The Case for a New Paradigm in Health care Delivery

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CONFIDENTIAL

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In the Era of the $1000.00 Genome

"Information is not knowledge."--- Einstein

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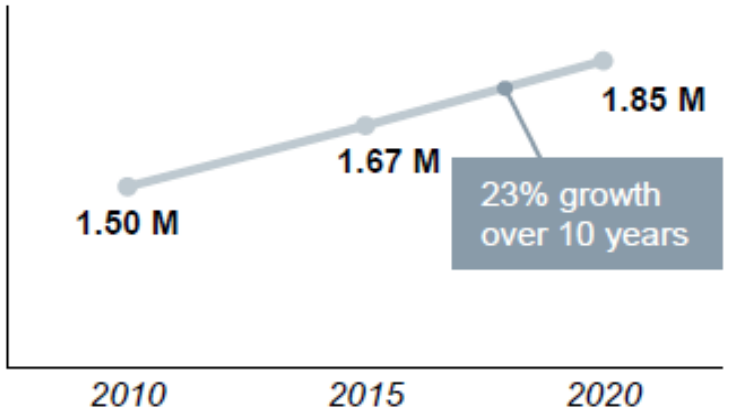
Market Forces Invoking New Care Paradigm

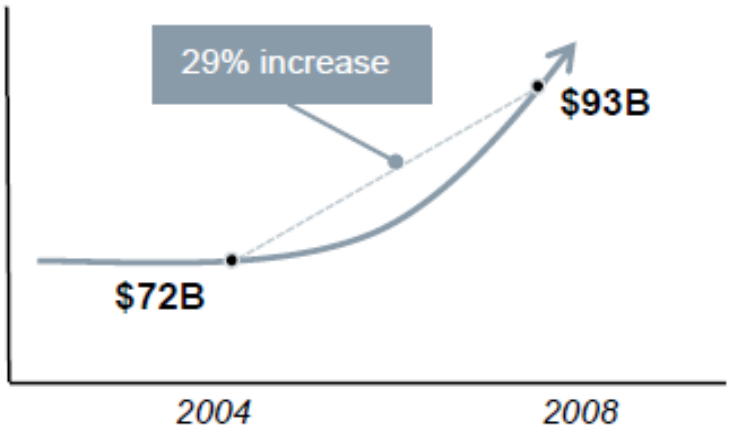
Volumes Increasing

Cancer Incidence



Costs Rising

Cost of Cancer Care



Emerging Trends

1. Focus on evidence-based medicine
2. Development of new care models
3. Shift in focus of clinical innovation
4. Increased role of consumer in decision-making

Source: American Cancer Society, available at: /www.cancer.org/cancer/cancerbasics/economic-impact-of-cancer, last accessed: August 23 2010; Oncology Roundtable Cancer Incidence Estimator, available at: www.advisory.com/or.

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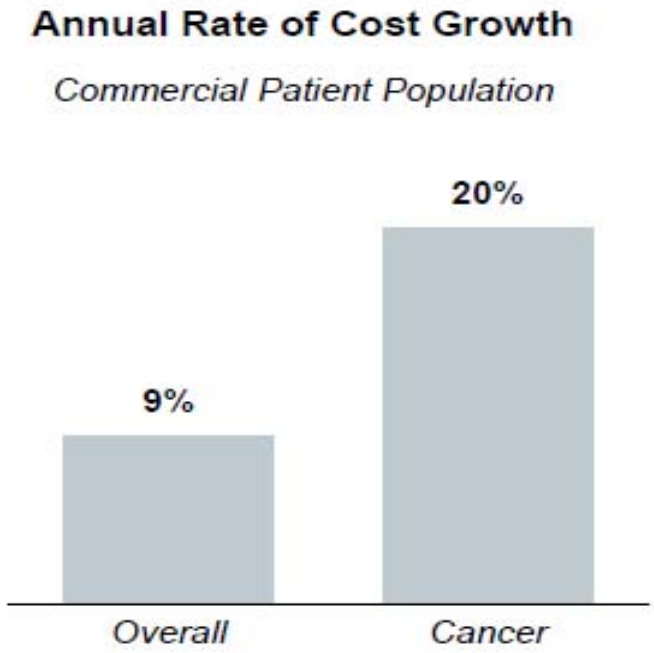
Commercial Payors Confront Startling Cost Growth

0.68% Cancer patients as a total of a commercially insured population

10% Cancer costs as a percentage of the total health care costs incurred



Source: "Cancer Patients receiving Chemotherapy: Opportunities for Better Management." *Milliman Client Report* available at: http://publications.milliman.com/research/health-rr/pdfs/cancer-patients-receiving-chemotherapy.pdf, accessed August 23 2010; *National Comprehensive Cancer Network*, "Managed Care Organizations to Focus on Value in Oncology," available at: http://www.nccn.org/about/news/ebulletin/2010-08-09/managed_care.asp?utm_source=NCCN+Global+List&utm_campaign=7b79e056c3-EB-N-0036-0810&utm_medium=email, accessed August 27 2010; Oncology Roundtable interviews and analysis.

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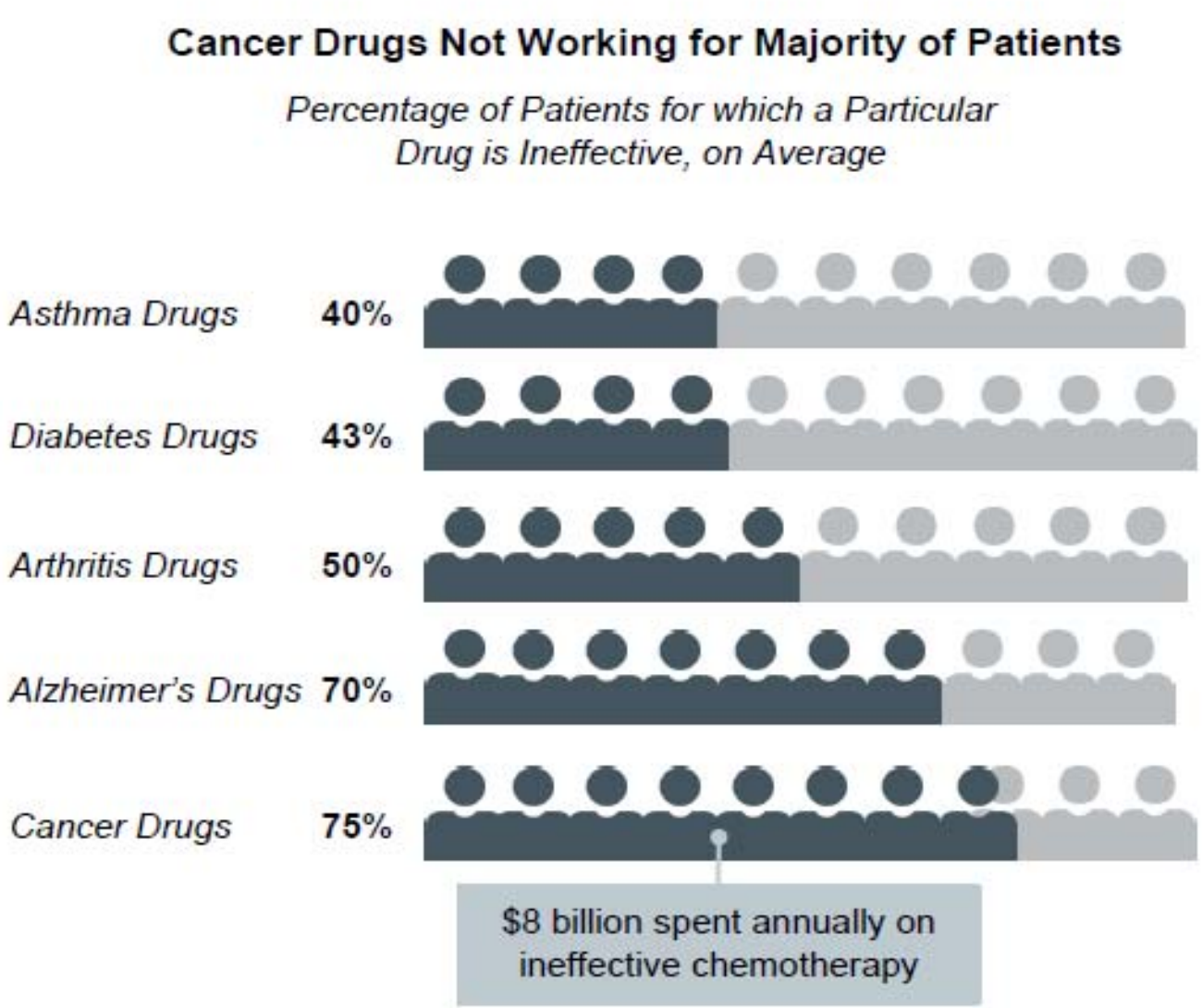
Ineffective Chemotherapy Wasting Health Care Dollars



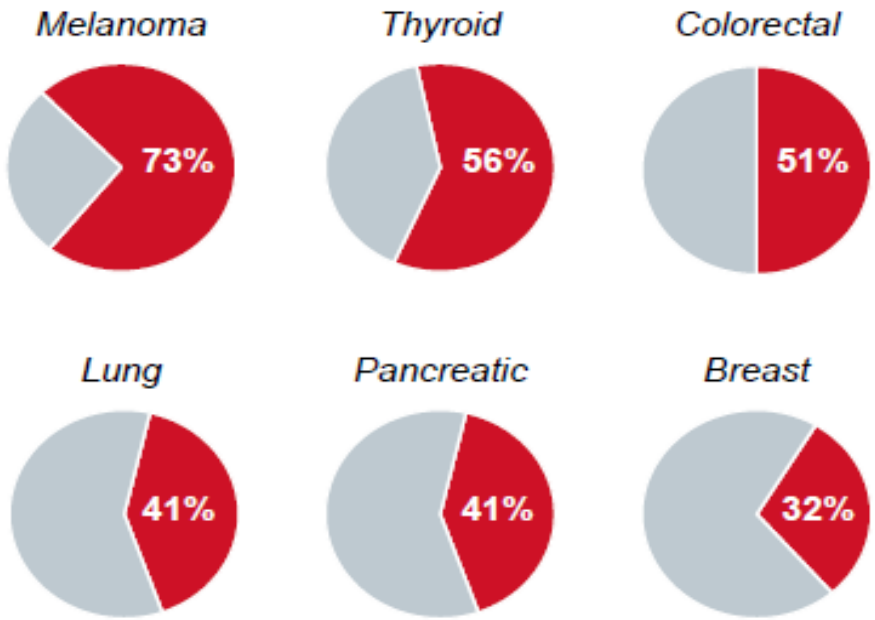
A More Accessible Option

Molecular Diagnostics Poised for Growth

In Near-Term, A Substitute for Full Genome Sequencing

Many Tumors Candidates for Targeted Therapy

Percentage of Tumors Driven by Genetic Mutations, by Type of Cancer



Drug Pipeline Increasingly Relying on Companion Diagnostics

30% of drugs in late clinical development

50% of drugs in early clinical development

60% of drugs in preclinical development

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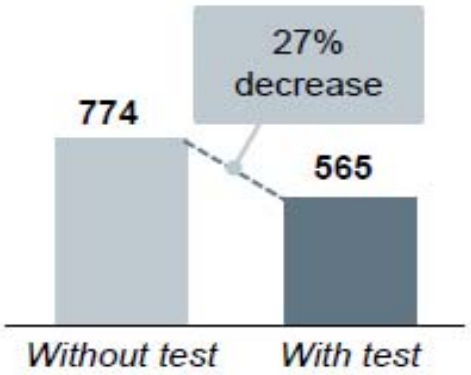
Evolving Business Case

