What Do Patients With Cancer Know, or Want to Know, About Genomic Tumor Sequencing and Genetic Testing? A State-of-the-Art Review

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Authors' disclosures of conflicts of interest are found at the end of this article.

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https://doi.org/10.6004/jadpro.2024.15.8.14

Abstract

Molecular profiling (MP), which involves testing tissue, blood, or other body fluids to identify biomarkers, has become increasingly important in cancer treatment. Genomic tumor sequencing, a specific type of MP, is commonly used to identify specific gene variants or proteins that can be targeted for treatment. Germline testing is also routinely recommended for certain cancers. Low levels of genomic literacy among cancer patients, coupled with increasingly complex test results, challenge clinicians to communicate results and provide appropriate education. In addition, patients may have varying preferences for the level of information they desire and are able to process. This state-of-the-art review explores cancer patients' expectations, attitudes, knowledge, satisfaction, and concerns as they undergo molecular profiling. A search was conducted through four databases to identify studies from 2016 to 2022 to explore cancer patients' knowledge and preferences regarding genomic testing. Nineteen studies met the inclusion criteria. Most studies revealed that people with cancer have low levels of knowledge regarding MP, albeit with significant variability. Patients primarily desired MP to identify new treatment options and increase survival. While patients relied on their providers to interpret test results, they wanted to be informed of all results, mainly if those results might guide treatment decisions or future care planning. Most patients, especially those with low genomic/genetic knowledge, tended to overestimate the personal benefits of MP. Further study is needed to provide tailored education to fulfill patients' information needs.

When a patient would present with advanced breast cancer in 1997, the pathology report would most likely have reported histology and hormone receptor information but would have lacked genetic test results such as *BRCA* variants or *HER2* expression that are commonplace today. Cancer diagnostics have evolved so tremendously that patients today are likely to have next-generation sequencing (NGS) of the tumor and possibly whole-exome sequencing of germline DNA. Molecular profiling (MP) refers to the testing of tissue, blood, or other body fluids to identify biomarkers, including specific gene variants or proteins of interest (Best et al., 2019). Tumor genomic sequencing findings may inform prognosis, predict treatment response, and sometimes identify appropriate matches for targeted therapies. Considering that therapies tailored to a molecular target are usually significantly more effective than other treatments, particular findings can be life-changing for some patients. In a small number of patients, tumor sequencing may also identify germline variants, with implications for patients and their families (Raymond et al., 2016). Germline testing is also routinely recommended for patients with certain cancers, for example in pancreatic cancer.

Genomic testing of tumors (a particular kind of MP) increased after the first US Food and Drug Administration (FDA) approvals of multigene NGS assays (FoundationOne CDx and the MSK-IMPACT) in 2017 (Colomer et al., 2020). This increase in testing was especially pronounced outside of academic settings (Colomer et al., 2020). Lower laboratory costs and improved understanding and identification of gene variants have further stoked demand for MP. An expanding list of tumor sequencing modalities ranges from single-gene assays and targeted panels to whole-exome and even whole-genome sequencing (Raymond et al., 2016). Increasingly, data generated from these tests may offer some patients additional treatment options as more and more genomic alterations are matched to precise treatment options (Roberts et al., 2019). Interestingly, these matched treatment options may include tumor-agnostic situations, such as using entrectinib (Rozlytrek) for solid tumors harboring an *NTRK* fusion. Specimen acquisition and sources have changed as well, with circulating tumor DNA and RNA (ctDNA, ctRNA) or "liquid biopsy" becoming routine in oncology practice and part of the standard of care for some cancers (Cavallo, 2021). Liquid biopsies offer a quicker, less invasive way to analyze some solid tumors using ctDNA shed into the blood (Cavallo, 2021).

The complexities of cancer diagnostics and treatment have become a challenge for some people with cancer to understand. Studies have shown that many patients with cancer do not comprehend even basic MP results (Adams et al., 2020; Blee et al., 2021; Solomon et al., 2020). In addition, poor genetic literacy has been associated with falsely elevated expectations of benefit. Clinicians also worry that many participants lack an understanding of germline findings and the potential implications for their relatives (Best et al., 2020).

