

# Uptake of a 21-gene expression assay in breast cancer practice: views of academic and community-based oncologists

M.A. O'Brien PhD,\* S. Dhesy-Thind MD MSc,<sup>†</sup> C. Charles PhD,<sup>‡a</sup> M. Hammond Mobilio MA,<sup>§</sup> N.B. Leigh MD MSc,<sup>||</sup> and E. Grunfeld MD DPhil<sup>\*#</sup>

## ABSTRACT

**Purpose** Advances in personalized medicine have produced novel tests and treatment options for women with breast cancer. Relatively little is known about the process by which such tests are adopted into oncology practice. The objectives of the present study were to understand the experiences of medical oncologists with multigene expression profile (GEP) tests, including their adoption into practice in early-stage breast cancer, and the perceptions of the oncologists about the influence of test results on treatment decision-making.

**Methods** We conducted a qualitative descriptive study involving interviews with medical oncologists from academic and community cancer centres or hospitals in 8 communities in Ontario. A 21-gene breast cancer assay was used as the example of GEP testing. Qualitative analytic techniques were used to identify the main themes.

**Results** Of 28 oncologists who were approached, 21 (75%) participated in the study [median age: 43 years; 12 women (57%)]. Awareness and knowledge of GEP testing were derived from several sources: international scientific meetings, participation in clinical studies, discussions with respected colleagues, and manufacturer-sponsored meetings. Oncologists observed that incorporating GEP testing into their clinical practice resulted in several changes, including longer consultation times, second visits, and taking steps to minimize treatment delays. Oncologists expressed divergent opinions about the strength of evidence and added value of GEP testing in guiding treatment decisions.

**Conclusions** Incorporation of GEP testing into clinical practice in early-stage breast cancer required oncologists to make changes to their usual routines. The opinions of oncologists about the quality of evidence underpinning the test affected how much weight they gave to test results in treatment decision-making.

**Key Words** Breast cancer, decision-making, gene expression profile testing

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## INTRODUCTION

Multigene expression profile (GEP) testing has been reported to have both prognostic and predictive value above the traditional clinical and histopathologic features in breast cancer<sup>1-3</sup>. One example of a GEP test in breast cancer is a 21-gene expression assay<sup>1,2</sup> that is funded in several Canadian provinces. That test uses real-time reverse transcriptase-polymerase chain reaction to measure messenger RNA levels in breast cancer tissue obtained during the patient's original surgery<sup>1,2</sup>. Results of testing are presented as a breast cancer recurrence score that is categorized as low (<18), intermediate (18–30), or high (≥31)<sup>1,2</sup>.

The test was originally developed for prognostic purposes in women with early-stage (stage I or II) lymph node-negative, estrogen receptor-positive, HER2-negative breast cancer who would receive tamoxifen<sup>1,2</sup>. The manufacturer (<http://www.genomichealth.com>) has since expanded the indications for use to node-positive disease and ductal carcinoma *in situ*, based on retrospective testing of archival samples from those patient groups. Health technology assessments in the United States<sup>4</sup>, the United

<sup>a</sup> Dr. Cathy Charles died 9 November 2015. She was Professor Emeritus during the conduct of this study and the drafting of the manuscript.

Kingdom<sup>5</sup>, and Canada<sup>6</sup> have reported that, although there is evidence of the test's prognostic value, the direct evidence is insufficient to determine its predictive value (clinical utility) in determining which patients are likely to respond to chemotherapy<sup>4–6</sup>.

Several clinical practice guidelines and consensus statements provide suggestions for using GEP testing in practice, although actual recommendations vary. For example, the U.S. National Comprehensive Cancer Network clinical practice guidelines<sup>7</sup> indicate that GEP testing is appropriate for women with intermediate-risk hormone receptor-positive breast cancer. The 2013 St. Gallen expert consensus panel<sup>8</sup> suggested that GEP testing might not be indicated in patients with low-risk disease (for example, tumour  $\leq 1$  cm, lymph node-negative) for whom chemotherapy is unlikely to be offered or in patients with high-risk disease (for example, tumour  $> 5$  cm, lymph node-positive) for whom chemotherapy is likely to be provided. Recent recommendations from Cancer Care Ontario specify that clinicians *could* offer GEP testing to eligible breast cancer patients. A qualifying statement that accompanies the recommendation specifies that GEP testing should not be requested “if the patient's management plan has been decided based on clinical, pathologic, and/or patient-related factors and is unlikely to change”<sup>9</sup>.

