Linking Oncotype Dx results to SEER data and patient report to assess challenges in individualizing breast cancer care

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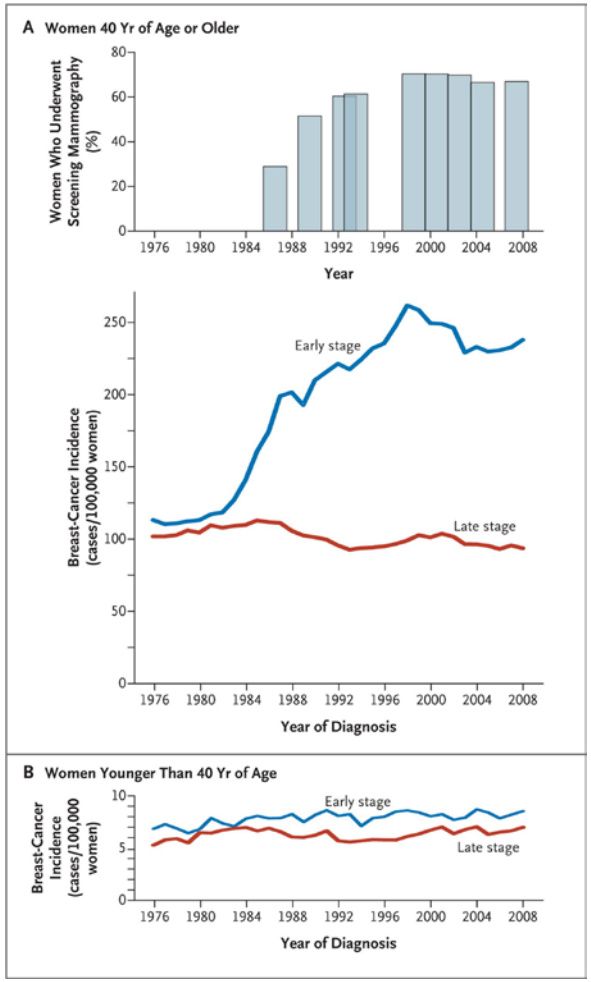
Previous treatment for early stage breast cancer

- Historically chemotherapy recommended for most women with tumor size >1 cm, regardless of lymph node involvement
- Previous levels of use chemo were: 75% of women <50 years of age, 30% 50-69, 5%≥70
- However adjuvant hormone therapy alone is sufficient for 85% of those with early stage, ER+, breast cancer
- Thus many undergo chemotherapy unnecessarily

Use of Screening Mammography and Incidence of Stage-Specific Breast Cancer in the United States, 1976–2008.



Bleyer A, Welch HG. N Engl J Med 2012;367:1998-2005

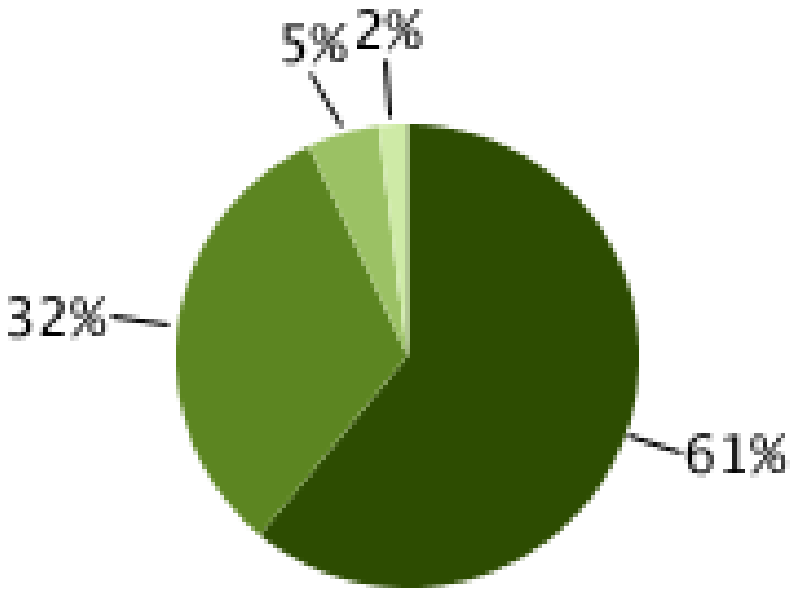
- Since onset of mammography screening among those 40+ there has been a large increase in early stage disease and relatively little decline in late stage
- Suggests that overtreatment of early stage disease may occur
- Genetic profiles of tumors such as done by Oncotype Dx may indicate which patients may need chemo (precision medicine)