As MP becomes more ubiquitous, patient understanding of the implications of test results will be essential, particularly since knowledge may influence treatment choices. For example, Yanes and colleagues (2019) found that patients who had MP of their tumors and knew their results were more likely to receive targeted therapy. Similarly, Freedman and colleagues (2015) noted that "improved general knowledge as well as improved understanding of one's tumor characteristics and the reasons for personalized treatment recommendations may improve adherence and, ultimately, outcomes" (p. 6, Freedman et al., 2015) When choosing treatment options, patient knowledge has been linked to decision-making satisfaction (Holmes-Rovner et al., 1996). The discovery of actionable variants in the germline may also give people with cancer options for treatment, for example, poly(ADP-ribose) polymerase (PARP) inhibition in patients who harbor pathologic *BRCA* variants. In addition, family members without cancer who also harbor germline variants may be able to take action to mitigate risk. For example, some women opt to have prophylactic mastectomies or oophorectomies in the setting of a germline *BRCA* finding. In this instance, informed decision-making may be critical to avoiding decisional regret (Bombard et al., 2014; Hoffman et al., 2017).

Recent literature reviews suggest patients have positive attitudes toward NGS despite having low

knowledge levels (Shirdarreh et al., 2021; Wolyniec et al., 2020). The complexity and importance of MP have created an unmet need for improved patient understanding of the implications of MP results, which is imperative for informed decision-making in cancer treatment. This state-of-the-art review explores the expectations, knowledge, and experiences of patients with cancer as they undergo molecular tumor profiling.

METHODS

A literature search was performed in October 2022, with search criteria formatted by an experienced health science librarian. A six-step approach for a state-of-the-art literature review was adapted from Barry and colleagues (2022). The search included years between 2016 and 2022 to capture the period after the FDA approved MP. The search was executed in Cumulative Index to Nursing and Allied Health Literature (CINAHL) full text, Medical Literature Analysis and Retrieval System Online (MEDLINE), Academic Search Complete, and Web of Science. Medical Subject Heading (MeSH) subject headings used in CINAHL, MEDLINE, and Academic Search Complete included "cancer patients," "knowledge or opinion or attitude or perception or awareness," and associated keywords "tumor profiling or genetic profiling or genomic profiling or liquid biopsy or circulating tumor DNA or personalized." Word variations were also searched. The search was limited to peer-reviewed articles published in English. Exclusion criteria included literature reviews, conference abstracts, non-English articles, pediatrics articles, and studies on the risk of developing malignancies. Publications based on theoretical scenarios were also excluded. The first author reviewed the journals for inclusion and exclusion.

This search yielded 229 publications from the CINAHL full text, MEDLINE, and Academic Search Complete databases, culled to 22 after reviewing titles and applying exclusion criteria. The same search strategy was used in Web of Science and yielded 287 publications, which were reduced to 19 after title reviews. Results were merged and duplicates removed, resulting in 33 articles. The abstracts of those 33 articles were reviewed, and eight more were excluded. An additional eight publications were excluded after a full manuscript review as they were related to hypothetical situations. Two other studies were identified from reference lists of eligible articles. In all, 19 publications met the inclusion criteria.

RESULTS

This review synthesizes information from the 19 included studies of patients undergoing tumor molecular profiling. Findings are described as related to patients' knowledge, attitudes, expectations, and concerns about test results and testing satisfaction (Table 1).

Knowledge

According to the articles reviewed in this paper, patients' knowledge of MP varies widely. Four studies measured self-perceived knowledge with contrasting results. In two studies, patients reported high levels of knowledge. In a German study, Pichler and colleagues (2021) found that, on average, a heterogeneous group of patients believed they had a high level of genomic knowledge. Adams and colleagues (2020) also reported a high level of "self-appraised ability and understanding" and questioned if this was inflated. In the other two studies, patients admitted they had limited knowledge but did not feel it hindered them from participating in MP and understanding the results (Best et al., 2019; Liang et al., 2017). Several studies noted that patients were aware of their lack of understanding. Still, they proceeded with testing, noting that discovering potential treatment options was more important than knowing the science behind it. Liang and colleagues (2017) found similar sentiments, with one patient commenting, "I'm probably more interested in getting the results and the solutions as opposed to 'Why is it so?'" (p. 7). This knowledge deficit was counterbalanced by confidence in the science and in clinicians. While they acknowledged their knowledge deficit, some patients still incorrectly understood the test results and their implications (Best et al., 2019).

