2021

Motivations and barriers to pursue cancer genomic testing: A systematic review

Megan Smith-Uffen

Nicci Bartley

Grace Davies

Megan Best

Follow this and additional works at: https://researchonline.nd.edu.au/ies_article

Part of the [Medicine and Health Sciences Commons](#)

This article was originally published as:

Smith-Uffen, M., Bartley, N., Davies, G., & Best, M. (2021). Motivations and barriers to pursue cancer genomic testing: A systematic review. *Patient Education and Counseling*, 104 (6), 1325-1334.

Original article available here:

[10.1016/j.pec.2020.12.024](https://doi.org/10.1016/j.pec.2020.12.024)

This article is posted on ResearchOnline@ND at . For more information, please contact researchonline@nd.edu.au.

©2021. This manuscript version is made available under the CC-BY-NC-ND 4.0 International license <http://creativecommons.org/licenses/by-nc-nd/4.0/>

This is the accepted manuscript version of an article published as:

Smith-Uffen, M., Bartley, N., Davies, G., & Best, M. (2021). Motivations and barriers to pursue cancer genomic testing: A systematic review. *Patient Education and Counseling*, 104(6) 1325-1334. <https://doi.org/10.1016/j.pec.2020.12.024>

This article has been published in its final form at:

<https://doi.org/10.1016/j.pec.2020.12.024>

Contents lists available at ScienceDirect

Patient Education and Counseling

journal homepage: www.elsevier.com/locate/pateducou

Review Article

Motivations and barriers to pursue cancer genomic testing: A systematic review

Megan Smith-Uffen^{a,*}, Nicci Bartley^b, Grace Davies^b, Megan Best^{a,b,c}

^a Faculty of Medicine and Health, University of Sydney, Sydney, Australia

^b Faculty of Science, School of Psychology, University of Sydney, Sydney, Australia

^c University of Notre Dame Australia, Sydney, Australia

ARTICLE INFO

Article history:

Received 2 August 2020

Received in revised form 21 November 2020

Accepted 23 December 2020

Keywords:

Motivation
Genome sequencing
Psychosocial
Risk perception
Systematic review
Decision making

ABSTRACT

Objectives: Single-gene testing is associated with psycho-social challenges for cancer patients. Genomic testing may amplify these. The aim of this study was to understand patients' motivations and barriers to pursue cancer genomic testing, to enable healthcare providers to support their patients throughout the testing process and interpretation of test results.

Methods: Five databases were searched for original peer reviewed research articles published between January 2001 and September 2018 addressing motivation for genomic cancer testing. QualSys was used to assess quality.

Results: 182 studies were identified and 17 were included for review. Studies were heterogeneous. Both somatic and germline testing were included, and 14 studies used hypothetical scenarios. 3249 participants were analyzed, aged 18 to 94. Most were female and white. The most common diagnoses were breast, ovarian, lung and colorectal cancer. Interest in testing was high. Motivations included ability to predict cancer risk, inform disease management, benefit families, and understand cancer. Barriers included concerns about cost, privacy/confidentiality, clinical utility, and psychological harm.

Conclusions: Despite concerns, consumers are interested in cancer genomic testing if it can provide actionable results for themselves and their families.

Practice Implications: Providers must manage understanding and expectations of testing and translate genetic information into health-promoting behaviours.

© 2020 Published by Elsevier B.V.

Contents

1. Introduction	00
2. Methods	00
2.1. Search strategy	00
2.2. Eligibility criteria	00
2.3. Screening	00
2.4. Quality assessment	00
2.5. Data extraction	00
2.6. Data analysis	00
3. Results	00
3.1. Study characteristics	00
3.2. Participant characteristics	00
3.3. Study quality	00
3.4. Key findings	00
3.4.1. Motivations	00

* Corresponding author at: University of Sydney, Faculty of Medicine and Health, School of Psychology, PoCoG, Level 6, Chris O'Brien Lifehouse, The University of Sydney, NSW, 2006, Australia.

E-mail address: mmsmi4314@uni.sydney.edu.au (M. Smith-Uffen).

3.4.2. Barriers	00
4. Discussion and conclusion	00
4.1. Discussion	00
4.2. Conclusion	00
4.3. Practice implications	00
Author contributions	00
Funding	00
Acknowledgements	00
References	00

1. Introduction

Rapid advances in DNA sequencing technology and our increasing understanding of cancer molecular biology are quickly moving us into an exciting new era of cancer medicine—cancer genomics [1]. Beginning relatively recently with the first identified somatic mutation in a human cancer gene in 1982, the *HRAS* gene in bladder carcinoma [2], single-gene cancer testing is now routinely used to identify at-risk individuals (e.g. *BRCA1/2* gene testing for breast cancer [3]) and tailor treatment to optimize care (e.g. *EGFR*, *ALK* and *ROS1* gene mutations for lung cancer [4]). Now, through somatic (tumour) and germline (blood) massive parallel genomic sequencing, we have an unprecedented amount of genetic information to inform, tailor, and optimize cancer prevention, diagnosis and treatment. Genomic sequencing involves examination of multiple genes. This may be a ‘panel’ of whole genes, single nucleotide polymorphisms (SNPs, genes with single mutations at specific positions in the sequence), the exome (all sequences which are eventually transcribed and translated into functional proteins), or the genome (all of the DNA in the organism). Testing is used in several ways, including assessing genes in the germline, which can be passed on to genetic relatives and therefore increase their cancer risk, or somatic changes within the subjects’ cancer, informing prognosis and guiding treatment choice. Some authors expect that genomic testing will become standard of care [5]. Further, patients are increasingly able to access direct-to-consumer genomic testing outside of a controlled clinical environment, such as through companies like 23andMe [6], increasing the technology’s reach.

