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Advanced Cancer Patient Knowledge of and Attitudes towards Tumor Molecular Profiling

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ABSTRACT

Limited research has indicated that despite their overwhelming interest in tumor molecular profiling (MP),[1] cancer patients have poor knowledge about MP. The current study aimed to investigate demographic and psychological predictors of knowledge and perceived importance of MP in an advanced cancer patient cohort. Eligible participants had advanced solid cancers of any histological type with sufficient accessible tissue for MP and were enrolled in the Molecular Screening and Therapeutics (MoST) Program. A questionnaire was completed by 1074 participants (91% response rate) after consent, prior to undergoing MP. Overall, participants had poor to moderate knowledge of MP, yet perceived MP to have high importance. Higher education, speaking English at home, and greater satisfaction with the decision to undergo MP were associated with higher knowledge scores. More negative attitudes towards uncertainty, greater self-efficacy to cope with results, and lower perceived likelihood of cancer progression were associated with greater perceived importance of MP. Less educated participants and those who do not speak English at home will need clear explanations, visual aids and ample opportunity to ask questions about MP at the time of their decision-making. Clinicians also need to consider psychological factors relevant to patients' decision to pursue MP. Given the increased awareness of and demand for cancer genomic information and the rapidly changing nature of the actionability of MP, these findings will help inform an important ongoing debate on how to facilitate ethical and informed consent and manage patient expectations about personalized treatments.

Introduction

Tumor molecular profiling (MP) is a form of genomic testing that involves characterization of tumor-derived DNA and RNA. MP aims to identify somatic driver pathogenic variants and other molecular characteristics, with a view to identifying tailored therapies. MP, paired with personalized treatment, offers new prospects for improvement in patient outcomes. It is anticipated that MP will increasingly facilitate identification of cancer patients who will benefit from targeted drugs and immunotherapy approaches, in contrast to the current 'scatter-gun' approaches of chemotherapy and radiotherapy [1]. The decreasing cost and increasing availability of molecularly-targeted therapies are expected to expand use of MP in oncology clinics [2].

The promise of personalized genomic medicine will only be realized, however, if patients understand their part in the process, likely outcomes and any potential implications of results, and make decisions concordant

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[1] *Abbreviations:* Accessibility and Remoteness Index of Australia (ARIA): an indication of the proximity of service centers relative to where the participant lives. Eastern Cooperative Oncology Group (ECOG): A performance status measure to quantify cancer patients' general well-being and activities of daily life. Molecular Therapeutics (MoST) Program: A research program which forms a component of the Australian Genomic Cancer Medicine Program. The Psychosocial Issues in Genomic Oncology (PiGeOn) Project: a longitudinal, mixed methods psychosocial sub-study of the MoST Program which aims to examine the psychosocial, behavioral and ethical impact of MP. Tumor molecular profiling (MP): a form of genomic testing, that involves characterization of tumor-derived DNA and RNA.

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with their values during the consent process. Managing patients' expectations is a challenge in this area, as patients commonly place unrealistic hope on novel therapeutic approaches [3,4]. One study reports that most participants (94%) enrolled in a clinical trial sought and expected significant medical benefit even though the likelihood of such benefit was very low [4].

An important aspect of traditional standards of informed consent is that participants have sufficient understanding about the treatment or research activity to make an informed decision about participation [5]. This criterion is made more complex by the uncertainties inherent in genomic testing regarding the chances of finding variants that can affect treatment (clinically actionable variants), how this might impact the patient's prognosis, and the additional chance of finding a germline variant with implications for the patient's blood relatives. Furthermore, some results may need to be updated as new gene targets are identified and new drugs developed, and their significance may change with time [6]. These challenges inherently apply within a research context, but also have implications for the 'real-world' setting as genomics enters the mainstream.

Currently, as shown by a recent systematic review [7], little is known regarding patients' understanding of and attitudes towards genomic testing, and the limited research conducted to date has been predominantly hypothetical. The published evidence has involved research participants who may or may not have cancer, where the potential benefit of detecting a gene variant to guide treatment was varied. A series of North American studies [8–10] presenting hypothetical scenarios to cancer patients found an overwhelming interest in and willingness to undergo MP for personalized treatment. However, the participants simultaneously expressed significant concerns about potential psychological harm, cost and discrimination. Moreover, participants felt they had insufficient knowledge to make an informed choice, and misunderstandings about MP were noted [8]. The few studies that have explored responses in patients facing real-world MP decisions have reinforced these findings, reporting a strong sense of information overload and misunderstanding, which has often led to unrealistic expectations, anxiety and uncertainty [11,12].

Research findings are mixed regarding patients' perceptions of MP. Patient hopes of MP benefits in one study were heightened by the potential for novel and targeted treatment but diminished by non-findings or limited access to relevant trials [3]. Past studies involving advanced cancer patients being offered MP found that patients had an overwhelming desire to seek new treatments [3,13]. Conversely, in studies exploring predictors of perceived barriers to genetic testing, advanced cancer stage was associated with greater perceived barriers to testing [14,15]. Receiving information relating to germline findings (while rare) is viewed as particularly burdensome by patients, when they are already trying to cope with their own progressive disease [13].

Almost no studies have explored predictors of knowledge and attitudes to MP. A useful framework to guide such an investigation is Protection Motivation Theory [16,17]. Protection Motivation Theory suggests that views on treatment options and decision making are influenced by a range of psycho-social factors such as self-efficacy, perceived susceptibility and attitudes towards uncertainty [16,17].

This study aimed to explore understanding of and attitudes towards MP among patients with advanced and/or metastatic solid cancer who are undergoing MP, to best inform clinical practice both prior to and following patients' decision to have MP.

Material and Methods

This study was approved by the St Vincent's Hospital Sydney Human Research Ethics Committee, Reference number HREC/16/SVH/23.