Objective knowledge was measured in nearly half of the studies, with different outcomes observed across different patient populations. Researchers used a range of instruments and methods to measure knowledge, including interviews and instruments with varying levels of

Table 1. Evidence Summary

Study	Dimensions measured	Sample size and population	Methodology	Survey or instrument	Main findings
Adams et al. (2020)	Assessment of patient psychological factors, perceptions, and comprehension of tumor genomic testing.	58 patients with metastatic breast cancer at a single institution.	Questionnaires pre- and post-tumor genomic testing.	Epidemiologic Studies Depression Scale (CES-D), Beck Anxiety Inventory (BAI), Trust in Physicians/ Providers Scale (TPS), and Communication and Attitudinal Self-Efficacy Scale for cancer (CASE-cancer). All validated.	No significant longitudinal differences in depression, anxiety, physician trust, self-efficacy, or objective comprehension were found before and after testing. Depression and anxiety were negatively associated with self-efficacy and positively associated with each other. Objective comprehension was lower in non-White and lower-income patients.
Ahmed et al. (2022)	Attitudes toward and experiences of prognostic testing using a 31-gene expression profile test.	24 patients with stage IB–IIC cutaneous melanoma.	43-question online survey.	Shared Decision Making Process Scale (validated). Other questions were from previously published surveys, and new questions developed and reviewed by a committee which included the authors.	Reasons for undergoing testing: to obtain all information possible about the tumor 79%; provider recommended 69.2%; inform treatment decisions 46.2%; better understand their future 30.8%. 22/24 felt results were easy to understand and useful. 60.7% felt that their test results provided increased knowledge. 39.3% felt relief from uncertainty about the future with 17.9% getting information relevant to life planning. No patients regretted their decision to test.
Bartley et al. (2022; PiGeOn)	Patients' experience of uncertainty when receiving comprehensive tumor genomic profiling results.	37 patients with advanced cancer who have exhausted standard treatment options.	Semi-structured interviews done 2 weeks after patients received their tumor genomic profile results.	Interview guides were developed by a multidisciplinary team with questions about reaction to and communication of results with specific questions on perceptions of uncertainty. Interview guide not provided.	Results relieved future treatment uncertainty even if there were no actionable variants. Negative germline results reduced uncertainty about the risk to family members. Reducing illness and treatment uncertainty is a motivating factor in undergoing comprehensive tumor genomic profiling.
Best et al. (2019; PiGeOn)	Attitudes and expectations of patients toward MP.	569 patients with advanced cancer with no further treatment options.	Semi-structured interviews (n = 20) were done by phone after consent to undergo molecular tumor profiling and a survey.	The entire cohort was asked, "What are the benefits and drawbacks of molecular tumor profiling?" with a free text response. Interview questions are published in an additional file.	Three themes emerged: agreement to participate because of a desire for new treatments to increase survival, altruism, and encouragement from providers coupled with faith in the scientific process.

Note. MP = molecular profiling; VUS = variants of uncertain significance; WES = whole-exome sequencing; NSCLC = non–small cell lung cancer; WGS = whole-genome sequencing; ctDNA = circulating tumor DNA.

Table 1. Evidence Summary (cont.)