Single-gene testing, particularly germline testing, has been associated with psycho-social challenges for patients [7–9]. Patients can find the idea of genetic ‘determinism’ associated with inherited mutations distressing [7], often struggle to align their perceived risk of disease occurrence with their actual risk [8] and, when faced with the uncertain clinical utility of somatic or germline test results, may be unsure if they want the test at all [10]. Genomics will likely amplify these issues, generating large amounts of data that may predict disease risks for which there are no available interventions, are of uncertain significance, or are related to diseases that participants were not initially considering [11,12]. Rather than relieving patients’ anxiety, the complexity of this data could actually increase uncertainty [13]. Awareness of patient motivations for seeking genomic testing can alert healthcare providers to their expectations, allowing them to manage expectations [7]. Furthermore, familial risk assessment for cancer is most informative when the index case has been tested. Identification of a pathogenic variant in an affected family member enables predictive testing of the known variant among family members.

Why would patients pursue cancer genomic testing in the face of these challenges and how can healthcare providers address patient expectations of these new testing platforms? While there is an existing body of research investigating motivation for single-gene testing [14,15], it is not well understood how this will translate to genomics. Therefore, we conducted this review with

the aim of assessing what is currently known about the motivations to pursue cancer genomic testing, both germline and somatic, among participants along the trajectory of cancer occurrence and recurrence risk (i.e. personal history of cancer, family history, neither).

2. Methods

2.1. Search strategy

We searched MEDLINE, Embase, PsycINFO, CINAHL and Scopus databases. The search used keywords and medical subject headings (Fig. 1) selected based on keyword lists of relevant papers. The search terms were grouped into four main concepts: psychology/psychiatry, motivation for testing, cancer, and genomic testing. We included the concept of ‘psychology/psychiatry’ to focus on themes of motivation and attitude, excluding technical guidelines for implementation and use of testing. We hand-searched the references of the studies included in the final review for relevant papers. This review was registered on PROSPERO (registration: CRD42019117714) prior to the conduct of the review. Ethics approval was not required.

2.2. Eligibility criteria

A list of eligibility criteria was developed to guide study selection (Table 1). Both qualitative and quantitative studies were included to comprehensively assess the limited research available. A study was considered eligible for inclusion if it was original research published between January 2001 and September 2018 and included information about motivations for participants to pursue genomic testing. We chose 2001 for the start of our study period to capture attitudes towards testing introduced after the completion of the sequencing of the human genome in 2003.

We defined genomic testing as any test panel that involved analysis of multiple genes. Testing of both germline and somatic cells were included. We limited our studies to adult participants, peer-reviewed journal articles in English. Grey literature was excluded due to its heterogeneity and lack of peer-review in the context of this already-heterogenous research space. We included studies with participants who had a personal history of cancer, a family history of cancer, or were members of the general population. Healthcare professionals, students, and researchers were excluded. We included studies that used hypothetical scenarios because these captured attitudes towards testing either not yet implemented or not yet fully understood.

2.3. Screening

One hundred eighty-two papers were identified and 6 were removed as duplicates. The remaining 176 had titles and abstracts reviewed by two authors (MSU and NB), eliminating 143 studies. The full text of the remaining 33 studies were reviewed in detail by both MSU and NB, excluding a further 16 studies (Fig. 2). Any disagreements were resolved through discussion.

Fig. 1. Literature search terms across the four search categories (grey boxes). Terms within each category were combined with “OR”, terms between each category were combined with “AND”. Bolded terms represent Medical Subject Headings, un-bolded represent key words. * This term was combined with “AND” with the other terms in its category.

2.4. Quality assessment

We used the systematic review tool “QualSyst” [16] quantitative and qualitative checklists to assess the quality of the papers included for data extraction. Seventeen percent of the studies (three of 17) were analyzed by both MSU and NB for both data extraction and quality assessment to ensure consistency between researchers.

2.5. Data extraction

Study design and methods, participant characteristics, and research findings were extracted by two authors (MSU and NB) from the included articles (Table 2). Given the broad definition of genomic testing, findings were initially compared within each testing technology (somatic, germline, and SNP testing). Differences between each testing technology were also assessed.

Table 1
Eligibility criteria.

Category	Eligibility criteria
Date of publication	01/01/2001 – 30/09/2018
Language of publication	English
Publication type	Original, peer reviewed research journal articles. Excluded: <ul style="list-style-type: none"> • Grey literature • Proceedings of conferences • Unpublished abstracts • PhD theses • Books • Professional guidelines • Non-original research (e.g. opinion pieces, commentaries, editorials, reviews)
Population	Human, adult participants (18 years or older). Includes participants with a personal history of cancer, family history of cancer, both, neither. Excluded: healthcare workers, researchers, students.
Topic	Motivation for genomic cancer testing, defined as any cancer genetic test investigating more than 1 gene. Includes both somatic and germ cell testing. Excluded: tests that analyzed only 1 gene.

Fig. 2. Study selection process.

2.6. Data analysis

Demographic data were tabulated and summarized. Descriptive statistics (frequencies, means, medians) were used to summarize the data. Meta-analysis was not possible due to the heterogeneity of the studies (in methodology, participants, tools and analyses). The results section of qualitative papers were analyzed by content analysis [17]. Extracted data was reviewed by all researchers and aggregated. Quantitative and qualitative findings were merged in the final analysis.

3. Results

3.1. Study characteristics

Seventeen studies were identified that met the inclusion criteria. Details of the included studies are found in Table 2. Studies were published between 2011 and 2017. All were cross-sectional, with two utilizing mixed methods [18,19]. Although all papers included for analysis met our definition of genomic testing, many labelled the testing as “genetic” and many used the two terms interchangeably. The purpose of the testing varied. Thirteen investigated testing for cancer risk of occurrence (e.g. hypothetical multiplex testing for risk of developing breast cancer, SNP testing for colorectal or prostate cancer), three to inform risk of recurrence (e.g. Oncotype Dx), and seven to guide therapy (e.g. tumour profiling). Five of these studies included a combination of the three. Only four studies specifically discussed germline testing, however nine described testing that could have the potential to reveal germline variants. Most (n = 14) used hypothetical genomic testing scenarios. Those that used non-hypothetical scenarios investigated Oncotype Dx and CYP2D6 testing for breast cancer recurrence risk and treatment response and SNP testing for

prostate cancer occurrence risk. Two studies analyzed participant views on direct-to-consumer testing. There was no significant difference in motivation found between the hypothetical and non-hypothetical scenarios, nor between the different types of tests investigated in these studies, and so detailed subgroup analyses are not presented here.

