risk categories.[8,9] Clinical trials are actively investigating how PRS guided screening compares with conventional screening for breast and colorectal cancer.[10,11]

Nonetheless, any benefit of PRSs for cancer prevention and early detection relies on the willingness of individuals to undergo testing in the first place. Although clinical utility refers to the potential for a PRS test to improve cancer outcomes, in health economics, utility refers to the benefit obtained by an individual from choosing one alternative over another. It is integral that researchers and policymakers understand the various factors that may influence utility to better inform facilitators and barriers to PRS test uptake.

Much research has focused on participant views related to PRS testing for individual cancer types, however we do not know whether people have a preference to test for specific cancer types or whether they would like to be tested for multiple cancers at the same time.[12-14] Previous genomic studies have indicated a wish for individuals to know their personal risk of a condition regardless of whether there is a preventative or treatment option available, although if measures do exist, lifestyle interventions have been preferred over medication or surgery.[15-17] From a service delivery perspective, the broad accessibility of primary care physicians (PCPs) means that they are likely to be central in providing PRS information to the public. Although this is acceptable to specialist clinicians, there is mixed evidence as to whether this will be acceptable to patients.[14,18,19] Additional variables of concern to the public include privacy protections and the potential impact of genomic test results on life insurance plans.[12,13,16,20] Despite the importance of understanding public preferences regarding PRSs, there is a lack of data to adequately understand how these variables are traded off and the subsequent impact on implementation.

Discrete choice experiment (DCE) is a quantitative method for eliciting preferences that have been used extensively in health economics and across other disciplines ranging from transportation to marketing.[21] Given a vignette describing the situation in which a choice is to be made, participants complete a series of choice tasks, where they choose between alternative goods or services, described by their underlying characteristics, or attributes, that vary across questions.[22] The choices made by participants enable their preferences between attributes to be estimated.[22] Discrete choice models draw on the assumption that the decision maker will choose the alternative that provides them with the greatest utility. DCEs have been used to assess preferences for a range of genomic tests using both generic designs and for specific disease types.[17,20,23,24] One DCE has examined preferences for PRS testing for breast cancer risk.[14] To our knowledge, no DCE has been conducted assessing how cancer type is traded off against other attributes of a PRS test.

This study used a DCE to examine which attributes of a PRS test most influence the likelihood that members of the Australian public will choose to undertake a PRS test.

Materials and Methods

DCE attributes and levels

A DCE was developed to elicit preferences for different aspects of a PRS test on the basis of accepted good research practices for stated preference methods.[25] Attributes and levels were derived from 3 main sources: literature review, expert opinion, and consumer focus groups. The literature review was undertaken by searching PubMed and Medline databases to identify studies examining public preferences regarding genomic testing and PRSs. A provisional list of attributes and levels was subsequently devised and incorporated into a brief questionnaire that was provided to 6 researchers and clinicians with expertise in cancer genomics. The revised attributes and levels incorporating the feedback from those experts were subsequently discussed in a focus group with 7 consumers from the Primary Care Collaborative Cancer Clinical Trials Group. Consumers had a lived experience of cancer, either as cancer survivors or carers. Focus group participants were asked to rank the attributes they viewed in order of importance to guide final attribute inclusion. An iterative process was undertaken to further refine the attributes and levels based on what the authors deemed most relevant to the current PRS policy context and decision-making setting.[25]

For example, concern regarding PRS accuracy was evident from the existing literature and was important to our consumer group.[13,26] Although the validation statistic that most closely encompasses this concept is calibration, it was evident that calibration would not be well-understood by members of the lay public and the most understandable way to convey this concept was to present it as accuracy. To determine feasible levels of accuracy of a PRS for cancer, we used the calibration results of a validation study of 16 PRS for colorectal cancer.[27] We calculated an overall observed vs expected risk of colorectal cancer for each of the PRSs in the study—this study provided calibration statistics per decile, but to present 1 figure of accuracy, we combined them into 1 statistic. We took the lowest calibration observed in this validation study as an indication of the poorest accuracy and the highest as the best accuracy.

A final list of 8 attributes with levels ranging from 2 to 6 was devised as outlined in Table 1.

Designed experiment

A generator developed design was used, as outlined by Street and Burgess.[28] The initial design was an orthogonal array with 108 runs.[29] In total, 4 generators were used,

Table 1 Attributes and attribute levels

Attribute	Survey Description	Level
Impact of result on life insurance	The result of the DNA test can impact on whether you would qualify for life insurance or if your life insurance premiums would be affected	Yes No
Testing process	To have the test and receive the results you would	Order the test online, perform the cheek swab at home, send the swab back, and then receive the results online Go to your GP, have a cheek swab taken, and then see your GP for the results Obtain a referral to a genetic specialist, have a cheek swab taken, and then see your genetic specialist for the results
Price	The test will cost you	$0 (no cost) $75 ($53 US) $150 ($107 US)
Test accuracy	The accuracy of the test at estimating your risk of developing cancer is	60% accurate 75% accurate 90% accurate
Chance the result will change cancer screening	The chances that the recommended cancer screening for you changes as a result of the test is	10 out of 100 people will have different screening. This may be more screening for some, for others it would be less screening 25 out of 100 people will have different screening. This may be more screening for some, for others it would be less screening. 50 out of 100 people will have different screening. This may be more screening for some, for others it would be less screening.
Privacy	Who has access to the result	Only me Me and my family members Me and my health professionals
Cancer type	The type of cancer you will be having the test for is	Pancreatic cancer Breast cancer/prostate cancer (reflexive level based on gender) Bowel cancer Melanoma Lung cancer Pancreatic, breast, prostate, bowel, melanoma, and lung cancer (multiple cancer test)
Risk reduction measures	If the test indicates you are at high risk, to help reduce your risk you can	There are no specific changes you can make to reduce your risk of this cancer Participate in cancer screening Make lifestyle changes Participate in cancer screening and make lifestyle changes Take a medication that reduces your cancer risk Have surgery to reduce the chance the cancer will occur

