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Psychological predictors of advanced cancer patients' preferences for return of results from comprehensive tumor genomic profiling

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Running title: Preferences for return of molecular profiling results

Abstract

This study assessed the psychological predictors of preferences for return of comprehensive tumor genomic profiling (CTGP) results in patients with advanced cancers, enrolled in the Molecular Screening and Therapeutics Program. Patients completed a questionnaire prior to undergoing CTGP. Of the 1,434 who completed a questionnaire, 96% would like to receive results that *can guide treatment* for their cancer, and preference for receiving this type of result was associated with lower tolerance of uncertainty. Sixty-four percent would like to receive results that *cannot guide treatment*, and lower tolerance of uncertainty, self-efficacy and perceived importance were associated with this preference. Fifty-nine percent would like to receive *variants of unknown significance*, which was associated with lower tolerance of uncertainty, higher self-efficacy and perceived importance. Eighty-six percent wanted to receive *germline results that could inform family risk.* This was associated with higher self-efficacy, perceived importance and perceived susceptibility. Although most patients wanted to receive all types of results, given the differing patient preferences regarding the return of results depending on the utility of the different types of results, it appears critical to safeguard patient understanding of result utility to achieve informed patient choices. This should be accompanied by appropriate consent processes.

Key words: Tumor testing, advanced cancer, patient preferences, attitudes, genomic sequencing, personalized medicine

INTRODUCTION

The field of cancer genomics is at the cusp of unprecedented change, driven by major advances in genomic testing technology (Jackson et al., 2015). Rapid advances in genomic technology are revolutionizing cancer management in people at increased risk, by informing therapeutic decisions, and enabling accurate diagnosis of disease susceptibility and targeted implementation of risk management. Survival rates for many people with a variety of cancers have seen little improvement (Australian Institute of Health and Welfare, 2014). Therefore, new approaches to prevent and treat cancers, increase patient survival and reduce morbidity are urgently needed. In some cases, effective personalized cancer treatments exist, but the therapy may not be accessible to the patient. Genomics provides perhaps the greatest promise for improved cancer outcomes at a time when increased costs of clinical research have slowed the development of therapeutic options (Jackson et al., 2015).

Comprehensive tumor genomic profiling (CTGP) involves testing tumor tissue for molecular characteristics including gene mutations and fusions, which can be linked to cognate therapies (Sicklick et al., 2019). Comprehensive tumor genomic profiling can identify variants that: a) affect treatment (clinically actionable), b) do not affect treatment (non-actionable), c) are variants of uncertain significance (VUS) in terms of therapeutic potential, and/or d) may have a germline origin (and thus have relevance to the patient's genetic relatives as well as potentially for the patient). These categories are not mutually exclusive. If a clinically actionable result is returned, the relevant therapy may or may not be accessible to the patient. While estimated rates of clinical actionability range from 10-40%, more than half of all patients undergoing CTGP will receive a non-actionable result (Zehir et al., 2017). In addition, less than half of all of patients who receive an actionable result will go onto a cognate treatment (Malone et al., 2020).

Qualitative studies have reported that patients with advanced cancer offered tumor testing had positive views about, and unequivocally accepted, screening for somatic tumor genetic variants linked to possible cancer treatments (Best et al., 2019; Best et al., 2020; Hamilton et al.; Liang et al., 2017). In a quantitative assessment of advanced cancer patients' perceived value of CGTP, we found that as many as 89% of such patients would have CGTP for as little as a 1% actionable return rate (Butow, Davies, et al., 2020). In these studies, patients perceived CGTP to have high importance even though they had had poor to moderate knowledge of CGTP (Davies et al., 2020; Liang et al., 2017). They preferred that discussion focused on practical matters relevant to treatment (Liang et al., 2017) and information that could inform treatment options rather than other information, which they felt might confuse them (Best et al., 2020). Indeed patients considering hypothetical (Miller et al., 2014) and actual CTGP (Best et al., 2019) were confused about the utility of non-actionable findings (Miller et al., 2014). Additional qualitative studies of advanced cancer patients offered CTGP found that patients did not consider receiving screening results burdensome but identified information overload and cancer-related distress as key barriers to test comprehension (Liang et al., 2017). Furthermore, some patients perceived germline findings as worrying due to their incapacity to understand results or to share the results with family members as a result of having advanced cancer (Best et al., 2019; Catenacci et al., 2015) and because of concerns about being able to obtain health or life insurance (Yushak et al., 2016). It has also been reported that patients misunderstood results, which led to anxiety and uncertainty about the future (Pellegrini et al., 2012). In summary, many qualitative studies have been conducted on preferences and attitudes towards tumor testing, but there is a dearth of quantitative studies on this topic.

Our group recently reported quantitative data on patients' preferences for CGTP results, as well as demographic and disease predictors of these preferences (Best et al., 2020). However, this paper did not explore the influence on preferences of patients' psychological approaches to uncertainty and genomic testing. Understanding the latter is important, since psychological factors are potentially modifiable, contrary to demographic/disease variables. Thus, the aim of this analysis was to quantitatively assess the relationship between preferences regarding return of CGTP results and psychological variables.