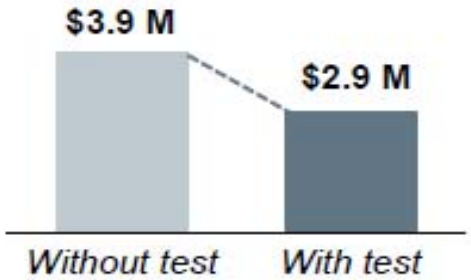
Oncotype DX® : Decreasing Chemo Use in Breast

Breast Cancer Volumes, Revenue Projections for Leslie Cancer Center[1] After Adopting OncotypeDX®

Estimated Change in Chemotherapy Volumes



Estimated Change in Chemotherapy Revenues[2]



Nationwide Impact

$330 M

Potential national savings from Oncotype DX

Test in Brief: Oncotype Dx®

- 21-gene assay developed by Genomic Health that provides a recurrence score for women diagnosed with estrogen receptor-positive breast cancer
- Studies show no significant benefit to providing adjuvant chemotherapy to women with low risk of recurrence

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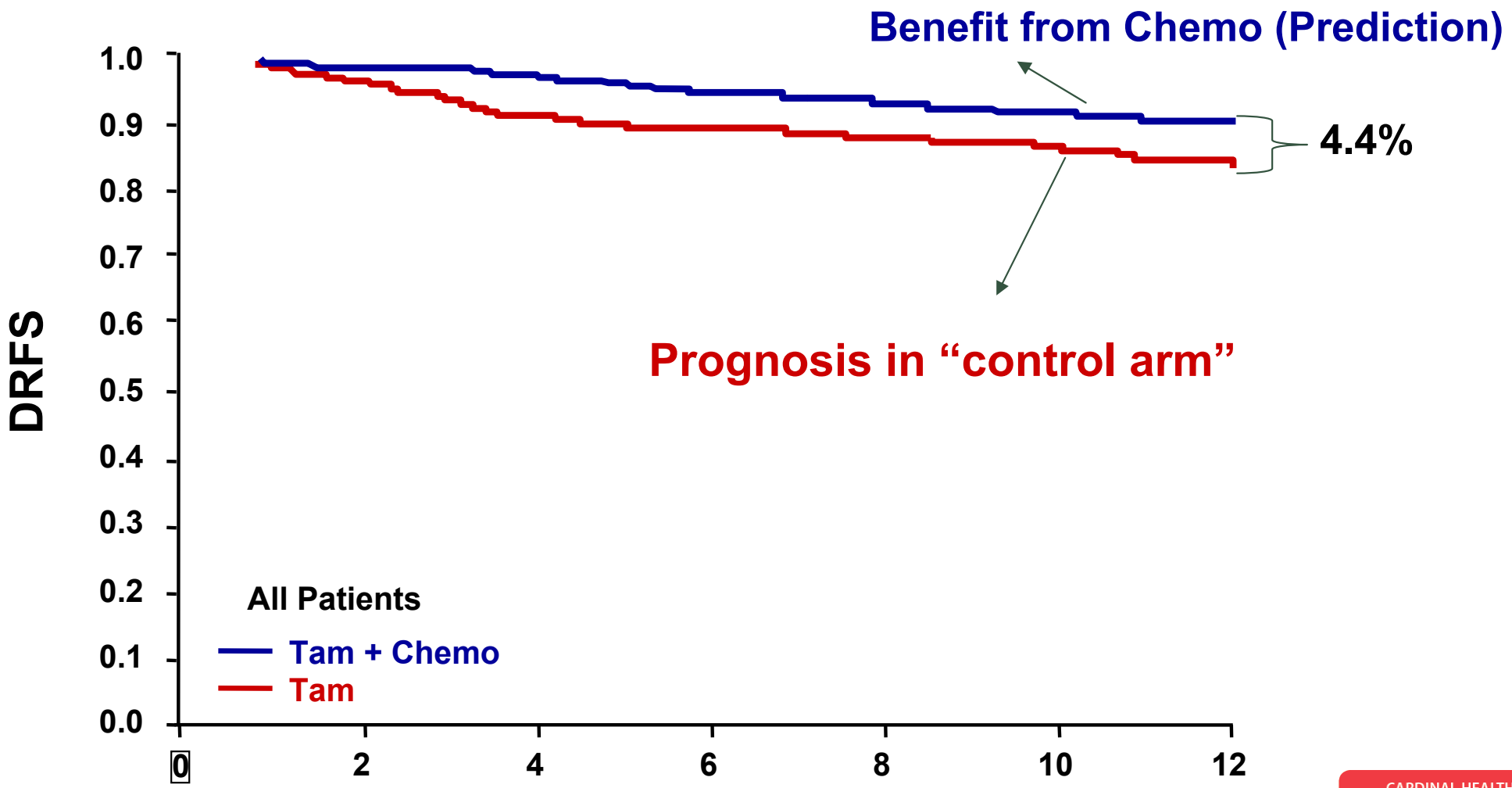
NSABP-20 TRIAL SHOWED OVERALL BENEFIT OF CHEMOTHERAPY IN TAMOXIFEN-TREATED PATIENTS

Tam vs Tam + Chemo – All 651 Patients



Paik et al. *J Clin Oncol*. 2006.

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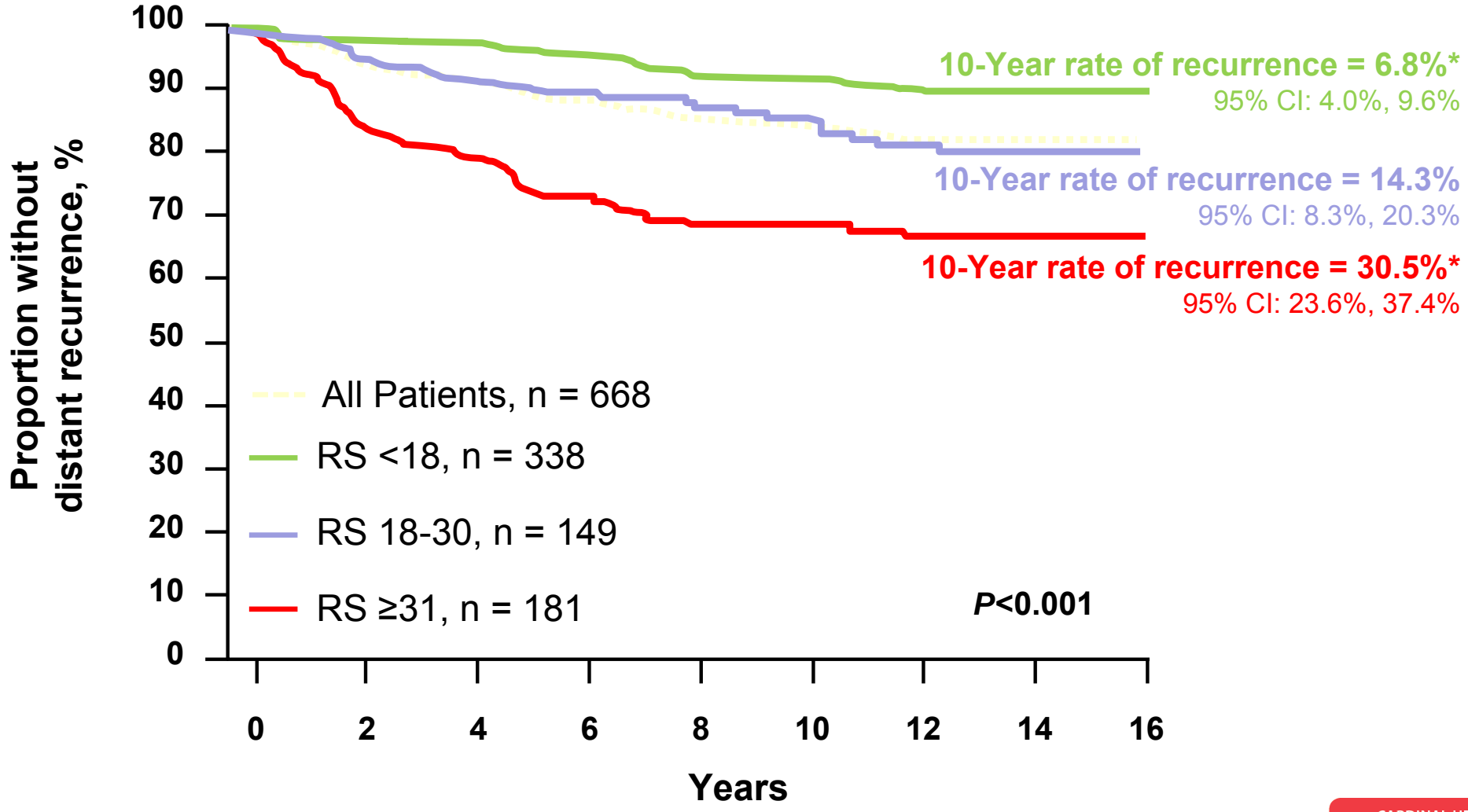
CLINICAL VALIDITY: THE ONCO*TYPE* DX® ASSAY IS PROGNOSTIC OF DISTANT RECURRENCE (NSABP B-14 STUDY)

Distant recurrence over time



RS, Recurrence Score® result

*10-Year distant recurrence comparison between low- and high-risk groups: $P < 0.001$

Paik S, et al. *N Engl J Med.* 2004;351:2817-2826.