USD conversions are based on exchange rate of 1 AUD to 0.71 USD.
AUD, Australian dollar; *GP*, general practitioner; *USD*, US dollar.

together leading to a final design with 432 choice sets. The choice sets were divided into 36 blocks of 12 choice sets. A minimum of 20 respondents for each block is considered sufficient to estimate a reliable model,[30] which in this study would be achieved with a minimum sample size of 720 participants. To reduce task complexity and improve respondent efficiency, partial profiles with 2 overlapping attributes were used. To foster realism, 2 restrictions were placed on the attribute combinations tying the appearance of (1) pancreatic cancer (cancer type) to the level indicating no specific changes could be made to reduce cancer risk and (2) ordering the test online to the privacy level "only me."

Instrument design

The survey consisted of 6 sections: (1) plain language statement and consent form including the purpose and length of the survey as well as a description of PRS testing, (2) description of the study attributes and levels, (3) a vignette describing a scenario in which the participant's PCP is offering a DNA test to estimate their cancer risk, (4) 12 choice tasks, (5) ranking of attribute importance, and (6) health and sociodemographic questions. Within each choice task (section 4), the level of prostate/breast cancer was designed to be reflexive, with participants allocated to respective cancer types on the basis of gender. Hovers were used to clarify terms, for

example, accuracy was described to participants as "*this is an estimate of your cancer risk, this means how closely the score reflects your true risk of cancer*." Icon arrays were included to improve the communication of probability-based levels. After completing the DCE questions, participants were asked to nominate their most and least important attribute. Appendix 1 provides an illustration of the survey components.

Pilot testing

The survey was pretested on 105 individuals. After completing the 12 choice tasks, participants were asked a series of post survey evaluation questions about the clarity of the survey instructions, explanation of PRS testing, and the difficulty of the choice tasks. The results of pretesting indicated participants' difficulty in understanding the attribute "chance the result will change cancer screening." On the basis of this, refinements were made to the wording of the attribute and attribute levels, and further hovers and icon arrays were added to facilitate participant understanding.

Data collection

The survey was administered to the Pureprofile online panel (http://www.pureprofile.com.au). Pureprofile has an independent, actively managed panel of online consumer account holders (panel members), who are sourced through a variety of online and offline sources including internal referral programs, paid acquisition, social media, search engine marketing, offline marketing, and location-based registration. Pureprofile consumer panel members have a profile homepage. Invitations can be seen in the "feed" of their homepage, where they can see basic information about the survey content including the length and the maximum/minimum payment they will receive, depending on the time taken. Participants can opt to find out more information about the study and then elect to proceed with the survey. Participants are paid directly by Pureprofile, on a continuous per-minute basis and payment is also provided if participants opt out during the survey based on the time spent. The final survey in this study was administered to Australian participants aged 18 years or older via an invitation available through their Pureprofile membership page. Quotas for age and gender were used to match the sample to the Australian adult population based on Australian Bureau of Statistics data. The response rate, defined as the number of participants starting the survey divided by the number of Pureprofile members invited to the survey was 83%. The completion rate, defined as total number of participants who completed the survey divided by the total number of participants who started the survey was 92%.

Statistical analysis

Data analyses were conducted in Stata 17 (StataCorp). Descriptive statistics were used to summarize the sociodemographic characteristics, which were compared with population-based values from the Australian Bureau of Statistics.[31] Stated attribute importance was summarized as the percentage of participants who ranked the respective attributes as most and least important, on the basis of responses to the attribute ranking in section 5 of the survey (see Instrument design). Relative attribute importance, the proportion that each attribute contributed to the choice decision, was calculated by dividing the range of coefficients for each attribute by the sum of the ranges for all attributes.

Two approaches, mixed logit modeling (MXL) and latent class analysis (LCA), were used to model preferences. The mixed logit model accounts for the panel nature of the data and allows for possible heterogeneity in preferences, by assuming preference weights vary between respondents.[32] Attributes containing levels with statistically significant standard deviations were included as random parameters in the final MXL model. These included attribute levels for privacy, cancer type, and risk reduction measures. Each model was estimated using 1000 Halton draws.

Latent class model assumes that distinct response groups exist within a sample, and it is possible to estimate the probability of individuals exhibiting similar preferences.[30] Membership to each group is characterized by latent or unobserved variables that may relate to observed characteristics of respondents such as sociodemographic characteristics.[22,29] The appropriate number of latent classes was determined by comparing the Akaike information criteria and Bayesian information criterion along with what was deemed most relevant to the research question.[32] We hypothesized that the preferences of respondents across the sample may vary according to the following characteristics: male sex, age >50 years, university-level education, having a life insurance policy, and a family history of cancer.