Although the results of health technology assessments raise questions about the clinical utility of the 21-gene expression assay, medical oncologists are using test results in clinical practice to help inform decision-making with respect to patients who can safely avoid adjuvant chemotherapy<sup>10–12</sup>. The short- and long-term risks of adjuvant chemotherapy have been well documented, and there are concerns about the overtreatment of patients having breast cancer with low-risk features<sup>13</sup>.

Relatively little is known about the post-marketing adoption of breast cancer GEP testing in actual oncology practice. Research in this area can yield valuable information about how oncologists use new technologies in less-controlled, non-research settings. For example, Hassett *et al.*<sup>11</sup> used a prospective registry that collected data from 17 comprehensive and community cancer centres to assess GEP test adoption for women diagnosed with breast cancer between 2006 and 2008. They found that GEP testing increased over time, with an overall reduction in use of adjuvant chemotherapy in hormone receptor-positive breast cancer. Although most tests were ordered for patients with intermediate-risk cancer, 20% of tests were ordered for patients in whom testing is not recommended according to the U.S. National Comprehensive Cancer Network guideline<sup>11</sup>. The same authors also found that chemotherapy was sometimes ordered even when GEP test results indicated that the risk was low; the converse was also true, in that chemotherapy was not provided when GEP test results indicated that the risk was high. Those findings suggest that, in some circumstances, factors other than GEP test results play a role in the decision by the oncologist to institute chemotherapy for breast cancer patients who are eligible for GEP testing.

The purpose of the present study was to better understand the perspectives of oncologists about how the 21-gene expression assay was adopted in breast cancer clinical

practice and about how the results of testing were used in decision-making under circumstances in which robust evidence for the test's clinical utility was still emerging. It is anticipated that the results of our study will assist researchers and clinicians alike to better understand the perceptions of oncologists with respect to the diffusion of information about testing into practice and the various information sources (academic and manufacturer-based) used by oncologists; our results might also uncover additional challenges in incorporating testing into actual practice rather than in more controlled research settings.

The specific objectives of the present study were to understand the experiences of medical oncologists in using GEP testing in clinical practice and to describe the views of medical oncologists about the influence of test results on clinical decision-making.

## METHODS

### Design

We conducted a qualitative descriptive research study<sup>14,15</sup>. This method is appropriate when relatively little is known about the topic (for example, post-marketing adoption of GEP testing in practice) and when the research focuses on the perspectives of those who have encountered the phenomenon of interest (for example, use of GEP testing by oncologists)<sup>14,16</sup>.

### Setting

Cancer care in Ontario is delivered through thirteen regional cancer programs. From within those programs, a convenience sample of 6 cancer centres and 2 hospital-affiliated cancer clinics belonging to five programs was selected. The selected sites were located in 8 different communities in five local health integration networks that provide care for approximately 38% of new breast cancer patients in the province<sup>17</sup>. Medical oncologists were eligible if they provided care for women with breast cancer at one of the selected sites. Purposive sampling<sup>14</sup> was used to identify a diverse group of medical oncologists [varying in sex, years in practice, and type of cancer centre (academic or community) as classified by the Ontario Ministry of Health and Long-Term Care (<http://www.health.gov.on.ca/en>)]. Using a publicly accessible database (<http://www.cpsso.on.ca/Public-Register/Public-Register>), a list of medical oncologists at each centre was created. One team member (SDT) contacted the oncologists by e-mail to determine interest in the study. The study received institutional ethics board approval. All medical oncologists provided written informed consent.

As an example of GEP testing, we used a 21-gene breast cancer assay (Oncotype Dx: Genomic Health, Redwood, CA, U.S.A.). One of the goals of GEP testing is to identify women with breast cancer who are unlikely to benefit from chemotherapy<sup>1,2</sup>. Beginning in 2010, the Ontario Ministry of Health and Long-Term Care paid for the assay on a per-case basis for patients meeting eligibility criteria. Concurrent with the present study, most cancer centres voluntarily participated in a field study that examined GEP testing and treatment decision-making by oncologists and patients<sup>12</sup>. While our study was underway, the Ontario

Ministry of Health and Long-Term Care changed the payment criteria for GEP testing; a new criterion required mandatory oncologist participation in the field study. Of 21 participants in our study, 7 were recruited before that change in funding criteria.

