



PATIENT CARE
RESEARCH
EDUCATION
COMMUNITY

Processing of Breast Cancer Risk of Recurrence Results Following Genomic Tumor Testing

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A Comprehensive Cancer Center Designated
by the National Cancer Institute

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Precision Medicine through Tumor Genomic Profiling

NATIONAL CANCER INSTITUTE PRECISION MEDICINE IN CANCER TREATMENT

Discovering unique therapies that treat an individual's cancer based on the specific genetic abnormalities of that person's tumor.



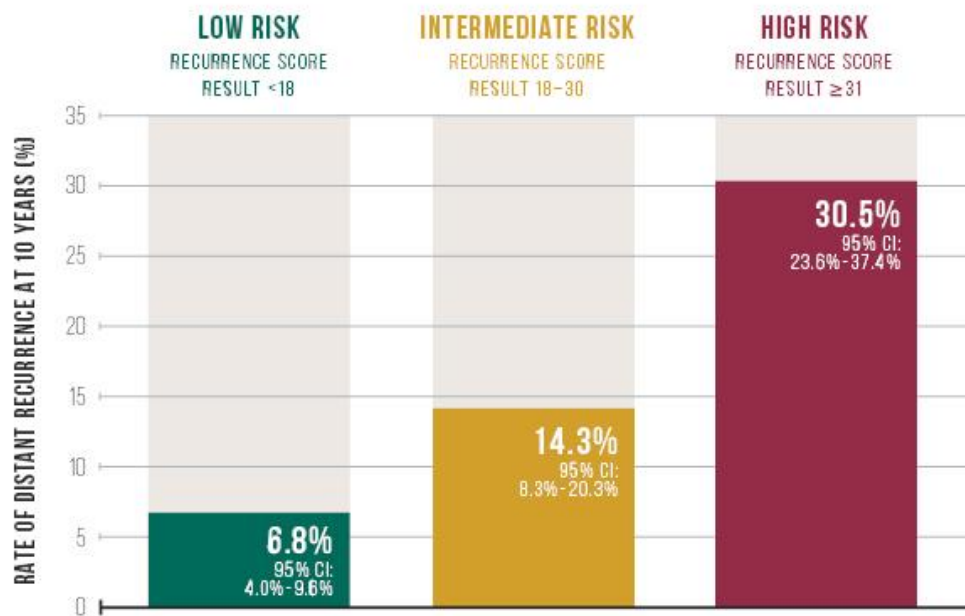
Genomic Testing for Risk for Recurrence

- Gene expression tumor analysis for early stage, ER+ breast cancers:
 - Estimate risk of recurrence
 - Aid prognosis
 - Predict treatment benefit
 - Chemotherapy
 - Extending hormonal therapy

Oncotype DX[®]

NSABP B-14 Study

10-year rate of distant recurrence was significantly lower for patients with low Recurrence Score results compared to high results¹



LOW RECURRENCE SCORE RESULT =
LOWER RATE OF DISTANT RECURRENCE¹



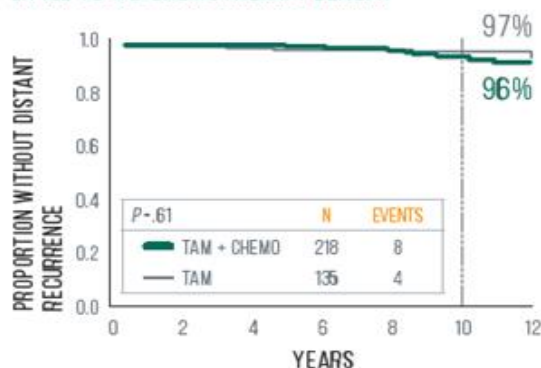
HIGH RECURRENCE SCORE RESULT =
HIGHER RATE OF DISTANT RECURRENCE¹