All attributes were dummy coded across both models. To examine gender subgroups for breast and prostate cancer, interactions were created for female and breast cancer as well as male and prostate cancer. Marginal willingness to pay (mWTP) was estimated by taking the ratio of the coefficients for attribute levels over the mean scaled coefficient for cost. This was performed for statistically significant attributes from the MXL model only.

Results

Participant characteristics

A total of 1002 participants completed the study. Participant characteristics are outlined alongside those of the Australian adult population (Supplemental Table 1). Participants were comparable to the Australian adult population across sex, age, Aboriginal and/or Torres Strait Islander status, country of birth, and geographic distribution. Participants with a vocational or university qualification were over-represented, and higher rates of self-reported screening were recorded for breast and bowel, but not cervical, cancer. Compared with

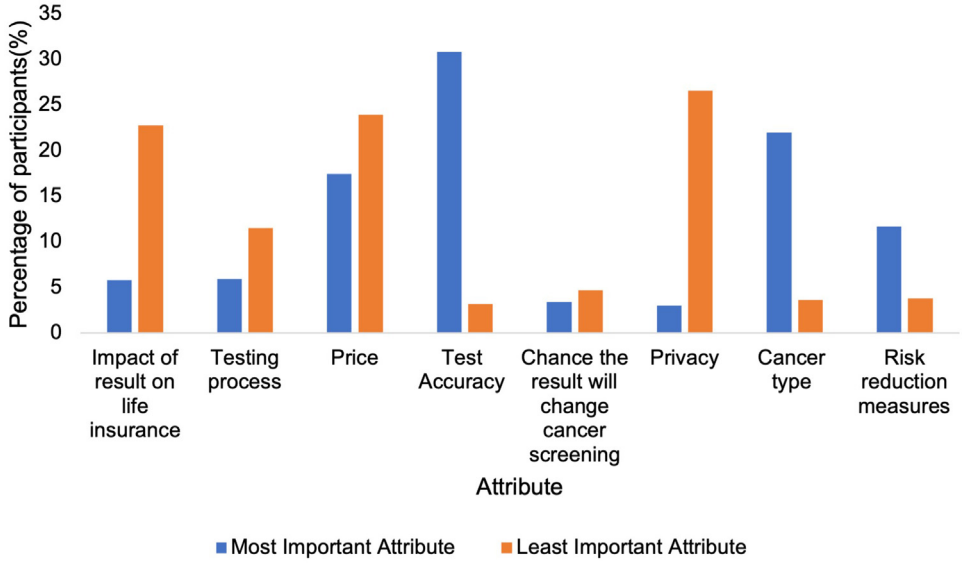

Figure 1 **Stated attribute importance**.

the Australian adult population, the sample had lower rates of self-reported very good or excellent health.

Stated attribute importance

Figure 1 represents the proportion of times that attributes were ranked as the most or least important. "Test accuracy" and "cancer type" were most often ranked as the most important attributes, whereas the attributes most often ranked as the least important attributes were "privacy" and "impact of result on life insurance." In relation to cost, 24.0% reported this as the least important attribute, whereas 17.5% stated that it was the most important.

MXL

Results of the MXL model are presented in Table 2. The relative importance of PRS test attributes is displayed in Figure 2. Relative to the reference level pancreatic cancer, a multicancer PRS test was preferred over individual PRS tests for prostate cancer followed by breast cancer and then bowel cancer. There was no significant preference for lung cancer or melanoma. A test for cancer in which participants could employ measures to reduce their risk through lifestyle modification, screening, or medication ($P < .001$) were preferred over no preventative measure or surgical procedures. There was heterogeneity in preferences for the use of a multiple cancer test ($P < .001$) and surgery as a preventative measure ($P < .001$).

There was a preference for testing through a PCP ($P < .001$) rather than online or through a genetic specialist. Participants indicated that a test that did not impact life insurance eligibility or premiums was preferred over the one that did ($P < .001$). There was no statistically significant preference depending on the test's ability to alter participant screening requirements. Increasing the price of the test resulted in larger negative coefficients.

LCA

We identified 3 distinct classes on the basis of the Akaike information criteria/Bayesian information criterion and what was considered to be most informative (Supplemental Table 2). The coefficients and 95% CIs are available in Supplemental Table 3. Membership classes were relative to the reference group, class 3. The relative importance of each attribute across classes is shown in Figure 3. Members of class 1, termed "more is better," had significant attribute levels for test accuracy and the cancer levels breast cancer, prostate cancer, bowel cancer, and multiple cancers, highlighting a preference for an accurate test of multiple cancer types. "More is better" were more likely to identify a family history of cancer. For members of class 2, termed "aim for accuracy," accuracy was most important, indicated by statistical significance across all levels of the accuracy attribute. "Aim for accuracy" were more likely to be males and those aged >50 years. For class 3, termed "choose cheaper," the only significant attribute levels were for cost, which had a negative impact on preferences. All classes were similar in size, representing shares of 31.8% for "more is better," 32.6% for "aim for accuracy," and 35.5% for "choose cheaper."