Semi-structured face-to-face interviews lasting approximately 40 minutes were conducted in the cancer centres by an experienced researcher (MAO). An interview guide was pilot-tested with 2 oncologists. Topics for the interview guide were based on the study objectives and included questions about the experiences of the oncologists when using GEP testing in clinical practice and the effect of test results on treatment decision-making. Interviews were conducted iteratively. For example, in interviews 14–21, oncologists were asked how they learned about GEP testing because that topic had been raised as an issue in an earlier interview. In qualitative research, it is usual practice to modify an interview guide based on new interview data.

Interviews were digitally recorded and transcribed verbatim. Demographic characteristics were collected.

## Data Analysis

Two researchers (MAO, MHM) independently coded the interview transcripts<sup>18</sup>. Codes were assigned by each coder according to the main meaning in a specific sentence or paragraph of the transcript. The constant comparative method, whereby codes were compared within and across interview transcripts, was used<sup>19–21</sup>. Subsequently, higher-order categories were derived by grouping similar codes. Any coding discrepancies were resolved through discussion. Lastly, qualitative analytic techniques were used to inductively identify the main themes<sup>19–21</sup>. The concept of data saturation determined when the analytic process was complete<sup>22</sup>. Data saturation with respect to the effect of GEP testing on treatment decision-making was reached after 18 interviews, but another 3 oncologists were interviewed to ensure that additional important information was not missed. To ensure study rigour and transparency, we kept an audit trail, including interview summaries and memos to document all major analytic decisions<sup>23</sup>. Data management and analysis software (NVivo 9: QSR International, Melbourne, Australia) was used to facilitate data analysis.

## RESULTS

### Demographics

The 21 medical oncologists who agreed to participate [78% of those approached (Table 1); median age: 43 years; 12 women (57%)] had practiced for a median of 11 years since medical oncology training. Oncologists practiced in academic ( $n = 9$ , 43%) or community hospital-affiliated ( $n = 12$ , 57%) cancer centres.

### Main Themes

Two main themes were derived from the interview data:

- Learning about GEP testing and incorporating the test into clinical practice
- Factors affecting the use of GEP test results in treatment decision-making

In the sections that follow, we describe each theme and provide exemplar quotes from study participants. Additional quotations for each theme are provided in Tables II and III.

### *Learning About GEP Testing and Incorporating the Test into Clinical Practice*

As oncologists recounted their experiences with GEP testing, the pattern described by most about how they came to use GEP testing in their clinical practice was similar (Table II). They described becoming aware of GEP testing, then gaining personal experience with the testing procedures and interpretation of recurrence scores by participating in clinical studies (for some), and then incorporating the test into actual practice. Oncologists said they first heard about GEP testing at international conferences such as an American Society of Clinical Oncology annual meeting or from faculty supervisors when they were residents. Oncologists then described becoming more familiar with testing at regional or departmental meetings. However, several oncologists expressed concern that manufacturer representatives had played a role in how they learned about GEP testing. For example:

The people who fund the test went around teaching us. They invited us to days where we learned about the test. We didn't learn about it from our teachers at [name of cancer centre or teaching hospital]. We learned about it from industry.  
— P16

Oncologists also described how the introduction of GEP testing necessitated several adjustments to their clinical practice. The adjustments included increasing the length of consultations to explain testing to patients, scheduling an extra visit when test results were ready, and developing procedural workarounds to minimize treatment delays as a result of GEP testing.

Oncologists indicated that they had increased the length of the consultation to explain testing to patients. They described how breast cancer consultations had become increasingly complex and challenging and thus required more time with patients. Discussions about GEP testing were perceived to have added to the complexity, resulting in longer

**TABLE I** Demographics of the study physicians

Characteristic	Value
Sex [ $n$ (%)]	
Men	9 (43)
Women	12 (57)
Age (years)	
Median	43
Range	35–67
Time since medical oncology training (years)	
Median	11
Range	4–33
Type of hospital [ $n$ (%)]	
Academic	9 (43)
Community	12 (57)

consultations. In addition, oncologists indicated that longer consultations meant that clinics often ran over the allotted time, which oncologists and patients found stressful.

