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ORIGINAL ARTICLE

# Patients' perceptions of gene expression profiling in breast cancer treatment decisions

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## ABSTRACT

### Introduction

Determining the likely benefit of adjuvant chemotherapy for early-stage breast cancer patients depends on estimating baseline recurrence risk. Gene expression profile (GEP) testing of tumours informs risk prediction, but evidence of its clinical utility is limited. We explored patient perceptions of GEP testing and the impact of those perceptions on chemotherapy decisions.

### Methods

We conducted one focus group ($n = 4$) and individual interviews ($n = 24$) with patients who used GEP testing, recruited through clinics at two hospitals in Ontario. Data were analyzed using content analysis and constant comparison techniques.

### Results

Patients' understanding of GEP testing was variable, and misapprehensions were common. Patients valued the test because it provided them with certainty amidst confusion, with options and a sense of empowerment, and with personalized, authoritative information.

They commonly believed that the test was better and fundamentally different from other clinical tests, attributing to it unique power and truth-value. This kind of "magical thinking" was derived from an amplified perception of the test's validity and patients' need for reassurance about their treatment choices. Despite misperceptions or magical thinking, GEP was widely considered to be the deciding factor in treatment decisions.

### Conclusions

Patients tend to overestimate the truth-value of GEP testing based on misperceptions of its validity. Our results identify a need to better support patient understanding of the test and its limitations. Findings illustrate the deep emotional investment patients make in GEP test results and the impact of that investment on their treatment decisions.

## KEY WORDS

Gene expression profiling, breast cancer, patient perceptions, chemotherapy, decision-making, genomics, risk recurrence, personalized medicine

## 1. INTRODUCTION

Current guidelines for the management of early-stage breast cancer result in thousands of women receiving chemotherapy without benefit[1]. Clinical guidelines suggest that 90% of the 22,600 Canadian patients with human epidermal growth factor receptor 2–negative, node-negative, hormone receptor–positive disease should be offered adjuvant chemotherapy[1–4]. Yet it is estimated that only 15% of such cancers will recur, suggesting that about 8500 Canadian patients will be treated without benefit each year[2–5].

Distinguishing patients who likely will benefit from those who might not depends on baseline recurrence risk. Traditionally, recurrence risk assessments are based on several prognostic factors, including tumour size, tumour grade, nodal involvement, and hormone receptor status[2,3,5]. Gene expression profiling (GEP) tests measure the expression levels of a set of prognostically relevant genes to predict the likelihood of distant recurrence at 10 years and the likely benefit from chemotherapy. In retrospective studies, several GEP tests have been validated as prognostic of distant disease recurrence and predictive of the benefit of adjuvant chemotherapy for patients with estrogen receptor–positive disease[6–10]. The resultant recurrence scores classify patients into groups with poor or good prognosis (likelihood of recurrence outside the breast in the next 10 years). Those with low recurrence scores

have a low likelihood of recurrence and will likely derive little or no benefit from chemotherapy; those with high risk recurrence scores have a higher likelihood of recurrence and will likely derive high benefit from adjuvant chemotherapy. The likelihood of benefiting from chemotherapy among those receiving intermediate recurrence risk scores is unknown and is the subject of the TAILORx study[11].

Thus, GEP testing might further inform baseline risk prediction, potentially reducing unnecessary treatment, exposure to toxicity, and considerable health care costs[12]. Health technology assessment agencies in the United Kingdom, the United States, and Canada have evaluated GEP tests[13–15]. Although the assessments have raised questions about the predictive and prognostic validity of GEP tests[13,14,16], the tests have been recommended for clinical practice to complement conventional risk-of-recurrence assessments and are increasingly being integrated into clinical practice in the United States and Canada[3,5,17].