Study	Dimensions measured	Sample size and population	Methodology	Survey or instrument	Main findings
Best et al. (2020; PiGeOn)	Preferences for receiving somatic MP results.	1,299 patients with advanced cancer who have exhausted therapeutic options.	Self-administered questionnaire done after consent. A subset of 20 patients underwent a qualitative interview.	Questionnaire asked if they would like to receive actionable, nonactionable, VUS, or germline results. Interview schedule is published in the supplementary table.	96% wanted to receive actionable results; 64% elected to receive nonactionable results; 60% wanted to receive VUS; and 86% wanted to receive germline results that could inform family risk. Priority was to obtain results that could inform of possible cancer treatment.
Blee et al. (2021)	Patient understanding of molecular testing terminology.	60 patients with cancer undergoing molecular testing.	A patient-physician conversation about molecular results was observed, recorded, and transcribed. Patient interviews were done after the result disclosure to assess their understanding of the technical terms. Patients were also asked to provide definitions of the technical terms that were used.	Data obtained from physician-patient conversations and interviews with patients (done just after results disclosure) were evaluated using multilevel semantic content analysis.	Patients understood about half of the technical terms regardless of whether terms were defined in the result disclosure. "Mutation" was understood by less than half, with (21/43; 48.8%) correctly defining the word. "Genomic testing" was also difficult for patients to understand, with (4/11; 36.3%) correctly defining the term despite being defined by clinicians 72.7% of the time in the result disclosure conversation. The only significant demographic correlate to patient understanding was family income.
Bradbury et al. (2022; COMET)	Serial measurements of knowledge, anxiety, depression, and cancer-specific distress.	594 patients with advanced cancer undergoing tumor-only genetic sequencing.	A randomized trial comparing the effect of a genetic educational intervention vs. standard return of results with patients doing online surveys at baseline, post education, and after receiving results.	Genetic knowledge was evaluated with an adapted version of the ClinSeq knowledge scale modified for tumor genetic testing. General anxiety and depression were assessed with 4-item short forms of the Patient-Reported Outcomes Measurement Information System (PROMIS). State anxiety was assessed with 20 items from the State-Trait Anxiety Inventory. Cancer-specific distress was measured with an adapted 14-item version of the Impact of Events Scale.	Patients in the intervention arm had greater increases in knowledge but no significant differences in distress outcomes. Women, but not men, in the intervention arm, had less cancer-specific distress. Patients with lower health literacy in the intervention arm had greater increases in cancer-specific distress and less decline in general anxiety, and greater increases in depression in comparison with those receiving usual care.

Note. MP = molecular profiling; VUS = variants of uncertain significance; WES = whole-exome sequencing; NSCLC = non–small cell lung cancer; WGS = whole-genome sequencing; ctDNA = circulating tumor DNA.

Table 1. Evidence Summary (cont.)

Study	Dimensions measured	Sample size and population	Methodology	Survey or instrument	Main findings
Davies et al. (2020; PiGeOn)	Knowledge and attitudes toward MP profiling.	1,299 patients with advanced cancer who have exhausted therapeutic options.	Questionnaire within a month of consent and prior to getting results of MP.	Comprised of study-specific, adapted, and previously validated scales. A two-item measure adapted from Hay et al. (2012) assessed the perceived importance of learning whether gene variants affect the chance of responding to particular cancer treatments and learning more about how lifestyle affects the chance of living longer with cancer. An eight-item, multiple choice, study-specific scale assessed participants' knowledge regarding the purpose of MP, its utility in guiding treatment and understanding future cancer risk, and whether the likely frequency of informative results differs across cancer types. The seven-item Attitude Towards Uncertainty scale measured attitudes toward uncertainty in the specific context of medical testing. Four Likert-scale items adapted from Rosenberg et al. (2013) assessed perceived ability to cope if actionable, non-actionable, or germline results were found.	96% wanted to receive actionable results, 64% elected to receive non-actionable results, 60% wanted to receive VUS, 86% wanted to receive germline results that wished to receive VUS, and 86% wanted to receive germline results that could inform family risk. Priority was to obtain results that could inform of possible cancer treatment.
Gray et al. (2016; CanSeq)	Genetic knowledge and preferences for learning WES findings.	167 patients with stage IV lung or colorectal adenocarcinoma at Dana Farber Cancer Institute.	Patient consent forms and surveys.	Surveys included validated measures (not specifically identified) to assess patients' attitudes about undergoing a genetic test, experience with genetic testing, genetic knowledge, subjective numeracy, health literacy, self-reported Eastern Cooperative Oncology Group performance status, quality of life, and decision-making preferences. The patient consent form elicited patients' preferences for disclosure of WES results.	Genetic knowledge was moderately low (mean 4 of 7). The majority of patients wanted to learn cancer-related, carrier status, and pharmacogenetic findings.