A number of theoretical frameworks can guide our understanding of psychological predictors of preferences for CTGP. Protection Motivation Theory (Maddux et al., 1983; Rogers et al., 1997) is particularly well-suited to guide research into this topic, because it is a multidimensional theory, which has been used previously in other genomic studies, e.g. by Fisher et al. (2012) and Yanes et al. (2017). This theory proposes that attitudes to treatment options and decision-making about these options are influenced by a range of psychological factors including perceived susceptibility, perceived importance of learning whether gene variants affect the chance of responding to particular cancer treatments, attitudes towards uncertainty, and self-efficacy (Maddux et al., 1983; Rogers et al., 1997). Based on Protection Motivation Theory, we hypothesized that preferences for wanting to receive results from CTGP would be associated with higher perceived susceptibility, perceived importance, tolerance of uncertainty, and self-efficacy.

MATERIALS AND METHODS

Parent study

The methodology for this study is described in detail in our protocol paper (Best et al., 2018). In brief, participants were recruited through the Molecular Screening and Therapeutics (MoST)

program (Thavaneswaran et al., 2018), which is being conducted nationally in Australia. MoST is recruiting adult patients with pathologically confirmed advanced or metastatic solid cancers of any histological type with a particular focus on rare or neglected cancers who have exhausted therapeutic options. Participants undertake CTGP and receive results at approximately 11 weeks, and if an actionable variant is found, are enrolled in a related therapeutic trial or receive an indicated targeted therapy if available. Participants were recruited by the parent program (MoST) from incident and prevalent cases nationally.

The inclusion criteria for the parent study were: at least 18 years old; pathologically confirmed advanced and/or metastatic solid cancer or an earlier diagnosis of a poor prognosis cancer; sufficient and accessible tissue for CTGP; all standard anticancer therapy failed or at time or enrolment was given last line of standard therapy; Eastern Cooperative Oncology Group Performance Status Measure (ECOG) performance status 0, 1 or 2; was interested and capable to observe with all requirements of the study; and provided written informed consent. Exclusion criteria were: suitability for standard therapy, if the patient has not been previously treated; has specific health conditions which suggest that individual should not participate or that assessment of key outcomes may be compromised; history of another malignancy within two years prior to registration: pregnancy, lactation, or inadequate contraception.

Procedure for Psychosocial Issues in Genomics in Oncology (PiGeOn) Project

Participants in MoST were also invited to participate in the PiGeOn Project, which is a longitudinal, mixed-methods psychosocial sub-study of MoST. It aims to examine the psychosocial and behavioral impacts of CTGP and ethical issues involved in that process (Best et al., 2018). Patients give written consent to the PiGeOn study at the same time as giving consent to

the parent study. Both studies were approved by the St Vincent's Hospital Human Research Ethics Committee (Reference HREC/16/SVH/23). All participants were asked to complete either an online or hard copy questionnaire just after the MoST patient information sheet was explained and consent was given (prior to CTGP).

Measures

The following predictor variables were assessed (see Supplementary File 1).

Demographics and disease data: Participants' gender, age, education, language spoken at home, socio-economic status, urban versus rural/remote place of residence according to the Accessibility and Remoteness Index of Australia (ARIA), previous attendance at a family cancer clinic, occupation, parental status, family history (first-degree relative with cancer), marital status, multiple primary cancer, time since diagnosis, and cancer incidence (common, less common or rare) were collected or determined based on responses in the questionnaire, or were collected within the parent study (MoST Program).

Fear of cancer progression: Three items from the Concerns about Recurrence Questionnaire, (Thewes et al., 2015) were adapted to measure fear of cancer progression, e.g. "How often have you worried about your cancer progressing?" Summed scores range from 0 to 30, with higher scores indicating greater fear.

Self-efficacy: Four items adapted from Rosenberg et al. (2013) assessed perceived ability to cope if actionable, non-actionable, VUS and/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". Summed scores range from 1 to 5, with higher scores indicating greater perceived ability to cope.

Attitudes towards uncertainty: The seven-item Likert-type scale (Braithwaite et al., 2002) assessed 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". Summed scores range from 1 to 5, with higher scores indicating a lower tolerance of 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. Responses were on a visual analogue scale (0–100%). The item was adapted from a previous study (Kasparian et al., 2009).

Perceived importance: A two-item measure adapted from Hay et al. (2012) assessed perceived importance of learning whether gene variants affect the chance of responding to particular cancer treatments, and 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 range from 1 to 5, with higher scores indicating greater importance.

The outcome variables of the analyses were:

Preferences for being informed of results. Four Likert-scale items adapted from Tabor et al. (2012) were used to assess desire for results informing: treatment, prognosis and family risk of cancer as well as gene variants that no-one knows anything about (response options: "yes", "no", "maybe" and "don't know"). The wording of the items can be found in Tables 3 and 4.