Oncotype DX®

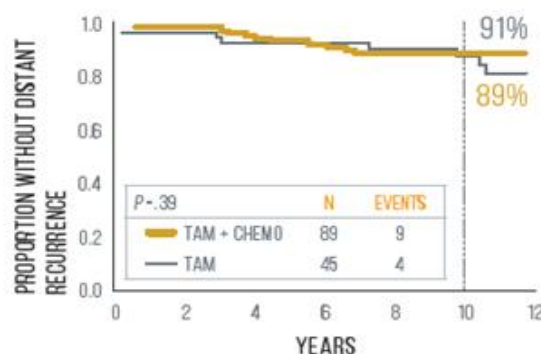
NSABP B-20 Study

Low Recurrence Score result predicted little to no benefit from chemotherapy²

LOW RECURRENCE SCORE RESULT (<18) LITTLE TO NO CHEMOTHERAPY BENEFIT



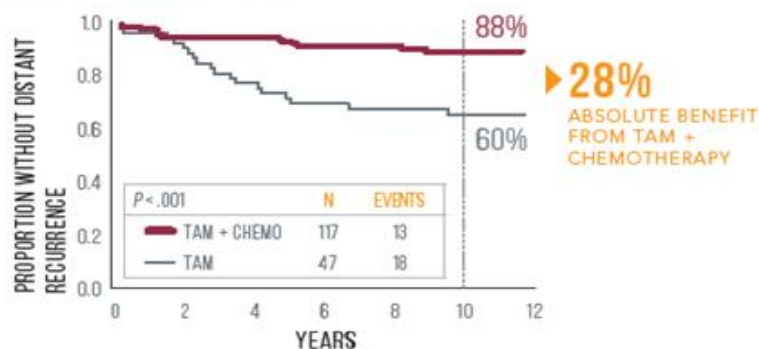
INTERMEDIATE RECURRENCE SCORE RESULT (18–30) NO SUBSTANTIAL CHEMOTHERAPY BENEFIT



