The Influence of Gene Expression Profiling on Decisional Conflict in Chemotherapy Treatment Decisions for Early Stage Breast Cancer

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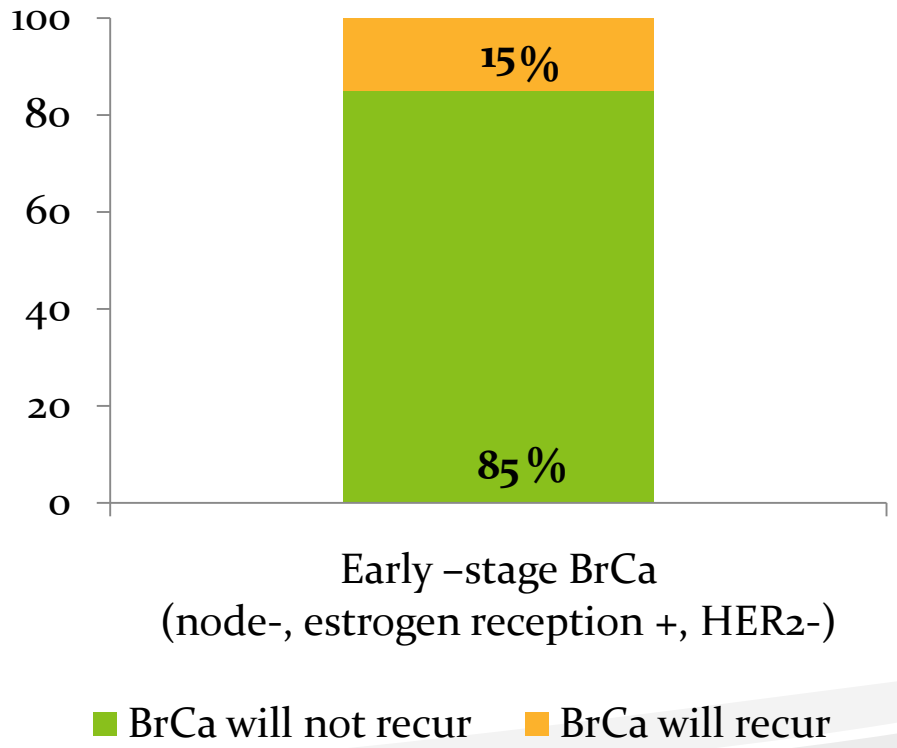
Background

Issue

- Women with early stage breast cancer (BrCa) are faced with challenging treatment decisions
- Guidelines recommend adjuvant chemotherapy for early-stage BrCa (node -, estrogen receptor +, HER2-)
  - Only 15% of these cancers will recur
  - Suggests 85% may be treated without benefit