Data analysis

Demographic data were tabulated, and summary statistics used to describe questionnaire results. To check which variables were associated with the desire to receive each type of result, logistic

regressions were performed using SPSS Version 25. The following demographic variables, found to be significant in the previous analysis (Best et al., 2020), were included in the current analyses to control for their potentially confounding influence: age, education, language spoken at home (as a proxy for English as a second language), remote/rural versus urban location, whether participants had biological children, and whether any first-degree relatives were diagnosed with cancer. The outcome variables relating to preferences for being informed of results were categorized as "Yes" versus "No"/"Maybe"/"Don't know" due to the small number of "No", "Maybe" and "Don't know" responses. The logistic regression analyses investigated the effects of attitudes towards uncertainty, perceived susceptibility, self-efficacy, perceived importance of CTGP, and concerns about cancer progression. Due to the low event rate for being informed about gene variants that can guide treatment, a Firth's bias-reduced penalized-likelihood logistic regression was also carried out using the function *logistf* in library *logistf* in R (Version 1.24), which has been shown to give unbiased odds ratios and p-values in low event data (van Smeden et al., 2016). This Firth's bias-reduced penalized-likelihood logistics regression gave very similar results to those reported in the article indicating no bias from the low event rate of this sample.

RESULTS

Of 1,545 participants who provided consent for the study, 1,434 (93% response rate) completed the questionnaire. Participants were evenly distributed in gender (52% female), had a mean age of 55 years, with a median Eastern Cooperative Oncology Group (ECOG) Performance Status rating of 1 (restricted in physically strenuous activity). See Table 1 for demographic and ECOG details.

[Insert Table 1 about here]

Of the 1,434 study participants who completed the questionnaire, 1,380 (96%) would like to receive results that could guide treatment for their advanced cancer, 920 (64%) would like to receive results that could not guide treatment, and 673 out of 1,137 (59%) would like to receive VUS (see Table 2). In the case of germline results which could inform family risk, 1,227 (86%) wanted to receive these results. As shown in Table 2, to the question as to whether they wanted to receive each type of result, it was quite rare for participants to respond with a definite "No", and similar numbers answered "Maybe" or "Don't know".

[Insert Table 2 about here]

Controlling for the demographic variables listed above, logistic regression indicated that low tolerance of uncertainty was significantly associated with wanting to be informed about gene variants that *can guide treatment* for their cancer (Table 3). For every category increase in low tolerance of uncertainty (e.g. agree – strongly agree) the odds of wanting to be informed about gene variants that *can guide treatment* increased by 2.02-fold (95% CI, 1.14 to 3.58), p=0.016.

Controlling for the demographic variables listed above, lower tolerance of uncertainty, higher self-efficacy, and higher perceived importance were significant predictors of patients' preference to be informed about gene variants that *cannot guide a treatment* for their cancer (Table 3). For every category increase in lower tolerance of uncertainty the odds of wanting to learn about this type of result increased by 2.19-fold (95% CI, 1.70-2.81), p<0.001. For every category increase in patients' perceived self-efficacy to cope with results (e.g. agree – strongly agree) the odds of wanting this result increased by 1.37-fold (95% CI, 1.13-1.67), p=0.001. For every category increase in perceived importance to learn about gene variants (e.g. moderately important

– very important) the odds of wanting this result increased by 1.27-fold (95% CI, 1.04-1.56), p=0.019.

[Insert Table 3 about here]

In terms of preferences to be informed about gene variants that *no-one knows anything* about (or *VUS*), controlling for the above demographic variables, lower tolerance of uncertainty, higher self-efficacy, and higher perceived importance were significant predictors of wanting to be informed about this result (Table 4). For every one-category increase, the odds of wanting this result increased by 1.91-fold (95% CI, 1.43-2.54, p<0.001) for low tolerance of uncertainty; by 1.48-fold (95% CI, 1.19-1.84, p<0.001) for higher self-efficacy; and by 1.61-fold (95% CI, 1.26-2.05, p<0.001) for higher perceived importance.

Controlling for sociodemographic variables, in terms of being informed about gene variants that provide information about *family members' risk* of developing cancer, higher self-efficacy, higher perceived importance, and higher perceived susceptibility were significant predictors of wanting to be informed about *family member's risk*. For every category increase, the odds of wanting this result increased by 1.61-fold (95% CI, 1.27-2.04, p<0.001) for self-efficacy; and by 1.86-fold (95% CI, 1.48-2.35, p<0.001) for perceived importance. For every ten percent increase in patients' perceived susceptibility of cancer progression (e.g. 80% chance of cancer progression – 90% chance of cancer progression) the odds of wanting to be informed about this type of result increased by 1.08-fold (95% CI, 1.01-1.15), p=0.031.

[Insert Table 4 about here]

Discussion

This analysis shows that the vast majority of advanced cancer patients (96%) who have consented to CTGP would like to receive results that could guide treatment for their cancer and germline results, which would inform family risk (86%). Interest in receiving results that could not guide treatment was lower (64%), as was interest in receiving a VUS (59%). These varying preferences depending on the type of result demonstrate that the perceived utility of different types of results impacted on patient preferences for the return of results, with the result type with the greatest utility being associated with the highest proportion of patients wanting to receive results.