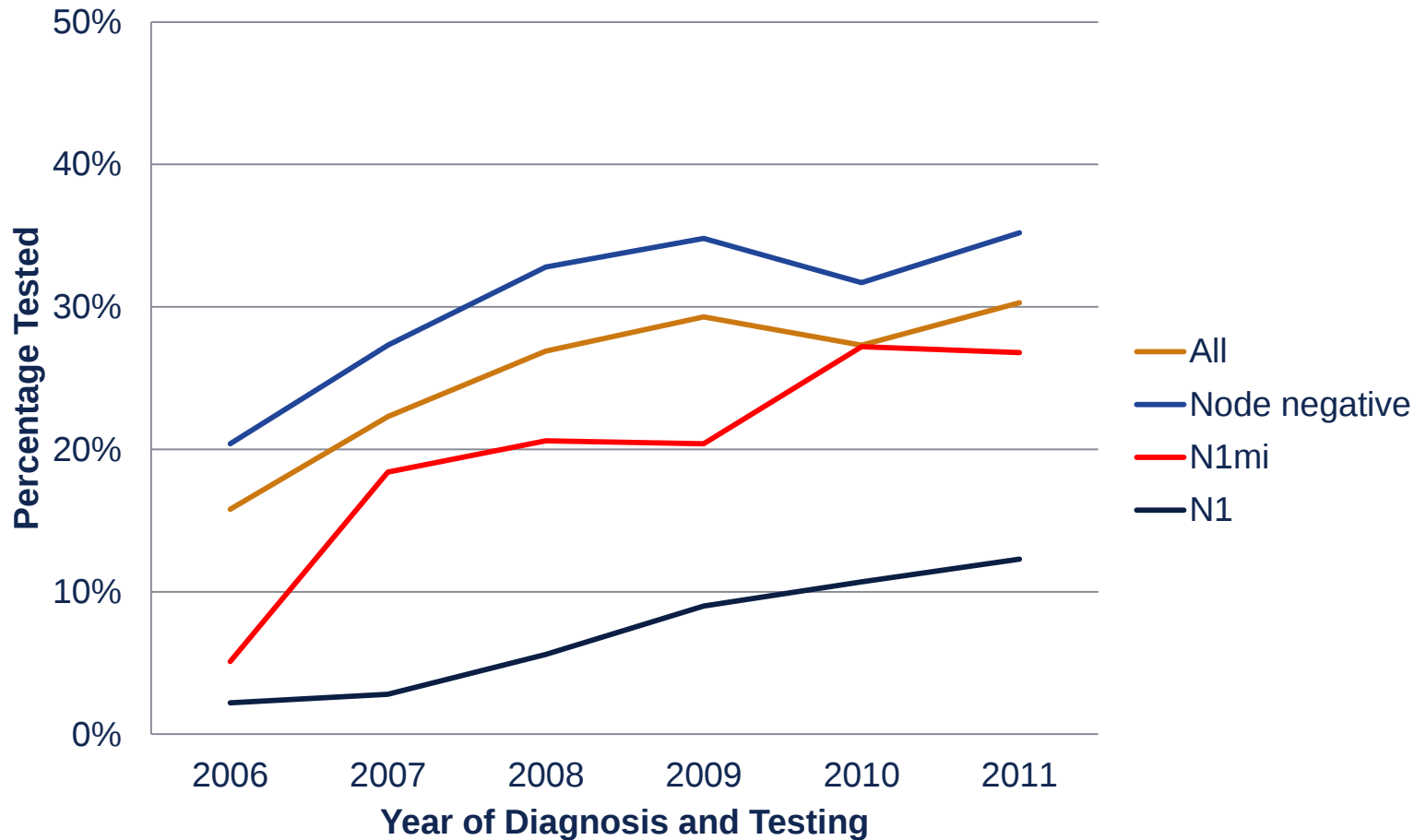
NSABP B-20 Study

High Recurrence Score result predicted large benefit from chemotherapy²

HIGH RECURRENCE SCORE RESULT (≥31) LARGE CHEMOTHERAPY BENEFIT



Rates of testing by year (2006-2011)



Testing = Standard of Care

ASCO | Guidelines

12th St.Gallen International Breast Cancer Conference

Primary Therapy of Early Breast Cancer
with Treatment Consensus Update

16 - 19 March 2011
St. Gallen, Switzerland



National
Comprehensive
Cancer
Network

Sample Report



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1 Breast Cancer Report - Node Negative Prognosis

Patient/ID: DOE, JANE ELIZABETH

Gender: Female

Date of Birth: 01-Jan-1950

Medical Record/Patient #: 556677771

Date of Collection: 10-Oct-2015

Specimen Type/ID: Breast/C83P0ZDYQ

Study #: ReportStudy1055

Report Number: OR123456789-01

Specimen Received: 30-Oct-2015

Date Reported: 10-Nov-2015

Client: Community Medical Center

Ordering Physician: Dr. Harry D Smith

Additional Recipient: Dr. Sally M Jones

3 Recurrence Score® Result

6

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

The findings are applicable to women who have stage I or II node negative (N-), estrogen receptor positive (ER+) breast cancer, and will be treated with 5 years of tamoxifen (tam). It is unknown whether the findings apply to other patients outside these criteria.

Clinical Experience: The following results are from a clinical validation study that included 668 patients from the NSABP B-14 study. The study included female patients with stage I or II, N-, ER+ breast cancer treated with 5 years of tam.

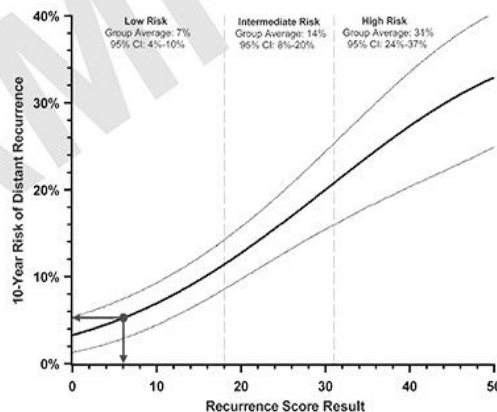
4 Prognosis: 10-Year Risk of Distant Recurrence after 5 Years of Tam, Based on the Recurrence Score Result (from NSABP B-14)

10-Year Risk of Distant Recurrence

Tam Alone

5% —

(95% CI: 3%-7%)



¹ Paik et al. N Engl J Med. 2005.

Laboratory Director(s): S. Shak, MD; J. Anderson, MD; F. Baehner, MD & P. Joseph, MD

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.