Despite the diffusion of GEP tests into clinical practice, relatively little is known about their impact on chemotherapy decisions. Several studies have demonstrated that GEP results are an important factor in the treatment recommendations made by oncologists[18–21]. Studies also indicate that patients are interested in receiving GEP tests and that, in surveys posing hypothetical questions, GEP results would affect patient treatment preferences to a greater extent than do standard recurrence measures. However, patients' understanding of the results varies depending on their knowledge and health literacy scores[22–28]. Yet, in this era of shared decision-making, no study has addressed patient perceptions and experiences of GEP testing in informing actual treatment decisions in breast cancer or cancer contexts. Moreover, there is a paucity of evidence on why and how the tests inform treatment decisions made by patients, taking into account the range of clinical and contextual factors at play during the decision-making process. The aim of the present study was to gain insight into patient perceptions of the value of GEP testing and the perceived impact of the results on chemotherapy treatment decisions.

## 2. METHODS

### 2.1 Study Design

This qualitative study is part of a larger, mixed-methods study to examine the value of the GEP test for breast cancer patients and medical oncologists. The first phase was the present qualitative study, which used a focus group and interviews. In the second phase, a quantitative survey that included a discrete choice experiment to estimate the utility of the GEP test relative to other factors was completed by a nationally representative sample of oncologists, women with a history of breast cancer, and adult women from the public, with survey sampling performed using an online survey panel (manuscripts forthcoming). The research ethics boards at St. Joseph's Hospital, Sunnybrook Health Sciences Centre, and Princess Margaret Hospital approved the study. All participants provided informed consent before taking part in this study.

### 2.2 Sample Recruitment

We recruited early-stage (stage I–II) breast cancer patients who had completed surgical treatment and used GEP testing in their chemotherapy decisions. We targeted patients who were offered the GEP test after initiation of public funding in Ontario in March 2010. Participants in the TAILORx trial[11] were ineligible, because that trial began before initiation of public funding for GEP testing, creating inherent differences in how patients accessed and used the GEP test.

Eligible patients who were scheduled for routine follow-up visits were identified from clinical records by participating oncologists and designated site coordinators at two academic hospitals in Toronto, Ontario. Coordinators attended follow-up clinics and offered information about the study to eligible patients. Interested patients were invited to contact the qualitative researcher to discuss the study, arrange participation, and give consent. The qualitative researcher contacted eligible patients who indicated interest but who did not call the qualitative researcher within a few weeks. At one of the clinics, the study was introduced to patients by their oncologist at their follow-up visit, and the site coordinator then provided further information if the patient was interested in participating in the study.

### 2.3 Data Collection

We conducted a focus group and interviews to accommodate patient schedules and to encourage maximum participation. A semistructured discussion guide developed through literature review and clinical consultation elicited details of patient experiences of decision-making about treatment and the role that the GEP test played in that process (Appendix A). Areas of discussion included feelings previously held about chemotherapy, treatment discussions with the oncologist and other health care providers, attitudes toward and understanding of the GEP test, the treatment decision and factors influencing that decision, and impact of the GEP test on the decision-making process. Demographic data were collected in questionnaires administered before the interviews and the focus group.

### 2.4 Data Analysis

All qualitative data (focus group and interviews) were digitally audio-recorded for verbatim transcription.

All corrected transcripts were then merged into a single dataset and entered into a software program to code for both anticipated and emergent themes. Qualitative data were analyzed using content analysis and constant comparison techniques, which involved collecting data until saturation of themes was reached and included searches for disconfirming evidence[29]. Data were validated through peer-debriefing, during which developing themes and analyses were identified and discussed with the study team.

## 3. RESULTS

### 3.1 Patient Demographics

A total of 28 patients participated in the study from 2010-2011 (focus group: $n = 4$; telephone interviews: $n = 24$). Most of the patients in our sample were married (61%), had children (67%), were highly educated (79%), and did not undergo chemotherapy (68% ; Table I).