Oncologists explained that they often scheduled an extra patient visit before treatment because they believed that patients needed extra time to understand complex

**TABLE II** Views of oncologists concerning learning about gene expression profile (GEP) testing and adjusting clinical practice

Aspect of GEP testing	Exemplar quotations (study participant ID)
<i>Learning about GEP testing</i>	
Major international meetings	I heard about [GEP testing] at one of the ASCO meetings. (P14)
Clinical studies	We then obviously participated in the field studies, so [learning] was a gradual thing. (P20)
Manufacturer-sponsored meetings	This test we learned a lot through the company that did it, and they pushed it hard. (P21)
<i>Adjustments to clinical practice</i>	
Increased consultation time	<p>The more tests you have, the more time you need to discuss with patients [the test] limitations and what it really means, and so it takes more time. (P7)</p> <p>The number of decision-making points has dramatically increased. You might have a discussion about 3 or 4 or 5 of these decision points with one patient. So there are many factors that have significantly increased the complexity—the time both with the patient and with things that you do outside of that. (P11)</p>
Scheduling an extra visit	I think in general our current model isn't adequate, and ... that is why I tend to bring people back for a second session in the majority of cases. Because even a single session, I think, is overwhelming to absorb the current state of information that we have in someone who is in a highly anxious and vulnerable state. (P10)
Developing procedural workarounds	That happened to me yesterday. So I had no [hormone] receptors, so you can't go too far, so we talked in generalities and she was okay with that, she understood, but I got her to sign the [name of consent form] just in case we needed it. So instead of having her come back—another delay—"let's have you sign this in case we need it" and I said, "If we don't need it, I will call you" ... to make it a little bit more efficient, and [patients] like it because they don't have to come back and sign a form. (P19)

ASCO = American Society of Clinical Oncology.

**TABLE III** Views of oncologists concerning factors affecting the use of gene expression profile (GEP) testing in treatment decision-making

Factor	Exemplar quotations (study participant ID)
Concerns about the overtreatment of women with early-stage breast cancer	
	<ul style="list-style-type: none"> <li>My concern is definitely in overtreating patients and wanting to avoid chemotherapy if possible. (P20)</li> </ul>
Interpreting GEP test results in the context of other clinicopathologic features	
	<ul style="list-style-type: none"> <li>Usually we look at a bunch of things. We look at the tumour size, the grade, the [estrogen receptor], the [progesterone receptor], HER2, then the node status and then the [name of test] just gives us another thing to look at. So then you try to put all those things into a matrix and come up with as best a solution as you can. (P21)</li> </ul>
GEP test results have potentially to be meaningful and affect oncologist and patient treatment decision-making	
	<ul style="list-style-type: none"> <li>Is there any chance that I might consider chemotherapy for this patient? Or is it a clear no-brainer? So, number one, if the patient comes to me and says, "There's absolutely no way I'm ever going to take chemotherapy from you," well, then, I think that's probably not a valid use of the test if it's not going to change what I'm going to do. So ... the test has to some way affect my management. (P1)</li> </ul>
GEP test results serve to affirm the oncologist's opinion	
	<ul style="list-style-type: none"> <li>I am really looking at the test just to give me more information to say, okay, the score is low, I am right, you know, you don't need chemo. Or the score is high and I was wrong and you probably do need to at least to consider chemo. (P21)</li> </ul>
Perceived confidence in evidence underpinning GEP testing	
	<ul style="list-style-type: none"> <li>So, I actually don't feel that it's poor data. I don't think that we are jumping the gun, because I don't think that we are making, that is, why I again I am talking node negative.... I don't think that we are making rash decisions by using this. So when I sort of look at it in the whole context of things, I think the data is not too bad. You can nitpick anything you want. You can find flaws and you can find good things in anything you want.... I'm comfortable with what we have. (P9)</li> <li>I think a lot of this data is still based on retrospective analysis of prospective studies and not a prospective assessment of the [name of test], which is, if we want to go for the gold standard, is always an area of concern. (P8)</li> </ul>
Desire for clarity and difficulties with intermediate results: "back to where you started"	
	<ul style="list-style-type: none"> <li>Sometimes the very patients that you have some uncertainty about, which is why you have ordered the test, sometimes the results come back in the middle.... Then you are in the same situation. (P8)</li> </ul>



information. The GEP testing was viewed as introducing additional information that patients needed to understand. When GEP testing was ordered, the second visit after 2 weeks was necessary so that the patient could receive test results.

In addition to increasing the length of consultations and adding an extra visit, many oncologists described having to develop alternative or additional procedures. Strategies such as preparing patients for GEP test results or having patients pre-emptively sign GEP test consent forms in advance when hormone receptor results were unavailable at the time of the consult (so that patients did not have to return to the cancer centre solely to sign the consent form) became part of usual practice for the participants.