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GH004 Rev007



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1 Breast Cancer Report - Node Negative Prediction of Chemotherapy Benefit

Patient/ID: DOE, JANE ELIZABETH

Gender: Female

Date of Birth: 01-Jan-1950

Report Number: OR123456789-01

Specimen Received: 30-Oct-2015

Date Reported: 10-Nov-2015

3 Recurrence Score® Result

6

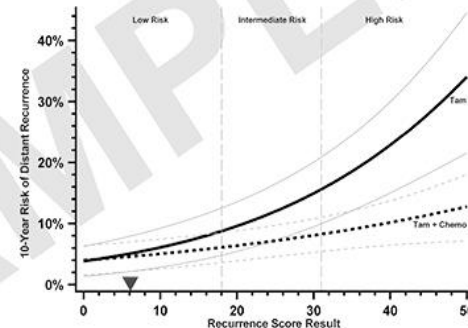
The findings are applicable to women who have stage I or II node negative (N-), estrogen receptor positive (ER+) breast cancer and will be treated with 5 years of tamoxifen (tam). It is unknown whether the findings apply to other patients outside these criteria.

Clinical Experience: The following results are from a clinical validation study that included 651 patients from the NSABP B-20 study. The study included female patients with stage I or II, N-, ER+ breast cancer. Patients were randomized to either tam alone or tam plus CMF or MF chemotherapy. For patients in the pre-specified group with Recurrence Score results ≥ 31 , the group average 10-year risks (95% CI) of distant recurrence were 40% (25%, 54%) for tam alone and 12% (6%, 18%) for tam + CMF/MF.¹

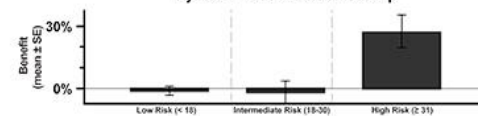
4 Prediction of Chemotherapy Benefit after 5 Years of Tam, Based on the Recurrence Score Result (from NSABP B-20)

Tam Alone —

Tam + Chemo - - -



Absolute Benefit of Chemotherapy at 10 Years by Recurrence Score Risk Group



¹ Paik et al. J Clin Oncol. 2005.

Laboratory Director(s): S. Shak, MD; J. Anderson, MD; F. Baehner, MD & P. Joseph, MD

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GH004 Rev007

EGAPP Recommendations--2015



Evaluation of Genomic Applications in Practice and Prevention (EGAPP)

- Research gaps:
 - “Further research (is needed) to clarify how women **understand** and **use** the risk information.”

What we know to date:

- Most women accurately recall their perceived risk of recurrence
 - 71% of tested women recalled a perceived risk of recurrence within 4% of the Recurrence Score
 - Mean perceived risk for recurrence for women with low (9.6%), intermediate (18%) and high (25.8%) Recurrence Score reflected actual risk

Questions:

How do women perceive their risk of recurrence before and after the receipt of their Recurrence Score?

How many women over- or underestimate their risk?

What are the correlates of over- or underestimation?

Methods and Participants

Newly diagnosed breast cancer patients (N = 193)

- Stage I/II
- Pre-test/Post-test design
- High RS = 17
- Intermediate RS = 60
- Low RS = 116

Demographics

- Mean age = 57 (range = 37-83)
- 65% White, 27% African American, 5% Asian, 3% Other
- 60% college degree

Perceived Risk of Recurrence:

“What do you think the chance is that your breast cancer will come back or spread to other parts of your body? Please choose a number from 0-100?”