Oncotype DX

Oncotype DX^{R} (Genomic Health, Redwood, CA) is:

- Meant to be used for ER-positive, HER2 negative, early stage breast cancer
- A validated 21-gene diagnostic assay
- Provides a Risk Score (RS) that predicts the benefit of chemotherapy and rate of cancer recurrence at 10 years (RS<18=Low; RS18-30=Intermediate; RS≥31=High).

Distribution of Breast Cancer Cases by Stage at Diagnosis SEER 18 2003-2009 (SEER.Cancer.Gov)



- **Localized (61%)**
  Confined to Primary Site
- **Regional (32%)**
  Spread to Regional Lymph Nodes
- **Distant (5%)**
  Cancer Has Metastasized
- **Unknown (2%)**
  Unstaged

iCanCare Study

(Individualized Cancer Care)

The Challenge of Individualizing Treatments for Patients with Breast Cancer

Steven Katz, MD, University of Michigan, Overall PI
LA: Ann Hamilton, PI, Dennis Deapen, Co-I.
Georgia: Kevin Ward, PI

- A challenge to physicians is in determining breast cancer treatment plan for disease with favorable prognosis.
- Screening has resulted in tripling of incidence of in situ and early invasive stage disease and only slight (or no) reduction in late stage disease. (61% localized, 32% regional)
- Treatments impose substantial morbidity.
- Concern about potential harm of over-treatment

Overall Goals of the Project

1) Examine challenges of individualizing treatment for women diagnosed with loco-regional breast cancer.

   Population based study of ~5200 patients and their physicians from Los Angeles County and state of Georgia,

   P1: surgeons and patients (loco-regional therapy)

   P2: medical oncologists and patients (systemic therapy)

2) Improve decision quality

   P3: surgeon practice-based online decision tool (Los Angeles not involved)

3) Disseminate SEER-based research findings to clinicians.

4) Advance methods in SEER population translational research on quality of cancer care.

Understand use of evaluative tests

- Use of MRI to determine extent of disease. Increased sensitivity could lead to unnecessary aggressive treatment.
- 21 gene assay (personalized assessment adding to previous use of ER and HER2 testing). Little is known about use of the test and impact of the assay results on treatment decision making.
- BRCA testing. What are the patterns of use in community setting among those not from high risk families?

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Study Methods

Cases selected by the registries using RCA from surgical reports

Patients contacted at least one month after surgery date

Sent survey in the mail and extensive telephone and other follow-up methods employed to increase response

5200 participants from Los Angeles and Georgia

Currently in the field (Oct 2013—July 2015).

70% response rate

Linkages

1. SEER Variables (among others)

- CS Site Specific Factor 1: ER status
- CS Site Specific Factor 22:Multigene signature method
  - 010=Oncotype DX
  - 020=Mammaprint
  - 030=Other
  - 040=Test performed, type unknown
- CS Site Specific Factor 23: Multigene signature results
  - 000-100 actual score
  - 200=Low risk of recurrence
  - 300=Intermediate risk of recurrrence
  - 400=High risk of recurrence

2. Planned linkage of dataset with Genomic Health (not yet completed).

Data used in these preliminary results:

1) Patient self-reported questionnaire data from 1498 cases from Los Angeles and Georgia who completed their questionnaire prior to Dec. 31, 2014 and for whom SEER data was available (and not missing).
2) SEER data on ER status, nodes positive, CS 22 and CS-23 on use of Oncotype DX and risk score.