Willingness to pay

Results for mWTP are displayed in Supplemental Table 4. The largest mWTP values were for attributes pertaining to test accuracy, whereby respondents had a mWTP of A$176.26 (Australian dollar) ($125.35 US [US dollar]) to move from a PRS test with an accuracy of 90% compared

Table 2 Mixed logit model results

Attribute Level	Coefficient	95% CI	*P* Value	SD	*P* Value
Impact of result on life insurance					
Yes	Base				
No	0.12	(0.06 to 0.17)	<.001		
Testing process					
Online	Base				
GP	0.18	(0.08 to 0.27)	<.001		
Specialist	–0.02	(–0.11 to 0.08)	.74		
Price					
No cost	Base				
$75	–0.56	(–0.66 to 0.46)	<.001		
$150	–1.04	(–1.16 to –0.91)	<.001		
Test accuracy					
60%	Base				
75%	0.50	(0.41 to 0.59)	<.001		
90%	1.22	(1.07 to 1.37)	<.001		
Chance the result will change cancer screening					
10/100	Base				
25/100	–0.012	(–0.09 to 0.06)	.75		
50/100	–0.03	(–0.11 to 0.45)	.44		
Privacy					
Only me	Base				
Me and family	–0.05	(–0.15 to 0.40)	.29	0.67	.02
Me and HPs	0.05	(–0.04 to 0.14)	.26	0.18	.81
Cancer type					
Pancreatic	Base				
Breast/prostate	0.27	(0.12 to 0.41)	<.001	0.38	.47
Breast (females)	0.24	(0.07 to 0.41)	<.001	0.13	.82
Prostate (males)	0.30	(0.12 to 0.48)	<.001	0.71	.07
Bowel	0.15	(0.01 to 0.29)	.043	0.31	.62
Melanoma	0.06	(–0.08 to 0.21)	.08	0.02	.48
Lung	–0.05	(–0.18 to 0.09)	.49	0.30	.64
Multiple	1.00	(0.79 to 1.22)	<.001	1.10	<.001
Risk reduction measures					
No preventative measure	Base				
Screening	0.25	(0.13 to 0.38)	<.001	0.01	.72
Lifestyle changes	0.26	(0.12 to 0.39)	<.001	0.06	.52
Screening and lifestyle	0.43	(0.30 to 0.56)	<.001	0.01	.29
Medication	0.49	(0.34 to 0.63)	<.001	0.34	.49
Surgery	0.11	(–0.02 to 0.24)	.11	0.91	<.001

A positive coefficient for an attribute indicates that its presence would increase the probability of a test being used, whereas a negative coefficient for an attribute level indicates that its presence would decrease the probability of a test being use.

GP, general practitioner; *HP*, health professional.

with 60%. Participants were willing to pay A$145.16 ($103.23 US) for a multicancer PRS test compared with a test for pancreatic cancer alone, A$25.66 ($18.25 US) to have a PRS test through a PCP compared with online, and A$16.79 ($11.94 US) if there was no impact of PRS test on life insurance eligibility or premiums, compared with there being an impact.

Discussion

There is potential for PRS testing to transform cancer prevention through personalized risk assessment and tailored preventative or early detection strategies. Although this remains an active area of investigation, the effective implementation and uptake of PRS testing relies on understanding the factors that influence choice. This study provides important insights into what consumers value in a PRS test to assess cancer risk across a large representative Australian sample. Our study found a preference for PRS testing that is undertaken through a PCP, has no impact on life insurance, is highly accurate, can be undertaken to assess risks of multiple cancer types, and enables risk reduction measures that include medication, lifestyle modification, and screening programs. The higher price of a PRS test had a significant negative impact on choice, evident through both the MXL and LCA results. In addition, mWTP estimates indicated that participants placed the greatest value on improvements in the accuracy of a PRS test and a test that includes multiple cancer types.

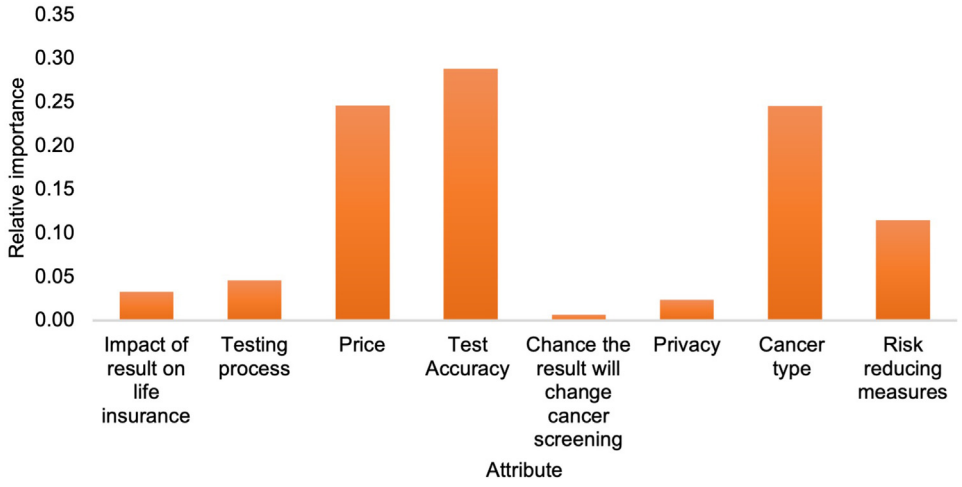

Figure 2 **Relative attribute importance for a PRS test to estimate cancer risk.** PRS, polygenic risk score.