TABLE I Patient demographics

| *Variable* | *Value [n (%)]* |
|---|---|
| Patients | 28 |
| Age group | |
| 30–39 Years | 3 (11) |
| 40–49 Years | 3 (11) |
| 50–59 Years | 11 (39) |
| 60–69 Years | 8 (29) |
| 70–79 Years | 3 (11) |
| Marital status | |
| Never married | 7 (25) |
| Married | 17 (61) |
| Separated, divorced, or widowed | 4 (14) |
| Children | |
| 1 or more | 18 (67) |
| Highest level of education ($n$=27) | |
| Elementary, some high school, or high school diploma | 4 (14) |
| Completed university or college | 22 (79) |
| Other | 1 (4) |
| Employment status ($n$=26) | |
| Employed | 14 (50) |
| Unemployed | 3 (11) |
| Retired | 8 (29) |
| Other | 1 (4) |
| Chemotherapy treatment | |
| Yes | 9 (32) |
| No | 19 (68) |

### 3.2 Patient Understanding and Misunderstanding of GEP

Many patients understood the predictive aspect of the GEP test, which is to provide an indication of whether chemotherapy would be beneficial in their case. However, many also appeared to be confused about the prognostic aspect of the test and what it could tell them about their chance of cancer recurrence. For example, one woman believed that the test would indicate what caused her cancer, that her cancer would certainly recur, and that the test would tell her whether it would recur sooner (without chemotherapy) or later (with chemotherapy):

> Because I have no family history of breast cancer, so that's why [the oncologist] would like to know more clear what was causing that, or something.... If I'll do the chemo it will be coming back in fifteen to twenty years, and if I'm not doing the chemo it will be five to ten years.
> — Patient 2 in focus group 2

In addition, many participants appeared to have been overwhelmed by the results, providing confused accounts of numbers, charts, and graphs showing recurrence risks that they found difficult to interpret. There were also misapprehensions about the laboratory analyses involved. For example, one woman believed that the test involved injecting tumour samples with chemotherapy drugs to determine response:

> My understanding is they actually take a sample of the tumour ... and they run it against the actual chemo to see how it responds.
> — Patient 17 in interview

### 3.3 The Value of GEP in Treatment Decisions

Patients described emotionally and socially complex reasons why they valued GEP testing in making their treatment decisions. Those reasons were often shaped by pre-existing beliefs and expectations of chemotherapy, which derived from sources such as prior experience of caring for a friend or relative with cancer, media representations of cancer treatment, and Internet or book-based research. Some held negative views of chemotherapy and anticipated undesirable effects on their work, lifestyle, and family. Others were open to taking chemotherapy because they wanted to feel that they had done everything possible to fight their cancer. Expectations about chemotherapy were also informed by the rapport with providers, often in relation to the willingness of the patient's oncologist to be consultative and the degree of confidence instilled as a result. It was against this backdrop of pre-existing beliefs about chemotherapy and

interactions with providers that patients valued the GEP test, because it provided them with certainty amidst confusion, with options, and a sense of empowerment, and with personalized, authoritative information.

#### *3.3.1 Certainty Amidst Confusion*

Many patients described discomfort in making decisions based on the opinions of their oncologist—despite considering those providers to be medically competent—because they had received conflicting opinions from other clinicians responsible for their care. For women in that position, GEP test results were perceived as providing a more stable platform from which to act and a degree of clarity that had otherwise been absent:

> It's hard because you get different people explaining their area to you. It's so specialized, you know? ... Well, let's just say it didn't paint a very clear picture ... and that's why the genome testing is so important.
> — Patient 10 interview

#### *3.3.2 Options and a Sense of Empowerment*

In situations in which rapport between the patient and oncologist was poor, or in which the patient had lost confidence in her oncologist, the test was experienced as compensating for the failure of the relationship. For example, one woman contrasted the doctrinaire manner of a first oncologist with the approach of a second who used the test as part of a shared decision-making process in which a number of options were considered:

> [The GEP test] also opened up a dialogue.... The first oncologist I talked to was just very cut-and-dry, like, ... "You have no options here." And so to deal with what you're dealing with, plus the fact that you have no options, no voice ... It was just overwhelming.... The two experiences were in stark contrast in terms of one oncologist saying, "Yeah, there are no other sources of information, you have no other options, you have to do this," versus, "Yeah, we do have options, we can do no chemo or we could do four rounds or we could do six rounds ... Let's gather our resources so we can figure out the right one for you."
> — Patient 14 interview

As the preceding example illustrates, the GEP test brokered a dialogue for some women where previously none had existed. As a consequence, it was perceived as providing options at a difficult moment in their lives, allowing them to feel like active agents rather than passive recipients of care, regardless of whether it changed their treatment decision.