The studies also varied considerably in how they defined the term “motivation”, which was described by some as “attitudes towards”, “interest in”, and “perceived benefits and barriers of” testing. Motivation for testing was a primary focus of most of the studies, with only two including it as a secondary focus to participant preferences for modes of genomic information communication.

3.2. Participant characteristics

Across the 17 papers there were 3249 participants (sample sizes ranged from 23 to 829). Ages ranged from 18 to 94. Most were female and white. Ten studies reported on participants with a personal history of cancer, four with a family history, two with neither and one did not specify. The most common cancer diagnoses among the participants and their families were breast, ovarian, lung and colorectal. Four studies also included subgroups of healthcare workers, students and/or researchers. These subgroups were not included in the analysis.

3.3. Study quality

Overall, the quality of the studies was high (Table 2). Methodological weaknesses among the quantitative studies included inadequate controlling for confounding variables, poor definition of outcome measures and insufficient sample size. Insufficient descriptions of study participants and unclear study design were problem areas identified among qualitative studies.

Table 2

Characteristics, quality and outcomes of included studies.

Reference	Population	Female	Ethnicity	Study design*	Patient cancer history	Purpose (type) of test**	Outcomes	Quality
Anderson et al. 2014	n = 272 Mean = 51.2 (9.63) 30–74	64%	White: 100%	Quantitative – questionnaires (hypothetical)	Family history of cancer (CRC), no personal cancer history	Risk of CRC cancer occurrence (SNP)	Motivators: inform management. Associated with younger age, greater cancer-related fear/worry, female gender.	100%
Birmingham et al. 2013	n = 23 Mean = 57 (6.3) 45–70	0%	White: 74% African American: 13% Latino: 13%	Qualitative – focus groups, surveys	Family history of cancer (prostate), no personal cancer history	Risk of prostate cancer occurrence (SNP)	Motivators: inform management, cancer understanding. Barriers: clinical utility, false sense of security.	90%
Blanchette et al. 2014	n = 98 Median = 59 22–77	76%	Not reported	Quantitative – questionnaires (hypothetical)	Cancer diagnosis, current (CRC (26%), breast (25%), ovarian (16%), lung (7%), sarcoma (4%), endometrial (4%), other (18%))	Guide treatment (tumor profiling)	Motivators: inform cancer risk, management, cancer understanding, contribute to cancer research. Barriers: privacy/confidentiality, clinical utility, technical concerns, delay/distract from treatment.	85%
Defrank et al. 2013	n = 132 Mean received test = 57.5 (10.2) Mean did not receive test = 62.2 (11.1)	100%	White: 88% Other: 12%	Qualitative – questionnaires	Cancer diagnosis, current (breast (100%))	Risk of breast cancer recurrence, guide treatment (Oncotype Dx)	Motivators: inform management. Associated with younger age, lower perceived risk, greater sense of self-efficacy. Barriers: cost, clinical utility. Associated with advanced cancer stage.	90%
Flores et al. 2017	n = 149 Mean = 53 (9.4)	100%	White: 98%	Quantitative – questionnaires (hypothetical)	Family history of breast cancer, no personal cancer history	Risk of breast cancer occurrence (multiplex)	Motivators: inform prevention. Associated with greater cancer-related fear/worry, perceived risk.	100%
Graves et al. 2011	n = 105 Mean = 53.1 (12.8)	100%	White: 67.6% African American: 26.7% Other: 5.7%	Qualitative – interviews (hypothetical)	Family history of breast or ovarian cancer, no personal cancer history	Risk of breast cancer occurrence (SNP)	Motivators: inform cancer risk. Associated with greater cancer-related fear/worry, perceived risk. Barriers: cost.	100%
Gray et al. 2012	n = 69 Median = 59 32–86	71%	White: 58% Black: 42%	Qualitative – interviews (hypothetical)	Cancer diagnosis, current (lung (38%), CRC (27%), breast (35%))	Risk of cancer occurrence, recurrence, guide treatment, including germline testing	Motivators: inform cancer risk, inform management, benefit family, cancer understanding, contribute to cancer research. Barriers: cost, privacy/confidentiality, psychological impact.	90%
Leventhal et al. 2013	n = 24 Mean = 54.3 28–77	62%	White: 37% African American: 42% Other: 21%	Qualitative and quantitative – focus groups and surveys (hypothetical)	Cancer diagnosis, prior (20.8% total; breast (40%), carcinoid (20%), throat (20%), colon (20%))	Risk of CRC occurrence	Motivators: inform cancer risk, benefit family, contribute to cancer research, physician recommendation. Barriers: privacy/confidentiality, clinical utility, psychological impact.	90%
Meisel et al. 2013	n = 56 Mean = 44.9 (13.2)	84%	White: 66%	Qualitative – focus groups (hypothetical)	No cancer diagnosis, current (100%)	Risk of ovarian cancer occurrence	Motivators: inform management, benefit family. Barriers: psychological impact.	100%
Meisel et al. 2016	n = 829 Mean = 46 (15.5) 18–74	100%	White: 93%	Quantitative – questionnaires (hypothetical)	Not specified	Risk of ovarian cancer occurrence	Motivators: inform cancer risk, inform management. Barriers: associated with ethnic minorities.	95%
Miller et al. 2014	n = 29 Mean = 57 41–80	59%	Not reported	Qualitative – interviews (hypothetical)	Cancer diagnosis, current (breast (24%), CRC (14%), lung (7%), ovarian (14%), prostate (7%), other (34%))	Guide treatment (tumor profiling)	Motivators: inform management.	80%

Table 2 (Continued)