This is further underscored by our finding that perceived importance of learning whether gene variants affect the chance of responding to particular cancer treatments and how lifestyle may affect the chance of living longer with cancer (as measured by the 'Perceived importance' variable) were significant predictors of patients' preference for wanting to be informed about gene variants that cannot guide treatment for their cancer, VUS, and variants that provide information about family member's risk. These results demonstrate that patients' preferences for the return of different types of results directly reflect how much they perceive variants will impact on their response to specific cancer treatments, and whether they believe they can influence their cancer outcome by changing their lifestyle in response to genomic findings. These findings suggest that patient education on the likelihood of a result indicating additional treatment options and the role of lifestyle factors on survival are important to promote value-informed decision-making about results return. Indeed it is possible that behind the association between perceived utility and preferences are personal utility dimensions, rather than clinical ones (Kohler et al., 2017), which may need to be explored in patient education.

In accordance with the hypothesis based on Protection Motivation Theory, lower tolerance of uncertainty was a significant predictor for wanting to receive results that can guide treatment, cannot guide treatment and VUS. Although preference for being informed about germline gene variants that provide information about one's family members' risk was not significantly associated with low tolerance of uncertainty, the association was in the predicted direction. Given that many people hope that genomic testing will reduce uncertainty (Bartley et al., 2020), it is perhaps not surprising that low tolerance of uncertainty was significantly associated with a preference to receive different types of results. These results confirm those by Bombard et al., who assessed patient perceptions of gene expression profiling in breast cancer treatment decisions and found that the perceived benefits included the ability to reduce uncertainty (Bombard et al., 2014). In our previous qualitative study, we found that advanced cancer patients desired immediate, clear and simple information that promotes certainty, thus highlighting that health professionals' communication skills are critical in meeting patient expectations ((Bartley et al., Early view Patient Education and Counseling).

In accordance with Protection Motivation Theory, self-efficacy was also a significant predictor of wanting to be informed about variants that cannot guide a treatment, VUS, and results that informed family members' cancer risk. While self-efficacy was not significantly associated with wanting to be informed about variants that can guide treatment for advanced cancer, the results were in the predicted direction. These findings are consistent with those of DeFrank et al. (2013), who examined uptake of genomic testing results for breast cancer recurrence risk in women with early-stage breast cancer and found that interest in testing was associated with self-efficacy to cope with, and act on, results. These results show that self-efficacy is an important predictor of interest in CTGP, underscoring the important role of confidence in one's ability to deal with the

information received. Indeed, Butow et al. (2020) reported that patients with low self-efficacy were significantly more distressed by non-actionable CTGP results. These findings suggest that screening for self-efficacy prior to testing may be useful in guiding delivery of care, with those low in self-efficacy offered additional counseling and support before and after result receipt.

Perceived susceptibility was a significant predictor of wanting to be informed about germline results that inform family member's risk. These findings are consistent with other studies, which found that perceived risk was associated with interest in testing for single nucleotide polymorphisms related to breast cancer risk (Graves et al., 2011), as well as interest in panel testing for genes that confer modest and moderate breast cancer risk (Flores et al., 2017). These findings are also consistent with a large number of studies on interest in single gene testing showing an association with perceived risk in cancer (Meiser, 2005) as well as non-cancer settings (Studwell et al., Early view).

The limitations of this study should be mentioned. Firstly, CTGP was offered in the context of a research study, and thus patient preferences in the routine clinical setting may be different. Secondly, a higher proportion of university-educated participants (42%) than the general public (24%) (Australian Bureau of Statistics, 2017) were included, possibly reflecting that people with higher levels of education may be more likely to participate in research. On the other hand, our sample was comparable to the general population in terms of the percentage speaking a language other than English at home (22% compared to 26% in the general population) and in terms of the percentage who had biological children (23% compared to 24% in the general population) (Australian Bureau of Statistics, 2017), indicating good generalizability in terms of these characteristics. Thirdly, some patients were self-referred (Best et al., 2020), perhaps reflecting higher health literacy. Finally, since participants in MoST do not receive a VUS result as a result

from their CTGP, this was a hypothetical question for these participants. The strengths of this study include a large sample size and that patients were actually offered CTGP as opposed to many other studies that assessed preferences to a hypothetical testing. This is important, as it is well-established that attitudes to hypothetical genetic testing do not always translate into actual testing uptake (Meiser et al., 2000).

Conclusion

This study reported advanced cancer patients' preferences regarding the return of CTGP results. An awareness of which psychological drivers influence patients' preference for the return of results assists healthcare providers to adapt their consultations to manage preferences. Our findings demonstrated that the perceived utility of different types of results impacted on patient preferences for the return of results. Given that differing patient preferences regarding the return of results depended on the perceived utility of the different types of results, it seems critical to enhance patient understanding of result utility in order to achieve informed patient choices. This needs to be accompanied by appropriate consent processes promoting the return of results that is tailored to patient preferences. Given the lack of time of oncologists, other providers may need to be involved to supplement the consenting process to assist, such as oncology nurses or primary care physicians. The consenting process may also need to be supported with use of technology such as web-based platforms to achieve dynamic consent (Haas et al., 2021).