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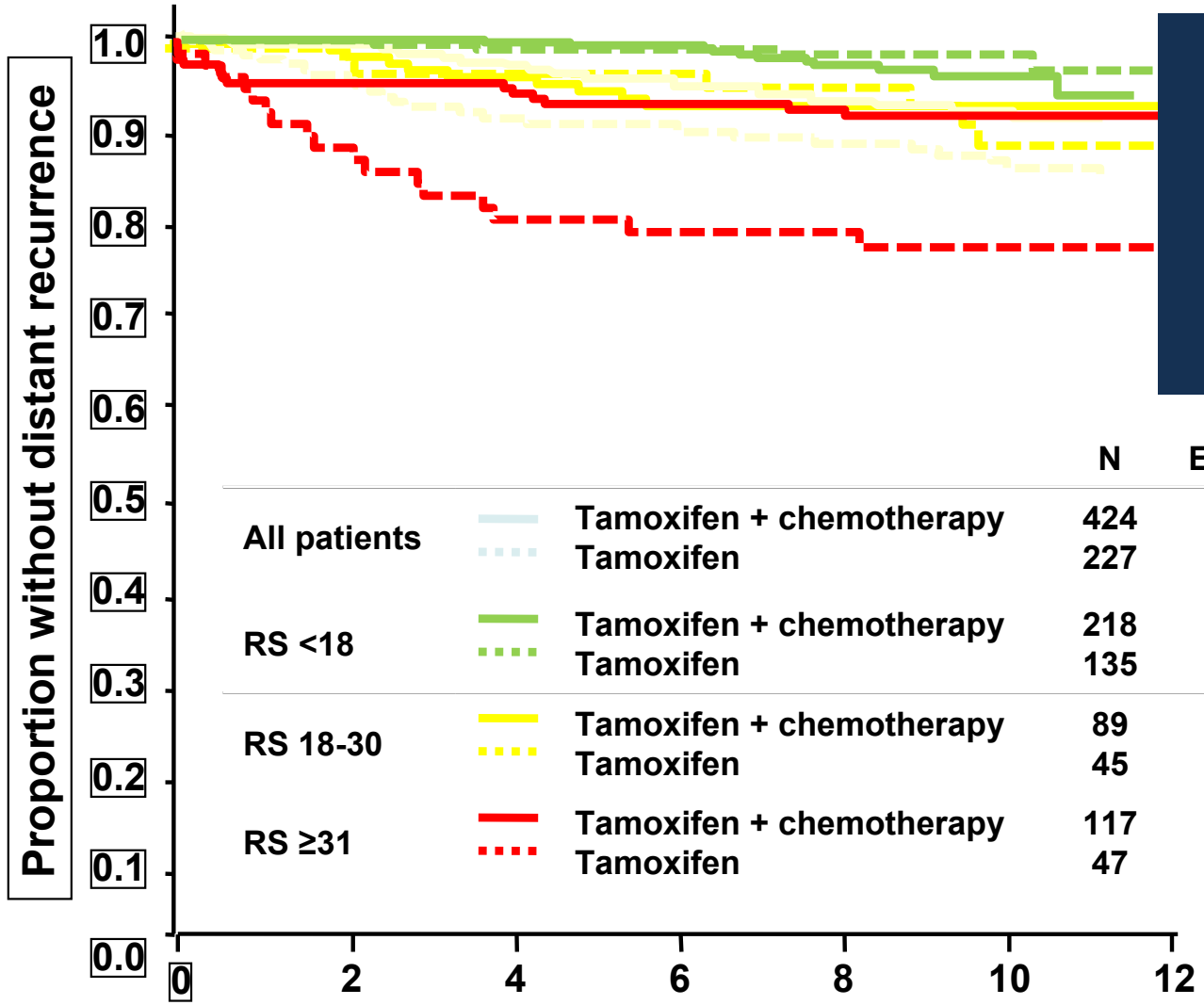
CLINICAL VALIDITY: THE ONCO*TYPE* DX® ASSAY IS PREDICTIVE OF CHEMOTHERAPY BENEFIT (NSABP B-20 STUDY)



Patients With High RS
28% absolute benefit from tamoxifen + chemotherapy

Interaction p-value for continuous RS = 0.038

		N	Events	
All patients	Tamoxifen + chemotherapy	424	33	*P* = 0.02
	Tamoxifen	227	31	
RS <18	Tamoxifen + chemotherapy	218	8	*P* = 0.61
	Tamoxifen	135	4	
RS 18-30	Tamoxifen + chemotherapy	89	9	*P* = 0.39
	Tamoxifen	45	4	
RS ≥31	Tamoxifen + chemotherapy	117	13	*P*<0.001
	Tamoxifen	47	18	

4.4% absolute benefit from tamoxifen + chemotherapy

RS, Recurrence Score® result

Paik S, et al. *J Clin Oncol*. 2006;24:3726-3734.

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THE ONCO*TYPE* DX® ASSAY CHANGED TREATMENT DECISIONS IN OVER ONE-THIRD OF PATIENTS

Treatment Plan After Onco*type* DX
Treatment Plan Prior to Onco*type* DX
Women Diagnosed with Breast Cancer

- Chemotherapy recommended for 62% of patients
- **Over a 37% Change in Treatment Decisions**

Chemotherapy No Chemotherapy

*Based on meta-analysis of seven studies with 912 patients.

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Say Yes to the Mess

"*It is cookbook medicine. Yes, guidelines are something like a cookbook. However, all great chefs and expert pilots use cookbooks and checklists, and diners and flyers are grateful that their experiences are not created entirely from scratch. Perhaps it would help if we thought of guidelines as jazz scores. AS practitioners we work from a basic chord structure and melody line (clinical science) with a great deal of latitude for improvisation (the art of medicine).*"

James Reinersten, MD
Annals of Internal Medicine 138;922 2003

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Relationship between Oncotype DX® Testing and the Use of Chemotherapy in High-Risk Patients

Wong W,[1] Cooper J,[2] Richardson S,[3] Feinberg B[2]

[1]CareFirst BlueCross BlueShield

[2] Cardinal Health Specialty Solutions, Dublin, OH

[3] Genomic Health Inc., Redwood City, CA

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The New Standard of Care

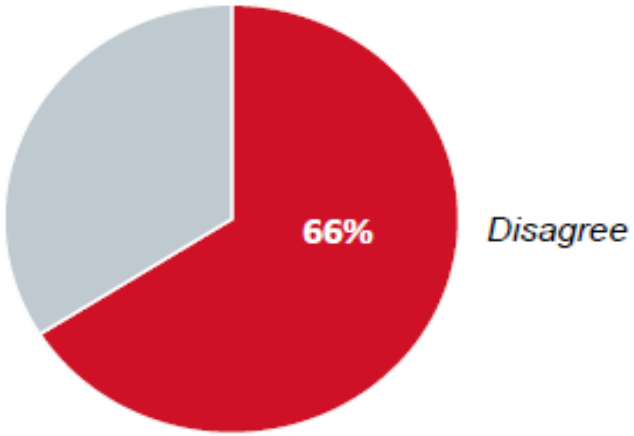
Physician Resistance to Guidelines Waning

Physician Attitudes Toward Clinical Guidelines

"Guidelines reduce my autonomy as a physician"

Commonwealth Fund[1]

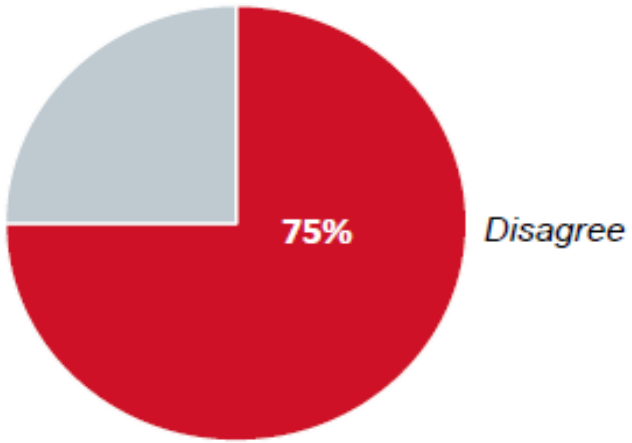
2002



"Guidelines undermine my autonomy as a physician"

NEHI Physician Survey Respondents[2]

2008



1) Survey of U.S. clinicians attitudes towards clinical guidelines.
2) New England Healthcare Institute.

Source: Kenefick H, et al., "Improving Physician Adherence to Clinical Practice Guidelines," Cambridge: New England Healthcare Institute, 2008; Farquhar C et al. "Clinicians' Attitudes to Clinical Practice Guidelines: A Systematic Review," *Medical Journal of Australia*, Nov. 4, 2002 177(9): 502–06.

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CareFirst and Clinical Pathways Goals

- Provide high quality care while attempting to reduce cost
  - Creating rules to biologic use that will result in appropriate usage, without strict authorization tactics
- Keep community rheumatology vigorous in Mid-Atlantic
  - Moving the money away from drug reimbursement to services, while maintaining community infusion
- First program of its kind for treatment of rheumatoid arthritis

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Breast Cancer Treatment Pathways
Adjuvant Therapy

ER Positive

The 21-gene recurrence assay (or the 70- gene expression assay) should be considered for all women with node negative and ER positive breast cancer whom you would consider appropriate for adjuvant chemotherapy. Patients with extremely small primary tumors (<0.5 cm) or those with large tumors greater than 5 cm, or those that are medically unsuitable for chemotherapy may omit this test.

Oncotype DX®

Low Risk	<18	Endocrine Therapy
Intermediate Risk	18-31	Endocrine Therapy +/- Chemotherapy
High Risk	>31	Endocrine Therapy + Chemotherapy

**Low Risk: National Steering Committee Comment: "Uncomfortable with low risk cut off of 18, less than 10 may be optimal, pending results of the TAILORx trial".

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Materials and Methods

- A total of 1,174 patients who were treated on the CFBCBS clinical care pathways program between August 2008- June 2011 and received Onco*type* DX® testing were retrospectively identified using CHSS proprietary claims software.

- The number of patients with a Recurrence Score® value in the low- (<18), intermediate- (18-30), and high-risk (≥31) groups and the number of patients who subsequently received chemotherapy were descriptively analyzed by age group and by time window from when the assay was ordered.
  - Window 1: August 1, 2008-July 31, 2009; window 2: August 1, 2009- July 31, 2010; window 3: August 1, 2010- June 30, 2011.