Reference	Population	Female	Ethnicity	Study design*	Patient cancer history	Purpose (type) of test**	Outcomes	Quality
Ngoi et al. 2013	n = 200 Median = 55 27–82	100%	Chinese: 78% Malay: 14% Indian: 6% Other: 3%	Quantitative – questionnaires	Cancer diagnosis, prior (100%)	Risk of breast cancer recurrence, guide treatment (Oncotype Dx and CYP2D6)	Motivators: inform cancer risk, inform management, cancer understanding. Associated with cancer-related fear/worry. Barriers: cost, privacy/confidentiality, clinical utility, lack of interest.	95%
Selkirk et al. 2014	n = 689 Mean = 53.3 18–94	90.9%	White: 81.4% Asian: 4.5% Multi-ethnic: 4.4% Hispanic: 3.9% African American: 3.1% Middle Eastern: 1.7% Unknown: 1%	Quantitative – clinical data (hypothetical)	Cancer diagnosis, prior (61.4% total; breast (100%))	Risk of cancer occurrence	Motivators: associated with older age, male gender. Barriers: cost, clinical utility, lack of interest, delay/distract from treatment.	82%
Smit et al. 2015	n = 34 Mean = 56 19–82	73%	Caucasian: 79% South Asian: 9% Middle Eastern: 3% Pacific Islander: 3% Other: 6%	Qualitative – focus groups (hypothetical)	No personal history of cancer (melanoma)	Risk of melanoma occurrence	Motivators: benefit family, cancer understanding. Associated with older age, female gender. Barriers: cost, privacy/confidentiality.	95%
Walsh et al. 2012	n = 27 Age note reported	59%	Asian/Pacific Islander: 15% African American: 15% Caucasian: 59% Latino/Hispanic: 7% Other: 11%	Qualitative – focus groups (hypothetical)	Cancer diagnosis, average risk CRC (45%), current diagnosis or high-risk CRC (19%)	Risk of CRC occurrence, including germline testing	Motivators: inform cancer risk, inform management, benefit family. Barriers: cost, psychological impact.	80%
Yushak et al. 2016	n = 413 Mean = 59 29–87	74%	White: 78% Other: 21%	Quantitative – questionnaires (hypothetical)	Cancer diagnosis, current or previous (breast (50%), GIT (19%), lung (31%))	Risk of cancer occurrence, including germline testing	Motivators: inform management, contribute to cancer research. Associated with identifying as white. Barriers: cost, privacy/confidentiality.	91%
Yusuf et al. 2015	n = 100 Mean = 55.3	100%	White: 71.4% Hispanic: 16.3% African American: 10.2% Asian: 2%	Quantitative – questionnaires (hypothetical)	Cancer diagnosis, previous (breast (100%))	Risk of cancer occurrence, guide treatment, including germline testing	Motivators: inform cancer risk, inform management, contribute to cancer research. Associated with identifying as white. Barriers: cost.	95%

*All studies were cross-sectional.

** Specific tests are listed if provided by the study.

SNP: Single nucleotide polymorphism.

CRC: Colorectal cancer.

3.4. Key findings

3.4.1. Motivations

Overall, interest in genomic testing was high although the decision to undergo testing was described as weighing barriers versus benefits. The four primary motivators for pursuing testing were: interest in the tests' ability to predict cancer occurrence [19–24] and recurrence risk [21,25], inform management decisions [18,21–31], benefit participants' families [19,21,26,28,32], and provide participants with a better understanding of their cancer [18,21,23,25,32]. These personal benefits from genomic testing were more important to participants than a desire to contribute more broadly to cancer research [21,23,24,31] or respond to physician recommendations to pursue testing [19].

3.4.1.1. Predict risk of cancer occurrence and recurrence. A strong motivator to pursue genomic testing was the tests' ability to

predict risk of occurrence or recurrence. Risk of occurrence was defined as the participant's risk of developing cancer in the first instance [19–24,26], and recurrence as the risk of developing cancer after treatment concluded and a period of time passed during which the cancer could not be detected [21,25,27]. Most of these studies included participants with a personal [19,21,23,24,26] or family [20] history of cancer (even if it wasn't the type of cancer investigated in the study). In one study in which 20% of participants had a prior history of cancer (breast, carcinoid, throat, colon), 75% wanted SNP testing if it would indicate any increased risk for colorectal cancer (CRC) occurrence [19]. Interest in testing increased as the level of occurrence risk conveyed by the test increased [20,22], for example, in one study, more participants were interested in a test that indicated a 75% increase in relative risk than a test indicating a 25% increase [20]. Participants reported that knowing their risk gave them both emotional reassurance about the future

[20] and could inform risk-reducing behaviours like life-style changes and screening uptake [19,22,26,30,33].

“I’d like to know. I’d like the knowledge so that I could prevent it, take early action, rather than just taking a chance. If there’s some way to find out if you have a specific gene, and you’re predisposed to a certain type of cancer, I think that knowledge is valuable.” [26] – participant at ‘high-risk’ of CRC occurrence (as determined by their oncologist).

Importantly, however, interest in prevention was not consistent across all studies, with some reporting less interest if testing required them to change their behaviour [20,30], or that, although they wanted the test results, they were unlikely to actually act on them [18]. Interestingly, the participants who reported this had no personal history of cancer [18,20,30].

“I wish it were true that when I received information that I would act on it in the way I ought to, but I don’t always. I mean, you get back your cholesterol results or whatever and they aren’t in nearly such a wonderful graphical form, but you still know, ‘Oh, I need to cut down on steaks,’ or whatever. But have I? I have a father who’s died of prostate cancer, but I’m still 30–40 pounds overweight. So is this going to change my behaviour? I wish I could say it would, but I don’t know that it’s going to.” [18] – first-degree relative of a patient with prostate cancer.

3.4.1.2. Inform treatment management. Participants were very interested in somatic genomic testing that could inform more effective therapy [18,21–31], including Oncotype DX testing [25,27]. This type of testing served as a source of hope that participants may have better treatment outcomes, prolonging or saving their life [21,29]. In a study of hypothetical tumour profiling across multiple cancer types, 70% of participants reported they would be interested in testing to guide their treatment choice, and 35% *only* wanted to receive results that would impact treatment decisions, to the exclusion of other information [23]. In one study, 61% were willing to undergo tumour profiling even if there was only a 1% chance that the information might improve their treatment options [31]. When offered testing for ovarian cancer, just having the test results on-file was viewed as supportive of receiving better and more targeted care, even if the participants didn’t want to know the results themselves [28].