Furthermore, as low tolerance of uncertainty and self-efficacy to cope with results were associated with preferences, clinicians could administer to patients prior to CTGP the scales used in this study to assess low tolerance of uncertainty and self-efficacy to cope with results to identify patients likely to experience negative psychological reactions. Patient-reported outcomes are

increasingly used in cancer settings to identify patients at risk, and have been shown to improve doctor-patient communication and improve quality of life (Chen et al., 2013; Kotronoulas et al., 2014). Those with high scores on the scales to assess low tolerance of uncertainty and self-efficacy to cope with results may need more support if non-actionable or complex results eventuate. In particular, it may be necessary to schedule a longer appointment to disclose and discuss nonactionable or complex results at length and/or refer patients for counseling. Clinicians need to be adequately resourced to administer the scales and discuss the results such in more depth.

Author statement

Bettina Meiser, Phyllis Butow, Megan Best, Timothy Schlub, Ilona Juraskova, Mandy Ballinger, David Thomas, Kathy Tucker, David Goldstein and Barbara Biesecker were responsible for the conception and initial study design, and for refining the study design. Megan Best, Phyllis Butow, Nicci Bartley and Christine Napier were responsible for co-ordinating the acquisition of study data. Grace Davies was responsible for statistical analyses. Bettina Meiser and Grace Davies drafted the manuscript, and all authors were involved in editing and approving the final manuscript.

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Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Table 1: Demographics of participant cohorts

Characteristics	Total participants (n=1434)
Age (years)	
Mean (SD)	55.34 (14.30)
Median (IQR)	57 (20)
Range	18-89
	n (%)
Gender	
Female	742 (51.74)
Highest level of education completed:	
Primary school	17 (1.20)
Year 7 or 8	37 (2.61)
Year 9 or 10	239 (16.87)
Year 11 or 12	246 (17.36)
Vocational Training	272 (19.19)
University did not graduate	18 (1.27)
University graduated	588 (41.50)
Accessibility and Remoteness Index of Australia (ARIA)	
Urban (versus rural/remote)	1295 (91.39)
Language spoken at home	
Language other than English	313 (21.83)
Has biological children	1098 (77.49)
Cancer diagnosis	
Bone and soft tissue	331 (23.08)
Brain	152 (10.60)
Colon and/or rectum	132 (9.21)
Pancreas	133 (9.27)
Breast	75 (5.23)
Uterus	5 (0.35)
Ovary	56 (3.91)
Unknown primary	63 (4.39)
Lung	50 (3.49)
Prostate	37 (2.58)
Other	400 (27.89)
Eastern Cooperative Oncology Group (ECOG) Performance Status rating	
0	716 (50.32)

1 2 3	643 (45.19) 60 (4.22) 4 (0.28)
Has a first-degree relative diagnosed with cancer	711 (49.58)
Previously had genetic testing Yes No Don't know Missing	 250 (17.43) 1144 (79.78) 31 (2.16) 9 (0.63)
Attitudes towards uncertainty	
Mean (SD)	4.30 (0.56)
Range	1.43-5
Perceived susceptibility	
Mean (SD)	66.52 (26.74)
Range	0-100
Self-efficacy	
Mean (SD)	4.27 (0.69)
Range	1-5
Perceived importance	
Mean (SD)	4.71 (0.60)
Range	1-5
Concerns of cancer progression	
Mean (SD)	17.55 (8.07)
Range	0-30

Legend: SD=standard deviation, IQR=inter quartile range

Table 2: Survey results- What sort of gene variants you would like to be informed about

Preference	**n (%)**
Wanted to receive gene variants that <u>can guide</u> treatment for my advanced cancer	
Yes	1380 (96)
No	3 (0.2)
Maybe	26 (2)
Don't know	17 (1)
Missing	8 (0.6)
Wanted to receive gene variants that <u>can NOT guide</u> a treatment for my advanced cancer	
Yes	920 (64)
No	156 (11)
Maybe	190 (13)
Don't know	137 (10)
Missing	31 (2)
Wanted to receive gene variants that <u>no-one knows</u> anything about	**(**N = 1137)*
Yes	673 (59)
No	120 (11)
Maybe	140 (12)
Don't know	172 (15)
Missing	32 (3)
Wanted to receive gene variants that provide information about my <u>family members' risk</u> of developing cancer	
Yes	1227 (86)
No	53 (4)
Maybe	84 (6)
Don't know	44 (3)
Missing	26 (2)

*Version 2 of the questionnaire only

Table 3. Multiple Logistic Regressions for preferences to be informed about gene variants (Yes vs No/Maybe/Don't Know)

	I would like to be informed about gene variants that <u>can guide</u> treatment for my advanced cancer		**I would like to be informed about gene variants that <u>can NOT guide</u> a treatment for my advanced cancer**	
Independent Variable	Odds ratio (95% CI)	*p* value	Odds ratio (95% CI)	*p* value
Age (for every 10-year increase)	0.88 (0.69-1.12)	0.291	0.98 (0.90-1.08)	0.728
Education	1.33 (1.09-1.61)	0.005**	1.09 (1.01-1.17)	0.019*
ARIA				
Remote/Rural	1.92 (0.44-8.34)	0.386	1.85 (1.19-2.87)	0.006**
Urban	Ref.		Ref.	
Language spoken at home				
Language other than English	0.62 (0.30-1.26)	0.186	0.88 (0.66-1.18)	0.389
English	Ref.		Ref.	
Biological Children				
Yes	2.35 (1.06-5.19)	0.035*	0.88 (0.64-1.21)	0.424
No	Ref.		Ref.	
First-Degree Relative with Cancer				
Yes	2.00 (0.98-4.08)	0.055†	1.04 (0.82-1.33)	0.739
No	Ref.		Ref.	
Attitudes towards Uncertainty	2.02 (1.14-3.58)	0.016*	2.19 (1.70-2.81)	< 0.001***