Previous studies have emphasized the importance of PRS accuracy in relation to breast cancer. Yanes et al (2019) found that concerns regarding test inaccuracy was the reason stated by 35% to 40% of women who declined a PRS test for breast cancer.[13] Accuracy was also a key concern for participants in a qualitative study by Wong et al (2017), in which women expressed an expectation that a PRS test should have an accuracy of at least 90% before they would proceed with testing.[26] Accuracy was a meaningful factor in decision making in this study, accounting for a large portion of the relative importance in the MXL model and influenced decision making in one of the 3 latent classes (Figure 2). Although the variable performance of PRSs across ancestry groups was not outlined to participants in this study, the value placed on accuracy by participants is likely to be most problematic for those of non-European ancestry, in whom differences in PRS performance across ancestry groups continues to be a well-recognized limitation to their wide-scale use.[33] This study therefore reinforces the importance of improving the performance of PRSs, including across ancestry groups, to ensure all members of the public can access accurate PRS information.[3]

Research examining preferences for a cancer PRS have focused on single cancer types.[13,19,26,34] Our study is the first to examine how cancer type, as well as a multicancer PRS test, are traded off when choosing between alternative PRS testing approaches. Results from the MXL model showed a preference for a multicancer test and cancer types including breast cancer, prostate cancer, and bowel cancer whereas no significant preference was found for pancreatic cancer, lung cancer, or melanoma. In addition, the latent class "more is better," represented a subgroup of individuals, making up approximately one-third of participants, with a preference for a multiple cancer test. A possible explanation for the preferred cancer types includes greater public awareness and the promotion of existing screening programs, whereas conversely, limited risk reduction options (pancreatic cancer) or the perception that lifestyle factors are the primary mediators of risk (eg, smoking for lung cancer, UV radiation for melanoma) may be why the alternative cancers were less important. Interestingly, there was a strong preference for a multicancer PRS, despite some of the cancers in this option not being preferred individually. Evidence suggests that the public value the notion of knowing about their cancer risk, and when multiple cancer types are bundled together, this may offset other cancer types that are not valued to the same degree individually.[12,13,15,17]

The class memberships identified in the LCA provides a greater understanding of the features of a PRS test that are most important to population subgroups. For instance, the accuracy of a PRS test and the type of cancer are critical to those with a family history of cancer (see class 1). Identifying the specific groups such as these within the LCA allows us to better target messaging to increase the likelihood of PRS uptake.

Generic preference studies for genomic testing have found a preference for testing when preventative options, specifically lifestyle interventions, are available.[17,20] Whereas these studies used generic designs, our study provided a more realistic choice scenario by comparing actual cancer types to available preventative options. Furthermore, our results differed in that medication was a more attractive form of risk reduction, compared with either lifestyle modification or screening, individually and combined. This finding has important implications for how chemoprophylactic medications, such as aspirin for bowel cancer or serum estrogen receptor modulators for breast cancer, may be applied to individuals with a high-risk PRS.

In the Australian setting, PCPs act as the first point of contact within the health system for nonurgent health issues, and more than 80% of Australians have a consultation with a PCP each year.[35] Although our study identified a preference for having a PRS test arranged through a PCP, a previous DCE examining PRS testing for breast cancer identified a specialist doctor as the preferred clinician to see

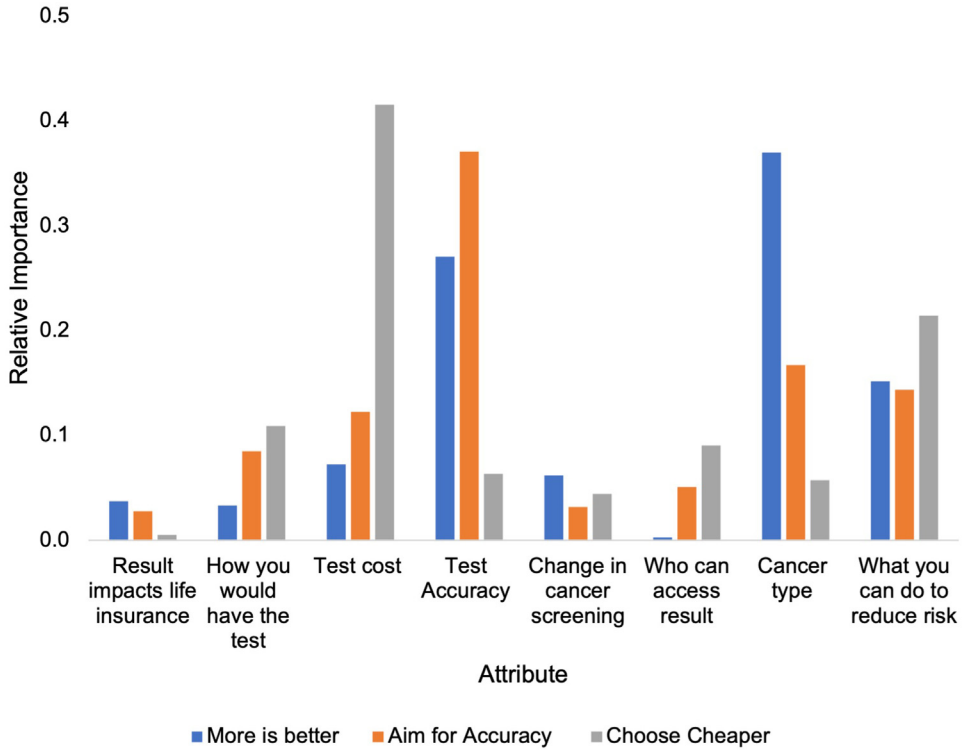

Figure 3 **Relative importance of PRS test attributes across 3 latent classes.** PRS, polygenic risk score.