### ***Factors Affecting the Use of GEP Test Results in Treatment Decision-Making***

Oncologists described several factors that affected their use of GEP testing in treatment decision-making (Table III), including concerns about overtreatment in early-stage breast cancer, interpretation of the GEP test results in the context of clinicopathologic factors, the potential to use GEP test results in patient and oncologist decision-making, whether GEP test results served to reaffirm the oncologist's own opinion, perceived confidence in the evidence underpinning GEP test results, and difficulties with intermediate test results.

***Concerns About Overtreatment in Early-Stage Breast Cancer:*** Oncologists raised concerns about overtreatment in patients with early-stage breast cancer and hoped that GEP testing could be used to avoid chemotherapy. Several oncologists reflected that they had been trained to overtreat patients with chemotherapy, and they questioned the benefit of such therapy when the patient's risk of recurrence was low. Other oncologists described changes that they had experienced over time, with chemotherapy increasingly being offered to patients with smaller tumours, which contributed to the potential for overtreatment.

I do worry more about overtreating, because I think we have spent the last 30 years saying that chemo is good, more is better, and now we are treating tumours that are less than a centimetre in size. Well, the benefit that you are getting there is so small, is it really correct to do that?

— P21

One oncologist described having been trained to overtreat patients and becoming “unusually comfortable with overtreating; we are trained to overtreat” (P16).

***Interpretation of the GEP Test Results in the Context of Clinicopathologic Features:*** Most participants viewed GEP test results as another tool to guide treatment decision-making. They were reluctant to devalue the contribution of traditional clinicopathologic features of the patient's breast cancer in favour of test results. However, when oncologists were uncertain about the value of chemotherapy, they were willing to place more emphasis on test results. Oncologists commonly referred to these patients as being in the “grey zone.”

I use [GEP testing] as an additional tool apart from all the clinical characteristics and the patient assessment. There [are] a lot of things that go into whether we have to give chemo to this patient, whether or not this patient can tolerate chemo.... [Name of test] is one extra piece, not the only piece. But it might help me in those grey-zone patients.

— P12

However, in situations in which test results differed from the expected, and particularly when scores were higher, oncologists said that they might weigh GEP testing results more heavily when recommending treatment to patients.

### ***Potential to Use GEP Test Results in Oncologist and Patient Treatment Decision-Making:***

Most oncologists were comfortable with ordering GEP testing for patients who met the eligibility criteria; however, they indicated that the results had to be potentially useful for oncologist and patient decision-making. If the oncologist believed that the results would not affect decisions about treatment (for example, if the patient would not consider chemotherapy regardless of results), they would not order the test. Similarly, if the patient wanted to do everything possible to reduce their risk of recurrence and if the oncologist already believed that the patient had high-risk features, then the oncologist would not order the test. As one oncologist explained:

If [the GEP test] changes the clinical decision ... then I order the test. If it doesn't change the clinical decision, then I would not.

— P12

### ***GEP Test Results Serve to Affirm the Oncologist's Opinion:***

Approximately half the oncologists indicated that GEP test results provide an opportunity to reaffirm the oncologist's expectations and treatment recommendations. When the test results reaffirmed their own opinion, it gave them more confidence in their treatment recommendation.

### ***Perceived Confidence in the Evidence Underpinning GEP Test Results:***

Most oncologists reported feeling confident that GEP tests are based on good science. They acknowledged that, although the tests are not perfect, they are the “best we have for now.” However, several oncologists indicated that the evidence underpinning the test was not sufficiently robust for them to place a high weight on test results for decision-making; they were awaiting stronger evidence from studies then underway. Those oncologists relied more heavily on clinicopathologic features such as tumour size and grade.

### ***Difficulties with Intermediate Test Results—“Back to Where You Started”:***

Every oncologist expressed some frustration with intermediate test results. Oncologists indicated that some patients might have only 1 concerning clinical feature, and they had doubts about whether the benefits of chemotherapy would outweigh the risks. When GEP test results were intermediate, they described being back to where they had started with respect to treatment decision-making.

## DISCUSSION

In the present study, we examined the experiences of medical oncologists in incorporating GEP testing into clinical practice and the views of those oncologists about the effect of test results on treatment decision-making under circumstances in which robust evidence for the test's clinical utility was still emerging. Our work contributes to the literature by describing formal and informal learning about GEP testing, adjustments that oncologists made to their clinical practice when using GEP testing, and the views of those oncologists about factors affecting the use of GEP testing in treatment decision-making.