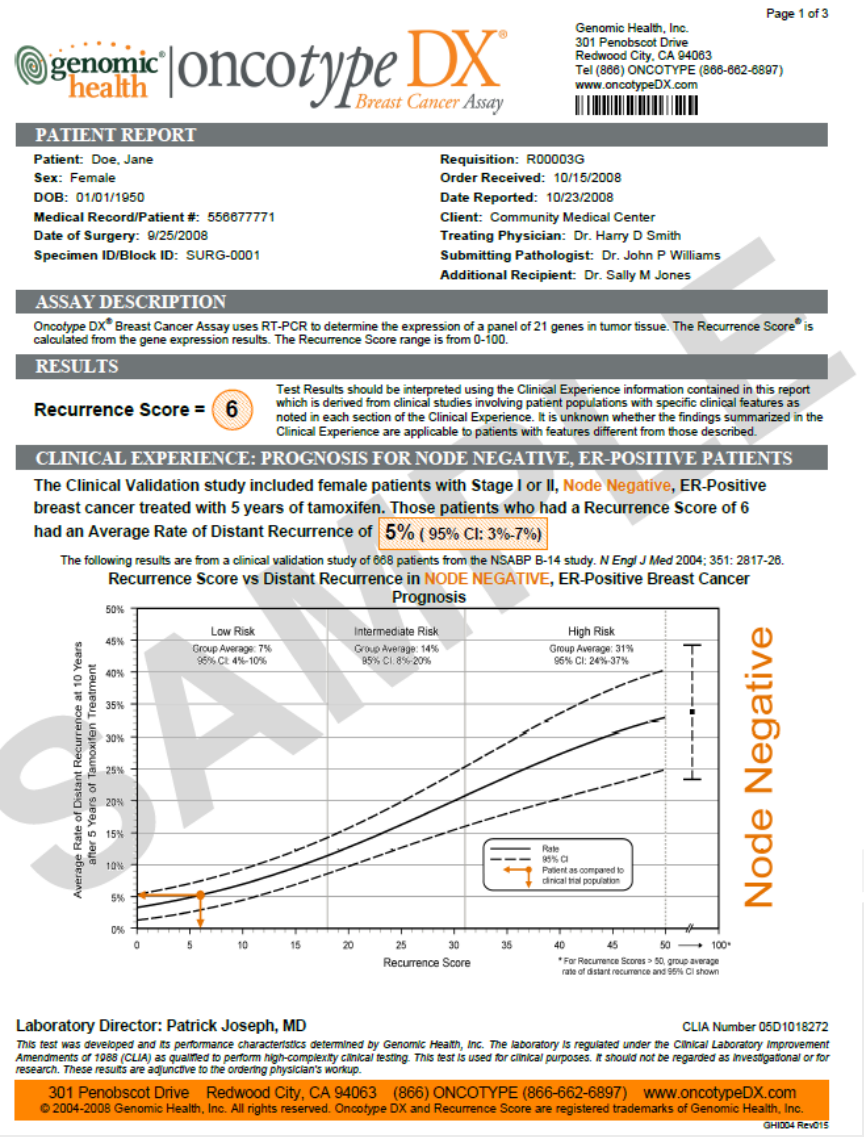
Patients potentially treated without benefit[1,2,3]



[1] Marchionni L, et al. Systematic review: Gene expression profiling assays in early-stage breast cancer. *Ann Intern Med* 2008.
[2] National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Breast Cancer V.I.2010. 2010.
[3] Goldhirsch A, et al. Highlights of the international expert consensus on the primary therapy of early breast cancer 2007. *Ann Oncol* 2007.

Gene Expression Profiling (GEP)

- Gene expression profiling (e.g. Oncotype DX) is a form of personalized medicine
- GEP provides information about the likelihood of BrCa recurrence in 10 years
- Identifies patients who may not benefit from chemotherapy
- Costs ~$4000
- Cost of test is currently covered in Saskatchewan, Ontario and Quebec



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genomic health | oncotype DX® Breast Cancer Assay

Genomic Health, Inc.
301 Penobscot Drive
Redwood City, CA 94063
Tel (866) ONCOTYPE (866-662-6897)
www.oncotypeDX.com

PATIENT REPORT

Patient: Doe, Jane
Sex: Female
DOB: 01/01/1950
Medical Record/Patient #: 556677771
Date of Surgery: 9/25/2008
Specimen ID/Block ID: SURG-0001

Requisition: R00003G
Order Received: 10/15/2008
Date Reported: 10/23/2008
Client: Community Medical Center
Treating Physician: Dr. Harry D Smith
Submitting Pathologist: Dr. John P Williams
Additional Recipient: Dr. Sally M Jones

ASSAY DESCRIPTION

Oncotype DX® Breast Cancer Assay uses RT-PCR to determine the expression of a panel of 21 genes in tumor tissue. The Recurrence Score® is calculated from the gene expression results. The Recurrence Score range is from 0-100.

RESULTS

Recurrence Score = 6

Test Results should be interpreted using the Clinical Experience information contained in this report which is derived from clinical studies involving patient populations with specific clinical features as noted in each section of the Clinical Experience. It is unknown whether the findings summarized in the Clinical Experience are applicable to patients with features different from those described.

CLINICAL EXPERIENCE: PROGNOSIS FOR NODE NEGATIVE, ER-POSITIVE PATIENTS

The Clinical Validation study included female patients with Stage I or II, Node Negative, ER-Positive breast cancer treated with 5 years of tamoxifen. Those patients who had a Recurrence Score of 6 had an Average Rate of Distant Recurrence of **5%** (95% CI: 3%-7%)

The following results are from a clinical validation study of 668 patients from the NSABP B-14 study. *N Engl J Med* 2004; 351: 2817-26.