#### *3.3.3 Personalized, Authoritative Information*

Patients also valued the GEP test because they believed it provided them with more personalized, authoritative information than other clinical tests and medical opinions. Many expressed discomfort with the notion that treatment decisions based on traditional risk stratification markers (tumour size, tumour grade, nodal involvement, and hormone receptor status) would be protocol-driven or statistically-derived. They believed that the GEP test reflected their unique circumstances, detached from statistics:

> It meant that I wasn't just going to be lumped in with statistics.... I certainly felt that with this kind of tailored or personalized kind of investigation ... "guesswork" was going to disappear.
> — Patient 9 interview

Moreover, patients did not generally understand that the test is based on population-based estimates derived from sample cohort data. They believed that information unique to them was being returned, in contrast with the statistical estimates patients receive based on the pathology assessment of their tumours (size, grade, nodal involvement, and hormone receptor status):

> It would actually take something concrete from my body and it would use a finer scientific way of actually deciding ... what treatment would best benefit me. It would not be based on others people's statistics, mortality rates.... It would define my risk factors.
> — Patient 26 interview

In addition, the test was valued for providing what was perceived to be higher-calibre information. The feeling that the GEP test was state-of-the-art, more scientific, and therefore more reliable was commonly expressed:

> He delineated them as fantastically precise measurement. They showed that there was absolutely no, no reason, a zero factor, to participate in chemo or radiation.... I said, "There couldn't have been a better gift in my life than that...." It was the greatest gift I'd ever been given.
> — Patient 26 interview

This amplified perception of GEP's scientific accuracy characterized a type of emotionally-invested "magical thinking" that underpinned perceptions of the test.

### 3.4 Magical Thinking

Perceptions of the GEP test by patients were linked to the value and the symbolic importance that some

patients ascribed to it. In this sense, a type of "magical thinking" underpinned their perceptions of the test, which was founded on a belief that GEP testing had unique scientific power and, therefore, truth-value. The presumed validity of the results was a key feature of the test for many patients, with very few questioning or even discussing the test's potential limitations with their oncologist. When prompted to think about why they hadn't considered the possible limitations of the test, several participants identified emotional reasons for not doing so:

> I didn't ask, and it's something I would normally ask.... I think probably I just wanted to take it at face value. I don't know.... I didn't think about it 'til just now, but when you said that, I thought, "Well, why didn't I ask?" I don't know why I didn't. I think I was so happy about what I was seeing on that paper, and hearing from her, that I didn't question it.
> — Patient 2 in focus group 2

> You want to believe something like that because you don't want to go through something so horrible ... [and] so, I mean, there's a willful ... suspension of disbelief, you know?
> — Patient 17 interview

The suggestion that there might be cause to question the validity of the test led one woman to become angry. Like others, she admitted (in this case, unwittingly) that her emotional investment in the test had precluded any such questioning:

> The terminology here is very scientific.... It tells you how many patients that this research is based on, in what situation.... You even get graphs.... It's statistically significant information; nothing here is fluff the way I see it.... I would not even want anybody to question that, because for me this test is my reassurance that I did the right thing. I think it's bogus that people would question the validity of testing 21 genes.
> — Patient 10 interview

In one exceptional case, a patient did conduct more detailed, independent research and discovered that the test was limited in ways that proved disappointing:

> The recurrence score was based on people who had larger tumours, or a higher grade, or had already taken the tamoxifen ... which I kind of didn't realize at the time—that it was a very limited population that they got their results from.
> — Patient 7 interview

For some, an additional factor bolstering the presumed validity of the test was the public funding for it:

> I had no idea there was even another world out there that wouldn't be supporting the test.... The fact that's covered tells me that it's absolutely supported, right?
> — Patient 4 in focus group 1

A high emotional investment was placed in the test. The test was perceived as more emotionally significant than other conventional risk stratification marker information (tumour size, tumour grade, nodal involvement, and hormone receptor status) that they had received. The investment is reflected in the structure of narratives that frequently position the test as a beacon of hope in the darkest hour:

> Anything that happened after that [diagnosis] was like pulling me out of a pit, [and] so to have a little bright light like the suggested possibility that I won't have to fill my body with toxic chemicals, take six months off work, interrupt my entire life and live for a disease and lose my mind halfway—that became the biggest flicker of hope.
> — Patient 17 interview

Several women who had their scheduled chemotherapy cancelled at the last minute saw the GEP test result as a quasi-miraculous occurrence:

> I was just getting ready to do chemo, [and] so it was ... like I'd won the lottery.
> — Patient 20 interview

For these patients, the turnaround heightened the importance that they had attached to the test because of the sense of having been "rescued" from additional hardship.

### 3.5 The Deciding Factor in Treatment Decisions

Some patients described the test as one of many factors considered in their decision, but the indication most widely shared was that the test results had been the deciding factor, over and above all other considerations. This was true for patients who were initially reluctant to undergo chemotherapy, but who were persuaded of its importance because of the test results, and for patients facing the opposite scenario of wanting reassurance that foregoing chemotherapy would be justified in their case despite the popular notion that it is the standard of care:

> I may not have done chemotherapy. I'm pretty sure I wouldn't. I was resisting it all the way

> along the line, and I hadn't heard anything ... up to that point that was convincing me to do something I didn't want to do.... But the test, it was, like, staring me in the face, saying, "This is recommended. This would be the treatment option that would be beneficial for you." ... Well, how do you fly in the face of that? ... It really was, for me, the definitive thing. Without that test, I don't know. I don't think I would have.
> — Patient 3 in focus group 1

> Had I not done the test, I would have done chemo.... If they had said to me, "You need to do chemo," I would have just done it. I wouldn't have questioned that, but because of the results I had, I felt comfortable not doing chemo.
> — Patient 20 interview

Ultimately, patients followed the course of action that their results suggested, despite the misperceptions or magical thinking that the test engendered. A number of patients received intermediate test results that pointed to no clear course of action. In those cases, patients generally interpreted the results to mean whatever they wanted them to mean, aligning them with their pre-existing treatment preferences. That finding might provide a further indication of emotionally-informed magical thinking.

## 4. DISCUSSION

As one of the first qualitative studies of patients' perceptions of GEP testing, this work presents novel insights into how and why patients valued the GEP test in their treatment decisions. Patients often viewed their GEP results as providing information that was more scientifically valid, uniquely personalized, and emotionally significant than any other information they had received. In many of the patient narratives, the test figured as a transformational element that empowered them, allowed them to feel confident in their decisions, and in many cases, rescued them from unnecessary chemotherapy.

Participants understood that the test would indicate whether chemotherapy would or would not be beneficial in their care, but they generally did not understand that their results were founded on a population-based derivative. Furthermore, the suggestion that the test should be viewed as critically as any other technology was very uncomfortable for them to consider. Some acknowledged that they had willingly suspended critique because they needed something to provide a sense of certainty in the midst of such a difficult situation.

Our study has several limitations. The participant group comprised mainly highly educated women, all of whom used GEP testing and who were drawn from two tertiary centres. The findings might also reflect a degree of self-selection, in that some participants had seen their oncologist's original recommendation overturned by the test results, which might have provided motivation to share their story. Also, the subgroup of participants receiving intermediate results did not include anyone who experienced ongoing indecision after receiving their results.

This study did not interview matched sets of patients and oncologists. Nor was it designed to test patient comprehension or to explore provider efforts to explain the GEP test. For those reasons, it is not possible to describe a direct causal relationship between oncologists' explanation of GEP testing and what patients understood. However, our results are consistent with the literature demonstrating variability in how patients understand the tests and the interest of patients in using GEP tests to inform treatment decisions[22–28]. Nonetheless, no study has addressed patient perceptions and experiences of GEP testing in informing actual treatment decisions. Our study thus provides novel insights into how and why patients valued the test: it was seen as providing them with certainty amidst confusion, with options and a sense of empowerment, and with personalized, authoritative information. Ultimately, GEP was widely considered to be the deciding factor in treatment decisions, despite the misperceptions or magical thinking the test engendered.