Oncologists described several sources of information about GEP testing. Many of the listed sources were not unexpected; they can be considered to be familiar and traditional venues—such as the American Society of Clinical Oncology annual meeting. However, the concerns expressed by several oncologists about the role of manufacturer-supported meetings in their learning about GEP testing was unexpected. Several oncologists were critical of those sources and questioned the role in learning that those sources played compared with sources such as academically-based oncologists. The extent of the manufacturer role as a key source of new GEP testing-related knowledge for oncologists is not well known, and further research is required.

In adopting GEP testing, oncologists described adjustments to their day-to-day work, including longer consultations and extra visits. The GEP test was not the sole reason for the changes, but was perceived to be a significant contributing factor. Oncologists described an increased level of stress with the longer consultations and delayed clinics, which suggests that the addition of GEP testing and the increasing complexity of breast cancer management might contribute to broader negative issues in the day-to-day work of oncologists. Grunfeld *et al.*<sup>24</sup> conducted a survey and 17 focus groups with Canadian cancer workers including medical oncologists, allied health professionals, and clerical staff. Survey results indicated that 46% of the oncologists endorsed having high job stress. Results from the focus groups indicated that a heavy and increasing workload was a key source of job stress. More recently, Shanafelt *et al.*<sup>25</sup> reported that approximately 45% of surveyed oncologists in the United States reported at least 1 symptom of burnout. Moreover, an independent predictor of burnout in the study was the number of hours per week spent in direct patient care<sup>25</sup>. The introduction of GEP testing might not solely contribute to burnout, but longer consultations and delays in clinics might result in additional hours of direct patient care.

Oncologists also expressed concerns about treatment delays with GEP testing. Similarly, Bombard *et al.*<sup>26</sup>, who interviewed oncologists and patients about access to GEP testing, found concerns about treatment delays. The extent to which and the ways in which oncologists adjust their clinical practice to accommodate new technologies and the resulting implications for their day-to-day work needs further investigation.

During the interviews, oncologists raised concerns about overtreating women with early-stage breast cancer

using chemotherapy, a view supported by others<sup>13,27</sup>. It is possible that the backdrop of overtreatment concerns might predispose oncologists to order GEP testing where uncertainty exists about the risk of recurrence, despite some having misgivings about the quality of the evidence underpinning the test. Moreover, several oncologists believed that they had been trained to overtreat patients, which raises considerations for future residency training.

Oncologists had various views about the strength of the evidence supporting GEP testing, with several oncologists expressing some skepticism about the existing data. Their opinions of the evidence appeared to affect their views of GEP test results in decision-making, with several oncologists using test results as one piece of a larger puzzle rather than relying more heavily on the results, as was the case for other oncologists. Our findings are similar to those of Spellman *et al.*<sup>28</sup>, who found that oncologists were concerned that too much weight was given to test results rather than to other clinical data.

At the time of the interviews, the preliminary results of TAILORX<sup>29</sup> were not available. Early results from that trial demonstrated that patients who had a very low recurrence score (0–10) and who received endocrine therapy alone (that is, no chemotherapy) experienced very low recurrence rates at 5 years<sup>29</sup>. Had those results been available, participants might have had a different view of the evidence. Nevertheless, our results underline the challenges in using information from new technologies such as GEP testing for treatment decision-making when evidence based on rigorously designed studies is still emerging.

Despite misgivings by some oncologists about the evidence underpinning the tests, those individuals are incorporating GEP testing into treatment decision-making. Augustovski *et al.*<sup>10</sup> conducted a systematic review and summarized the effect of GEP test results on treatment decision-making by oncologists. The review indicated that GEP test results were associated with changes in the oncologist's treatment recommendation for about 30% of patients, leading to a reduction in chemotherapy of about 12% in patients with low risk scores<sup>10</sup>. Levine *et al.*<sup>12</sup> recently published results from a population-based cohort study that evaluated the influence of GEP test results on treatment decision-making by oncologists. They found that GEP test results were associated with changes in recommendations for about 50% of patients, with the major effect of avoidance of chemotherapy for patients with intermediate or high risk of recurrence as assessed using Adjuvant! Online (Ravdin PM, San Antonio, TX, U.S.A.)<sup>12</sup>. Specifically, they found that oncologists changed their recommendation from unsure or chemotherapy to no chemotherapy in 365 of 972 patients and from unsure or no chemotherapy to chemotherapy in 143 of 972 patients<sup>12</sup>. Our study, which included oncologists who participated in the Levine *et al.* study, supports their findings. In our study, oncologists described changing their treatment recommendation in the face of “surprising” test results. They recalled more often changing their recommendation away from chemotherapy to hormonal treatment alone, but also recalled patients for whom they recommended chemotherapy after receiving test results. Oncologists appeared to seek confirmation of their treatment recommendation through GEP testing. In circumstances

in which the results of GEP testing did not confirm their original opinion, oncologists might be more likely to change their treatment recommendation. Our results were similar to those of Bombard *et al.*<sup>30</sup>, who found that the self-perceived confidence of oncologists in their decision-making was enhanced through the use of GEP testing.