Perceived Susceptibility (for every 10% increase)	1.12 (0.98-1.27)	0.090†	1.02 (0.98-1.07)	0.348
Self-Efficacy	1.24 (0.78-1.97)	0.368	1.37 (1.13-1.67)	0.001**
Perceived Importance	1.49 (0.98-2.26)	0.065†	1.27 (1.04-1.56)	0.019*
Fear of Cancer Progression	1.00 (0.96-1.04)	0.990	0.99 (0.98-1.01)	0.247

*** $p < 0.001$ | ** $p < 0.01$ | * $p < 0.05$ | † $0.05 < p < 0.1$

Legend: Ref. = Reference category; ARIA=Accessibility and Remoteness Index of Australia.

Table 4. Multiple Logistic Regressions for preferences to be informed about gene variants (Yes vs No/Maybe/Don't Know)

I would like to be informed about gene variants that no-one knows anything about			**I would like to be informed about gene variants that provide information about my family members' risk of developing cancer**	
Independent Variable	Odds ratio (95% CI)	*p* value	Odds ratio (95% CI)	*p* value
Age (for every 10-year increase)	0.89 (0.80-0.98)	0.024*	0.84 (0.74-0.96)	0.012*
Education	1.01 (0.93-1.09)	0.867	0.97 (0.87-1.07)	0.504
ARIA				
Remote/Rural	1.63 (1.04-2.57)	0.035*	1.01 (0.55-1.83)	0.988
Urban	Ref.		Ref.	
Language spoken at home				
Language other than English	1.20 (0.87-1.66)	0.272	0.91 (0.60-1.36)	0.635
English	Ref.		Ref.	
Biological Children				
Yes	1.11 (0.79-1.56)	0.549	1.73 (1.14-2.61)	0.009**
No	Ref.		Ref.	
First-Degree Relative with Cancer				
Yes	1.21 (0.93-1.58)	0.166	1.35 (0.95-1.91)	0.093†
No	Ref.		Ref.	
Attitudes towards Uncertainty	1.91 (1.43-2.54)	< 0.001***	1.29 (0.93-1.78)	0.122

Perceived Susceptibility (for every 10% increase)	1.03 (0.98-1.08)	0.293	1.08 (1.01-1.15)	0.031**
Self-Efficacy	1.48 (1.19-1.84)	< 0.001***	1.61 (1.27-2.04)	< 0.001***
Perceived Importance	1.61 (1.26-2.05)	< 0.001***	1.86 (1.48-2.35)	< 0.001***
Fear of Cancer Progression	0.99 (0.97-1.01)	0.172	1.01 (0.98-1.03)	0.623

*** $p < 0.001$ | ** $p < 0.01$ | * $p < 0.05$ | $^{\dagger} 0.05 < p < 0.1$

Legend: Ref. = Reference category; ARIA=Accessibility and Remoteness Index of Australia.

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MoST Program Questionnaire 1

As part of the MoST Program, we hope to better understand the impact of new genetic testing technologies on emotions and behaviour. Thus we are inviting you to complete this questionnaire as someone who is participating in the MoST Program.

We would greatly appreciate if you completed this questionnaire within the next 1-2

weeks. It will take about 20 minutes to complete. Once completed the questionnaire can be returned using the reply paid envelope provided or it can be submitted online.

Your responses will be kept confidential and your identity will not be revealed in any reports or presentations. Information you provide will not be shared with any health professionals involved in your care.

Participation in this study is voluntary and you can withdraw from the study at any time. If you would prefer not to participate in this study, please let us know by contacting the MoST Program Senior Research Coordinator Tharindi Ip on (02) 9355 5874. Your participation (or non-participation) will not affect your relationship with any treating doctors, other health professionals or researchers involved with the MoST Program**.**

If you have any questions about filling in the questionnaire, or the study in general, please call the MoST Program Research Coordinator Christine Napier on (02) 9355 5839 or send an email to most@garvan.org.au.

Participant number:

Date issued:

Date completed:

1. **What has been your main occupation? _____**

2. **What was the highest level of education that you completed?**

❑ Primary school (some or all)
❑ Secondary school – year 7 or 8
❑ Secondary school – year 9 or 10
❑ Secondary school – year 11 or 12
❑ Vocational training
❑ Undergraduate university
❑ Postgraduate university

3. **Do you speak a language other than English at home?**

❑ No

❑ Yes *(please specify)*

4. A family cancer clinic focuses on genetic risk factors for cancer, and is usually run by a geneticist (a clinician with expertise in genetics). a. Have you ever been to a family cancer clinic?