Recurrence Score vs Distant Recurrence in NODE NEGATIVE, ER-Positive Breast Cancer Prognosis

Laboratory Director: Patrick Joseph, MD

CLIA Number 05D1018272

This test was developed and its performance characteristics determined by Genomic Health, Inc. The laboratory is regulated under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high-complexity clinical testing. This test is used for clinical purposes. It should not be regarded as investigational or for research. These results are adjunctive to the ordering physician's workup.

301 Penobscot Drive Redwood City, CA 94063 (866) ONCOTYPE (866-662-6897) www.oncotypeDX.com

GHI004 Rev015

Issue

- Decisional conflict:
  - "**a state of uncertainty about a course of action**" which is
  - "**more likely when making choices involving risk or uncertainty of outcomes**, high stakes in terms of potential gains and losses, the need to make value trade-offs in selection a course of action, and anticipated regret over the positive aspects of rejected options"
  - Can be decreased with decision supporting interventions[4]

[4] O'Connor A. Validation of a Decisional Conflict Scale. *Med Decis Making*. 1995.

GEP and decisional conflict

- In populations of women with BrCa:
  - Decisional conflict decreases after receiving GEP scores in real-life treatment decisions [5-7]
- To our knowledge, this has not been studied in a general population sample

[5] Sulayman N. Psychosocial and Quality of Life in Women Receiving the 21-Gene Recurrence Score Assay. *J Cancer Epi.* 2012.
[6] Lo S. Prospective Multicenter Study of Impact of 21-Gene Recurrence Score on MO and Patient BrCa Treatment Selection. *J Clin Oncol.* 2010.
[7] Davidson J. A prospective clinical utility and pharmacoeconomic study of the impact of the 21-gene recurrence score. *Eur J Canacer.* 2013.

Objective

- Examine if **learning about and receiving GEP** results **decreases decisional conflict** in a sample of **general population women** making a hypothetical chemotherapy decision

Hypotheses

1. Receiving and learning GEP information decreases overall decisional conflict
2. Receiving GEP test results decreases decisional conflict the most in women unsure about taking chemotherapy

Study Design & Methods

Decisional Conflict Scale (DCS)

- Validated tool that quantifies personal uncertainty and factors contributing to uncertainty in decision making
- 5 subscales:

Uncertainty	• Level of uncertainty in decision
Informed	• Extent to which one is informed about their options, risks and benefits
Values clarity	• Extent to which one feels clear about personal values and value trade-offs in the decision
Support	• Extent to which one feels supported in making a choice
Effective decision	• Extent to which one agrees that their decisions were informed, consistent with personal values, and would be implemented

[4] O'Connor A. Validation of a Decisional Conflict Scale. *Med Decis Making*. 1995.

Component A

Suppose you were diagnosed with early-stage breast cancer:

- After meeting with your cancer doctor (whom you somewhat trust), they estimate that your **risk of cancer returning** is **intermediate** (for example: lymph node negative, the cancer is not responsive to Herceptin, the cancer is less responsive to hormone therapy, tumour size is between 2.1 and 3cm).

- Your risk of **temporary side effects** (may commonly occur during chemotherapy - may include nausea, vomiting, numbness or tingling in fingers, hair loss, fever and infection) is **moderate**.

- Your risk of **permanent side effects** (may occur after chemotherapy and last permanently - may include leukaemia (blood cancer), damage to the heart muscle, and early menopause) is **moderate**.

- If you had the choice to have chemotherapy, and if the scenario above was really your situation, what would you do?

  - **I would have chemotherapy**
  - **I would not have chemotherapy**
  - **Unsure**

Component B

Thinking about the choice you just made, please rate, how strongly you agree or disagree with these comments

	Strongly Agree	Agree	Neither Agree or Disagree	Disagree	Strongly Disagree
1. I know which options are available to me.	○	○	○	○	○
2. I know the benefits of each option.	○	○	○	○	○
3. I know the risks and side effects of each option	○	○	○	○	○
4. I am clear about which benefits matter most to me.	○	○	○	○	○
5. I am clear about which risks and side effects matter most.	○	○	○	○	○
6. I am clear about which is more important to me (the benefits or the risks and side effects).	○	○	○	○	○
7. I have enough support from others to make a choice.	○	○	○	○	○
8. I am choosing without pressure from others.	○	○	○	○	○
9. I have enough advice to make a choice.	○	○	○	○	○
10. I am clear about the best choice for me.	○	○	○	○	○
11. I feel sure about what to choose.	○	○	○	○	○
12. This decision is easy for me to make.	○	○	○	○	○
13. I feel I have made an informed choice.	○	○	○	○	○
14. My decision shows what is important to me.	○	○	○	○	○
15. I expect to stick with my decision.	○	○	○	○	○
16. I am satisfied with my decision.	○	○	○	○	○