for pretest counseling.[14] Previous studies support our findings that the public is accepting of the role of PCPs in providing personalized cancer risk information.[16,19,36] This is reinforced by the results of a recent survey that found that approximately half of health professionals viewed PCPs as the clinician likely to be involved in offering PRS testing.[18] Nevertheless, there are numerous barriers to the integration of genomics into primary care, particularly for clinicians, who report of lacking knowledge and confidence in discussing genomic risk information.[37]

In the Australian context, a current industry-led moratorium protects consumers from providing life insurers with the results of genetic test results for policies up to set thresholds (eg, A$500,000 for death cover), whereas similar protections do not exist in the United States.[38] Members of the public have concerns regarding the impact of genomic testing results on life insurance, and this may extend to the results of PRSs.[13,20,34,39] In our study, if a PRS test impacted life insurance, it was negatively associated with choosing the test, which reflects the influence that disclosing results to life insurers has on preferences for genomic sequencing in the Australian setting.[20] Compared with our sample, members of the public in countries such as the United States, where the same consumer protections do not exist with regards to life insurance, this result may be further amplified.

An unexpected result of our study was the lack of a clear preference for the ability of the test to change recommended screening options. Our a priori expectation was that participants would be positively influenced by the availability of a more personalized screening program, indicated by an increased likelihood of recommendations changing because of having a PRS test. There is no clear rationale for the result we observed. In describing the attribute, attention was paid to provide detailed explanatory material to clearly communicate that change in screening requirements were probability-based. That material was developed with input received directly from consumers and pilot tested with respondents, enabling further refinement of this attribute. In addition, we incorporated the use of an icon array and included the same denominator across probability information, which are suggested ways of improving the communication of probability attributes.[40] Nonetheless, it is possible that the absence of a clear preference for recommended screening options might reflect the complexity of this attribute for respondents.

This study has several strengths. First, our attributes were identified through 3 separate avenues, including a consumer advisory group. The latter helped to bolster the saliency of the issues addressed by our DCE, in part by accessing the lived experience of the consumer advisory group and by engaging its members in reviewing the clarity and appropriateness of our survey. Second, by performing this survey online, we were able to engage a large, representative sample of individuals aged 18 years or older. This adds depth to the existing literature on PRSs, which has tended to focus on specific cancer types and corresponding population groups limited by age and/or gender. In addition, we have examined the joint impact of aspects of PRS testing,

combining the elements of the focus of testing, how it is conducted and the implications arising from test results. Combined with analysis of participant factors, this provides a holistic view of the factors influencing potential participation in PRS testing.

Limitations of this study included the over-representation of participants with a vocational or university qualification. This may bias the transferability of these findings to groups with differing levels of educational attainment, particularly given the complex nature of the study content. Although the use of an online survey improved access to a range of population groups, it did limit the ability to address concerns that participants may have had regarding both content and task decisions. In addition, the vignette participants viewed before undertaking the survey asked them to imagine their PCP offering them a DNA test to estimate their cancer risk. This may have primed participants toward a preference for having the test through their PCP rather than online or through a specialist. This was a hypothetical study to examine stated preferences, and although the intention is a precursor to action, an intention–behavior gap may exist whereby decisions in hypothetical scenario may not always evolve to reflect real-life behaviors.

As PRSs for different cancer types continue to be developed and refined, the role of consumer preferences in determining how to implement PRS testing most effectively will be of increasing importance. Preference data are increasingly a focus of medical regulators, who recognize the value of consumer views on exploring the risks and benefits of different medical tests and treatments.[41] It is therefore prudent that patient-preference data continue to inform the scientific evidence base that underpins the implementation of PRS testing.

The results of this study raise several points that require further research. First, a preference for a multicancer test has uncertain clinical implications when it includes cancers (eg, pancreatic cancer) that have no effective preventative or screening options available. Testing for cancer types outside of existing screening programs will require further evidence to guide clinicians on how to manage results through surveillance or other means of follow up. The degree to which the public will accept shifts in screening recommendations because of a PRS test result should also be explored further. Given the importance placed on test accuracy, research to validate PRS tests that are applicable to individuals from varying ancestries will continue to be paramount. Finally, if future availability of PRS testing occurs through PCPs, further upskilling of the primary care workforce should be a focus for policymakers.

Data Availability

The data that support the results of this study are available on request from the corresponding author.

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Ethics Declaration

Ethics approval for this study was provided by the University of Melbourne Human Research Ethics Committee (HREC reference No: 2021-21701-18823-3). Informed consent was obtained from all participants as required by the Human Research Ethics Committee. All individual-level data were de-identified.

Conflict of Interest

The authors declare no conflicts of interest.

Additional Information

The online version of this article (https://doi.org/10.1016/j.gim.2022.07.011) contains supplementary material, which is available to authorized users.

References

1. Conran CA, Shi Z, Resurreccion WK, et al. Assessing the clinical utility of genetic risk scores for targeted cancer screening. *J Transl Med*. 2021;19(1):41. http://doi.org/10.1186/s12967-020-02699-w.