“Look, it showed me that one possible option for treatment isn’t available. And, so, with that information I now know, ok, that’s not an option. I’ve ticked it off my list. So now I need to search elsewhere. And I think that’s an important piece of information. Whether it was positive or negative” [29] – participant with a solid malignancy, in which no mutation was reported that could guide treatment decisions.

3.4.1.3. Family benefit. Participants were interested in germline testing—testing that could inform them of inherited cancer susceptibilities that could be passed on to their children or screened for among family [19,21,26,28,32]. Four studies included in this review addressed the issue of germline testing directly [21,24,26,31], however the concept surfaced as a main motivator in three other studies, unprompted [19,28,32]. Interestingly, none of the studies reporting this motivation included participants with a family history of cancer, although this may simply be because few studies reported on participants with a family history at all.

Some described this as a responsibility to family [28], particularly if there was a family history of cancer [19], and participants reported that the knowledge gained from testing would motivate behaviour changes among their family [19,26] such as early detection, treatment and lifestyle changes [26].

“One of the main reasons why I’m looking into this is because whatever’s going to happen to me will happen to me. But, I’m really looking at how I can best advise my grandchildren to get early detection. I want my son to exercise more . . . to get himself checked out, to get a colonoscopy regularly.” [19] – participant regarding SNP testing for CRC occurrence risk.

3.4.1.4. Cancer understanding. Some participants wanted testing that could give them a better understanding of cancer in general, even if it didn’t lead to actionable results like risk calculation or treatment choice [18,21,23,25,32]. Participants already diagnosed with cancer believed that testing could facilitate a better understanding of their condition [23,25], such as its cause [21].

Some were interested simply to satisfy their curiosity [18,21], or because they believed that this understanding would be empowering – ‘knowledge is power’ [32] – participant regarding lifetime risk of melanoma occurrence.

“I’d like to know if that’s where I’m headed. Maybe there’s nothing I could do about it—that doesn’t matter. I think there’s a benefit to knowing as much as you can about yourself.” [19] – participant regarding SNP testing for CRC occurrence risk.

3.4.1.5. Variables associated with motivation. High cancer-related fear or worry [19,20,25,30,33], a strong sense of self-efficacy to cope with and act on results (among cancer survivors pursuing tumour profiling for recurrence and treatment response) [27], and identifying as white [22,24,31] were associated with increased interest in genomic testing. Only three studies directly assessed interest with perceived risk of cancer occurrence, two of which reported that interest was associated with greater perceived risk [20,33] and one reported the opposite [27]. Overall interest in testing did not differ across studies regardless of whether participants had a personal history, family history, or no history of cancer. While some studies reported that age was inversely associated with interest to test (younger participants were more interested) [27,30], some reported the opposite [32,34]. In two studies, females were more interested in testing [30,32], while one reported that males were [34].

3.4.2. Barriers

Identified barriers to testing included concerns about: costs [20,21,24–27,31,32,34]; privacy/confidentiality of results [19,21,23,25,31,32]; clinical utility [18–20,23,25,27,34]; and psychological harm [19,21,26,28].

3.4.2.1. Cost. Cost was a commonly identified barrier, with participants concerned about low insurance coverage and high out-of-pocket costs [20,21,24–27,31,32,34], particularly in studies conducted in the United States [20,21,24,26,27,31,34].

Participants became less interested as testing became more expensive [20]. Only two studies assigned exact dollar amounts to tests and in both cases many participants reversed their initial interest if they had to pay out-of-pocket. In one study of a test indicating a 25% increased risk of developing cancer [20], 87.7% of participants were interested in a free test, while only 64.8% were interested if the out-of-pocket expense was 150USD, and only 20% if it cost 1500USD. In another study, 84% of participants who initially agreed to Oncotype Dx reversed their decisions because of cost (which ranged from 350–3500USD) [25]. Importantly though, participants were less concerned with cost if the test promised greater clinical utility (e.g. in informing cancer risk of occurrence) [20].

“If you’re talking about a significant investment of money and you’re looking at it’s only going to make it change a little bit on

this graph, do I really care?" [19] – participant regarding SNP testing for CRC occurrence risk.

3.4.2.2. Privacy and confidentiality. Concerns about the privacy and confidentiality of the test results were common, particularly regarding discrimination from health and life insurance companies for those identified to be at increased risk of developing disease [19,21,23,25,31,32].

"What are the implications of this? If you know this and you got an increased risk and it goes into your medical history, life insurance companies take those medical histories into account when they're coming up with plans. Does that impact what your rate is going to be?" [19] – participant regarding SNP testing for CRC occurrence risk.

3.4.2.3. Clinical utility. Some participants questioned whether their results would be useful to inform clinical decision-making, particularly if testing identified variants of unknown significance or indicated only slight increases in cancer risk [18,19,23,25,27,34].

"Being told that you are high risk and all we are going to do is do a blood test every three months but there's no advice we can give you about changing your lifestyle, I think that's downright cruel." [28] – participant without a current cancer diagnosis, regarding ovarian cancer occurrence risk.

Some were concerned that testing wouldn't provide any more useful information than a detailed family history [18].

"If you already know that, because of your family history, you have an elevated risk of getting prostate cancer, what more is this going to tell you other than what you already know?" [18] – first-degree relative of a patient with prostate cancer.

Some worried that testing was too new and that the limitations of science would reduce the value of results, but would be interested in the future, once more information about implementing test results became available [34].

3.4.2.4. Psychological impact. Participants were also concerned that knowledge of their results would cause them psychological distress, particularly given the uncertainty of interpretation of the findings [19,21,26,28]. Most of these studies included participants with a past or current history of cancer [19,21,26] and in one study, concern about psychological impact was higher specifically among cancer survivors [26]. Concern was also highest among those who had not undergone somatic testing previously [21].

"Sometimes being ignorant and blind is better than going out there and worrying yourself to death because I have 2.5 times the risk of somebody else getting it." [18] – first-degree relative of a patient with prostate cancer.

Advanced cancer stage [27], and identifying as an ethnic minority [22] were associated with greater perceived barriers to testing.