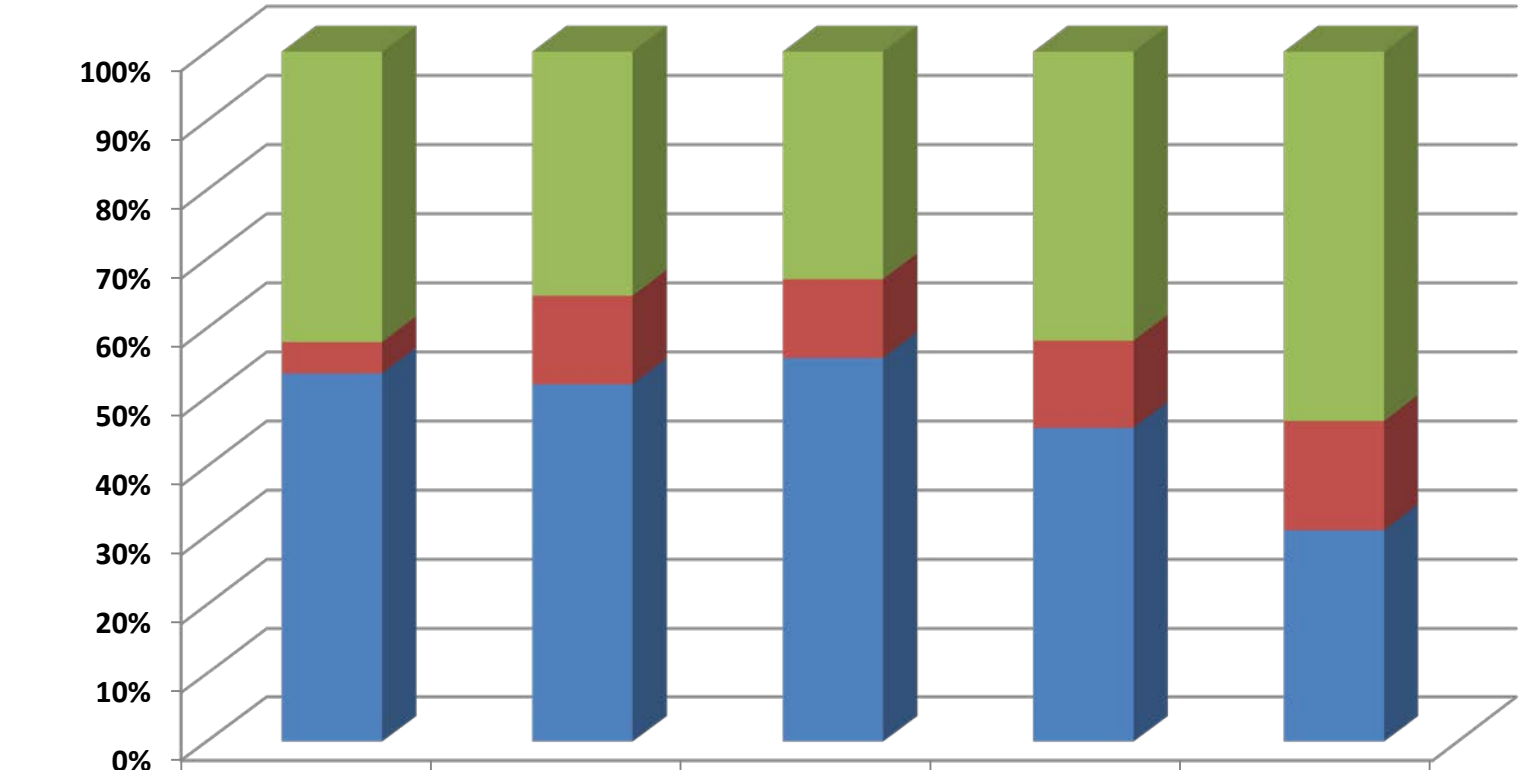
Percent distribution of self-reported use of Oncotype DX by Clinical subtype