Participants

The Molecular Screening and Therapeutics (MoST) Program is a component of the Australian Genomic Cancer Medicine Program [18]. The MoST Program is recruiting adult patients with pathologically confirmed advanced or metastatic solid cancers of any histological type, either during or after their last line of standard therapy. Eligibility criteria include: having an Eastern Cooperative Oncology Group (ECOG) Performance Status of 0, 1, 2 or 3; sufficient accessible tissue for MP; and ability to provide written informed consent. Individuals with rare or neglected cancers (defined as <6 cases/100,000 population) comprise approximately 77% of the MoST Program participants. Participants were recruited to the MoST Program from centers across Australia from 2016 to 2019. As part of the consent process, participants received education material in a Participant Information Sheet advising there was a 10-20% rate of actionable somatic mutations linked to treatment and that germline mutations were found "very rarely". Family members were sometimes present during the consent process to the MoST Program. MP is conducted on MoST Program participants' archived tumor tissue, and a report linking molecular characteristics with potential therapeutics is issued to their oncologist.

The Psychosocial Issues in Genomic Oncology (PiGeOn) Project is a longitudinal, mixed methods psychosocial sub-study of the MoST Program which aims to examine the psychosocial, behavioral and ethical impact of MP [19]. Patients gave written consent to participate in the PiGeOn Project while giving consent to participate in the MoST Program, using established procedures for genetic research [20,21]. The current paper reports results from the PiGeOn cross-sectional analysis of participants' knowledge of and attitudes towards MP within one month of having consented to undertake MP and prior to having MP results returned.

Measures

Participants completed a questionnaire (hard copy or online), which was comprised of a combination of the following study-specific, adapted, and previously validated scales.

Demographics and Disease Data

Participants' gender, age, marital status, education, language spoken at home, socio-economic status, Accessibility and Remoteness Index of Australia (ARIA-an indication of the proximity of service centers relative to where the participant lives), previous attendance at a family cancer clinic, medical or science occupation, parental status, family history of cancer (first-degree relative), multiple primary cancers, time since diagnosis and cancer incidence [common (>12 cases/100,000 population), less common (6-12 cases/100,000 population) or rare (<6 cases/100,000 population)] were collected via questionnaire or the parent study database (MoST Program).

Satisfaction with Decision to have MP

The six-item Satisfaction with Decision scale [22] measured participants' satisfaction with their decision to have MP e.g. "The decision I made was the best decision possible for me personally". Items were rated on a Likert-scale, from "strongly disagree" to "strongly agree" (scores range 1-5) with higher scores indicating greater satisfaction.

Self-Efficacy

Four Likert-scale items adapted from Rosenberg et al. (2013) [23] assessed perceived ability to cope if actionable, non-actionable, or germline results were found e.g. "I am confident that I would be able to cope if I get a test result that leads to a new treatment". Response options were on a Likert-scale ranging from "strongly disagree" to "strongly agree" (scores range 1-5) with higher scores indicating greater perceived ability to cope.

Attitudes Towards Uncertainty

The seven-item Attitude towards Uncertainty scale [24] measured attitudes towards uncertainty in the specific context of medical testing e.g. "The relief I would get from getting a result that would guide treatment is worth the risk that the result is bad". Items were rated on a Likert-scale, from "strongly disagree" to "strongly agree" (scores range 1-5) with higher scores indicating a more negative attitude towards uncertainty.

Perceived Susceptibility

Participants indicated their perceived likelihood of having a gene variant that increases their risk of cancer progression, in comparison with someone with the same cancer as themselves, via a visual analogue scale (0–100%) adapted from Kasparian et al. (2009) [25].

Knowledge

An eight-item, multiple choice, study-specific scale assessed participants' knowledge regarding the purpose of MP, its utility in guiding treatment and understanding future cancer risk, and whether the likely frequency of informative results differs across cancer types. Correct responses were determined by a multidisciplinary team of experts. As little variability was apparent on some items, a change to the knowledge questions was made after the first 345 participants of the study. Any analysis involving knowledge scores was therefore restricted to the final 777 participants. Higher scores (average number of items correct, possible range 0-100%) reflect greater knowledge about MP. A one-question difference in participants' correct responses resulted in a 12.5% change in overall knowledge score. Scores were divided into thirds, with the bottom third labelled as "poor", the middle as "moderate" and the top as "good" knowledge about MP.

Perceived Importance

A two-item measure adapted from Hay et al. (2012) [26] assessed perceived importance of learning whether gene variants affect the chance of responding to particular cancer treatments, and learning more about how lifestyle affects the chance of living longer with cancer e.g., "How important is it to you to learn about gene variants that may affect your chance of responding to particular cancer treatments?". Scores were averaged over both items, (scores range 1-5) with higher scores on the Likert-scale indicating greater importance.

Statistical Analysis

Descriptive statistical analysis and multiple regressions were conducted using IBM SPSS Statistics Version 25. A linear multiple regression was used to identify predictors of knowledge, and an ordinal regression was used to identify predictors of perceived importance. The outcome variable in the ordinal regression was calculated by taking the average of the two perceived importance item responses, which formed nine ordered categories, increasing in intervals of 0.5 and ranging between 1 and 5. Multivariable models were constructed with the inclusion of potential confounders, as well as predictors that were expected to share an association with the outcome variables based on the literature. All demographic, disease and psychosocial variables listed above were included as the predictor variables. Assumptions of normality of residuals and homogeneity of variance were checked visually through diagnostic residual plots with no violations found.

Results

One thousand and seventy-four of the 1174 participants enrolled in the MoST Program (91% response rate) completed the questionnaire. The knowledge sample was reduced to 777 participants, (94% response rate, see Methods). Regarding the total sample, participants were evenly distributed in gender (51% female), had a mean age of 55 years (Standard Deviation [SD] = 14 years), an average ECOG performance status between 0 (fully active and unrestricted performance) and 1 (restricted in physically strenuous activity), and a range of cancer diagnoses (see Table 1).