❑ Yes
❑ No – go to question 5
❑ Don't know – go to question 5

b. Which family cancer clinic did you go to? *(Please specify clinic and city)*

Clinic _____

City _____

5. Have you ever had genetic testing, before you were involved in the MoST Study?

❑ Yes
❑ No – go to question 6
❑ Don't know – go to question 6

What condition were you tested for? *(Please specify)*

_____

A **genetic panel test,** on a sample of a tumour taken during surgery, can identify changes in cancer genes. Genes contain the instructions for our body to function properly. Changes in genes, called **gene variants**, may affect how people respond to different treatments. Therefore, learning about gene variants may guide treatment options. Some gene variants also mean the person and their family have higher risks for other cancers.

6. **How important is it to you to learn about gene variants that may affect your chance of responding to particular cancer treatments?**

- ❑ Not at all important
- ❑ A little bit important
- ❑ Somewhat important
- ❑ Moderately important
- ❑ Very important

7. **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?**

- ❑ Not at all important
- ❑ A little bit important
- ❑ Somewhat important
- ❑ Moderately important
- ❑ Very important

This next section asks what you know about genetic panel testing. Please tick the **ONE** answer that you think is the most accurate. Just tick the "I don't know" option if you are not confident of the answer.

8. **Tests that can guide cancer treatment include:**

- ❑ Blood DNA
- ❑ Tumour DNA
- ❑ Both
- ❑ Neither
- ❑ I don't know

9. **Genetic panel testing of a help:**

- ❑ Guide treatment for the current cancer
- ❑ Manage the risk of future cancer
- ❑ Guide treatment for the current cancer and manage the risk of future cancer
- ❑ Neither
- ❑ I don't know

10. **Genetic panel testing is helpful for *guiding treatment* of:**

- ❑ No types of cancer
- ❑ Some types of cancer
- ❑ Most types of cancer
- ❑ All types of cancer
- ❑ I don't know

11. **Genetic panel testing is helpful tumour can for understanding *the risk of developing*:**

- ❑ No types of cancer
- ❑ Some types of cancer
- ❑ Most types of cancer
- ❑ All types of cancer
- ❑ I don't know

12. **Genetic panel testing is helpful for making decisions about *treatment for cancer*:**

- ❑ Never
- ❑ Rarely
- ❑ Sometimes
- ❑ Frequently
- ❑ Always
- ❑ I don't know

13. **Genetic panel testing is helpful for making decisions *about future cancer risks:***

- ❑ Never
- ❑ Rarely
- ❑ Sometimes
- ❑ Frequently
- ❑ Always
- ❑ I don't know

14. **The likelihood of finding a gene variant to guide treatment varies for different sorts of cancer.**

- ❑ Yes
- ❑ No
- ❑ I don't know

15. **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)
- ❑ Only available through a clinical trial (at no cost to the patient)
- ❑ Only available privately (at the patient's cost)
- ❑ I don't know

16. **From where have you learned most about genetic panel testing?**

- ❑ My oncologist
- ❑ The researchers of the MoST program
- ❑ School or university
- ❑ TV
- ❑ Online
- ❑ Other *(please specify)*

17. Please list any *benefits* you think genetic panel testing has:

_____

_____

_____

18. Please list any *drawbacks* you think genetic panel testing has:

_____

_____

_____

19. Considering your decision to have <u>genetic panel testing</u>, please indicate to what extent each statement is true for you AT THIS TIME.

	Strongly disagree	**Disagree**	**Neither agree or disagree**	**Agree**	**Strongly agree**
a. I am satisfied that I am adequately informed about the issues important to my decision	❑	❑	❑	❑	❑
b. The decision I made was the best decision possible for me personally	❑	❑	❑	❑	❑
c. I am satisfied that my decision was consistent with my personal values	❑	❑	❑	❑	❑

d. I expect to successfully carry out the decision I made	❑	❑	❑	❑	❑
e. I am satisfied that this was my decision to make	❑	❑	❑	❑	❑
f. I am satisfied with my decision	❑	❑	❑	❑	❑

20. The MoST Program is specifically trying to identify gene variants associated with cancer. The next few questions ask what sort of gene variants you would like to be informed about.

I would like to be informed about gene variants that:	**Yes**	**No**	**Maybe**	**Don't know**
a. Can guide treatment for my advanced cancer	❑	❑	❑	❑
b. Can NOT guide a treatment for my advanced cancer	❑	❑	❑	❑
c. No-one knows anything about	❑	❑	❑	❑
d. Provide information about my family members' risk of developing cancer	❑	❑	❑	❑

YOU ARE HALFWAY THROUGH THE QUESTIONNAIRE

This question asks how *confident* you are about having the genetic panel test of your tumour.

21. I am confident that I would be able to:

	Strongly disagree	**Disagree**	**Neither agree or disagree**	**Agree**	**Strongly agree**

a. Cope if I get a test result that leads to a new treatment	❑	❑	❑	❑	❑
b. Cope if I get a test result that does not lead to a new treatment	❑	❑	❑	❑	❑
c. Cope if a gene variant was found that no-one knew anything about	❑	❑	❑	❑	❑
d. Cope with telling other members of my family if an inherited gene variant was found	❑	❑	❑	❑	❑

The next questions ask about whether you would have genetic panel testing, and how much you would be prepared to pay, *depending on how likely finding information to guide your treatment is.*

As part of your participation in the MoST Program, you will be provided with genetic panel testing at no cost. However, we are interested to know whether people would consider having genetic panel testing if they had to pay for it, as part of routine care. For questions 22-24, please imagine you are being offered genetic panel testing by your doctor, where you would have to pay for it.