Note. MP = molecular profiling; VUS = variants of uncertain significance; WES = whole-exome sequencing; NSCLC = non–small cell lung cancer; WGS = whole-genome sequencing; ctDNA = circulating tumor DNA.

Table 1. Evidence Summary (cont.)

Study	Dimensions measured	Sample size and population	Methodology	Survey or instrument	Main findings
Halverson et al. (2016)	Patient perception of the utility of genomic sequencing.	19 patients with advanced cancer who had exhausted standard treatment.	In-depth semi-structured interviews by phone or in-person with patients and their family members.	Interview guide not provided.	Participants overwhelmingly reported that sequencing was worthwhile. They valued being empowered regardless of the clinical utility, enabling informed decision-making, contributing to scientific knowledge, and the feeling that they had done all they could.
Hamilton et al. (2017)	Patient perceptions of secondary germline findings.	40 patients with advanced breast, bladder, colorectal, or lung cancer had tumor profiling. Secondary findings not disclosed.	Qualitative semi-structured interviews.	Interview guide not provided.	57% were interested, 29% equivocal, and 14% disinterested in secondary germline findings. Benefits perceived included being informed, the opportunity for planning, and disease prevention/management. 53% did not anticipate harm though some were worried about privacy and misuse of information.
Liang et al. (2017)	Patient attitudes and experiences regarding somatic tumor screening.	24 patients with advanced NSCLC or melanoma.	Semi-structured face-to-face or telephone interviews.	Interview guide not provided.	20% did not remember having a sample sent for analysis. Two thirds noted results could help guide treatment. Wide acceptance of screening. Patients preferred to receive results from the oncologist with additional take-home materials and wanted the discussion to focus on practical matters relevant to treatment.
Marron et al. (2019; iCAT)	Hopes, expectations, and concerns about genomic tumor profiling, results of participation, and preferences regarding the return of tumor profiling results.	11 patients considered pediatric (age 18–30) at four academic centers with recurrent, refractory, or high-risk extracranial solid tumors. The majority was sarcoma.	A self-administered written survey consisting of items addressing participant understanding of the purpose of research, health perceptions, and genetic knowledge.	Surveys included scales that investigated participant understanding, which was assessed by four items, three of which were adapted from the validated Quality of Informed Consent. Genetic knowledge was measured in the surveys by the validated Genetic Knowledge Index (GKI). General health perception was assessed in the survey by the short form 36 general health perceptions question.	Most participants understood that the primary goal of this research was to help future patients, but they also cited a dual purpose of helping themselves. More understanding and genetic literacy were noted among higher-educated participants.

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Table 1. Evidence Summary (cont.)

Study	Dimensions measured	Sample size and population	Methodology	Survey or instrument	Main findings
Meiser et al. (2022; PiGeOn)	Psychological predictors of patients' preferences regarding the return of results from comprehensive tumor genomic profiling.	1,434 patients with advanced cancer who have exhausted therapeutic options.	Self-administered questionnaire, either online or hard copy.	The seven-item Likert-type scale (Braithwaite et al., 2002) assessed attitudes toward uncertainty in the specific context of medical testing and was adapted from a previous study (Kasparian et al., 2009). Three items from the Concerns about Recurrence Questionnaire (Thewes et al., 2015) were adapted to measure fear of cancer progression. Four items adapted from Rosenberg et al. (2013) assessed perceived ability to cope if actionable, nonactionable, VUS, and/or germline results were found. 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.	96% wanted to receive results that would guide treatment; 64% would like to receive results that cannot guide treatment; 59% wanted to receive VUSs; 89% wanted germline results that could inform family risk. Most patients wanted to receive all results.
Pichler et al. (2021)	Patients' information needs when undergoing comprehensive genomic profiling.	30 patients with refractory advanced cancer undergoing panel or WGS. Patients undergoing WGS had to be less than 50 years old.	After patients completed a questionnaire, a semi-structured interview was done face-to-face.	Questionnaire results were published in previous article (Rohrmoser et al., 2020). Interview guide provided in supplementary file.	Qualitative analysis revealed a limited understanding of the complex background of molecular diagnostics and uncertainties about personal benefits. Physician trust played a central role for many of the patients by "buffering" their limited understanding.
Relton et al. (2021)	Views on the potential use of ctDNA in endometrial cancer follow-up.	18 patients already enrolled in a nonintervention cohort study determining the ability of ctDNA to detect recurrent endometrial cancer.	Semi-structured interview.	Topic guide in supplementary data.	High level of patient acceptability of ctDNA monitoring with an overwhelming preference for blood test vs. pelvic exam for recurrence. Strong preference for being informed of results despite acknowledging associated anxiety should the test reflect recurrence.