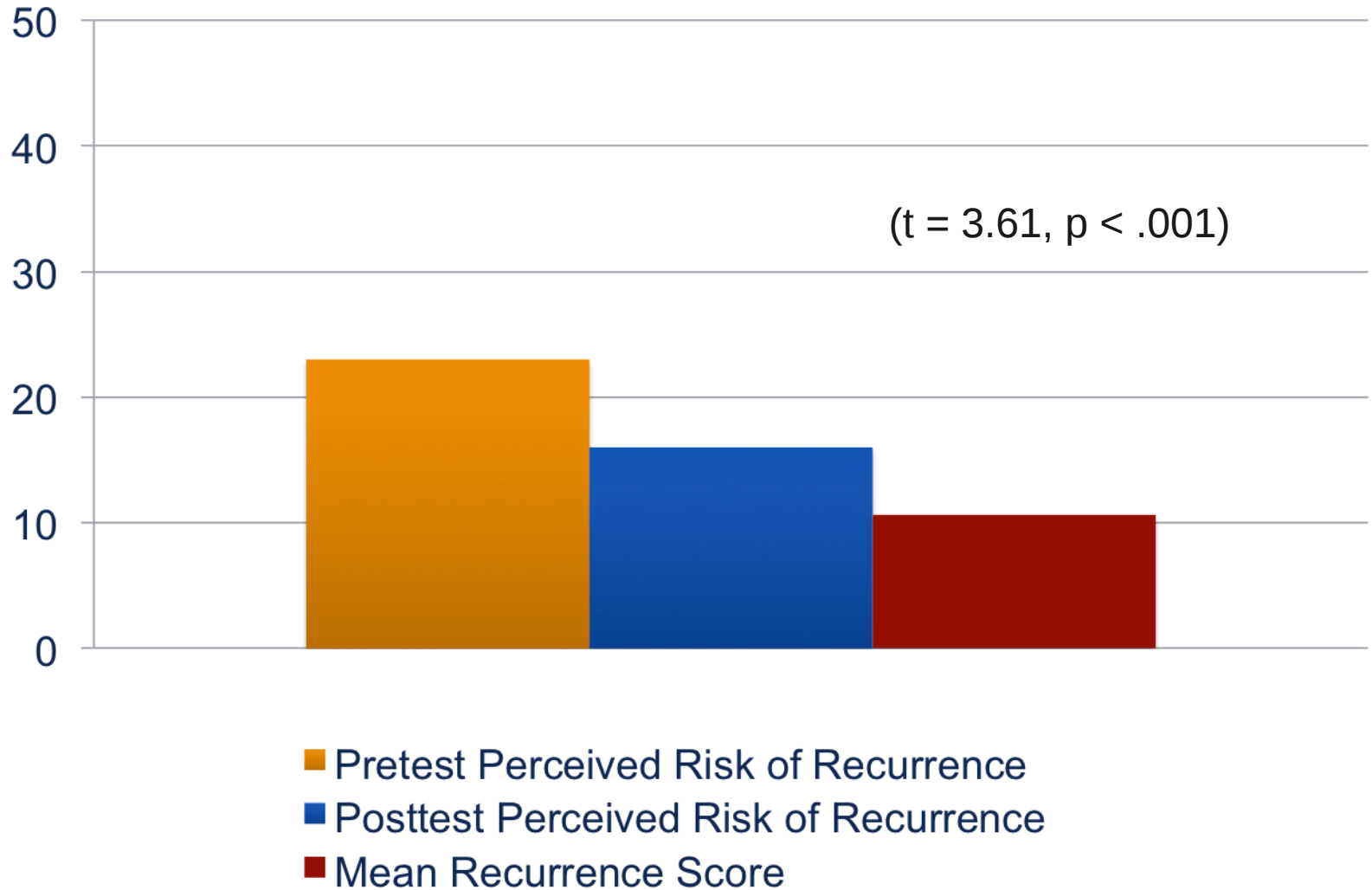
Accuracy: Alignment of post-test perceived risk and their Oncotype category