Knowledge

Overall, participants had poor to moderate knowledge about MP at the time they gave consent to have MP, with an average correct response score of 43% (SD = 20%). The individual scores from the knowledge scale items are presented in Table 2. Seventy-one percent of participants correctly answered (yes) *The likelihood of finding a gene variant to guide treatment varies for different sorts of cancer* and 66% of participants correctly answered (yes) *Tests that can guide cancer treatment include both blood DNA and tumor DNA*. Although 64% of participants correctly responded (guide treatment for the current cancer and manage the risk of future cancer) *Genetic panel testing of a tumor can help:*, a number of participants (34%) overlooked the ability of MP to help manage future cancer risk. Only 19% of participants correctly answered (all types of cancer) *Genetic panel testing is helpful for guiding treatment of:* and only 3% of participants correctly responded (rarely) to *Genetic panel testing is helpful for making decisions about future cancer risks*, with 20% acknowledging they did not know the answer to this question. Participants reported that the most common source of their knowledge about genetic panel testing was their oncologists.

The multiple regression analyses revealed that higher education, speaking English at home and having a rare cancer type were significant predictors of higher knowledge about MP (Table 3). For every category increase in participants' level of education completed (e.g. undergraduate university vs. postgraduate university) we found an increase in knowledge scores of 2%, $P = .001$. Participants from a non-English-speaking home scored on average 5% lower than those from an English-speaking home, $P = .012$. Participants with a common cancer type scored on average 4% lower than those with a rare cancer type regarding the knowledge questions, $P = .028$. The variable most strongly associated with participant knowledge was satisfaction with decision to have MP. Specifically, for every category increase in participants' overall satisfaction with decision (e.g. agree to strongly agree) we observed that knowledge scores increased by 5%, $P < .001$. Overall, demographics and psychosocial variables accounted for 16% of the variance in knowledge scores. No other psychosocial variables were associated with knowledge.

Perceived Importance

Participants had primarily positive attitudes to MP at the time that they gave consent to have MP (mean = 4.71, SD = 0.61). Individual item responses are presented in Table 4. The majority of participants (84%) rated learning about *gene variants that may affect your chance of responding to particular cancer treatments* as "very important". Slightly fewer participants (80%) considered it "very important" to *learn more about how your lifestyle, such as exercise, smoking and diet, affects your chance of living longer with your disease*.

The ordinal regression revealed a number of factors were associated with perceived importance of MP (Table 5). Among the demographic and disease variables, being female, having children, being married and having been diagnosed with cancer more recently were all significant predictors of higher perceived importance of MP. The ordered odds of having higher scores for perceived importance were: for females: 1.45 times that of male participants, $P = .02$; for participants with children: 1.62 times that of participants without children, $P = .02$; and for married participants: 1.57 times that of participants who were not married, $P = .015$. With every year since diagnosis the ordered odds of perceiving MP as very important decreased by a factor of 0.96, $P = .017$.

Higher perceived self-efficacy to cope with results, more negative attitudes to uncertainty and lower perceived susceptibility for cancer progression were significant psychosocial predictors of greater perceived importance of MP. Having a negative attitude towards uncertainty was the strongest predictor of participants' perceived importance of MP, such that for every category increase in participants' negative attitudes towards uncertainty (e.g. agree to strongly agree), the ordered odds of having greater perceived importance increased by 2.29-fold, $P < .001$. For every category increase in participants' perceived *self-efficacy* to cope with results, the ordered odds of having greater perceived importance increased by 1.40-fold, $P = .011$. For every ten per cent increase in participants' *perceived susceptibility* of cancer progression (e.g. 80% chance of cancer progression – 90% chance of cancer progression) the ordered odds of having greater perceived importance of MP decreased by 0.93-fold, $P = .016$.

Discussion

This study explored the experiences of adults with advanced cancer after they had consented to have MP, but prior to receiving MP results.

Table 1
Descriptive statistics for participants' demographics, disease and psychosocial variables

	Sample post knowledge questions change (N = 777)	Total sample (N = 1074)
	N (%)	N (%)
Sex		
Female	405 (52)	552 (51)
Male	372 (48)	522 (49)
Highest level of education completed		
Primary school (some or all)	9 (1)	12 (1)
Secondary school - year 7 or 8	23 (3)	27 (3)
Secondary school - year 9 or 10	124 (16)	176 (16)
Secondary school - year 11 or 12	133 (17)	173 (16)
Vocational training	137 (18)	197 (18)
[7]	Undergraduate university: 177 (23)	University – did not graduate: 18 (2)
	Postgraduate university: 168 (22)	University - graduated: 458 (43)
Missing	6 (0.8)	13 (1)
Culturally and linguistically diverse (CALD)		
Yes	184 (24)	242 (23)
Accessibility and remoteness index of Australia (ARIA)		
Urban	702 (90)	978 (91)
Rural and remote	75 (10)	94 (9)
Missing	0	2 (0.2)
Visited a family cancer clinic		
Yes	86 (11)	112 (10)
Medical/science occupation		
Yes	59 (8)	80 (7)
Parental status		
Yes, has children	574 (74)	794 (74)
Family history of cancer (first degree relatives)		
Yes	383 (49)	521 (49)
Marital status		
Married	578 (74)	804 (75)
Single, divorced, never married, separated, widowed, de facto	179 (23)	242 (23)
Missing	20 (3)	28 (3)
Multiple primary cancers		
Yes	110 (14)	148 (14)
Cancer incidence		
Common (>12 cases/100,000)	151 (19)	193 (18)
Less common (6-12 cases/100,000)	103 (13)	136 (13)
Rare (< 6 cases/100,000)	519 (67)	739 (69)
Missing	4 (0.5)	6 (0.6)
Primary site		
Bone and soft tissue	146 (19)	211 (20)
Brain	93 (12)	120 (11)
Colorectal	71 (9)	93 (9)
Pancreas	69 (9)	88 (8)
Breast	44 (6)	55 (5)
Uterus	44 (6)	57 (5)
Ovary	37 (5)	43 (4)
Unknown primary	27 (3)	44 (4)
Lung	24 (3)	37 (3)
Prostate	20 (3)	29 (3)
Other	202 (26)	297 (28)
Eastern Cooperative Oncology Group (ECOG) performance status		
0	393 (51)	537 (50)
1	345 (44)	479 (45)
2	31 (4)	44 (4)
3	2 (0.3)	4 (0.4)
Missing	6 (0.8)	10 (0.9)
	Mean (SD)	**Mean (SD)**
	Range	**Range**
Age	55.47 (14.26)	55.37 (14.31)
	19-90	18-90
Socio-economic status (SES)	6.78 (2.86)	6.83 (2.84)
Index of relative socio-economic disadvantage based on postcode, low scores reflect most disadvantaged (0-10)	0-10	0-10
Time since diagnosis (years)	3.14 (3.96)	3.28 (4.21)
	0-22.2	0-40.3
Satisfaction with decision	4.40 (0.75)	4.42 (0.71)
	1-5	1-5
Self-efficacy	4.29 (0.73)	4.26 (0.70)
	1-5	1-5
Attitudes to uncertainty	4.31 (0.56)	4.31 (0.57)
	1.5-5	1.5-5
Perceived susceptibility	65.07 (27.32)	66.85 (26.62)
	0-100	0-100
Knowledge (% correct)	43 (20)	