Note. MP = molecular profiling; VUS = variants of uncertain significance; WES = whole-exome sequencing; NSCLC = non–small cell lung cancer; WGS = whole-genome sequencing; ctDNA = circulating tumor DNA.

Table 1. Evidence Summary (cont.)

Study	Dimensions measured	Sample size and population	Methodology	Survey or instrument	Main findings
Roberts et al. (2019; MI-ONCOSEQ)	Understanding, expectations, and outcomes after participating in research with matched tumor and germline sequencing.	297 patients with refractory metastatic cancer.	A self-administered questionnaire, web-based or in person, at baseline and after the return of results.	Validated self-report measures and questionnaire items were created specifically for this study.	Discordance between pre-test expectation of benefit and post-test realization of that benefit though most patients had low levels of regret. The mean satisfaction score was 4.06 on a scale of 1 to 5.
Rohrmoser et al. (2020)	Expectations of cancer patients undergoing molecular diagnostics.	30 patients with refractory, advanced cancer undergoing panel or WGS. Patients undergoing WGS had to be less than 50 years old.	After patients completed a questionnaire, a semi-structured interview was done face-to-face.	Questionnaire on Stress in Cancer Patients revised version QSC-R23. Interview guide not provided.	Patients expected to discover an improved treatment, contribute to research, and learn additional information about their cancer. Patients noted two emotional benefits from participation in molecular diagnostics: it improved their hope for prolonged life or recovery and made them feel special individually.
Wing et al. (2021)	Patients' knowledge of genetic test results.	85 patients at a comprehensive cancer center who had undergone genomic testing.	Patient survey included demographics, disease characteristics, receipt of genetic counseling, cancer genomic knowledge, and germline genetic knowledge. Personal genomic knowledge measured by comparing self-reported recall with the medical record.	Cancer genomic knowledge questions adapted from Blanchette et al. (2014).	About one third of patients did not recall having had testing. Of the patients who remembered testing, 44% of patients with pathogenic germline mutations and 57% of patients with somatic alterations did not accurately recall their specific gene or variant.

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validation. Across studies, certain subgroups of patients scored higher on genomic knowledge testing, for example, patients with rare cancer (Davies et al., 2020), patients with lung cancer (Wing et al., 2021), patients with higher incomes (Blee et al., 2021), and patients who received a copy of their results (Wing et al., 2021). Two studies found that a substantial proportion of patients did not remember being tested at all (Liang et al., 2017; Wing et al., 2021). Comparing patient-reported findings with electronic health records, Wing and colleagues (2021) noted that roughly half of the patients with actionable findings could not recall their specific results. Blee and colleagues (2021) found that many patients do not understand key terminology used to describe molecular test results, with only about half the patients able to define terms such as "mutation," "gene," and "genetic testing." Despite differences in measurement instruments and populations, Caucasians, English speakers, and those with higher education tended to score higher on knowledge measures.

The Communication and Education in Tumor Profiling (COMET) study was the only study in this review that evaluated an educational program designed to help patients understand tumor genomics. COMET compared a web-based intervention to usual care in patients in the Molecular Analysis for Therapy Choice (MATCH) trial. COMET evaluated knowledge, anxiety, depression, and cancer-specific distress and found that the educational intervention increased patient understanding and significantly reduced distress in women but not men (Bradbury et al., 2022). Bradbury and colleagues (2022) concluded there is an ongoing need for communication strategies and tailored education to improve patient understanding of MP and genomic sequencing.