4. Discussion and conclusion

4.1. Discussion

We found that interest in cancer genomic testing was high overall, with motivations largely outweighing barriers. Key motivations for pursuing testing were the tests' ability to predict cancer occurrence and recurrence risk, inform management decisions, benefit participants' families through germline testing, and provide a better understanding of a patients' cancer. Key barriers included concerns about cost, privacy/confidentiality, clinical utility, and psychological harm.

Underlying many motivations was a strong interest in the clinical applicability of test results. In fact, some participants only wanted to receive genomic information that could influence therapeutic decisions, to the exclusion of other information. This aligns with single-gene research that shows that patients are highly motivated to get testing if it will influence their treatment decisions [7,35,36].

Interestingly, however, two of our studies found that, although participants valued a test's clinical utility, they were less interested if the result required them to change their behaviour to reduce their risk of developing disease [20,30]. Influencing behaviour based on genetic test results is a well-documented challenge for healthcare professionals [37,38], with several studies finding that communicating genetic risk does not actually change behavioural outcomes like smoking cessation, diet, or physical activity [37,39]. While the studies in our review did not directly investigate why participants were unwilling to adopt risk-reducing behaviours, it is interesting to note that unwilling participants also reported no personal history of cancer. It has been shown that a personal experience of disease [40] and a high fear of its recurrence [41] are strong motivators for adopting behavioural change to reduce disease risk, and it is possible that the opposite is true of the participants reported on here. Given their lack of personal cancer experience, our participants may have had a lower perceived risk of developing cancer, not recognizing the gravity of a cancer diagnosis and the importance of prevention efforts.

It is difficult to help patients align their perceived disease risk with their actual risk. Single-gene research has shown that even once patients receive genetic results, their perceived risk of developing cancer can be very hard to shift, with patients often focusing on an intuitive understanding of their risk (e.g. from their experience coming from a high-risk family), instead of objective risk information [7,42]. In our review, most of the participants with a strong interest in testing also reported a personal or family history of cancer [19–21,23–26], potentially indicating they had a greater perceived or intuitive understanding of their risk, increasing their motivation to test. Three studies specifically assessed the impact of perceived cancer risk on motivation to test, two of which reported that motivation was higher among those with higher perceived risk [20,33]. However, it should be noted that these were hypothetical studies with low proportions of participants with a personal or family history of cancer. They were also contrasted by another study which reported motivation to test was actually lowest among those at highest perceived risk of cancer recurrence [27]. In this study, patients with advanced cancer stage and nodal involvement were slightly less likely to pursue testing that would predict likelihood of cancer recurrence risk and treatment benefit. This may indicate that these high-risk patients were uncomfortable relying on the results of genomic testing to decide whether they would pursue treatment, opting instead to receive treatment regardless of test results. Unfortunately, none of the studies directly compared perceived risk with actual risk or directly investigated why these impacted motivation to test. Clearly, more research is needed in this space.

Cost is a well-recognized barrier to single-gene genetic testing [43,44] and was a common concern in the studies analyzed here. While some tests do remain expensive, for example Oncotype Dx is currently ~5000AUD [45], costs are trending down over time [46]. For example, 23andMe's Health and Ancestry Test is now only 199USD and has been approved to assess risk for 10 conditions in the USA including Parkinson's, Alzheimer's, and Celiac Disease [47]. The cost barrier may be reduced as technology improves in the future.

Concerns about insurance discrimination were also common. Interestingly, the studies that reported this as a barrier were conducted in countries that currently have prohibitions on genetic discrimination. The studies conducted in Canada and Singapore

were published before these countries introduced their respective prohibitions on genetic discrimination [48,49], so it is understandable that participants may have seen this as a barrier. However, most of the studies that reported this barrier were conducted in the USA, in which a Genetic Information Nondiscrimination Act [50] prohibits health and life insurance companies from using genetic information to influence premium or policy decisions. Most of these USA-based studies were published after the act came into effect in 2008, indicating that participants may be unaware of current legislation. It should also be noted that in Australia (the location of our research team and one of the studies included for analysis [32], which interestingly did not report privacy/confidentiality as a barrier), patients are required to disclose results of all genetic tests they've received to private mutually-rated insurance providers, and this information can be used to alter insurance premiums and policies [51]. It could therefore be expected that patients in Australia would view this as a barrier to genomic testing uptake, although there is no such data at this time to support this. Regardless, there is a clear need for counselors and healthcare workers to understand local legislature and inform patients of their rights to genetic information privacy prior to testing.

Concern about psychological impact is an important barrier for those considering testing. Single-gene research has shown that although most mutation carriers cope well, some report increased levels of anxiety and cancer-related worry after receiving their results [7–9]. In this review, test-related distress and psychological harm were commonly reported concerns [19,21,26,28], however one study measuring willingness to undergo testing reported that several participants' concerns were associated with germline, rather than somatic, testing [12]. Patients may misattribute some of the benefits and costs related to germline testing to somatic testing because there has been a longer public discourse related to germline testing and the term 'genetic testing' may raise family-related concerns through implicit associations. Given the low number of studies focusing on somatic testing included in this review, the relationship between lower health literacy and greater psychological concerns remains unclear. Irrespective, it is crucial that genetic counselors and health professionals explicitly inform patients about the implications of the test that they are consenting to.

Many participants reported limited knowledge about genomics and its potential role in determining and reducing cancer risk and optimizing treatment [18,20,28], emphasizing the need to ensure the decision to pursue testing is well-informed. This is an area of importance that has already been identified among genetic counseling groups anticipating the era of genomic counseling [52].

Ethnic minority groups were associated with greater perceived barriers to testing. This may reflect lower levels understanding of genomic testing and its implications, and/or lower self-efficacy to act on results [53]. However, the studies included in this review were largely comprised of white female participants, and ethnic subgroups were too small to draw any significant conclusions from the analyses. This highlights the importance of investigating attitudes towards genomic testing in patients from ethnic minority subgroups in future research.

Concerns about costs, confidentiality and the psychological impact of test results are major concerns to address when patients are considering testing. However, some of these barriers appear resolvable, as the cost of testing decreases, policies protecting patients from insurance discrimination are developed and communicated, and patient education and awareness of testing indications and implications improves.