Table 1 (*continued*)

	Sample post knowledge questions change (N = 777)	Total sample (N = 1074)
	N (%)	N (%)
Perceived importance	0-88 [4]	4.71 (0.61) 1-5

[7] A change to the responses for the education measure occurred following the change to the questionnaire (see Material and Methods).

Table 2
Study-specific knowledge scale: items and correct responses

Knowledge items	Number (%)
Tests that can guide cancer treatment include:	
Both	516 (66)[a]
Blood DNA	15 (2)
Tumor DNA	92 (12)
Neither	1 (0.1)
I don't know	153 (20)
Genetic panel testing of a tumor can help:	
Guide treatment for the current cancer and manage the risk of future cancer	498 (64)[a]
Guide treatment for the current cancer	156 (20)
Manage the risk of future cancer	16 (2)
Neither guide treatment for current cancer nor manage the risk of future cancer	2 (0.3)
I don't know	105 (14)
Genetic panel testing is helpful for guiding treatment of:	
All types of cancer	148 (19)[a]
Most types of cancer	124 (16)
Some types of cancer	334 (43)
No types of cancer	1 (0.1)
I don't know	167 (22)
Missing	3 (0.4)
Genetic panel testing is helpful for understanding the risk of developing:	
All types of cancer	125 (16)
Most types of cancer	132 (17)
Some types of cancer	338 (44)[a]
No types of cancer	2 (0.3)
I don't know	178 (23)
Missing	2 (0.3)
Genetic panel testing is helpful for making decisions about treatment for cancer:	
Always	116 (15)
Frequently	146 (19)
Sometimes	361 (47)[a]
Rarely	22 (3)
Never	1 (0.1)
I don't know	129 (17)
Missing	2 (0.3)
Genetic panel testing is helpful for making decisions about future cancer risks:	
Always	126 (16)
Frequently	119 (15)
Sometimes	347 (45)
Rarely	24 (3)[a]
Never	2 (0.3)
I don't know	156 (20)
Missing	3 (0.4)
The likelihood of finding a gene variant to guide treatment varies for different sorts of cancer	
Yes	552 (71)[a]
No	3 (0.4)
I don't know	218 (28)
Missing	4 (0.5)
Sometimes cancer treatment, screening or preventative surgery can be offered to people with a disease-causing gene variant. The costs of this would be:	
Covered in full by Medicare (at no cost to the patient)	113 (15)[a]
Only available through a clinical trial (at no cost to the patient)	128 (17)[a]
Only available privately (at the patient's cost)	15 (2)
I don't know	513 (66)
Missing	8 (1)
From where have you learned most about genetic panel testing?[b]	
My oncologist	343 (44)
The researchers of the MoST program	318 (41)
School or university	13 (2)
TV	16 (2)
Online	88 (11)
Other	87 (11)

[a] Correct responses
[b] Not included in the knowledge score calculation.

Table 3
Summary of multiple linear regression analysis for predictors of knowledge about MP, $n = 777$

Independent variables	Regression coefficient (95% CI)	*P* value
Sex		
Female	2.97 (-0.93 to 5.12)	.174
Male	Ref.	
Age (for every 10-year increase)	-0.97 (-2.23 to 2.82)	.128
Education	1.84 (0.78 to 2.89)	.001**
CALD		
Yes	-4.70 (-8.37 to -1.03)	.012*
No	Ref.	
SES	3.82 (-2.00 to 9.64)	.197
ARIA		
Urban	0.83 (-4.61 to 6.28)	.763
Rural/remote	Ref.	
Family cancer clinic		
Visited	-0.19 (-4.91 to 4.53)	.938
Not visited	Ref.	
Medical/science occupation		
Yes	5.67 (-0.05 to 11.38)	.052
No	Ref.	
Parental status		
Yes	0.29 (-3.94 to 4.52)	.893
No	Ref.	
Family history of cancer (first degree relative)		
Yes	2.11 (-0.96 to 5.18)	.177
No	Ref.	
Married		
Yes	2.95 (-0.83 to 6.72)	.126
No	Ref.	
Multiple primary cancers		
Yes	-0.07 (-4.45 to 4.32)	.976
No	Ref.	
Time since diagnosis	0.20 (-0.19 to 0.58)	.317
Cancer incidence		
Common	-4.24 (-8.03 to -0.45)	.028*
Less common	-0.90 (-5.45 to 3.65)	.696
Rare	Ref.	
Satisfaction with decision	4.56 (2.16 to 6.96)	<.001***
Self-efficacy	1.15 (-1.65 to 3.95)	.420
Attitudes to uncertainty	3.06 (-0.20 to 6.32)	.065
Perceived susceptibility (for every 10-unit increase)	0.03 (-0.59 to 5.39)	.927

*** $P < .001$; ** $P < .01$; *$P < .05$.
Ref. = Reference category.

The findings suggest that participants have poor to moderate knowledge about MP whilst also having primarily positive attitudes towards MP at the time of consent to undergo MP.

Signed, written informed consent was obtained from participants before commencing the MoST Program. However, questionnaire responses demonstrate that participants did not clearly understand the purpose of MP nor its implications for treatment decision-making and risk management.