Component B

	Strongly Agree	Agree	Neither Agree or Disagree	Disagree	Strongly Disagree
1. I know which options are available to me.	○	○	○	○	○
2. I know the benefits of each option.	○	○	○	○	○
3. I know the risks and side effects of each option	○	○	○	○	○
4. I am clear about which benefits matter most to me.	○	○	○	○	○
5. I am clear about which risks and side effects matter most.	○	○	○	○	○
6. I am clear about which is more important to me (the benefits or the risks and side effects).	○	○	○	○	○
7. I have enough support from others to make a choice.	○	○	○	○	○
8. I am choosing without pressure from others.	○	○	○	○	○
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10. I am clear about the best choice for me.	○	○	○	○	○
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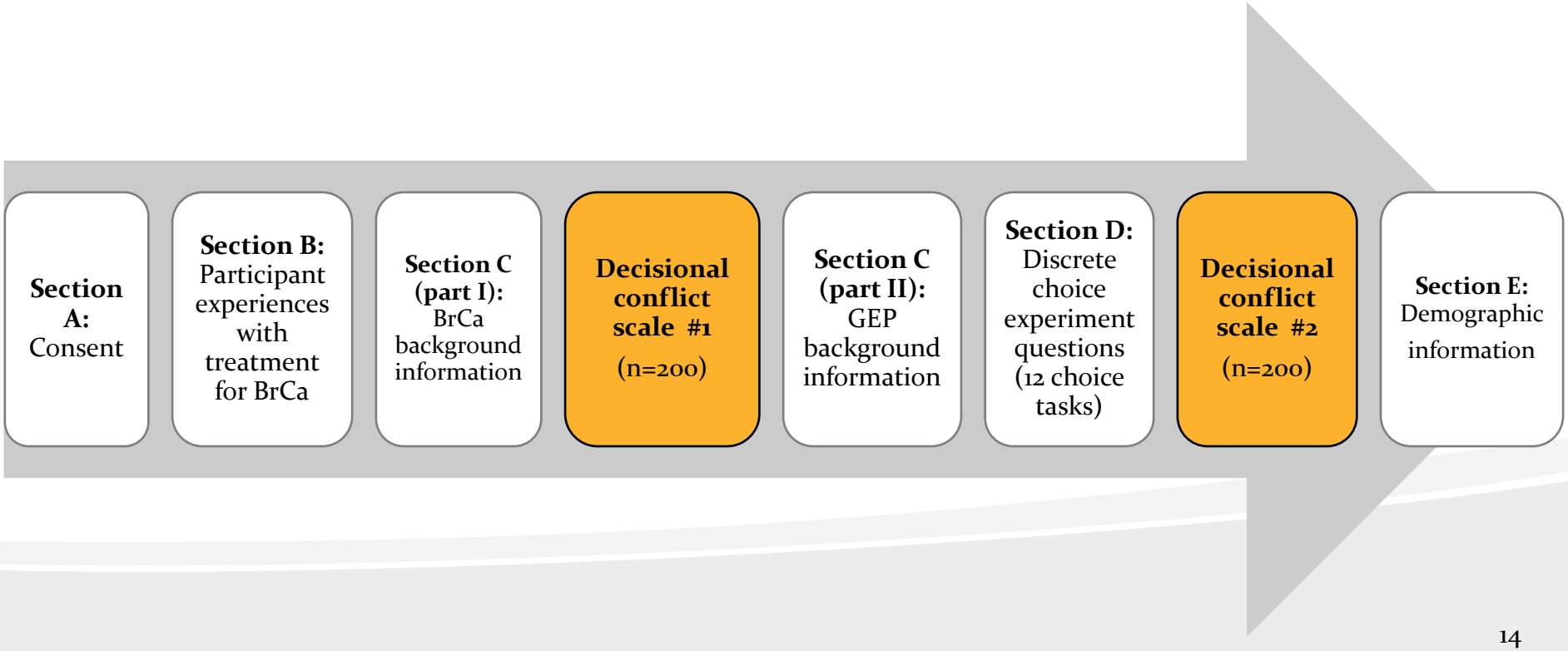
14. My decision shows what is important to me.	○	○	○	○	○
15. I expect to stick with my decision.	○	○	○	○	○
16. I am satisfied with my decision.	○	○	○	○	○