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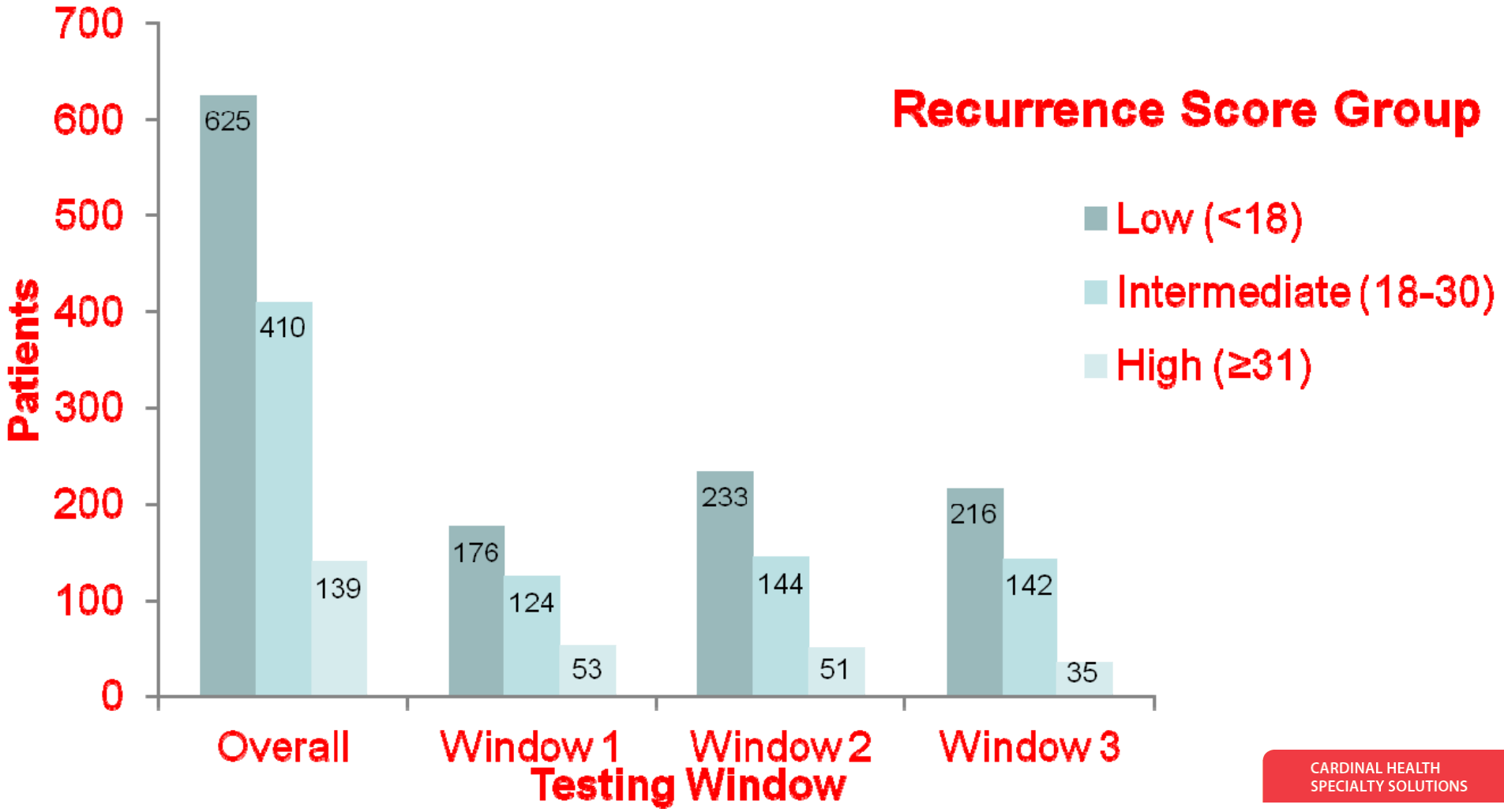
Distribution of Recurrence Score® Results



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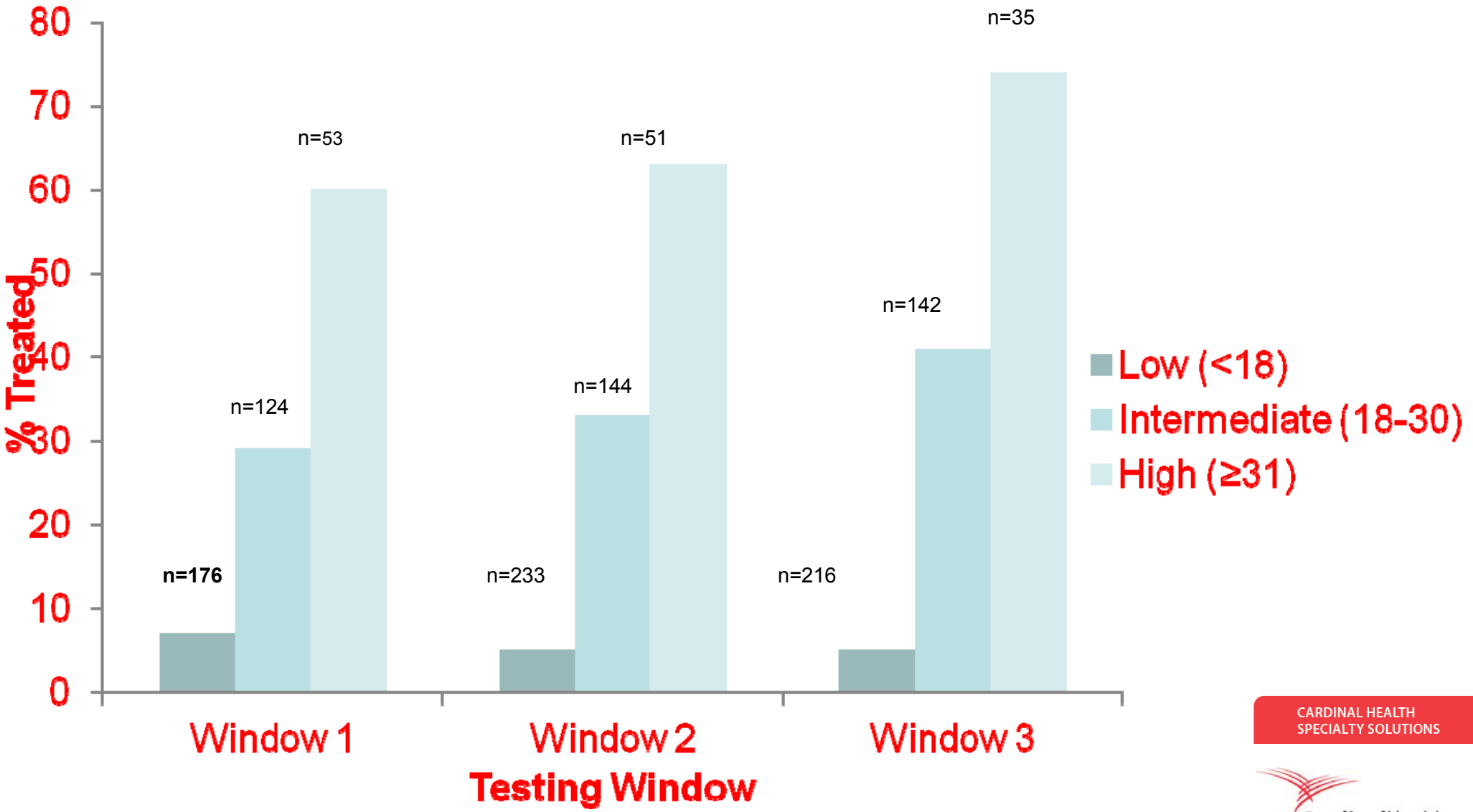
Chemotherapy Treatment Rate by Recurrence Score® Result



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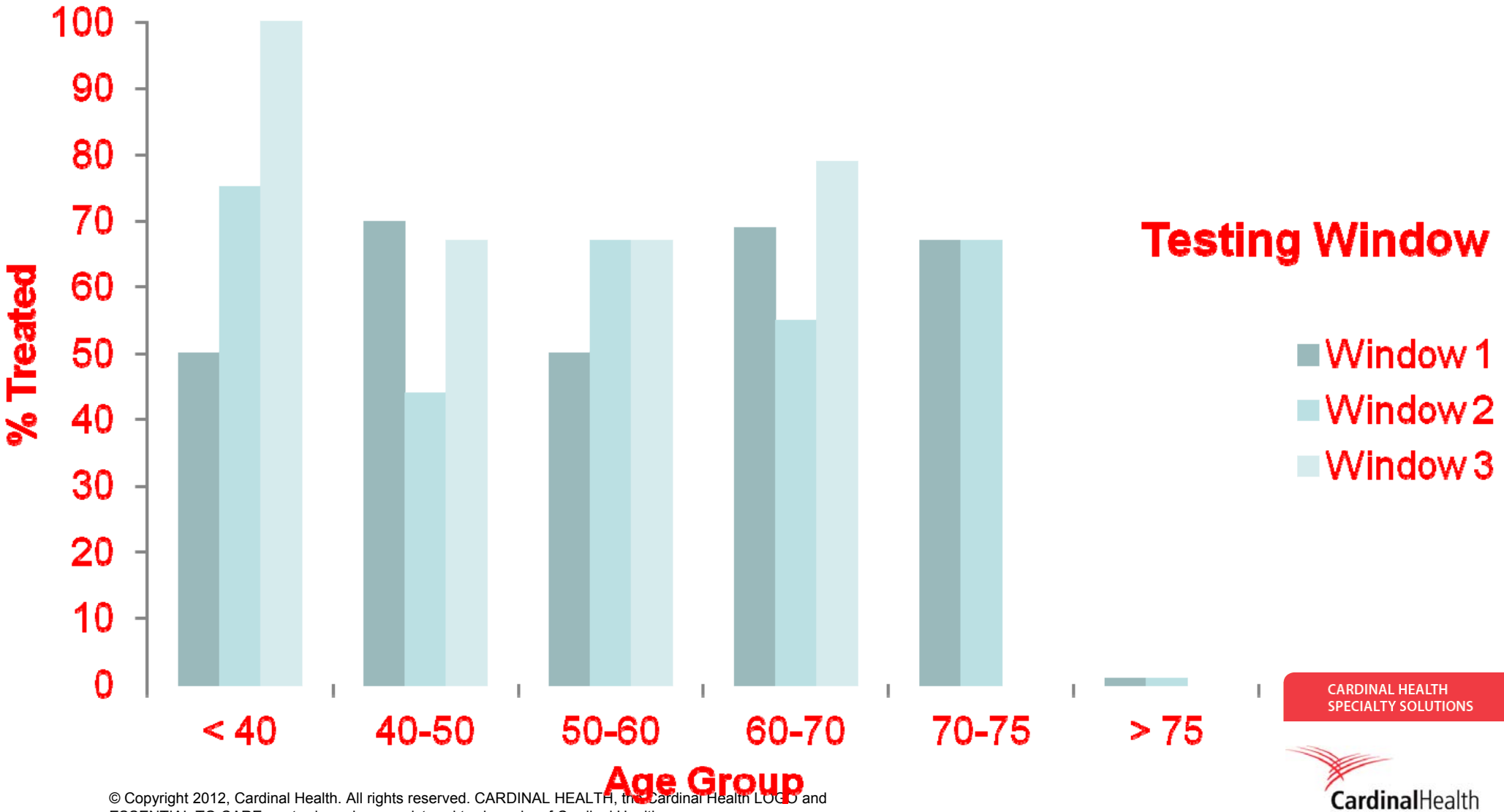
High Recurrence Score® and Chemotherapy Treatment Rate