Table 5
Summary of ordinal regression analysis for predictors of perceived importance of MP, $n = 1074$

Independent variables	Ordered odds ratio (95% CI)	*P* value
Sex		
Female	1.45 (1.06-1.98)	.020*
Male	Ref.	
Age (for every 10-year increase)	0.95 (0.84-1.08)	.442
Education	0.96 (0.87-1.06)	.401
CALD		
Yes	1.42 (0.96-2.11)	.080†
No	Ref.	
SES	1.02 (0.96-1.08)	.609
ARIA		
Urban	0.86 (0.47-1.55)	.614
Rural/Remote	Ref.	
Family cancer clinic		
Visited	1.49 (0.88-2.55)	.140
Not visited	Ref.	
Medical/science occupation		
Yes	0.98 (0.53-1.79)	.944
No	Ref.	
Parental status		
Yes	1.62 (1.08-2.43)	.020*
No	Ref.	
Family history of cancer (first degree relatives)		
Yes	1.00 (0.72-1.37)	.974
No	Ref.	
Married		
Yes	1.57 (1.09-2.27)	.015*
No	Ref.	
Multiple primary cancers		
Yes	1.10 (0.70-1.74)	.681
No	Ref.	
Time since diagnosis	0.96 (0.93-0.99)	.017*
Cancer incidence		
Common	0.98 (0.65-1.47)	.927
Less common	1.03 (0.65-1.66)	.889
Rare	Ref.	
Satisfaction with decision	0.93 (0.72-1.20)	.572
Self-efficacy	1.40 (1.08-1.80)	.011*
Attitudes to uncertainty	2.29 (1.68-3.12)	<.001***
Perceived susceptibility (for every 10-unit increase)	0.93 (0.87-0.99)	.016*

*** $P < .001$; ** $P < .01$; *$P < .05$.
Ref. = Reference category.

They tended to over- rather than under-estimate the MP benefits, with the majority (76%) significantly overestimating the utility of MP for making decisions about future cancer risks, and 20% acknowledging they did not know the answer to this question. Participants also demonstrated a lack of knowledge about the ability of MP to help guide treatment for *all* types of cancer. Although participants were told about the rates of finding actionable somatic mutations and germline mutations, it is possible that this did not change their understanding as participants were shown to largely rely on the knowledge of their clinicians. These two items, with

Table 4
Perceived importance of MP: item responses

Perceived importance of MP Items	Number (%)
1. How important is it to you to learn about gene variants that may affect your chance of responding to particular cancer treatments?	
Very important	903 (84%)
Moderately important	92 (9%)
Somewhat important	55 (5%)
A little bit important	20 (2%)
Not at all important	4 (0.4%)
2. How important is it to you to learn more about how your lifestyle, such as exercise, smoking and diet, affects your chance of living longer with your disease?	
Very important	861 (80%)
Moderately important	113 (11%)
Somewhat important	63 (6%)
A little bit important	27 (3%)
Not at all important	8 (0.7%)
Missing	2 (0.2%)

particularly low correct response rates, may assist in identifying areas to target for further clinician and patient education. Results from a qualitative study with a subset of this cohort [13] reported that participants confused somatic with germline results, which could lead to overestimations of the outcomes provided by somatic testing and also add to participants' concerns.

Overestimation of *benefit* is not surprising, given the media hype surrounding genomic testing [27], however, the potential for greater disappointment when actionable results are not returned concerns many clinicians [3]. Finding ways to manage participant expectations remains a challenge in this area. Since all research is predicated on fundamental uncertainty, this finding likely has implications for patient perception of research-led care in general. A key and unanswered issue is the extent to which unrealistic hope regarding genomics has characteristics specific to this context. A secondary and related issue is the readiness of genomics for 'real-world' practice, given the rapidly changing nature of the actionability of MP.

A lack of knowledge about MP can also lead to overestimated *concerns*. As reported in our qualitative paper [13], participants were primarily concerned that MP results may negatively impact insurance policies or employment opportunities for their younger family members and future generations (although currently in Australia there is a Moratorium on Genetic Tests in Life Insurance, which prohibits insurance companies from legally basing decisions on genetic test results [28]). It is important to elicit and address such concerns during the consent process.

When asked about the benefits of testing, a third of participants indicated that they were not aware that MP could help to manage the risk of future cancer. This suggests that they were either unaware of the potential germline implications of MP or that they did not know if this information could be used for clinical management in the context of their cancer. Communicating germline results may be an added burden on advanced cancer patients coping with treatment and a poor prognosis [13,19]. This implies that in the rare instances of germline result return, some participants may be unprepared for this outcome. It is arguable that a greater focus on germline results may not be appropriate during informed consent procedures focused on MP to guide treatment, particularly where patients have few treatment options and an anticipated shortened lifespan, as in the current study. Nonetheless, it is important to continue to explore ways to convey such information simply, clearly and according to patient preferences.

Greater knowledge about MP was apparent in those with higher education, who speak English at home or with a rare cancer type. Past studies have shown that patients with rare cancers are more likely to undertake individual research regarding their treatment options given the absence of clear clinical treatment pathways, a lack of expertise from healthcare providers and a lack of online information or support [29,30]. Current findings suggest particular efforts are required in the clinic to ensure adequate understanding and informed consent in vulnerable sub-groups.

In terms of psychosocial characteristics, higher satisfaction with the decision to have MP was a significant predictor of participant knowledge about MP. There is an established link between satisfaction with decisions and knowledge in medical decision-making [22]. The current study replicates this association in relation to the knowledge of cancer patients who have agreed to undergo MP. This finding reinforces the importance of ensuring adequate understanding before providing consent, so that patients are satisfied they have made the right decision.

Despite having poor to moderate knowledge about MP, all participants gave consent to undergo testing, reflecting the findings from our earlier qualitative paper that participants had an overwhelming desire to undertake MP while simultaneously referring to it as 'the black box' [13]. Participants acknowledged their lack of understanding and were seemingly untroubled by this limited understanding. This is consistent with a body of literature highlighting the issues in obtaining informed consent in a cancer trial setting. One past study, in a women's healthcare setting, showed that the majority of participants spent less than 30 seconds reading consent forms that were expected to take no less than three minutes (one form) or seven minutes (another form) [31]. This implies that patients' low genomic knowledge may not necessarily be a problem as individuals prefer to depend on and trust the accuracy of the advice of their clinicians.