## Study Limitations

Our study was conducted in 8 communities, including both academic and community practices, with 78% of oncologists agreeing to participate. Although we reached saturation after 18 interviews, we interviewed another 3 oncologists to ensure that important information was not missed. Oncologists volunteered to participate in the study, and we cannot be certain that participant views would be similar to the views of oncologists who did not volunteer.

The experience of many oncologists in our study could have been influenced by their participation in a field study that was conducted concurrently by other investigators<sup>12</sup>. In that study, oncologists were asked to state their recommendation for chemotherapy before and after reviewing GEP test results. Their experiences would likely have made them more aware of how GEP test results affected their decision-making. We do not know if their opinions would have been different had they not participated in the field study.

## CONCLUSIONS

The process by which oncologists learned about GEP testing was gradual and appeared largely unstructured, with some influence of manufacturer-sponsored meetings on awareness about and adoption of the test. Incorporation of the test into clinical practice in early-stage breast cancer required oncologists to make changes to their usual practice routines. Opinions about the quality of evidence underpinning the test affected the weight given to test results in treatment decisions.

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## CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology's* policy on disclosing conflicts of interest, and we declare that we have none.

## AUTHOR AFFILIATIONS

\*Department of Family and Community Medicine, University of Toronto, Toronto; <sup>†</sup>Department of Oncology and <sup>‡</sup>Department of Epidemiology and Biostatistics, McMaster University, Hamilton; <sup>§</sup>The Wilson Centre, University of Toronto, Toronto; <sup>||</sup>Division of Medical Oncology, Princess Margaret Cancer Centre, Toronto; and <sup>#</sup>Ontario Institute for Cancer Research, Toronto, ON.