Survey

- Embedded the DCS into our discrete choice experiment survey examining preferences for chemotherapy treatment in BrCa



DCS#1 vs DCS#2

Suppose you were diagnosed with early-stage breast cancer:

- After meeting with your cancer doctor (whom you somewhat trust), they estimate that your **risk of cancer returning** is **intermediate** (for example: lymph node negative, the cancer is not responsive to Herceptin, the cancer is less responsive to hormone therapy, tumour size is between 2.1 and 3cm).

- Your risk of **temporary side effects** (may commonly occur during chemotherapy - may include nausea, vomiting, numbness or tingling in fingers, hair loss, fever and infection) is **moderate**.

- Your risk of **permanent side effects** (may occur after chemotherapy and last permanently - may include leukaemia (blood cancer), damage to the heart muscle, and early menopause) is **moderate**.

- The result of your **GEP test is a score of 9** (low benefit from chemotherapy).

- If you had the choice to have chemotherapy, and if the scenario above was really your situation, what would you do?

  - **I would have chemotherapy**
  - **I would not have chemotherapy**
  - **Unsure**

Study Sample

- Survey was administered online to Canadian women(18 years and older) from the general population (n=1004)
- Subgroup of n=200 completed the DCS components of survey

Statistical methods

We examined:

- Changes in component A

> If you had the choice to have chemotherapy, and if the scenario above was really your situation, what would you do?
>
> ○ I would have chemotherapy
> ○ I would not have chemotherapy
> ○ Unsure

- Changes in component B scores
  - Total decisional conflict
  - Five subscores

Results

Demographics

Variable		DCS Subgroup (n=200)	
		n	%
Average age (years)		200	**48 years**
Education	*College or university*	122	**61**
Employment status	*Employed*	106	53
Population centre	*Large (≥100,000)*	115	58
Marital status	*Married/living common-law*	137	69
Children living at home	*Yes*	65	33
2011 Household income	*≥$80,000*	74	37

Changes in total score and subscores

- 0.5 decrease in total score
  - Non-significant improvement in overall decisional conflict for decision around chemotherapy (32.8→32.2; p=0.3)
- 4 out of 5 subscores decreased
  - Non- significant improvements in:
    - personal uncertainty (42.8→42.0; p=0.3)
    - feeling informed about options, risks and benefits (30.7→29.5; p=0.15)
    - feeling clear about personal values and value trade-offs in the decision (29.3→28.7; p=0.15)
    - feeling supported in choice (28.4→27.9; p=0.3)
- Effective decision score increased
  - Non-significant decline in feeling decision was informed and effective
    - 32.7→32.9; p=0.45

Changes in component A and treatment decisions

Profile	n	%
1. Those who are sure of their decisions	**78**	**39**
chemotherapy to chemotherapy	54	
no chemotherapy to no chemotherapy	24	
2. Those originally unsure of their decisions but made a decision after receiving GEP testing information	**46**	**23**
unsure to chemotherapy	13	
unsure to no chemotherapy	33	
3. Those who selected chemo/no chemo originally, but became unsure after receiving GEP testing information	**29**	**14.5**
chemotherapy to unsure	25	
no chemotherapy to unsure	4	
4. Those who selected chemo/no chemo originally but changed their decision to chemo/no chemo after receiving GEP testing information	**19**	**9.5**
chemotherapy to no chemotherapy	17	
no chemotherapy to chemotherapy	2	
5. Those who remained unsure of their decision	**28**	**14**