Consistent with previous studies [3,10], the participants in our study displayed overwhelmingly positive attitudes towards MP. This is consistent with the phenomena known as the 'Gartner hype cycle' [32]. It suggests that for most technologies, initial hype leads to over-estimation of benefit in the short term and under-estimation (and cynicism) in the long-term. Therefore, it is possible that even clinicians are reacting to hype and communicating an overestimation of benefit. There remains an interesting debate as to the line between cynical hype by commercial and other interests, and the hope inevitably attached by patients to science in providing an option where they have none.

Not surprisingly in an advanced cancer cohort, participants attached slightly less importance to wanting to learn about how their lifestyle and behavior modifications can affect their chance of prolonging their life, compared with learning about potential cancer treatments. Previous studies have shown similar results, where participants were less interested in testing if presented with a situation in which they could reduce their genetic risk by changing their behavior (e.g. through diet, exercise, taking vitamins) [33,34]. Further, a systematic review and meta-analysis found a lack of evidence that communicating genetic risk estimates changed behavioral outcomes, such as diet, physical activity or smoking cessation [35]. Additional research is needed to better understand how to motivate patients to learn about and act on lifestyle changes that affect their chances of living longer.

In terms of individual factors that contributed to participants' perceived importance of MP, we found that participants with children perceived MP to have greater importance compared to participants without children. This association may be driven by overestimated chances of germline findings emerging from MP. Our earlier qualitative paper [13] found that some participants were eager to pursue testing to identify relatives' risk of cancer, even when told there is only a small chance of this outcome. Alternatively, previous studies have shown that advanced cancer patients with dependent children are particularly burdened over the impact that their death will have on their children [36,37]. These patients prefer a course of treatment that focuses on extending life over treatment aiming to relieve as much pain and discomfort as possible [36,37]. Further to this, being married and female were also predictive of greater perceived importance of testing in the current sample. Therefore, patients with close family members (children and spouses) may perceive MP to be highly important out of a sense of familial responsibility to try anything that might prolong their life.

A strong association exists between negative attitudes towards uncertainty and greater interest in undergoing genetic testing for hereditary cancers [24,38–40]. The current study replicated this relationship among advanced cancer patients. Counseling and testing programs should ensure that prior to consent, patients are adequately supported to understand, consider and cope with the inherent uncertainty of genomic testing. Greater confidence in one's ability to cope with test results, or self-efficacy, was associated with greater perceived importance of MP. This association aligns with Protection Motivation Theory [16,17], which proposes that perceived self-efficacy is a key factor in individuals' motivation to engage with a preventative behavior. In addition, there is a large literature base showing that confidence is an essential characteristic in an individual's ability to make informed decisions about a variety of health behaviors and tests [14].

Interestingly, perceived susceptibility of cancer progression was associated with lower perceived importance of MP. This finding is inconsistent with the principles of Protection Motivation Theory, which proposes that perceived health threat increases motivation to protect oneself [16,17]. Previous research has shown, however, that motivation to pursue genomic testing is lower among individuals with both high perceived risk of cancer and advanced performance status in a germline testing setting [14]. Additionally, greater perceived cancer risk has been shown to be associated with greater perceived barriers to genetic testing as well as greater skepticism about the utility of results in a germline testing setting, perhaps because these individuals perceive it is too late for genomic testing to help [41,42]. Further, patients might perceive germline findings to be particularly burdensome at a time that they are trying to cope with their own advanced cancer diagnosis [43].

Strengths and Limitations

The conclusions of the current study are limited by the cross-sectional analysis, as causality cannot be inferred from associations. Further insights into patient outcomes will be gathered within the PiGeOn project through longitudinal assessments following the return of MP results. The lack of a standardized knowledge scale in MP research limits the comparability of the outcomes of the current study. Also, the selection bias inherent in the study poses a potential limitation to the conclusions of the study. All participants included in the study had agreed to undergo MP, potentially representing a sample of individuals biased towards having positive attitudes towards MP, and therefore the results are not generalizable to all advanced cancer patients. However, the results are generalizable to those opting for MP.

Nonetheless, the current study has high ecological validity as participants were about to undergo MP in a context where their oncologists would be informed of results which could influence their care, making it similar to the routine care setting in which MP is likely to be implemented in the near future. The findings of this study can help to ensure that when MP becomes part of routine clinical care, ethical considerations are embedded into practice, and patients are adequately prepared and supported during and after decision-making to pursue MP.

Implications

From a clinical perspective, given that the majority of participants gain their understanding of testing from their oncologist, these findings suggest a need to: i) educate cancer patients about MP and its utility before making decisions to pursue testing and ii) provide training for clinicians to increase their MP knowledge, as well as confidence and skills in managing patient and family expectations regarding the test results. Patients' poor to moderate knowledge and overestimation of the utility of MP present an ethical dilemma, as clinicians wish to avoid setting vulnerable patients up for unrealistic expectations and disappointment [3]. Hence there is a strong need for information and decision tools to support medical professionals in communicating realistic benefits and risks associated with results. Patients with lower education levels, and especially those who do not speak English at home, will need clear explanations, visual aids and ample opportunity to ask questions about MP at the time of their decision-making to pursue MP.

Our findings also suggest that outcomes of attempts to increase genomic understanding will be largely dependent on individuals' ability and appetite for in-depth knowledge, and limited by patients' prevalent, deep-seated trust in medicine and a perceived impossibility of truly understanding the complex fields of science being assessed here. Further, the comprehension of genomic information may be particularly challenging for advanced cancer patients who are navigating both psychological and physical burdens. These complexities point to the need for ongoing research to determine optimal approaches to attaining consent to genomic tests that will ensure consent is informed, while respecting patient preferences, psychological issues, and need for information over time.

In the future it is likely that awareness and demand for genomic information and testing relating to cancer will increase. The findings of this study can be used to inform ongoing ethical debates on issues such as how to effectively obtain informed consent for genomic profiling results and manage patient expectations.