Attitudes

Across all included studies, patients felt positive in their opinions about molecular profiling. The positive attitudes observed toward tumor profiling were largely attributed to the opportunity for patients to gain new insights into their disease and potential treatment options, particularly the perceived utility and value of this information. Liang and colleagues (2017) found that tumor profiling was highly acceptable to all patients since it was inextricably linked with the prospect of receiving a matched targeted therapy. Davies and colleagues (2020) also found that patients had overwhelmingly positive attitudes toward MP, which they noted were consistent with the Gartner Hype Cycle, a model in which the initial hype of new technology leads to overestimating benefits in the short term and underestimating future benefits. Genomic testing was perceived to be more important to patients with children, possibly due to the overestimation of finding germline alterations and familial responsibility to extend their life (Davies et al., 2020).

Preferences and Expectations

Patients with cancer strongly prefer to receive all molecular profiling results, regardless of their level of understanding or potential for distress. According to multiple studies, they expect to be informed in person with the opportunity to ask questions. Gray and colleagues (2016) and Meiser and colleagues (2022) found that patients strongly preferred to receive all categories of MP results, including germline alterations, somatic alterations, and variants of unknown significance (VUS). Patients in the Halverson and colleagues (2016) study expressed a desire to know everything about themselves, stating that it would allow them to plan and be aware of things and inform themselves about new developments. Best and colleagues (2020) found that English-speaking patients were more likely to be interested in being informed about gene variants and that better-educated patients wanted to be informed even of non-actionable variants. Patients also wanted to know germline findings for their families' sake (Best et al., 2020; Meiser et al., 2022). Patients preferred results to be provided in person with the opportunity to discuss them and ask questions. They relied on their clinicians to interpret results and deal with the technical aspects of testing. Patients also wanted written material to take home and reference later.

Patients valued the ability to plan for future care when tumor sequencing availed them of pertinent prognostic information. Relton and colleagues (2021) found that patients with endometrial cancer wanted to know if serial ctDNA

measurements indicated cancer recurrence to plan future care. Similar sentiments were noted in patients with resected melanoma whose MP indicated a poorer prognosis (Ahmed et al., 2022).

The expectation of personal benefit from discovering treatment options, which offer hope, was the primary reason patients underwent MP or participated in studies that offered MP. Other motivations for testing included altruism and contributing to science (Best et al., 2019; Halverson et al., 2016; Marron et al., 2019; Relton et al., 2021; Rohrmoser et al., 2020). Across studies, patients overestimated potential personal benefit, as described by previous research (Bombard et al., 2014). Roberts and colleagues (2019) found that college-educated patients had less expectation of direct benefit than those with a high school education. Many patients did not appreciate just how slight the chance was of personal benefit (Adams et al., 2020; Best et al., 2019; Davies et al., 2020; Marron et al., 2019; Pichler et al., 2021). Most patients in the study by Liang and colleagues (2017) thought there was no disadvantage to testing, especially if they received mutation-positive results.

Patients also overestimated the information that tumor genomic profiling would provide. Roberts and colleagues (2019) noted that most patients believed incorrectly that they would receive unexpected sequencing results, that is, results irrelevant to their cancer diagnosis but with implications for their family or their health. Adams and colleagues (2020) found that many patients were under the misperception that somatic tumor sequencing would explain how they could change their behavior to lower their disease risk. Liang and colleagues (2017) described a patient who worried that a somatic mutation could be passed to her children, corroborating previous findings that patients may mistakenly believe somatic testing will routinely provide germline information. On the other hand, Davies and colleagues (2020) found that patients were unaware of potential germline implications and possible use in clinical management. Some patients perceived cancer genomic sequencing as routine in current practice, while others perceived the testing as the best and final end-of-the-line testing (Halverson et al., 2016; Roberts et al., 2019).

Concerns

Across studies, patients reported the need to protect themselves from being overloaded with information, particularly in the context of ongoing burdens from advanced cancer. Some participants noted that they could not take in any more negative information, while others had the confidence to manage any resulting distress (Hamilton et al., 2017). There was wide variability of concern among patients about how results affect them emotionally. Some patients thought results conveying a poor prognosis would be too upsetting (although they still wanted the information), while others had a more fatalistic approach. Patients reported feeling disadvantaged at receiving mutation-negative results, with limited or no treatment options causing emotional distress and hopelessness (Liang et al., 2017). Complaints of waiting for results were universal and frequently provoked anxiety.