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As Clear as Mud

Between the idea
And the reality
Between the motion
And the act
Falls the Shadow

-T.S.Eliot,The Hollow Men

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Evaluation of Variables that May Impact Chemotherapy (CT) Administration After Determination of Oncotype DX® Recurrence Score® Results

Bowen K,[1] Gilmore J,[1] Szabo S,[1] Haislip S,[1] Hassell R,[2]
Cooper J,[2] Richardson S,[3] Fitzgerald M,[2] Feinberg B[2]
[1]Georgia Cancer Specialists, Atlanta, GA
[2]Cardinal Health Specialty Solutions, Dublin, OH
[3]Genomic Health, Inc., Redwood City, CA

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Methods

- Patients treated at Georgia Cancer Specialists diagnosed with ER-positive, HER2-negative, node-negative early stage breast cancer between 2009-2011 were identified through a retrospective search of electronic medical records.

- Descriptive analyses included:
  - Onco*type* DX® assay utilization in all eligible patients
  - Proportion of chemotherapy-treated patients with or without Onco*type* DX assay testing
  - Recurrence Score® groups (low <18, intermediate 18-30, high ≥31) and chemotherapy use

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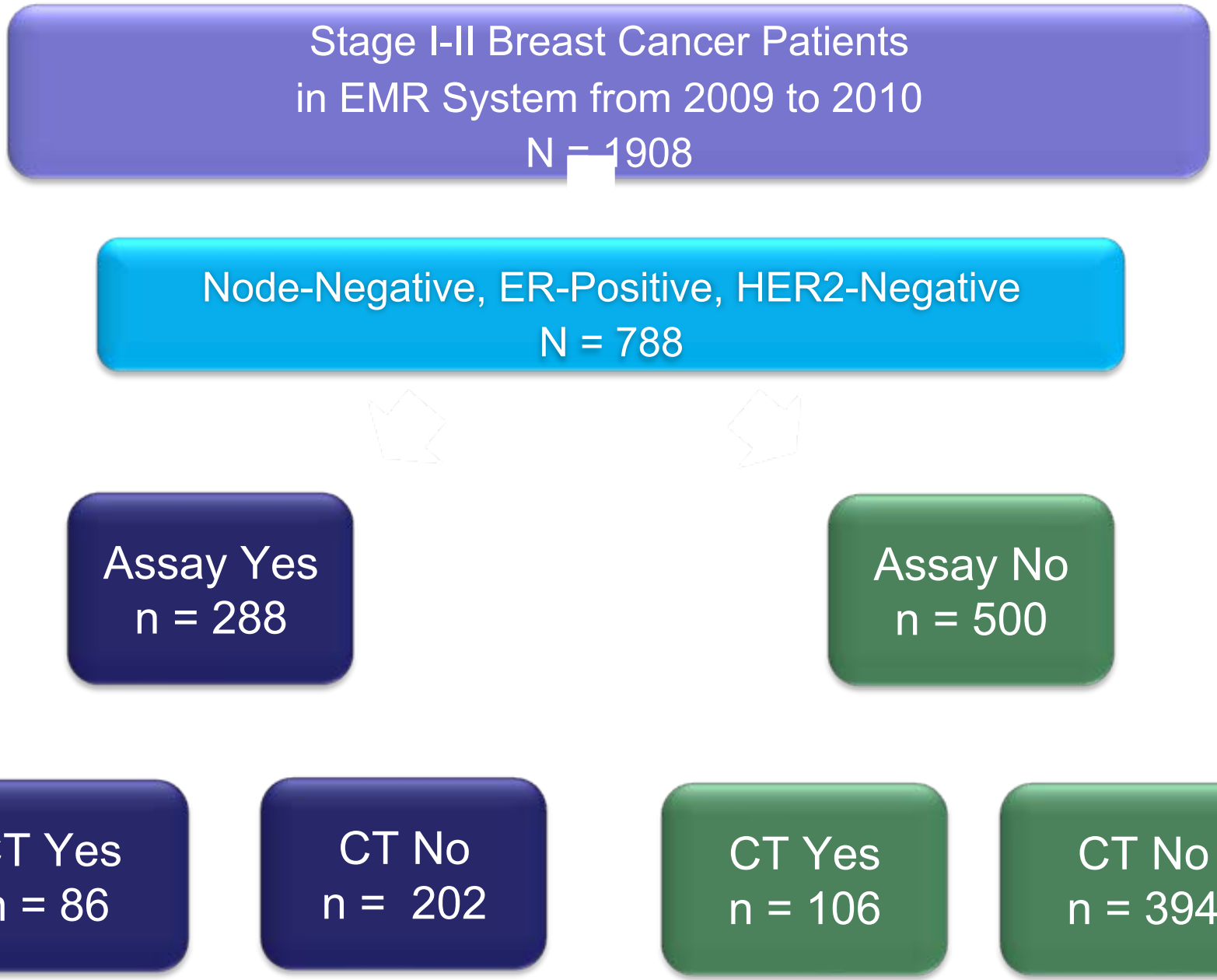
Patient Population



Oncotype DX® Assay Utilization

		Oncotype DX Assay Yes	Oncotype DX Assay No
Age (years)	≤ 45 (n=86)	29 (34%)	57 (66%)
	46-55 (n=219)	108 (49%)	111 (51%)
	56-65 (n=232)	85 (37%)	147 (63%)
	66-75 (n=161)	54 (34%)	107 (66%)
	≥ 76 (n=90)	12 (13%)	78 (86%)
Size (cm)	≤ 2.0 (n=602)	226 (38%)	376 (62%)
	2.0-5.0 (n=162)	59 (36%)	103 (64%)
	> 5.0 (n=22)	3 (13.6%)	19 (86%)
	n/a (n=2)	0 (0%)	2 (100%)
Grade	1 (n=62)	28 (45%)	34 (55%)
	2 (n=89)	38 (43%)	51 (57%)
	3 (n=27)	18 (67%)	9 (33%)
	n/a (n= 610)	204 (33%)	406 (67%)

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Oncotype DX® Assay and Chemotherapy Utilization

		Oncotype DX Yes		Oncotype DX No	
		CT Yes	CT No	CT Yes	CT No
Age (Years)	**≤ 45 (n=86)**	14/29 (48%)	15/29 (52%)	18/57 (32%)	39/57 (68%)
	46-55 (n=219)	39/108 (36%)	69/108 (64%)	33/111 (30%)	78/111 (70%)
	56-65 (n=232)	23/85 (27%)	62/85 (73%)	39/147 (27%)	108/147 (73%)
	66-75 (n=161)	7/54 (13%)	47/54 (87%)	7/107 (7%)	100/107 (93%)
	≥ 76 (n=90)	3/12 (25%)	9/12 (75%)	9/78 (12%)	69/78 (88%)
Size (cm)	**≤ 2.0 (n=602)**	62/226 (27%)	164/226 (73%)	50/376 (13%)	326/376 (87%)
	2.0-5.0 (n=162)	23/59 (39%)	36/59 (61%)	41/103 (40%)	62/103 (60%)
	> 5.0 (n=22)	1/3 (33%)	2/3 (67%)	15/19 (79%)	4/19 (21%)
	n/a (n=2)	0	0	0	2/2 (100%)
Grade	**1 (n=62)**	5/28 (18%)	23/28 (82%)	6/34 (18%)	28/34 (82%)
	2 (n=89)	11/38 (29%)	27/38 (71%)	19/51 (37%)	32/51 (63%)
	3 (n=27)	11/18 (61%)	7/18 (39%)	3/9 (33%)	6/9 (66%)
	n/a (n=610)	59/204 (29%)	145/204 (71%)	78/406 (19%)	328/406 (81%)

Distribution of Recurrence Score® Results

	Low (< 18)	Intermediate (18-30)	High ≥ 31)
Overall (n=288)	145 (50%)	97 (34%)	46 (16%)
Age Group (Years)			
≤ 45 (n=29)	13 (45%)	10 (34%)	6 (21%)
46-55 (n=108)	55 (51%)	31 (29%)	22 (20%)
56-65 (n=85)	40 (47%)	31 (36%)	14 (16%)
66-75 (n=54)	29 (54%)	21 (39%)	4 (7%)
≥ 76 (n=12)	8 (67%)	4 (33%)	0
Tumor Size (cm)			
< 2.0 (n=226)	120 (53%)	67 (30%)	39 (17%)
2.0-5.0 (n=59)	23 (39%)	29 (49%)	7 (12%)
> 5.0 (n=3)	2 (67%)	1 (33%)	0
Tumor Grade			
Grade 1 (n=28)	16 (57%)	11 (39%)	1 (4%)
Grade 2 (n=38)	21 (55%)	12 (32%)	5 (13%)
Grade 3 (n=18)	2 (11%)	5 (28%)	11 (61%)

You can bring a horse to water…

Yes, algorithms can be constructed to provide reasonable predictions about "what treatment [and how construed], by whom, is most effective for this individual with that specific problem, and under which set of circumstances?"

But, in the end it is one human being (the physician) who relates to another human being (the patient), and one cannot underestimate the power of relationship in medicine. Patient expectancies and belief in both the physician and process are extremely important in clinical effectiveness. (Paddock, 2012 in response to Paul, 1967).

Point: Medicine is an Art…but…it must be informed by and grounded in science.