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Data Statement

We are willing to make our data available.

Declaration of Competing Interests

The authors declare no competing interests.

References

[1] M.A. Glaire, M. Brown, D.N. Church, I. Tomlinson, Cancer predisposition syndromes: lessons for truly precision medicine, J. Pathol. 241 (2017) 226–235.
[2] M.L. Yushak, G. Han, S. Bouberhan, L. Epstein, M.P. DiGiovanna, S.S. Mougalian, T.B. Sanft, M.M. Abu-Khalaf, G.G. Chung, S.M. Stein, et al., Patient preferences regarding incidental genomic findings discovered during tumor profiling, Cancer 122 (2016) 1588–1597.
[3] F.A. Miller, R.Z. Hayeems, J.P. Bytautas, P.L. Bedard, S. Ernst, H. Hirte, S. Hotte, A. Oza, A. Razak, S. Welch, et al., Testing personalized medicine: patient and physician expectations of next-generation genomic sequencing in late-stage cancer care, Eur. J. Hum. Genet. 22 (2013) 391–395.
[4] J. Halpern, D. Paolo, A. Huang, Informed consent for early-phase clinical trials: therapeutic misestimation, unrealistic optimism and appreciation, J. Med. Ethics 45 (2019) 384–387.
[5] A.L. McGuire, L.M. Beskow, Informed consent in genomics and genetic research, Annu. Rev. Genomics Hum. Genet. 11 (2010) 361–381.
[6] R. Horton, A. Lucassen, Consent and autonomy in the genomics era, Curr. Genet. Med. Rep. 7 (2019) 85–91.
[7] T. Yanes, A.M. Willis, B. Meiser, K.M. Tucker, M. Best, Psychosocial and behavioral outcomes of genomic testing in cancer: a systematic review, Eur. J. Hum. Genet. 27 (2019) 28–35.
[8] P.S. Blanchette, A. Spreafico, F.A. Miller, K. Chan, J. Bytautas, S. Kang, P.L. Bedard, A. Eisen, L. Potanina, J. Holland, et al., Genomic testing in cancer: patient knowledge, attitudes, and expectations, Cancer 120 (2014) 3066–3073.
[9] R.A. Yusuf, D. Rogith, S.R.A. Hovick, S.K. Peterson, A.M. Burton-Chase, B.M. Fellman, Y. Li, C. McKinney, E.V. Bernstam, F. Meric-Bernstam, Attitudes toward molecular testing for personalized cancer therapy, Cancer 121 (2015) 243–250.
[10] S.W. Gray, K. Hicks-Courant, C.S. Lathan, L. Garraway, E.R. Park, J.C. Weeks, Attitudes of patients with cancer about personalized medicine and somatic genetic testing, J. Oncol. Pract. 8 (2012) 329–335.
[11] I. Pellegrini, M. Rapti, J.M. Extra, A. Petri-Cal, T. Apostolidis, J.M. Ferrero, T. Bachelot, P. Viens, C. Julian-Reynier, F. Bertucci, Tailored chemotherapy based on tumour gene expression analysis: breast cancer patients' misinterpretations and positive attitudes, Eur. J. Cancer Care 21 (2012) 242–250.
[12] R. Liang, B. Meiser, S. Smith, N.A. Kasparian, C.R. Lewis, M. Chin, G.V. Long, R. Ward, A.M. Menzies, J.N. Harris-Wai, et al., Advanced cancer patients' attitudes towards, and experiences with, screening for somatic mutations in tumours: a qualitative study, Eur. J. Cancer Care 26 (2017), e12600. .
[13] M.C. Best, N. Bartley, C. Jacobs, I. Juraskova, D. Goldstein, A.J. Newson, J. Savard, B. Meiser, M. Ballinger, C. Napier, et al., Patient perspectives on molecular tumor profiling: "Why wouldn't you?", BMC Cancer 19 (2019) 753.
[14] S.L. Manne, D.C. Chung, D.S. Weinberg, H.S. Vig, Z. Catts, M.K. Cabral, K. Shannon, N.J. Meropol, Knowledge and attitudes about microsatellite instability testing among high-risk individuals diagnosed with colorectal cancer, Cancer Epidemiol. Biomark. Prev. 16 (2007) 2110–2117.
[15] J.T. DeFrank, T. Salz, K. Reeder-Hayes, N.T. Brewer, Who gets genomic testing for breast cancer recurrence risk? Public Health Genomics 16 (2013) 215–222.
[16] J.E. Maddux, R.W. Rogers, Protection motivation and self-efficacy: a revised theory of fear appeals and attitude change, J. Exp. Soc. Psychol. 19 (1983) 469–479.
[17] Rogers, R.W., and Prentice-Dunn, S. (1997). Protection motivation theory. In Handbook of health behavior research 1: Personal and social determinants. (New York, NY, US, Plenum Press), pp 113-132.
[18] S. Thavaneswaran, L. Sebastian, M. Ballinger, M. Best, D. Hess, C.K. Lee, K.M. Sjoquist, W.E. Hague, P.N. Butow, R.J. Simes, et al., Cancer Molecular Screening and Therapeutics (MoST): a framework for multiple, parallel signal-seeking studies of targeted therapies for rare and neglected cancers, Med. J. Aust. 209 (2018) 354–355.
[19] M. Best, A.J. Newson, B. Meiser, I. Juraskova, D. Goldstein, K. Tucker, M.L. Ballinger, D. Hess, T.E. Schlub, B. Biesecker, et al., The PiGeOn project: protocol for a longitudinal study examining psychosocial, behavioural and ethical issues and outcomes in cancer tumour genomic profiling, BMC Cancer 18 (2018) 389.
[20] G.J. Mann, H. Thorne, R.L. Balleine, P.N. Butow, C.L. Clarke, E. Edkins, G.M. Evans, S. Fereday, E. Haan, M. Gattas, et al., Analysis of cancer risk and BRCA1 and BRCA2 mutation prevalence in the kConFab familial breast cancer resource, Breast Cancer Res. 8 (2006) R12.
[21] G. Mitchell, M.L. Ballinger, S. Wong, C. Hewitt, P. James, M.-A. Young, A. Cipponi, T. Pang, D.L. Goode, A. Dobrovic, et al., High frequency of germline TP53 mutations in a prospective adult-onset sarcoma cohort, PLoS One 8 (2013), e69026. .