- *Perceived risk = 0--underestimate*

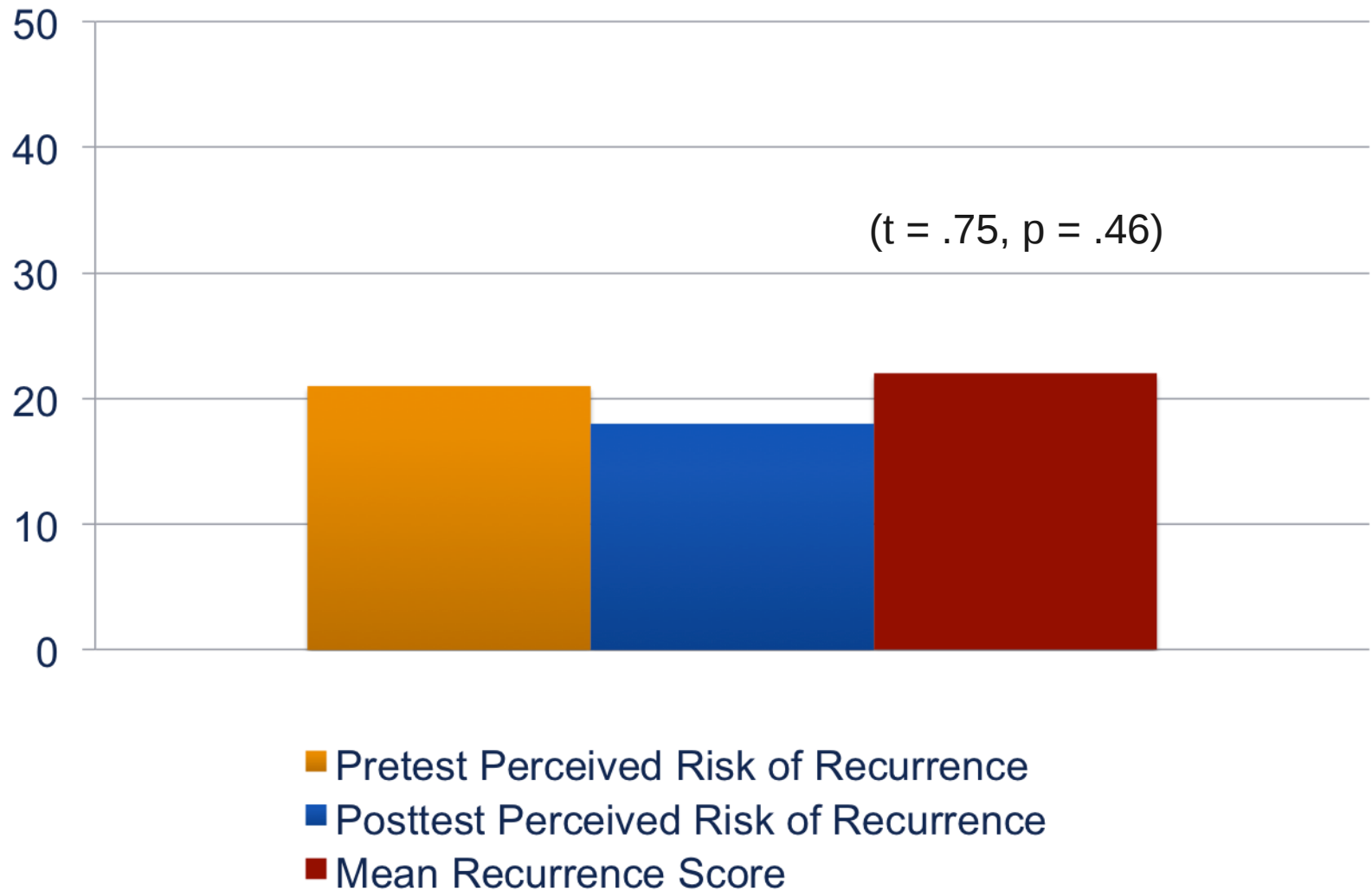
Correlates of over- and under-estimation:

- Recurrence Score
- Receipt of chemotherapy
- Age
- Race
- Education
- Cancer-related distress
- Perceived communication quality