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Evaluation of Oncotype DX® Testing and Subsequent Patterns of Care in Patients (pts) with Early-Stage Breast Cancer (ESBC)

Fitzgerald M,[1] Hassell R,[1] Haislip S,[2] Gilmore J,[2] Richardson S,[3] Cooper J,[1] Szabo S,[2] Feinberg B[1]

[1]Cardinal Health Specialty Solutions, Dublin, OH

[2]Georgia Cancer Specialists, Atlanta, GA

[3]Genomic Health, Inc., Redwood City, CA

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Objectives

The objectives of this study were:

To determine the uptake of the Onco*type* DX® assay by physicians with varying levels of experience

To assess the patterns of care that followed testing with the Recurrence Score® result

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Methods

A total 788 patients treated at Georgia Cancer Specialists diagnosed with ER-positive, HER2-negative, node-negative early stage breast cancer between 2009-2011 were identified through a retrospective search of electronic medical records.

Descriptive analyses included:

- Onco*type* DX® assay and chemotherapy use in all eligible patients
- Treating physician ordering and prescribing patterns

Eligible patients by physician was defined as low (<10), intermediate (10-25), and a high (>25) number of patients.

Onco*type* DX assay utilization was defined as low (<15% of eligible patients), low-moderate (15-40%), moderate-high (41-60%), and high (>60%) use.

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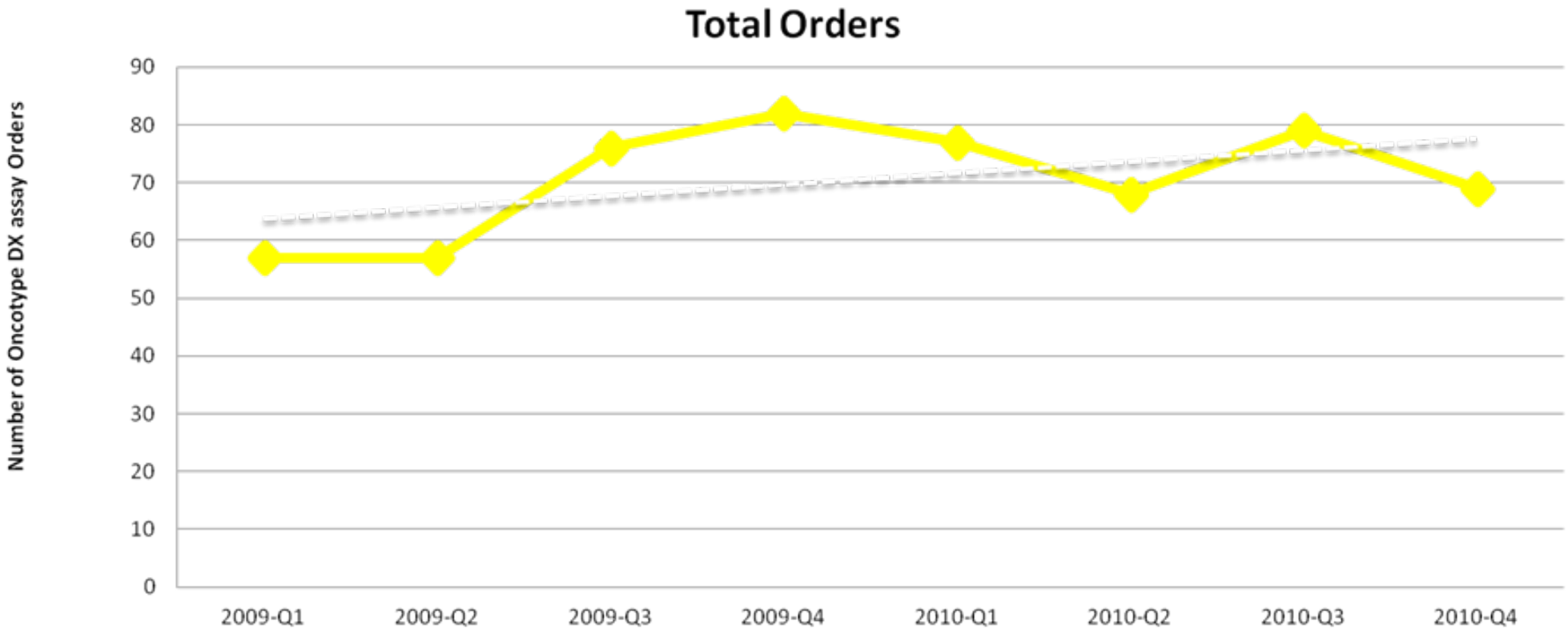
Oncotype DX® Utilization From Q1 2009 to Q4 2010



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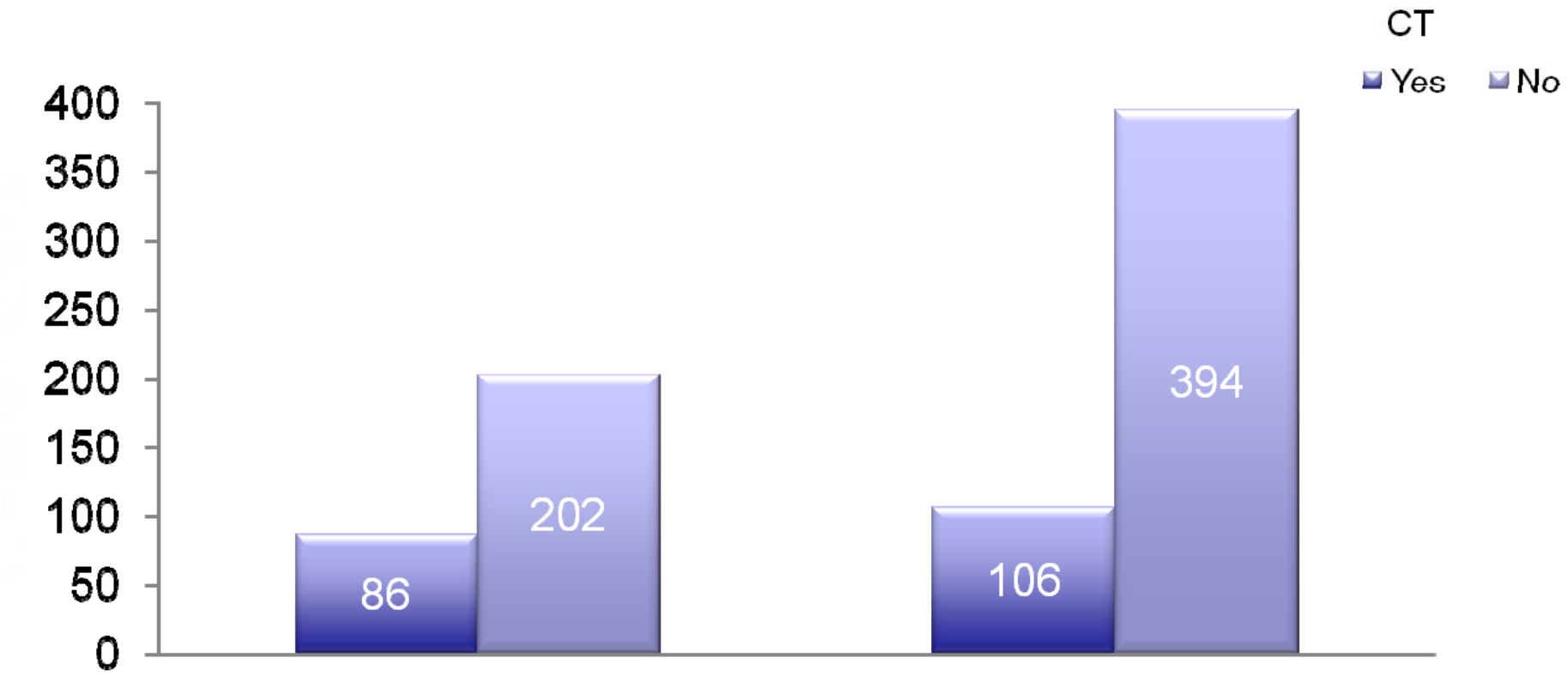
Overall Oncotype DX® Assay and Chemotherapy Use



Of the 788 patients eligible for the Oncotype DX assay, 288 (37%) underwent testing.

Within the tested group, 30% (86/288) received chemotherapy. Within the non-tested group, 21% (106/500) received chemotherapy.

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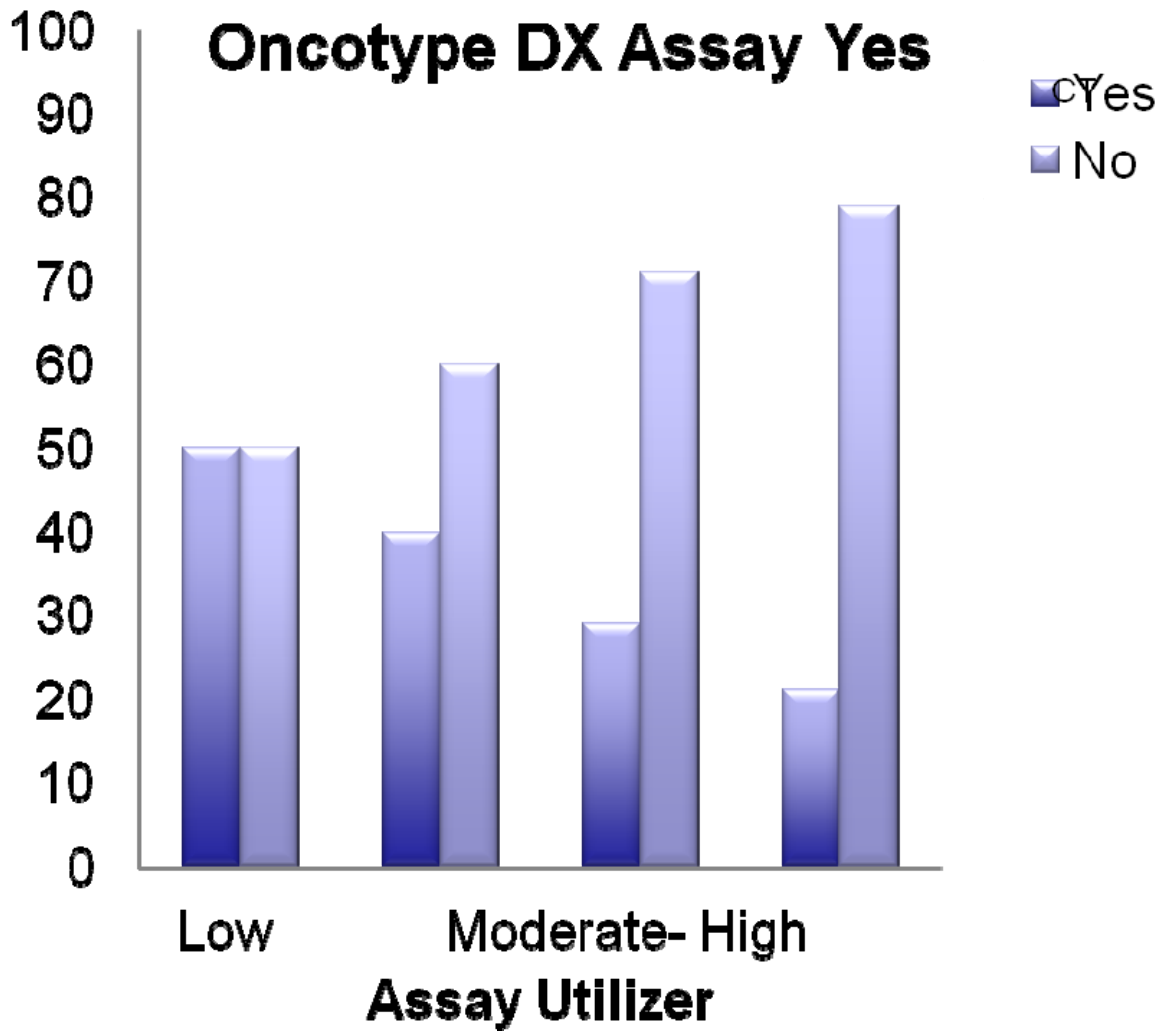
Chemotherapy Use (%) Based on Oncotype DX® Assay Use



Within the patient cohort that received the assay, use of CT decreased as physician assay utilization increased.