2. Torkamani A, Wineinger NE, Topol EJ. The personal and clinical utility of polygenic risk scores. *Nat Rev Genet*. 2018;19(9):581–590. http://doi.org/10.1038/s41576-018-0018-x.
3. Lewis CM, Vassos E. Polygenic risk scores: from research tools to clinical instruments. *Genome Med*. 2020;12(1):44. http://doi.org/10.1186/s13073-020-00742-5.
4. Kachuri L, Graff RE, Smith-Byrne K, et al. Pan-cancer analysis demonstrates that integrating polygenic risk scores with modifiable risk factors improves risk prediction. *Nat Commun*. 2020;11(1):6084. http://doi.org/10.1038/s41467-020-19600-4.
5. Choi J, Jia G, Wen W, Long J, Shu XO, Zheng W. Effects of screenings in reducing colorectal cancer incidence and mortality differ by polygenic risk scores. *Clin Transl Gastroenterol*. 2021;12(5):e00344. http://doi.org/10.14309/ctg.0000000000000344.
6. Guo F, Weigl K, Carr PR, et al. Use of polygenic risk scores to select screening intervals after negative findings from colonoscopy. *Clin Gastroenterol Hepatol*. 2020;18(12):2742–2751.e7. http://doi.org/10.1016/j.cgh.2020.04.077.
7. Thomas M, Sakoda LC, Hoffmeister M, et al. Genome-wide modeling of polygenic risk score in colorectal cancer risk. *Am J Hum Genet*. 2020;107(3):432–444. http://doi.org/10.1016/j.ajhg.2020.07.006.
8. Callender T, Emberton M, Morris S, et al. Polygenic risk-tailored screening for prostate cancer: a benefit-harm and cost-effectiveness modelling study. *PLoS Med*. 2019;16(12):e1002998. http://doi.org/10.1371/journal.pmed.1002998.
9. Dillon M, Flander L, Buchanan DD, et al. Family history-based colorectal cancer screening in Australia: A modelling study of the costs, benefits, and harms of different participation scenarios. *PLoS Med*. 2018;15(8):e1002630. http://doi.org/10.1371/journal.pmed.1002630.
10. Shieh Y, Eklund M, Madlensky L, et al. Breast cancer screening in the precision medicine era: risk-based screening in a population-based trial. *J Natl Cancer Inst*. 2017;109(5). http://doi.org/10.1093/jnci/djw290.
11. Australian New Zealand Clinical Trials Registry. Trial review. Australian New Zealand Clinical Trials Registry. Accessed February 17, 2022. https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=380786&isReview=true.
12. Saya S, McIntosh JG, Winship IM, et al. Informed choice and attitudes regarding a genomic test to predict risk of colorectal cancer in general practice. *Patient Educ Couns*. 2022;105(4):987–995. http://doi.org/10.1016/j.pec.2021.08.008.
13. Yanes T, Meiser B, Kaur R, et al. Uptake of polygenic risk information among women at increased risk of breast cancer. *Clin Genet*. 2020;97(3):492–501. http://doi.org/10.1111/cge.13687.
14. Wong XY, Groothuis-Oudshoorn CG, Tan CS, et al. Women's preferences, willingness-to-pay, and predicted uptake for single-nucleotide polymorphism gene testing to guide personalized breast cancer screening strategies: a discrete choice experiment. *Patient Prefer Adherence*. 2018;12:1837–1852. http://doi.org/10.2147/PPA.S171348.
15. Meulenkamp TM, Gevers SK, Bovenberg JA, Koppelman GH, van Hylckama Vlieg A, Smets EMA. Communication of biobanks' research results: what do (potential) participants want? *Am J Med Genet A*. 2010;152A(10):2482–2492. http://doi.org/10.1002/ajmg.a.33617.
16. Allen NL, Karlson EW, Malspeis S, Lu B, Seidman CE, Lehmann LS. Biobank participants' preferences for disclosure of genetic research results: perspectives from the OurGenes, OurHealth, OurCommunity project. *Mayo Clin Proc*. 2014;89(6):738–746. http://doi.org/10.1016/j.mayocp.2014.03.015.
17. Viberg Johansson J, Langenskiöld S, Segerdahl P, et al. Research participants' preferences for receiving genetic risk information: a discrete choice experiment. *Genet Med*. 2019;21(10):2381–2389. http://doi.org/10.1038/s41436-019-0511-4.
18. Smit AK, Sharman AR, Espinoza D, et al. Knowledge, views and expectations for cancer polygenic risk testing in clinical practice: a cross-sectional survey of health professionals. *Clin Genet*. 2021;100(4):430–439. http://doi.org/10.1111/cge.14025.
19. Saya S, McIntosh JG, Winship IM, et al. A genomic test for colorectal cancer risk: is this acceptable and feasible in primary care? *Public Health Genomics*. 2020;23(3-4):110–121. http://doi.org/10.1159/000508963.
20. Goranitis I, Best S, Christodoulou J, Stark Z, Boughtwood T. The personal utility and uptake of genomic sequencing in pediatric and adult conditions: eliciting societal preferences with three discrete choice experiments. *Genet Med*. 2020;22(8):1311–1319. http://doi.org/10.1038/s41436-020-0809-2.
21. Haghani M, Bliemer MCJ, Hensher DA. The landscape of econometric discrete choice modelling research. *J Choice Modell*. 2021;40:100303. http://doi.org/10.1016/j.jocm.2021.100303.
22. Ryan M, Gerard K, Amaya-Amaya M, eds. *Using Discrete Choice Experiments to Value Health and Health Care*. Vol. 11. Springer; 2008.
23. Buchanan J, Wordsworth S, Schuh A. Patients' preferences for genomic diagnostic testing in chronic lymphocytic leukaemia: a discrete choice experiment. *Patient*. 2016;9(6):525–536. http://doi.org/10.1007/s40271-016-0172-1.
24. De Abreu Lourenco R, McCarthy MC, McMillan LJ, Sullivan M, Gillam L. Understanding decisions to participate in genomic medicine in children's cancer care: A comparison of what influences parents, health care providers, and the general community. *Pediatr Blood Cancer*. 2021;68(8):e29101. http://doi.org/10.1002/pbc.29101.
25. Bridges JF, Hauber AB, Marshall D, et al. Conjoint analysis applications in health—a checklist: a report of the ISPOR Good Research Practices for Conjoint Analysis Task Force. *Value Health*. 2011;14(4):403–413. http://doi.org/10.1016/j.jval.2010.11.013.
26. Wong XY, Chong KJ, van Til JA, Wee HL. A qualitative study on Singaporean women's views towards breast cancer screening and Single Nucleotide Polymorphisms (SNPs) gene testing to guide personalised screening strategies. *BMC Cancer*. 2017;17(1):776. http://doi.org/10.1186/s12885-017-3781-8.
27. Saunders CL, Kilian B, Thompson DJ, et al. External validation of risk prediction models incorporating common genetic variants for incident colorectal cancer using UK Biobank. *Cancer Prev Res (Phila)*. 2020;13(6):509–520. http://doi.org/10.1158/1940-6207.CAPR-19-0521.
28. Street DJ, Burgess L. *The Construction of Optimal Stated Choice Experiments: Theory and Methods*. John Wiley & Sons; 2007. Accessed January 5, 2022. https://opus.lib.uts.edu.au/handle/10453/7760.
29. Kuhfeld WF. Orthogonal arrays. SAS. Accessed September 22, 2021. https://support.sas.com/techsup/technote/ts723b.pdf.
30. Lancsar E, Louviere J. Conducting discrete choice experiments to inform healthcare decision making: a user's guide. *Pharmacoeconomics*. 2008;26(8):661–677. http://doi.org/10.2165/00019053-200826080-00004.
31. Australian Bureau of Statistics. Population.| Australian Bureau of Statistics. Accessed January 6, 2022. https://www.abs.gov.au/statistics/people/population.
32. Hauber AB, González JM, Groothuis-Oudshoorn CG, et al. Statistical methods for the analysis of discrete choice experiments: a report of the ISPOR Conjoint Analysis Good Research Practices Task Force. *Value Health*. 2016;19(4):300–315. http://doi.org/10.1016/j.jval.2016.04.004.
33. Lewis ACF, Green RC. Polygenic risk scores in the clinic: new perspectives needed on familiar ethical issues. *Genome Med*. 2021;13(1):14. http://doi.org/10.1186/s13073-021-00829-7.
34. Smit AK, Espinoza D, Newson AJ, et al. A pilot randomized controlled trial of the feasibility, acceptability, and impact of giving information on personalized genomic risk of melanoma to the public. *Cancer Epidemiol Biomarkers Prev*. 2017;26(2):212–221. http://doi.org/10.1158/1055-9965.EPI-16-0395.
35. Australian Bureau of Statistics. Patient experiences in Australia: summary of findings. Australian Bureau of Statistics. Published November 17, 2021. Accessed February 22, 2022. https://www.abs.gov.au/statistics/health/health-services/patient-experiences-australia-summary-findings/latest-release.