22. If genetic panel testing found a genetic variant to guide personalised treatment for cancer ***in about 1 in 100 people* (1%),** would you have the test?

❑ Yes
❑ No – go to question 23

What is the *most* money you would be prepared to pay for it, if this was your 'out of pocket' expense? (Remember, your actual test is at no cost due to your participation in this research).

Highest amount you would be prepared to pay

❑ $0
❑ $300
❑ $1,000
❑ $3,000
❑ $10,000

23. If genetic panel testing found a genetic variant to guide personalised treatment for cancer ***in about 20 in 100 people*** **(20%),** would you have the test?

❑ Yes
❑ No – go to question 24

What is the *most* money you would be prepared to pay for it, if this was your 'out of pocket' expense?

Highest amount you would be prepared to pay

❑ $0
❑ $300
❑ $1,000
❑ $3,000
❑ $10,000

24. If genetic panel testing found a genetic variant to guide personalised treatment for cancer ***in about 40 in 100 people*** **(40%),** would you have the test?

❑ Yes
❑ No – go to question 25

What is the *most* money you would be prepared to pay for it, if this was your 'out of pocket' expense?

Highest amount you would be prepared to pay

❑ $0
❑ $300
❑ $1,000
❑ $3,000
❑ $10,000

The next question asks about how you cope with uncertainty.

25. Please indicate how much you agree or disagree with each statement by ticking the response that best represents your views.

	Strongly disagree	**Disagree**	**Neither agree or disagree**	**Agree**	**Strongly agree**
a. I would rather receive my genetic panel test results, and be certain whether or not there is a tailored treatment for me, even if the result is bad news	❑	❑	❑	❑	❑
	Strongly disagree	**Disagree**	**Neither agree or disagree**	**Agree**	**Strongly agree**
b. I would like to know now whether or not there is a tailored treatment for me, so I can get used to the news	❑	❑	❑	❑	❑

c. If I didn't receive my genetic panel test results, I would always be wondering whether there was another treatment for my cancer	❑	❑	❑	❑	❑
d. The relief I would get from getting a result that would guide treatment is worth the risk that the result is bad	❑	❑	❑	❑	❑
e. I think it is tempting fate to ask questions about future illness	❑	❑	❑	❑	❑
f. I would rather live with uncertainty, than find out there was no more treatment for my cancer	❑	❑	❑	❑	❑
g. Knowing the result of my genetic panel testing would mean I felt more in control	❑	❑	❑	❑	❑

26. Below is a list of statements that other people with your illness have said are important. Please indicate your response as it applies to the <u>past 7 days</u>.

	Not at all	**A little bit**	**Somewhat**	**Quite a bit**	**Very much**
a. I feel peaceful	❑	❑	❑	❑	❑
b. I have a reason for living	❑	❑	❑	❑	❑
c. My life has been productive	❑	❑	❑	❑	❑
d. I have trouble feeling peace of mind	❑	❑	❑	❑	❑
e. I feel a sense of purpose in my life	❑	❑	❑	❑	❑

f. I am able to reach deep down into myself for comfort	❑	❑	❑	❑	❑
g. I feel a sense of harmony within myself	❑	❑	❑	❑	❑
h. My life lacks meaning and purpose	❑	❑	❑	❑	❑
i. I find comfort in my faith or spiritual beliefs	❑	❑	❑	❑	❑
j. I find strength in my faith or spiritual beliefs	❑	❑	❑	❑	❑
	Not at all	**A little bit**	**Somewhat**	**Quite a bit**	**Very much**
k. My illness has strengthened my faith or spiritual beliefs	❑	❑	❑	❑	❑
l. I know that whatever happens with my illness, things will be okay	❑	❑	❑	❑	❑

27. Most people with cancer are worried about their cancer progressing. The next few questions ask about how worried *you* are about your cancer progressing. For each question please tick the box for the answer that best reflects how you felt in THE PAST MONTH.

a. How often have you worried about your cancer progressing?

0	1	2	3	4	5	6	7	8	9	10

None of the time All of the time

b. To what extent does worry about your cancer progressing spill over or intrude on your thoughts and activities?

0	1	2	3	4	5	6	7	8	9	10

Not at all A great deal

c. How emotionally upset or distressed have you been about your cancer progressing?

0	1	2	3	4	5	6	7	8	9	10

Not at all A great deal

For the next question, think about yourself in comparison with someone with the same cancer as you.

d. What do you think your chances of your cancer progressing are? Please place a vertical mark on the line below, where *0% = I am certain that my cancer will NOT progress*; and *100% = I am certain that my cancer WILL progress*.

0% 50% 100%

No chance of 50-50 chance Will definitely progression of progression progress

THANK YOU FOR COMPLETING THE QUESTIONNAIRE