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Distribution of Recurrence Score® Results and Chemotherapy Use

Assay Utilizer; % time (n=patients tested)	Recurrence Score Result					
	Low (RS <18)		Intermediate (RS 18-30)		High (RS ≥31)	
	Total	Rec'd CTX	Total	Rec'd CTX	Total	Rec'd CTX
Low; <15% (n=6)	3 (50%)	1 (33%)	3 (50%)	2 (67%)	0	n/a
Low-Moderate; 15-40% (n=58)	27 (47%)	2 (7%)	20 (34%)	12 (60%)	11 (19%)	9 (82%)
Moderate-High; 41-60% (n=157)	74 (47%)	4 (5%)	57 (36%)	19 (33%)	26 (17%)	23 (88%)
High; >60% (n=67)	41 (61%)	1 (2%)	17 (25%)	7 (41%)	9 (13%)	6 (67%)
Total (n=288)	145 (50%)	8 (6%)	97 (34%)	40 (41%)	46 (16%)	38 (83%)

A Different Paradigm is Needed

"Data is not information, information is not knowledge, knowledge is not understanding, understanding is not wisdom."

-- Clifford Stoll

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Evaluation of variables that may impact the use of Oncotype® DX testing

Gilmore J, Hassell R, Szabo S, Feinberg, B

[1] Cardinal Health Specialty Solutions, Dublin, OH

[2] Genomic Health Inc., Redwood City, CA

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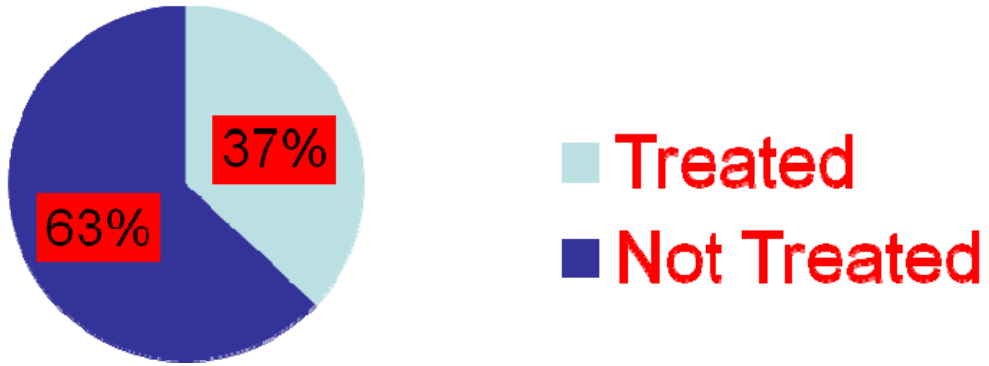
Study Results

- 1908 Early Stage BC Patients
- 788 Onco*type*® DX Eligible Patients
- 288 Onco*type*® DX Treated Patients
- 37% Utilization Rate

Oncotype DX Eligible Patients



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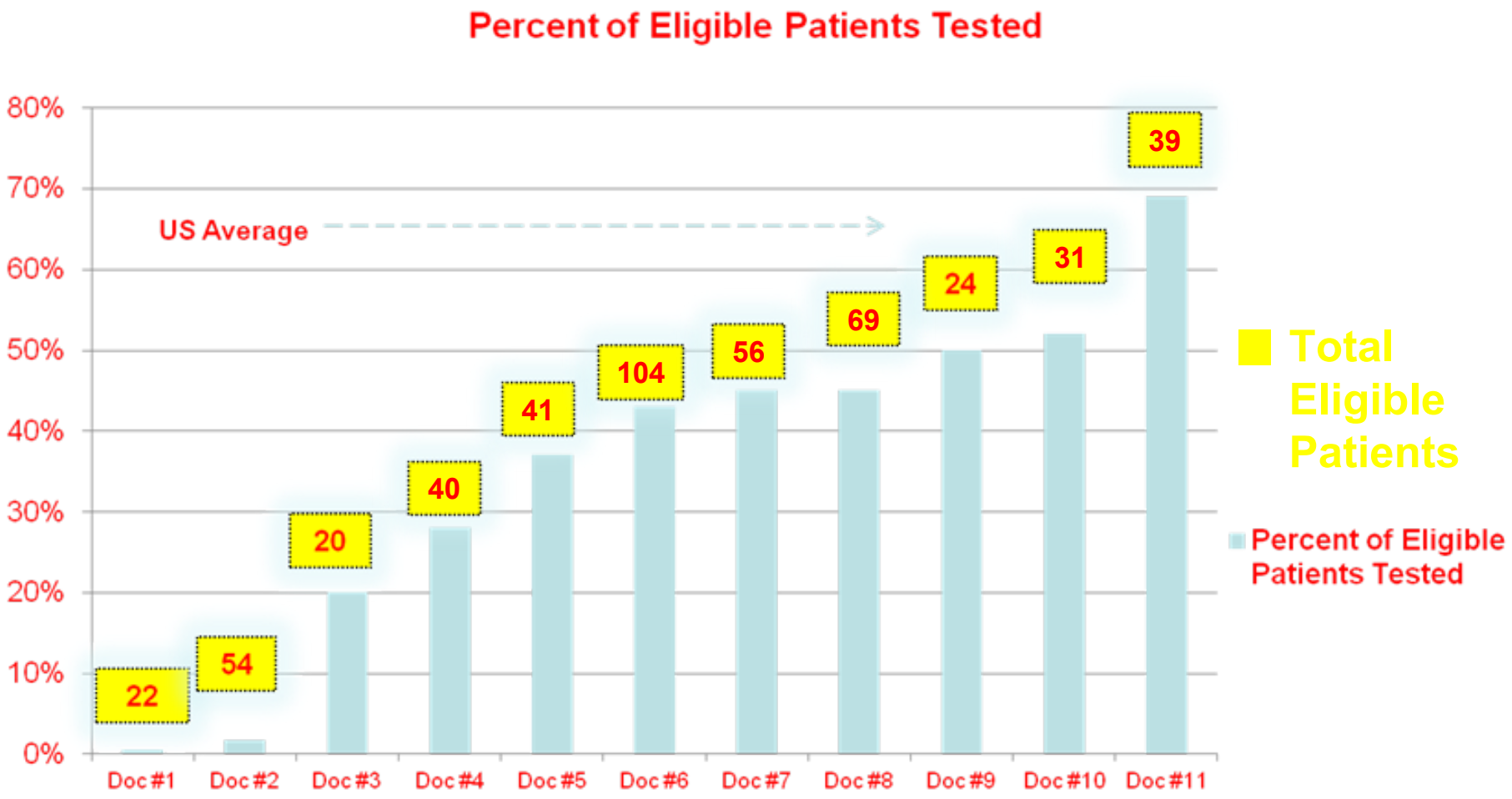
Oncotype® DX Utilization Patterns sorted by Physician



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THE END

Fact and truth are more complicated than one would imagine. Physicians are supposed to be scientists but they are not automatons, they are human . The wealth of information, the oft assailing of fact and truth as opinion and theory, the cognitive dissonance that allow people to listen and observe (learn) selectively, represent significant barriers for physician adherence to scientifically vetted guidelines. A new paradigm is need that embraces consensus guidelines, incents adoption and reports compliance in unobtrusive ways.

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Study Background

- To better understand physician behavior as it relates to **Onco*type*** **DX** testing, CHSS examined patterns of **Onco*type*** **DX** use in a large private practice oncology group with a robust electronic medical record (EMR), Georgia Cancer Specialists (GCS). We aimed to determine the variables that most impacted the use of Onco*type*® DX testing.

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Study Methods

- Using the Georgia Cancer Services EMR from 2009 to 2011, we retrospectively identified patients diagnosed with ESBC who were eligible for Onco*type* DX testing (stage I-II, node-negative, estrogen receptor-positive, HER2-negative). The use of Onco*type* DX testing was analyzed by patient age, tumor size, tumor grade, and physician prescribing patterns.