Strengths of this paper include a thorough literature search that generated high-quality studies. Limitations include a relatively small number of relevant studies and a high level of heterogeneity

which made it difficult to compare directly between the studies. As well, many of the studies included in this review used hypothetical scenarios to assess motivations to test, which may not reflect real-life use of testing. For example, in a study of patients at risk of Huntington's Disease, 80% reported that they would pursue single-gene genetic testing, however when the test became available only 20% actually did [54]. It is unclear how the reported motivations described in the hypothetical studies included here would translate to actual testing uptake.

4.2. Conclusion

We found a high level of interest in cancer genomic testing with primary motivators to test similar to those for single-gene testing, which included interest in predicting cancer risk, informing management decisions, benefitting patients' families, and providing a better understanding of cancer. Barriers identified were concerns about cost, privacy/confidentiality, clinical utility, and psychological harm.

4.3. Practice implications

As genomic testing takes on a larger role in cancer care, providers will be challenged to educate patients and their families about the usefulness of testing and its role in determining risk and optimizing treatment; manage expectations about the utility of results; align perceived with actual cancer risk; counsel regarding testing's potential clinical, psychological, confidentiality and financial consequences; and translate test results into health-promoting behaviours. Future research should focus on better understanding the role of perceived cancer risk in motivation to pursue testing, as well as how healthcare professionals can motivate those at high actual risk to be tested, act on results and communicate with family members.

Author contributions

MSU, NB, and MB made substantial contributions to the conception and design of this work, drafting and revising the work critically for important intellectual content, and final approval of the version to be published. GD contributed meaningfully to the drafting and revising of this manuscript. All authors read and approved the final manuscript.

Funding

This research was supported by the National Health and Medical Research Council (NHMRC) of Australia (1124749), and Cancer Institute of NSW (Post-Doctoral Research Fellowship for Megan Best). Neither funder had any role in the design of the study, data collection, analysis, interpretation of data, or writing of the manuscript.

Acknowledgements

The authors acknowledge the University of Sydney and the NHMRC for their support of this work.

References

- [1] S. Jackson, J. Chester, Personalised cancer medicine, *Int. J. Cancer* 137 (2) (2015) 262–266.
- [2] E. Reddy, et al., A point mutation is responsible for the acquisition of transforming properties by the T24 human bladder carcinoma oncogene, *Nature* 300 (1982) 149–152.
- [3] Anglican Breast Cancer Study Group, Prevalence and penetrance of BRCA1 and BRCA2 mutations in a population-based series of breast cancer cases, *Br. J. Cancer* 83 (10) (2000) 1301–1308.