36. Savard J, Hickerton C, Tytherleigh R, et al. Australians' views and experience of personal genomic testing: survey findings from the Genioz study. *Eur J Hum Genet*. 2019;27(5):711–720. http://doi.org/10.1038/s41431-018-0325-x.
37. Smit AK, Newson AJ, Keogh L, et al. GP attitudes to and expectations for providing personal genomic risk information to the public: a qualitative study. *BJGP Open*. 2019;3(1):bjgpopen18X101633. http://doi.org/10.3399/bjgpopen18X101633.
38. Tiller J, Winship I, Otlowski MF, Lacaze PA. Monitoring the genetic testing and life insurance moratorium in Australia: a national research project. *Med J Aust*. 2021;214(4):157–159.e1. http://doi.org/10.5694/mja2.50922.
39. Metcalfe SA, Hickerton C, Savard J, et al. Australians' views on personal genomic testing: focus group findings from the Genioz study. *Eur J Hum Genet*. 2018;26(8):1101–1112. http://doi.org/10.1038/s41431-018-0151-1.
40. Visschers VHM, Meertens RM, Passchier WWF, de Vries NNK. Probability information in risk communication: a review of the research literature. *Risk Anal*. 2009;29(2):267–287. http://doi.org/10.1111/j.1539-6924.2008.01137.x.
41. Johnson FR, Zhou M. Patient preferences in regulatory benefit-risk assessments: a US perspective. *Value Health*. 2016;19(6):741–745. http://doi.org/10.1016/j.jval.2016.04.008.