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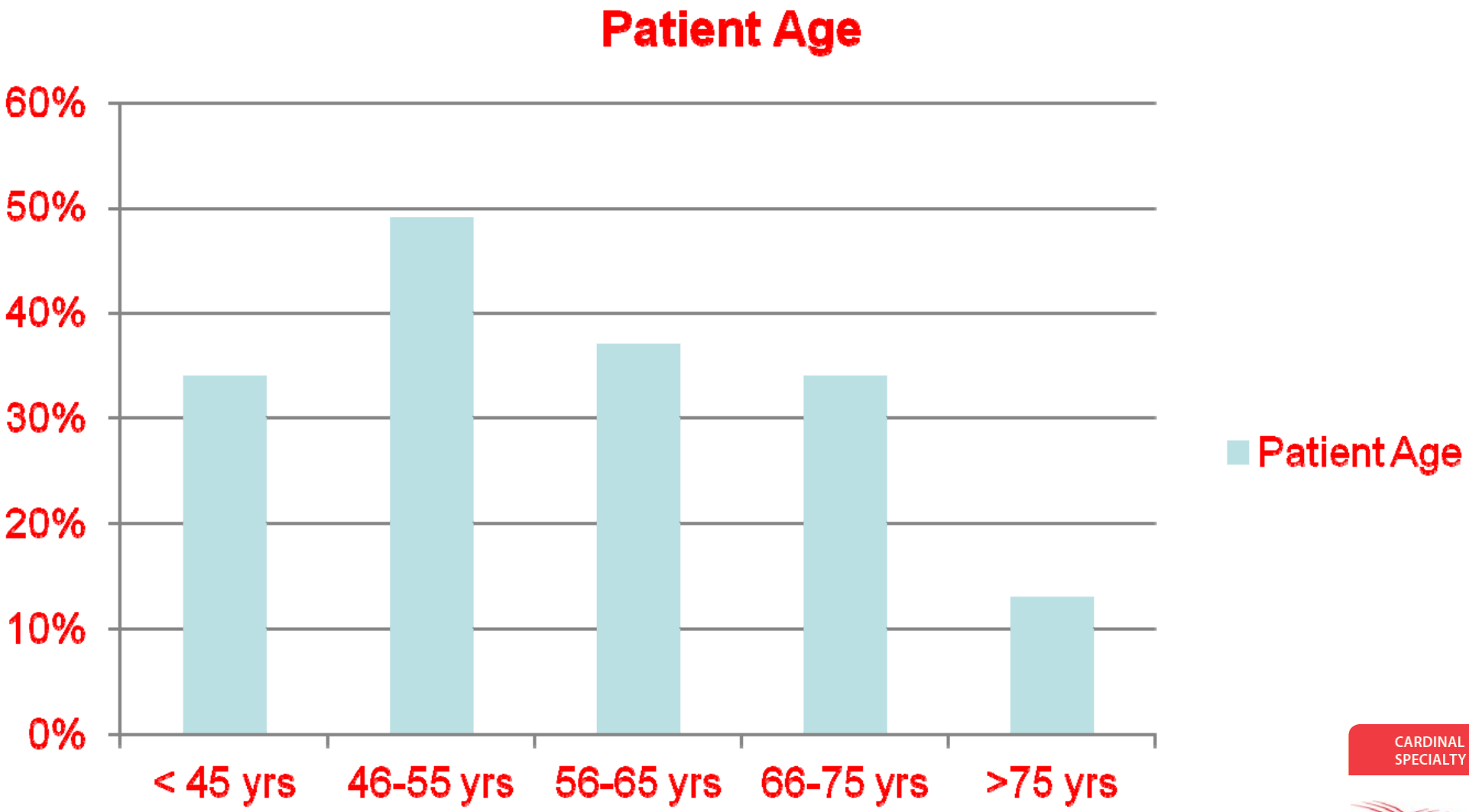
Oncotype® DX Utilization Patterns sorted by Patient Age



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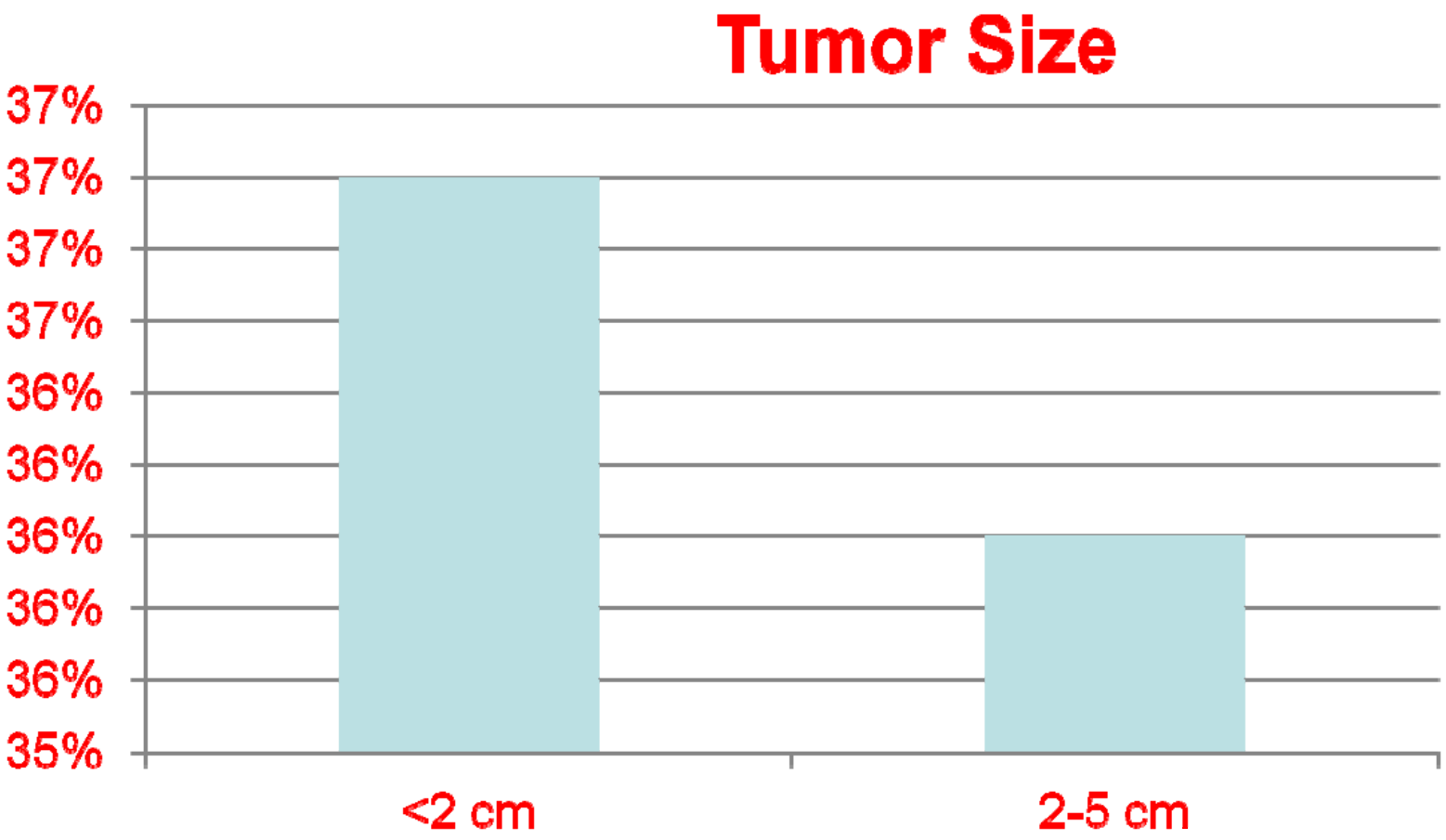
Oncotype® DX Utilization Patterns sorted by Tumor Size



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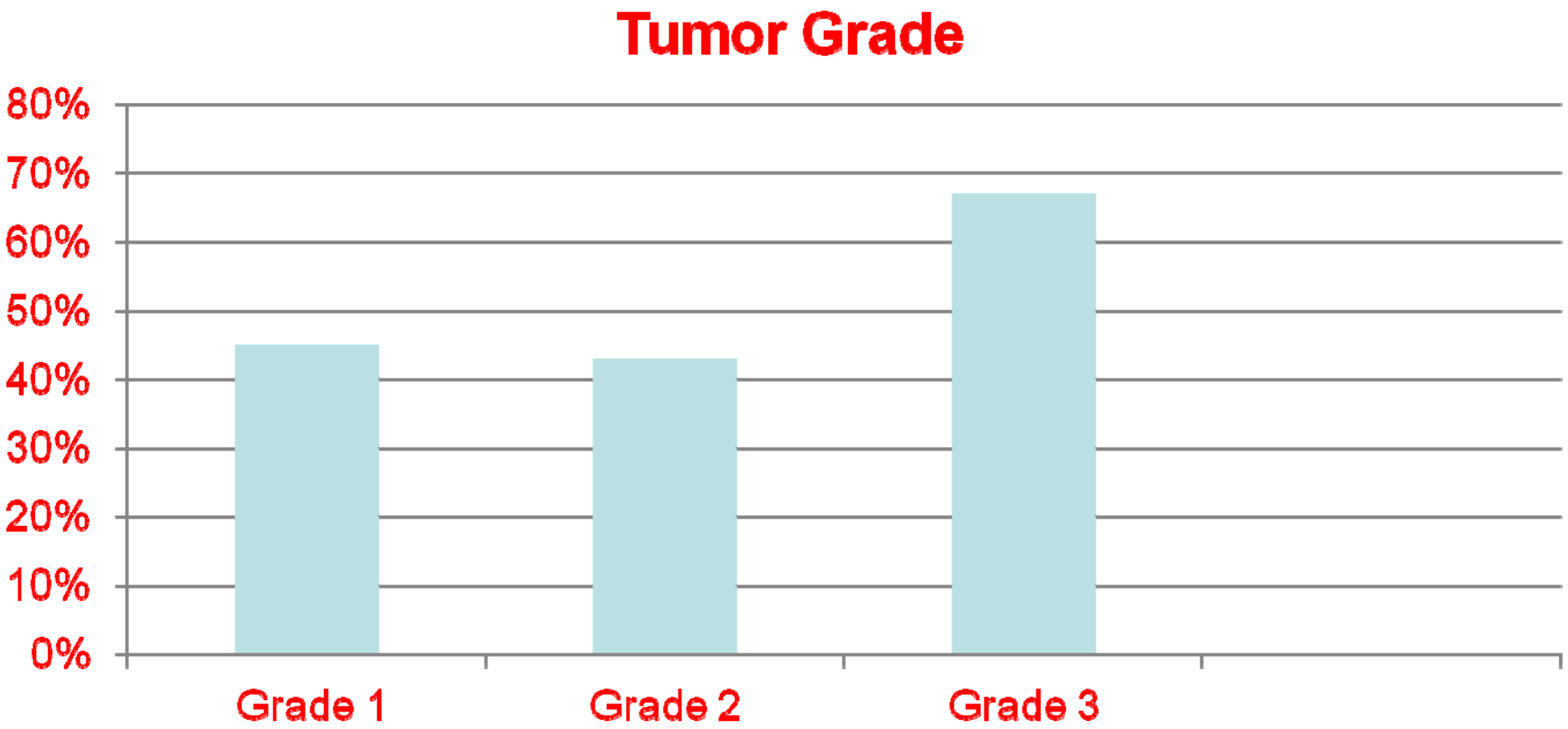
Oncotype® DX Utilization Patterns sorted by Tumor Grade



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Study Conclusions

- Based on this analysis, eligible patients with ESBC between 46-55 years of age, with small and intermediate sized tumors (<2-5 cm), and with grade 3 tumors were most likely to undergo Onco*type* DX testing. Although some trends in use were observed with specific tumor characteristics, physician behavior (choice) was the most significant variable in Onco*type* DX use.

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