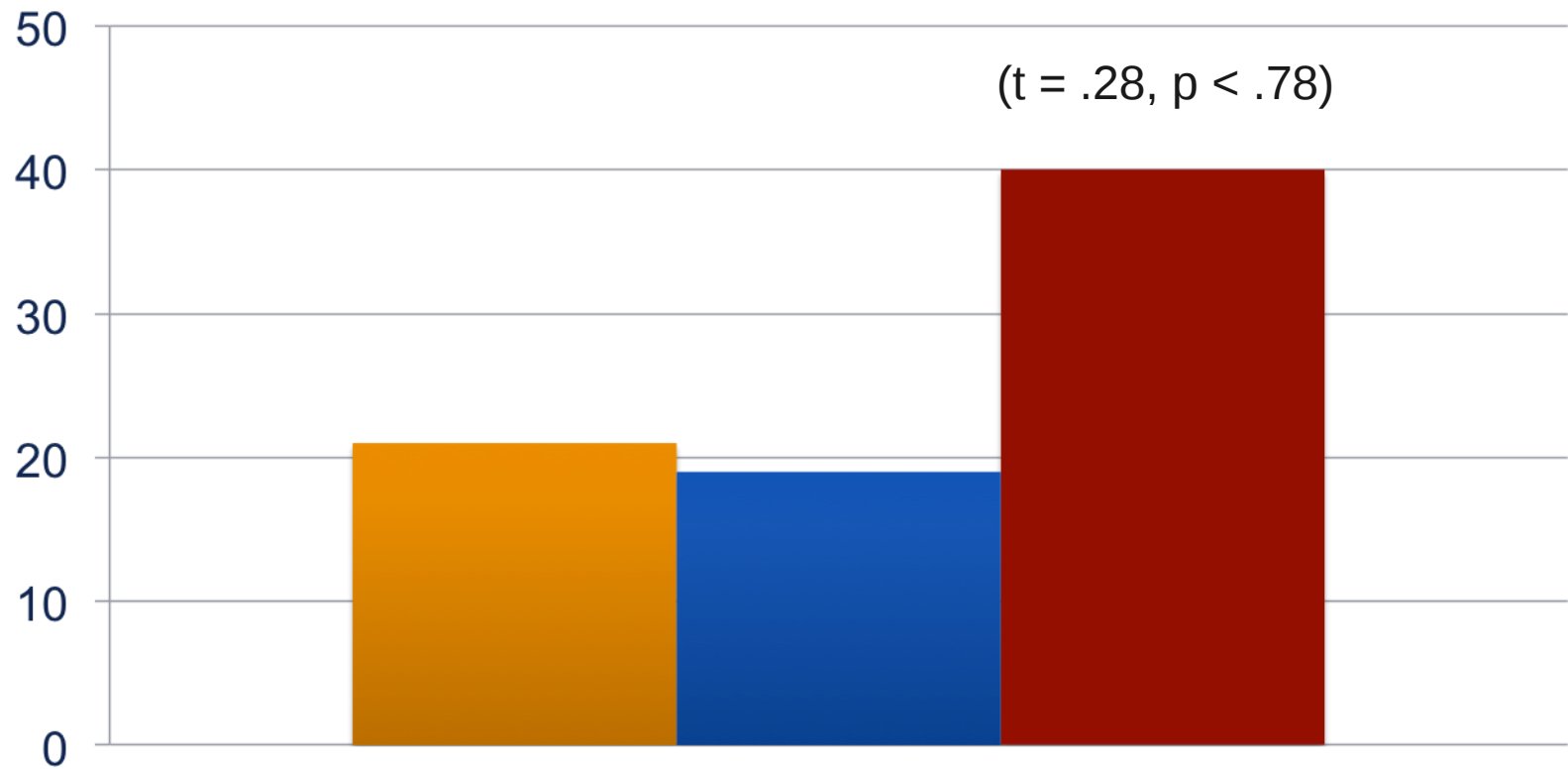
Low Risk of Recurrence



Intermediate Risk of Recurrence

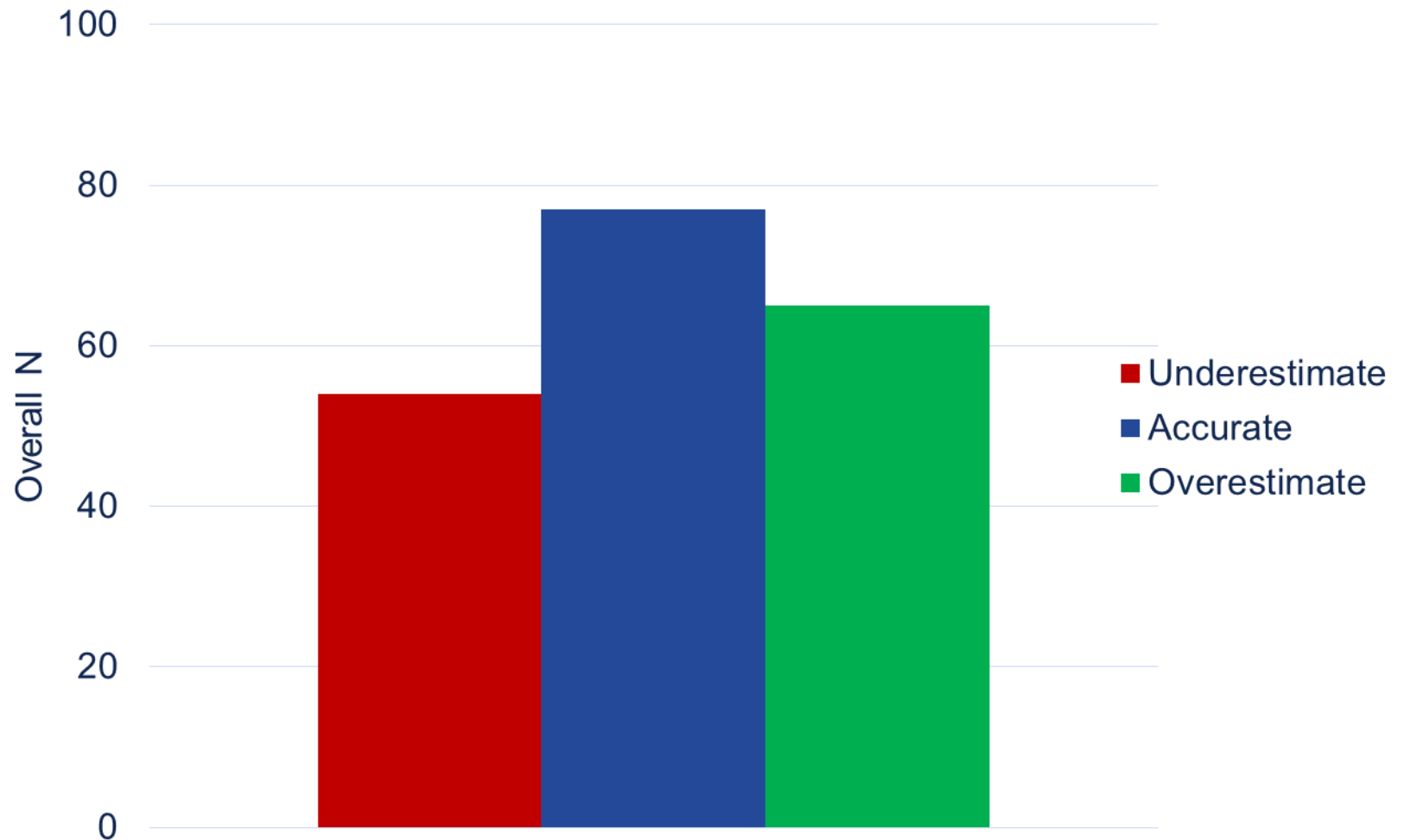


High Risk of Recurrence



- Pretest Perceived Risk of Recurrence
- Posttest Perceived Risk of Recurrence
- Mean Recurrence Score

Over- and under-estimation of risk



Correlates of over- and under-estimation

	Overestimated OR (95% CI)	Underestimated OR (95% CI)
Oncotype Score		
Low Score v. Intermediate	0.19 (0.03-1.39) ⁺	0.08 (0.02-0.41)**
Low Score v. High	2.88 (0.71-11.69)	0.03 (0.01-0.09)***
Age	1.01 (0.97-1.06)	0.95 (0.90-0.98)*
White v. non-White	1.36 (0.57-3.25)	2.18 (0.69-6.85)
College v. non-College	0.31 (0.13-0.75)**	2.50 (0.82-7.63)
Chemotherapy v. None	0.52 (0.12-2.18)	0.65 (0.17-2.51)
Post-test distress	1.03 (0.99-1.07)	0.97 (0.92-1.02)
Communication quality	0.88 (0.80-0.97)**	1.09 (0.97-1.22)

⁺<.10; *<.05; **<.01; ***<.001

Perceived risk: Women with high RS tumors

- Accurate integration of the risk-reduction afforded by chemotherapy

OR

- Defensive processing of high risk of recurrence

Over- and under-estimation

- Older women more likely to underestimate their risk for developing breast cancer (Jones et al., 2011)
- Lower levels of education is a common correlate of overestimation (Skinner et al., 1998; Leblond et al., 2012)
- Effective communication = greater accuracy
 - Family members (Himes et al., 2016)
 - Oncologists (Kelly et al., 2013)

Conclusions

- Perceived risk of recurrence does not uniformly reflect women's Recurrence Score results
- Future work will examine the impact of this for longer-term outcomes
 - Extend to 1 year post-dx
 - Adherence to treatment and surveillance
 - Quality of life

Acknowledgements

Chalanda Evans, BS
Marc Schwartz, PhD
Claudine Isaacs, MD
Susan Vadaparampil, PhD
Noel Brewer, PhD

ACS MRSG-10-110-01

Our participants

Oncologists, nurses and staff--LCCC, WHC, FSMC, MCC