When MP results included germline testing, some patients were concerned that the findings would distress their families. A few middle-aged patients believed this could be particularly emotionally burdensome for their parents (Hamilton et al., 2017). Despite some patients being concerned that sharing germline results with their families would cause them emotional upset, more than half of the patients thought there would be no downside to learning this information (Hamilton et al., 2017). When secondary germline findings were discovered, Hamilton and colleagues (2017) noted that most patients wanted to be informed, so they might use the information for life planning, disease prevention, and general knowledge.

Satisfaction With Testing

Participants overwhelmingly reported feeling that undergoing molecular profiling had been worthwhile. Despite unmet expectations, patients had little regret in undergoing MP (Best et al., 2019; Bradbury et al., 2022; Roberts et al., 2019; Rohrmoser et al., 2020). Halverson and colleagues (2016) found that patients valued testing, even if the results provided no clinical utility. Patients supported the use of the testing even if they did not understand or remember the test (Liang et al., 2017). There was high acceptability for ctDNA monitoring in early- and late-stage endometrial cancer, with an

overwhelming preference for ctDNA over pelvic exams (Relton et al., 2021). None of the patients with early-stage resected melanoma regretted having prognostic MP (Ahmed et al., 2022). In the 2019 publication, Best and colleagues concurred with other studies from the PiGeOn Project included in this review: Patients believed their results might help their family members or other patients even if they received no personal benefit.

DISCUSSION

This state-of-the-art review summarizes the most recent literature about cancer patients' knowledge and expectations of MP, as well as preferences regarding MP. Review findings confirm previous studies that patient knowledge regarding MP is low, although some patients with higher education and greater genetic understanding have more realistic expectations and view NGS, particularly whole-exome sequencing, as having altruistic value. Patients realized they had a knowledge gap regarding MP but were comfortable having their clinicians bridge that gap for them and guide treatment. Patients prioritized getting results over understanding the technical aspects. Patients' overwhelming support for MP was observed, even though expectations of additional treatment options were frequently unrealized, and some patients had unrealistic expectations of the benefits of the data. Some patients lacked an understanding of the purpose of testing and the logistics of the testing process, while other patients did not remember being tested at all. This is troubling, considering these patients may not fully appreciate their treatment options or inform their family members of a germline finding.

Patients' attitudes about germline findings were highly variable and influenced by the perceived benefits and harms of information about heritable variants. Patients identified three primary benefits if they happened to receive germline findings: being informed, future planning, and disease prevention and management. Patients also believed germline findings could prompt awareness and lead to disease prevention or management for biological family members. Concerns were expressed about emotional distress, particularly among their parents, and fear and anxiety in biological family members. For non-biologic family members such as spouses and partners, patients felt prognostic germline findings could be informative for care planning.

Limitations of this review include the small number of articles that fulfilled the search criteria. Nevertheless, a rigorous protocol was followed for identifying articles and decisions about inclusion and exclusion. The lack of multiple reviewers is another study limitation and could have introduced bias in interpreting the results. Most articles were based on studies done in academic settings, which limits the generalizability of the patient population. Strengths include broad search terms and the consistency of the findings with other studies.

IMPLICATIONS FOR PRACTICE

Molecular profiling in patients with cancer is complex, and it is unsurprising that college-educated patients have the most understanding/literacy. As genomic and genetic literacy disparities exist by race and education levels, the advanced practice provider (APP) must be aware of and assess the needs and preferences of particular patients and provide individualized assistance to support informed decision-making. Patients need education to mitigate unrealistic expectations and disappointment. Although understanding their cancer may lead to better adherence and decision-making, increasing patient genomic understanding may depend on the individual's ability and appetite for in-depth knowledge and may be challenging when patients have significant psychological and physical burdens (Davies et al., 2020). People with cancer need to be provided with easily understandable resources to help explain the outcomes, goals, and evidence-based practice. A return of results tool may assist patients in understanding complex results (Solomon et al., 2020). The APP is well situated to address these concerns and will be increasingly crucial as genomic sequencing increases and becomes more complex. ●

Disclosure

The authors have no conflicts of interest to disclose.

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