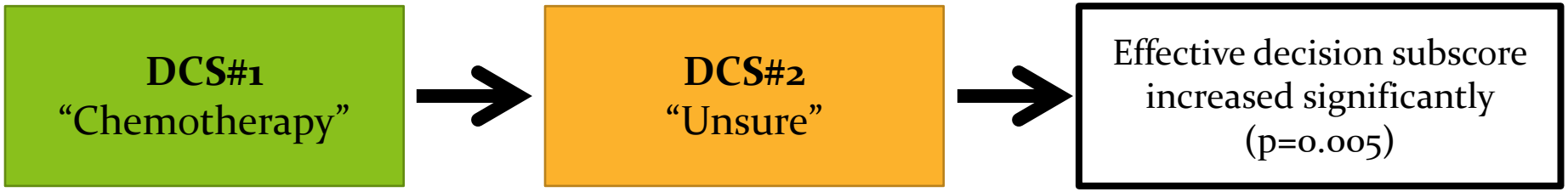
Those originally unsure of their decisions but chose no chemo after receiving GEP information

- N=33:

- Significant improvements in:
  - personal uncertainty
  - feeling informed about options, risks and benefits
  - feeling clear about personal values and value trade-offs in the decision
  - feeling supported in choice
  - feeling decision was informed and effective

Selected chemo originally, but became unsure after receiving GEP information

- N=25:



- Significant decline in:
  - feeling decision was informed and effective

Limitations

- Online survey panel
  - Demographic different than general population
  - Potential for incentive bias

Conclusions

Conclusions and hypotheses

Hypothesis #1:

- *Receiving and learning GEP information decreases overall decisional conflict*
  - GEP doesn't significantly decrease decisional conflict
  - **GEP may be more useful in certain populations**

Hypothesis #2:

- *Receiving GEP test results decreases decisional conflict the most in women unsure about taking chemotherapy*
  - **GEP significantly decreases decision conflict and is most useful in this population**

Conclusions

- Women unsure of their chemotherapy decision benefit from GEP results
- 2 groups of women have pre-determined decisions which they are unwilling to change, even after receiving a GEP test result
  - Decisional conflict does not significantly change with GEP test results
  - Aligns with Bombard et al. MO views of GEP
- GEP is costly to order for women who do not change, and are confident with, their treatment decisions, even after receiving GEP test results

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Research Team

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OICR Ontario Institute for Cancer Research

ARCC Canadian Centre for Applied Research in Cancer Control

McMaster University Inspiring Innovation and Discovery

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Thank you!

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Appendix slides

GEP and decisional conflict

- A few studies have examined GEP and decisional conflict in populations of women with BrCa and their Medical Oncologists faced with real-life chemotherapy treatment decisions
  - Decisional conflict decreases after receiving GEP scores in real-life treatment decisions [5-7]
- Studies by Lo and Davidson also found that GEP decreased patient anxiety and increased physician confidence[6,7]

[5] Sulayman N. Psychosocial and Quality of Life in Women Receiving the 21-Gene Recurrence Score Assay. *J Cancer Epi.* 2012.
[6] Lo S. Prospective Multicenter Study of Impact of 21-Gene Recurrence Score on MO and Patient BrCa Treatment Selection. *J Clin Oncol.* 2010. 31
[7] Davidson J. A prospective clinical utility and pharmacoeconomic study of the impact of the 21-gene recurrence score. *Eur J Canacer.* 2013.

Statistical methods

- Used the 0-100 scoring scale for total score and subscores
  - 100 is the highest decisional conflict possible
- DCS#1 and #2 mean total and subscores were calculated for the sample
- Matched pairs t-tests were used to measure if mean total score and subscores were significantly different from DCS#1 to DCS#2
  - $P<0.05$ was considered statistically significant

Changes in total score and subscores

- 0.5 decrease in total score not statistically significant
- All subscores had non-significant decreases
  - Exception was effective decisions, which increased

	DCS #1 Mean score	DCS#2 Mean score	Mean change in score	Std. dev.	Sign. (1-tailed)
Total score (n=200)	32.8	32.2	-0.5	13.3	0.3
Subscores (n=200)					
Uncertainty	42.8	42.0	-0.8	18.5	0.3
Informed	30.7	29.5	-1.2	15.9	0.15
Values clarity	29.3	28.7	-0.6	16.8	0.15
Support	28.4	27.9	-0.5	14.9	0.3
Effective decisions	32.7	32.9	0.2	15.8	0.45

*100 is the highest decisional conflict possible