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
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 and 1 (mean = 0.61). English at home and having a rare cancer type were significant predictors of higher knowledge about MP (Table 3). For every ten per cent 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

| Category                                                                 | Sample post knowledge questions change | Total sample |  |
|--------------------------------------------------------------------------|----------------------------------------|--------------|---|
|                                                                         | (N = 777)                              | (N = 1074)   | N (%) |
| Sex                                                                      |                                        |              | N (%) |
| Female                                                                   | 405 (52)                               | 552 (51)     |  |
| Male                                                                     | 372 (48)                               | 522 (49)     |  |
| Highest level of education completed                                     |                                        |              | N (%) |
| 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)     |  |
| Undergraduate university; 177 (23)                                      |                                        | University – did not graduate: 18 (2) |  |
| Postgraduate university: 168 (22)                                       |                                        | University - graduated: 458 (43) |  |
| Culturally and linguistically diverse (CALD)                             |                                        |              | N (%) |
| Yes                                                                      | 184 (24)                               | 242 (23)     |  |
| Accessibility and remoteness index of Australia (ARIA)                   |                                        |              | N (%) |
| Urban                                                                    | 702 (90)                               | 978 (91)     |  |
| Rural and remote                                                         | 75 (10)                                | 94 (9)       |  |
| Missing                                                                  | 0                                      | 2 (0.2)      |  |
| Visited a family cancer clinic                                           |                                        |              | N (%) |
| Yes                                                                      | 86 (11)                                | 112 (10)     |  |
| Medical/science occupation                                               |                                        |              | N (%) |
| Yes                                                                      | 59 (8)                                 | 80 (7)       |  |
| Parental status                                                          |                                        |              | N (%) |
| Yes, has children                                                        | 574 (74)                               | 794 (74)     |  |
| Family history of cancer (first degree relatives)                        |                                        |              | N (%) |
| Yes                                                                      | 383 (49)                               | 521 (49)     |  |
| Marital status                                                           |                                        |              | N (%) |
| 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                                                 |                                        |              | N (%) |
| Yes                                                                      | 110 (14)                               | 148 (14)     |  |
| Cancer incidence                                                         |                                        |              | N (%) |
| 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                                                             |                                        |              | N (%) |
| Bone and soft tissue                                                     | 146 (19)                               | 231 (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                                                                    | 27 (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             |                                        |              | N (%) |
| 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)     |  |
| Socio-economic status (SES)                                              |                                        |              | Mean (SD) |
| 0-10                                                                     | 6.78 (2.86)                            | 6.83 (2.84)  |  |
| Time since diagnosis (years)                                             |                                        |              | Mean (SD) |
| 0-22.2                                                                  | 3.14 (3.96)                            | 3.28 (4.21)  |  |
| Satisfaction with decision                                              |                                        |              | Mean (SD) |
| 0-40.3                                                                  | 4.40 (0.75)                            | 4.42 (0.71)  |  |
| Self-efficacy                                                            |                                        |              | Mean (SD) |
| 1-5                                                                     | 4.29 (0.73)                            | 4.26 (0.70)  |  |
| Attitudes to uncertainty                                                |                                        |              | Mean (SD) |
| 1-5                                                                     | 4.31 (0.56)                            | 4.31 (0.57)  |  |
| Perceived susceptibility                                                |                                        |              | Mean (SD) |
| 0-100                                                                   | 65.07 (27.32)                          | 66.85 (26.62)|  |
| Knowledge (% correct)                                                   |                                        |              | Mean (SD) |
| 43 (20)                                                                 |                                         |              |  |

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Table 1 (continued)

| Sample post knowledge questions change | Total sample |   |
|---------------------------------------|--------------|--|
| (N = 777)                              | (N = 1074)   |   |
| N (%)                                 | N (%)        |   |
| 0-88                                   | 4.71 (0.61)  |   |

* 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)*  |
| 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)* |
| 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)* |
| 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)   |
| 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)* |
| No types of cancer | 2 (0.3) |
| I don’t know     | 178 (23)   |
| Genetic panel testing is helpful for making decisions about treatment for cancer: | |
| Always          | 116 (15)   |
| Frequently      | 146 (19)   |
| Sometimes       | 361 (47)*  |
| 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)*    |
| 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)*  |
| 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)* |
| Only available through a clinical trial (at no cost to the patient) | 128 (17)* |
| 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? | |
| 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)    |

* Correct responses

b Not included in the knowledge score calculation.
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. 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 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) | .282   |
| Education             | 1.84 (0.78 to 2.89)             | .011   |
| CALD                  | Yes -4.70 (-8.37 to -1.03)      | .012   |
|                       | No Ref.                         |        |
| SES                   | 3.82 (-2.00 to 9.64)            | .019   |
| 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 (4.05 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* |
|                       | <.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.

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%)   |

Ref. = Reference category.
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 undergo 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.

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