## REFERENCES

- Paik S, Shak S, Tang G, *et al.* A multigene assay to predict recurrence of tamoxifen-treated, node-negative breast cancer. *N Engl J Med* 2004;351:2817–26.
- Paik S, Tang G, Shak S, *et al.* Gene expression and benefit of chemotherapy in women with node-negative, estrogen receptor-positive breast cancer. *J Clin Oncol* 2006;24:3726–34.
- Lo SS, Mumby PB, Norton J, *et al.* Prospective multicenter study of the impact of the 21-gene recurrence score assay on medical oncologist and patient adjuvant breast cancer treatment selection. *J Clin Oncol* 2010;28:1671–6.
- Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group. Recommendations from the EGAPP Working Group: does the use of Oncotype DX tumor gene expression profiling to guide treatment decisions improve outcomes in patients with breast cancer? *Genet Med* 2016;18:770–9.
- Ward S, Scope A, Rafia R, *et al.* Gene expression profiling and expanded immunohistochemistry tests to guide the use of adjuvant chemotherapy in breast cancer management: a systematic review and cost-effectiveness analysis. *Health Technol Assess* 2013;17:1–302.
- Health Quality Ontario. Gene expression profiling for guiding adjuvant chemotherapy decisions in women with early breast cancer: an evidence-based and economic analysis. *Ont Health Technol Assess Ser* 2010;10:1–57. [Available online at: [http://www.hqontario.ca/Portals/0/Documents/evidence/reports/gep\\_20101213.pdf](http://www.hqontario.ca/Portals/0/Documents/evidence/reports/gep_20101213.pdf); cited 22 February 2017]
- National Comprehensive Cancer Network (NCCN). *NCCN Clinical Practice Guidelines in Oncology: Breast Cancer. Ver. 2.2016*. Fort Washington, PA: NCCN; 2016. [Current version available online at: [https://www.nccn.org/professionals/physician\\_gls/pdf/breast.pdf](https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf) (free registration required); cited 22 February 2017]
- Goldhirsch A, Winer EP, Coates AS, *et al.* on behalf of the panel members. Personalizing the treatment of women with early breast cancer: highlights of the St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer. *Ann Oncol* 2013;24:2206–23.
- Chang MC, Souter LH, Kamel-Reid S, *et al.* on behalf of the Molecular Oncology Advisory Committee. *Clinical Utility of Multigene Profiling Assays in Early-Stage Breast Cancer*. Toronto, ON: Cancer Care Ontario; 2016. [Available online at: <https://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=362126>; cited 22 February 2017]
- Augustovski F, Soto N, Caporale J, Gonzalez L, Gibbons L, Ciapponi A. Decision-making impact on adjuvant chemotherapy allocation in early node-negative breast cancer with a 21-gene assay: systematic review and meta-analysis. *Breast Cancer Res Treat* 2015;152:611–25.
- Hassett MJ, Silver SM, Hughes ME, *et al.* Adoption of gene expression profile testing and association with use of chemotherapy among women with breast cancer. *J Clin Oncol* 2012;30:2218–26.
- Levine MN, Julian JA, Bedard PL, *et al.* Prospective evaluation of the 21-gene recurrence score assay for breast cancer decision-making in Ontario. *J Clin Oncol* 2016;34:1065–71.
- Gnant M, Steger GG. Fighting overtreatment in adjuvant breast cancer therapy. *Lancet* 2009;374:2029–30.
- Creswell JW. *Qualitative Inquiry and Research Design: Choosing Among Five Approaches*. 2nd ed. Thousand Oaks, CA: Sage Publications; 2006.
- Pope C, van Royen P, Baker R. Qualitative methods in research on healthcare quality. *Qual Saf Health Care* 2002;11:148–52.
- Patton MQ. The nature of qualitative inquiry. In: *Qualitative Research and Evaluation Methods*. 3rd ed. Thousand Oaks, CA: Sage Publications; 2001.
- Cancer Care Ontario (cco). Incidence and Mortality by Local Health Integration Network (LHIN) [Web page]. Toronto, ON: cco; 2012. [Available at: <https://www.cancercare.on.ca/cms/One.aspx?portalId=1377&pageId=121943#one-tab>; cited 22 February 2017]
- Crabtree B, Miller W, eds. *Doing Qualitative Research*. 2nd ed. Thousand Oaks, CA: Sage Publications; 1999.

19. Glaser BG, Strauss AL. *The Discovery of Grounded Theory: Strategies for Qualitative Research*. New Brunswick, NJ: Aldine Transaction Publishers; 1967.
20. Charmaz K. *Constructing Grounded Theory: A Practical Guide Through Qualitative Analysis*. Thousand Oaks, CA: Sage Publications; 2006.
21. Boeije H. A purposeful approach to the constant comparative method in the analysis of qualitative data. *Qual Quant* 2002;36:391–409.
22. Bowen G. Naturalistic inquiry and the saturation concept. *Qual Res* 2008;8:137–52.
23. Guba EG, Lincoln YS. *Fourth Generation Evaluation*. Thousand Oaks, CA: Sage Publications; 1989.
24. Grunfeld E, Zitzelsberger L, Coristine M, Whelan TJ, Aspelund F, Evans WK. Job stress and job satisfaction of cancer care workers. *Psychooncology* 2005;14:61–9.
25. Shanafelt TD, Gradishar WJ, Kosty M, *et al.* Burnout and career satisfaction among U.S. oncologists. *J Clin Oncol* 2014;32:678–86.
26. Bombard Y, Rozmovits L, Trudeau M, Leighl NB, Deal K, Marshall DA. Access to personalized medicine: factors influencing the use and value of gene expression profiling in breast cancer treatment. *Curr Oncol* 2014;21:e426–33.
27. Katz SJ, Morrow M. Addressing overtreatment in breast cancer: the doctors' dilemma. *Cancer* 2013;119:3584–8.
28. Spellman E, Sulayman N, Eggly S, *et al.* Conveying genomic recurrence risk estimates to patients with early-stage breast cancer: oncologist perspectives. *Psychooncology* 2013;22:2110–16.
29. Sparano JA, Gray RJ, Makower DF, *et al.* Prospective validation of a 21-gene expression assay in breast cancer. *N Engl J Med* 2015;373:2005–14.
30. Bombard Y, Rozmovits L, Trudeau M, Leighl NB, Deal K, Marshall DA. The value of personalizing medicine: medical oncologists' views on gene expression profiling in breast cancer treatment. *Oncologist* 2015;20:351–6.