[22] M. Holmes-Rovner, J. Kroll, N. Schmitt, D.R. Rovner, M.L. Breer, M.L. Rothert, G. Padonu, G. Talarczyk, Patient satisfaction with health care decisions: the Satisfaction with Decision Scale, Med. Decis. Mak. 16 (1996) 58–64.
[23] S.M. Rosenberg, M.S. Tracy, M.E. Meyer, K. Sepucha, S. Gelber, J. Hirshfield-Bartek, S. Troyan, M. Morrow, L. Schapira, S. Come, et al., Perceptions, knowledge, and satisfaction with contralateral prophylactic mastectomy among young women with breast cancer, Ann. Intern. Med. 159 (2013) 373–381.
[24] D. Braithwaite, S. Sutton, N. Steggles, Intention to participate in predictive genetic testing for hereditary cancer: The role of attitude toward uncertainty, Psychol. Health 17 (2002) 761–772.
[25] N.A. Kasparian, B. Meiser, P.N. Butow, J.M. Simpson, G.J. Mann, Genetic testing for melanoma risk: a prospective cohort study of uptake and outcomes among Australian families, Genet. Med. 11 (2009) 265–278.
[26] J. Hay, K. Kaphingst, R. Baser, Y. Li, S. Hensley-Alford, C. McBride, Skin cancer concerns and genetic risk information-seeking in primary care, Public Health Genomics 15 (2012) 57–72.
[27] M. Barbor, Precision medicine: hope or hype? https://wwwascopostcom/issues/february-10-2018/precision-medicine-hope-or-hype/ 2018.
[28] Centre for Genetics Education, Life insurance products and genetic testing in Australia, https://wwwgeneticseduau/publications-and-resources/facts-sheets/fact-sheet-20-life-insurance-products-and-genetic-testing-in-australia 2019.
[29] K. Budych, T.M. Helms, C. Schultz, How do patients with rare diseases experience the medical encounter? Exploring role behavior and its impact on patient–physician interaction, Health Policy 105 (2012) 154–164.
[30] S. Lea, A. Martins, S. Morgan, J. Cargill, R.M. Taylor, L.A. Fern, Online information and support needs of young people with cancer: a participatory action research study, Adolesc. Health Med. Ther. 9 (2018) 121–135.
[31] L. McNutt, E. Waltermaurer, R. Bednarczyk, B. Carlson, J. Kotval, J. McCauley, J. Campbell, D. Ford, Are we misjudging how well informed consent forms are read? J. Empir. Res. Hum. Res. Ethics 3 (2008) 89–97.
[32] C.V. Almario, The effect of digital health technology on patient care and research, Gastroenterol. Hepatol. 13 (2017) 437–439.
[33] M. Dieng, C.G. Watts, N.A. Kasparian, R.L. Morton, G.J. Mann, A.E. Cust, Improving subjective perception of personal cancer risk: systematic review and meta-analysis of educational interventions for people with cancer or at high risk of cancer, Psychooncology 23 (2014) 613–625.
[34] C. Lerman, E. Lustbader, B. Rimer, M. Daly, S. Miller, C. Sands, A. Balshem, Effects of individualized breast cancer risk counseling: a randomized trial, J. Natl. Cancer Inst. 87 (1995) 286–292.
[35] G.J. Hollands, D.P. French, S.J. Griffin, A.T. Prevost, S. Sutton, S. King, T.M. Marteau, The impact of communicating genetic risks of disease on risk-reducing health behaviour: systematic review with meta-analysis, Br. Med. J. 352 (2016) i1102.
[36] M.E. Nilsson, P.K. Maciejewski, B. Zhang, A.A. Wright, E.D. Trice, A.C. Muriel, R.J. Friedlander, K.M. Fasciano, S.D. Block, H.G. Prigerson, Mental health, treatment preferences, advance care planning, location, and quality of death in advanced cancer patients with dependent children, Cancer 115 (2009) 399–409.
[37] A.C. Muriel, C.W. Moore, L. Baer, E.R. Park, A.B. Kornblith, W. Pirl, H. Prigerson, J. Ing, P.K. Rauch, Measuring psychosocial distress and parenting concerns among adults with cancer, Cancer 118 (2012) 5671–5678.
[38] R.T. Croyle, D.S. Dutson, V.T. Tran, Y.C. Sun, Need for certainty and interest in genetic testing, Women Health 1 (1995) 329–339.
[39] A. Tibben, P.G. Frets, J.J.P. Van De Kamp, M.F. Niermeijer, M.V. Der Vlis, R.A.C. Roos, H.G.M. Rooymans, G.J.B. Van Ommen, F. Verhage, On attitudes and appreciation 6 months after predictive DNA testing for Huntington disease in the Dutch program, Am. J. Med. Genet. 48 (1993) 103–111.
[40] M. Decruyenaere, G. Evers-Kiebooms, H. Van den Berghe, Perception of predictive testing for Huntington's disease by young women: preferring uncertainty to certainty? J. Med. Genet. 30 (1993) 557–561.
[41] L. Kessler, A. Collier, K. Brewster, C. Smith, B. Weathers, E.P. Wileyto, C.H. Halbert, Attitudes about genetic testing and genetic testing intentions in African American women at increased risk for hereditary breast cancer, Genet. Med. 7 (2005) 230–238.
[42] L.D. Cameron, J. Reeve, Risk perceptions, worry, and attitudes about genetic testing for breast cancer susceptibility, Psychol. Health 21 (2006) 211–230.
[43] D.V.T. Catenacci, A.L. Amico, S.M. Nielsen, D.M. Geynisman, B. Rambo, G.B. Carey, C. Gulden, J. Fackenthal, R.D. Marsh, H.L. Kindler, et al., Tumor genome analysis includes germline genome: Are we ready for surprises? Int. J. Cancer 136 (2015) 1559–1567.