- [4] Cancer Council Australia Lung Cancer Guidelines Working Party, Clinical Practice Guidelines for the Treatment of Lung Cancer. (2017). Available from: https://wiki.cancer.org.au/australia/Guidelines:Lung_cancer/Treatment/Non_small-cell/Summary_of_recommendations.
- [5] M. Robson, et al., American Society of Clinical Oncology policy statement update: genetic and genomic testing for cancer susceptibility, *J. Clin. Oncol.* 33 (2015) 3660–3667.
- [6] 23 andMe Inc. 23andMe. 2019 [cited 2019; Available from: <https://www.23andme.com/en-int/>].
- [7] J. Heshka, et al., A systematic review of perceived risks, psychological and behavioral impacts of genetic testing, *Genet. Med.* 10 (1) (2008) 19–32.
- [8] M. Dieng, et al., Improving subjective perception of personal cancer risk: systematic review and meta-analysis of educational interventions for people with cancer or at high risk of cancer, *Psychooncology* 23 (6) (2014) 613–625.
- [9] C. Lerman, et al., Effects of individualized breast cancer risk counseling: a randomized trial, *J. Natl. Cancer Inst.* 87 (4) (1995) 286–292.
- [10] L. Keogh, et al., Choosing not to undergo predictive genetic testing for hereditary colorectal cancer syndromes: expanding our understanding of decliners and declining, *J. Behav. Med.* 40 (4) (2018) 583–594.
- [11] H. LaDuca, et al., Utilization of multigene panels in hereditary cancer predisposition testing: analysis of more than 2,000 patients, *Genet. Med.* 16 (11) (2014) 830–837.
- [12] J. Gagan, E. Van Allen, Next-generation sequencing to guide cancer therapy, *Genome Med.* 7 (1) (2015) 80.
- [13] P. Han, et al., A taxonomy of medical uncertainties in clinical genome sequencing, *Genet. Med.* 19 (8) (2017) 918–925.
- [14] M. Esplen, et al., Motivations and psychosocial impact of genetic testing for HNPCC, *Am. J. Med. Genet.* 103 (1) (2001) 9–15.
- [15] J. Balmaña, et al., Comparison of motivations and concerns for genetic testing in hereditary colorectal and breast cancer syndromes, *J. Med. Genet.* 41 (2004) 344.
- [16] L. Kmet, R. Lee, L. Cook, Standard Quality Assessment Criteria for Evaluating Primary Research Papers From a Variety of Fields, Alberta Heritage Foundation for Medical Research., 2004.
- [17] H. Hsieh, S. Shannon, Three approaches to qualitative content analysis, *Qual. Health Res.* 15 (9) (2005) 1277–1288.
- [18] W. Birmingham, et al., Patient and provider attitudes toward genomic testing for prostate cancer susceptibility: a mixed method study, *BMC Health Serv. Res.* (13) (2013) 279.
- [19] K. Leventhal, et al., “Is it really worth it to get tested?”: primary care patients’ impressions of predictive SNP testing for colon cancer, *J. Genet. Couns.* 22 (2013) 138–151.
- [20] K. Graves, et al., Interest in genetic testing for modest changes in breast cancer risk: implications for SNP testing, *Public Health Genomics* 14 (2011) 178–189.
- [21] S. Gray, et al., Attitudes of patients with cancer about personalized medicine and somatic genetic testing, *J. Oncol. Pract.* 8 (6) (2012) 329–335.
- [22] S. Meisel, et al., Genetic testing and personalized ovarian cancer screening: a survey of public attitudes, *BMC Womens Health* 16 (2016) 46–53.
- [23] P. Blanchette, et al., Genomic testing in cancer: patient knowledge, attitudes, and expectations, *Cancer* 120 (19) (2014) 3066–3073.
- [24] R. Yusuf, et al., Attitudes toward molecular testing for personalized cancer therapy, *Cancer* (121) (2015) 243–250.
- [25] N. Ngoi, et al., Interest and attitudes of patients, cancer physicians, medical students and cancer researchers towards a spectrum of genetic tests relevant to breast cancer patients, *Breast* 22 (2013) 47–52.
- [26] J. Walsh, et al., Preferences for genetic testing to identify hereditary colorectal cancer: perspectives of high-risk patients, community members, and clinicians, *J. Cancer Educ.* 27 (2012) 112–119.
- [27] J. DeFrank, et al., Who gets genomic testing for breast cancer recurrence risk? *Public Health Genomics* 16 (5) (2013) 215–222.
- [28] S. Meisel, et al., Population-based, risk-stratified genetic testing for ovarian cancer risk: a focus group study, *Public Health Genomics* 16 (2013) 184–191.
- [29] F. Miller, et al., Testing personalized medicine: patient and physician expectations of next-generation genomic sequencing in late-stage cancer care, *Eur. J. Hum. Genet.* 22 (3) (2014) 391–395.
- [30] A. Anderson, et al., Interest and informational preferences regarding genomic testing for modest increases in colorectal cancer risk, *Public Health Genomics* 17 (2014) 48–60.
- [31] M. Yushak, et al., Patient preferences regarding incidental genomic findings discovered during tumor profiling, *Cancer* (2016) 1588–1597.
- [32] A. Smit, et al., Exploring the potential emotional and behavioural impact of providing personalised genomic risk information to the public: a focus group study, *Public Health Genomics* 18 (5) (2015) 309–317.
- [33] K. Flores, et al., Factors associated with interest in gene-panel testing and risk communication preferences in women from BRCA1/2 negative families, *J. Genet. Couns.* 26 (3) (2017) 480–490.
- [34] C. Selkirk, et al., Cancer genetic testing panels for inherited cancer susceptibility: the clinical experience of a large adult genetics practice, *Fam. Cancer* 13 (2014) 527–536.
- [35] A. Kinney, et al., The impact of receiving genetic test results on general and cancer-specific psychologic distress among members of an African-American kindred with BRCA1 mutation, *Cancer* 104 (2005) 2508–2516.
- [36] K. Metcalfe, et al., The use of preventive measures among healthy women who carry a BRCA1 or BRCA2 mutation, *Fam. Cancer* 4 (2005) 97–103.
- [37] C. Bloss, N. Schork, E. Topol, Effect of direct-to-consumer genomewide profiling to assess disease risk, *N. Engl. J. Med.* 364 (6) (2011) 524–534.
- [38] T. Marteau, et al., Effects of communicating DNA-based disease risk estimates on risk-reducing behaviours, *Cochrane Database Syst. Rev.* 6 (10) (2010), doi: <http://dx.doi.org/10.1002/14651858.CD007275.pub2>.
- [39] G. Hollands, et al., The impact of communicating genetic risks of disease on risk-reducing health behaviour: systematic review with meta-analysis, *Br. Med. J.* 352 (2016) i1102.
- [40] L. Diseati, et al., Common genetic risk for melanoma encourages preventive behavior change, *J. Pers. Med.* 5 (2015) 36–49.
- [41] N. Hawkins, et al., Health-related behavior change after cancer: results of the American Cancer society’s Studies of Cancer survivors (SCS), *J. Cancer Surviv.* 4 (1) (2010) 20–32.
- [42] L. Heiniger, et al., Intuition versus cognition: a qualitative exploration of how women understand and manage their increased breast cancer risk, *J. Behav. Med.* 38 (2015) 727–739.
- [43] L. Cherkas, et al., A survey of UK public interest in internet-based personal genome testing, *PLoS ONE [Electronic Resource]* 5 (10) (2010) e13473.
- [44] A. Kinney, et al., Knowledge, attitudes, and interest in breast-ovarian cancer gene testing: a survey of a large African-American kindred with a BRCA1 mutation, *Preventative Medicine* 33 (6) (2001) 543–551.
- [45] Breast Cancer Network Australia, No Medicare Rebate for Oncotype DX Test, (2017) [cited 2019; Available from: <https://www.bcna.org.au/news/2017/10/no-medicare-rebate-for-oncotype-dx-test/>].
- [46] National Human Genome Research Institute, The Cost of Sequencing a Human Genome, (2019) 16/7/2019].
- [47] J. Boddy, FDA Approves Marketing of Consumer Genetic Tests for Some Conditions, (2017) [cited 2019].
- [48] Bill S-201: Statutes of Canada, Chapter 3: An act to prohibit and prevent genetic discrimination, 64-65-66 Elizabeth II, S.o. Canada, Editor. 2017, Parliament of Canada, (2017).
- [49] D. Vukcevic, J. Chen, Advances in Genetics and Their Impact on Life Insurance, Institute of Actuaries of Australia: Financial Services Forum, 2018.
- [50] Genetic Information Nondiscrimination Act of 2008., in Public Law 110–233, 122 STAT. 881., T.S.a.H.o.R.o.t.U.S.o. America., Editor, (2008) 110th Congress.
- [51] A. Newson, et al., Genetics and insurance in Australia: concerns around a self-regulated industry, *Public Health Genomics* 20 (2017) 247–256.
- [52] A. Sturm, K. Manickam, Direct-to-consumer personal genomic testing: a case study and practical recommendations for “genomic counseling”, *J. Genet. Couns.* 21 (3) (2012) 402–412.
- [53] A. Walker, et al., Results communication and patient education after screening for possible hemochromatosis and iron overload: experience from the HEIRS Study of a large ethnically and linguistically diverse group, *Genet. Med.* (9) (2007) 778–791.
- [54] B. Meiser, S. Dunn, Psychological impact of genetic testing for Huntington’s disease: an update of the literature, *J. Neurol. Neurosurg. Psychiatr.* 69 (2000) 574–578.