## 5. CONCLUSIONS

Our results provide insight into an important paradox: patients tend to overestimate the truth-value of GEP testing based on misperceptions of its validity. These results identify a need for communication or decision aids to support patients' understanding of the test and its limitations. Finally, our results might also help to support provider awareness of the ways in which patients can be emotionally invested in their GEP results and the impact of those investments on treatment decisions.

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## 7. CONFLICT OF INTEREST DISCLOSURES

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## APPENDIX A: DISCUSSION GUIDE

People sometimes describe their cancer experience as a journey. What we'd like to hear about today is the part of your journey that involved making decisions about whether or not to have chemotherapy and then, more specifically, about the part that genetic profiling played in that decision-making process.

1. When did your oncologist first discuss the possibility of chemotherapy with you?

    - How soon after your diagnosis did that discussion begin?
    - Did your oncologist explain what he/she would be basing his/her recommendation on?
    - Had you already been thinking about chemotherapy before that time?
    - Did you have a feeling about whether you'd want to have chemo or not? What was this based on?

2. When did the idea of having genetic profiling enter the conversation?

    - Suggested by the oncologist because ...
    - I knew about it from media coverage/Internet/own research and asked about it ...
    - I knew about it from some other person and asked about it ...

3. What did you think about this test when you first found out about it?

    - What was your understanding of what it would tell you or how helpful the results would be?
    - If it was the medical oncologist's suggestion, did you want the test?
    - Did you have any hesitations about having it?
    - Did it seem easier/harder to understand than other tests/clinical indicators
    - How important or helpful did it seem to you in terms of the decision-making about chemotherapy?

4. So, what factors did you weigh up when you were deciding whether to have the test?

    - Oncologist's opinion
    - Prior feelings about it
    - Practicalities linked to personal circumstances
    - Experiences of others
    - Desire to do everything possible to treat the disease
    - Concern about side effects of treatment

5. Apart from the results of the genetic profiling, what other factors did you weigh up when you were deciding whether to have chemotherapy?
    - Oncologist's opinion
    - Prior feelings about it
    - Practicalities linked to personal circumstances
    - Experiences of others
    - Desire to do everything possible to treat the disease
    - Concern about side effects of treatment

6. As you know, the results of that test are grouped into categories: high/medium/low risk of recurrence over the next 10 years. What did those categories mean to you?

    - Did you think about high/medium/low in terms of percentages?
    - Did you think about the different categories and what you would do depending on which one you fit into?

7. Did your oncologist ever discuss the accuracy of the test with you? Was this something you thought about or tried to find out about on your own?

    - What was your understanding of how accurate the test is?
    - What was your understanding of how well it could predict your risk of recurrence in the future?
    - Risk can be a difficult concept sometimes. What did it mean to you?

8. Do you think there are any downsides to having a test like this?

    - Did you ever consider not having it?
      - Concerns about protecting information from genetic testing
      - Cost relative to value added
      - Uncertainty/potential inaccuracy of the test
      - Anxiety associated with waiting for results
      - False impression of certainty about the future
      - Inequities of access

9. So, in the end, what was the deciding factor for you in relation to chemotherapy?

    - Oncologist's recommendation
    - Family history
    - Personal preferences/priorities based on ...?
    - gep test results
    - Other test results
    - How big a part did gep play in the overall picture for you?
    - If you were leaning one way or another prior to the test, did it have any impact on your final decision?

10. Do you think your experience of decision-making about chemotherapy would have been different without access to this test?

    - Was it a substantial help to you in any way?
    - Did it make things more or less complicated?
    - Did it make you feel more/less involved in the decision-making?
    - Did it help you feel like you made the right decision for you?
    - Did it affect the way you feel about the future?

11. As you may know, genetic profiling for breast cancer patients is now being funded by OHIP. How do you feel about this?

    - Definitely should be funded
    - Our tax dollars could be better spent on some other aspect of health care
    - Not sure