Clinical subtype	Yes		No		DK		Total		% of total
	%	N	%	N	%	N	%	N	
ER+,N-	45.6	(487)	13	(139)	41.3	(441)	100	(1067)	71.2%
ER+,N+ (1-3)	29.9	(72)	16.2	(39)	53.9	(130)	100	(241)	16.1%
ER-, N- or +	11.6	(22)	17.9	(34)	70.5	(134)	100	(190)	12.7%
Total	38.8	(581)	14.2	(212)	47.1	(705)	100	(1498)	100.0%

Agreement between Self-reported use of Oncotype DX and SEER Report for patients with ER+,N- cancer (N=1067) (Kappa=0.19 (0.17-0.23))

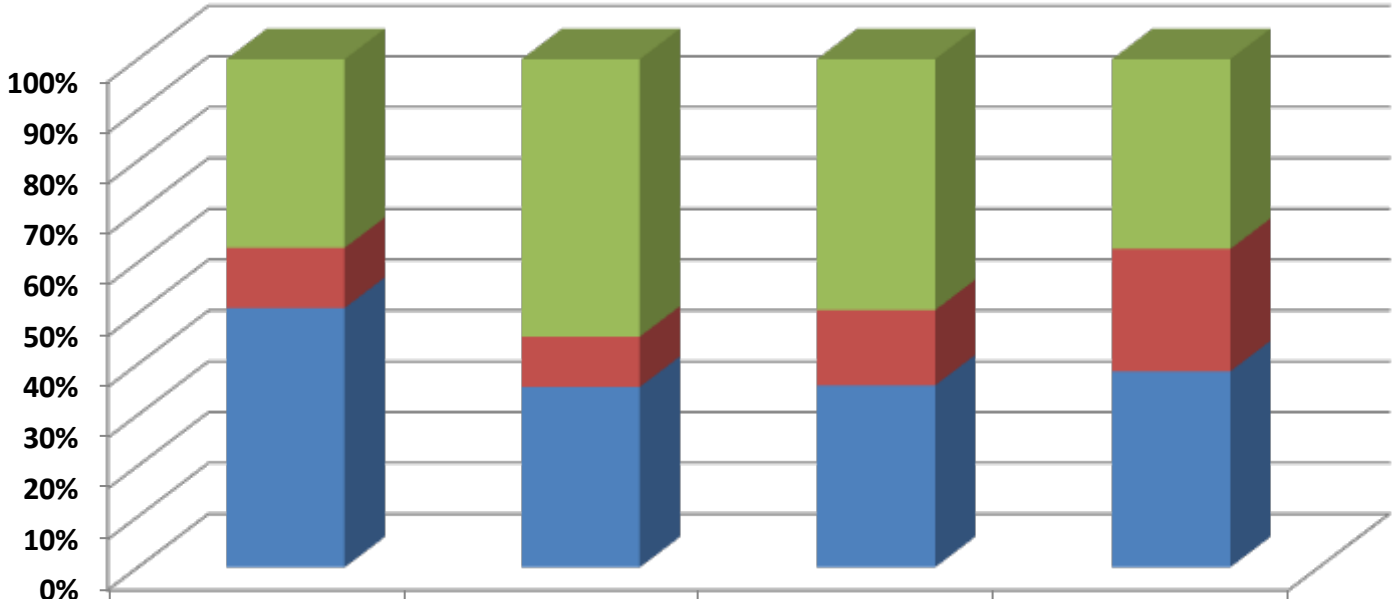
	SEER				
Self Report	Yes	No	DK	Total	
Yes	305	113	69	487	45.6%
No	9	81	49	139	13.0%
DK	57	247	137	441	41.3%
Total	371	441	255	1067	
	34.8%	41.3%	23.9%		100%

Self-reported use of Oncotype DX by patients with ER+,N- cancer, by age group (N=1015) (p<.0001)



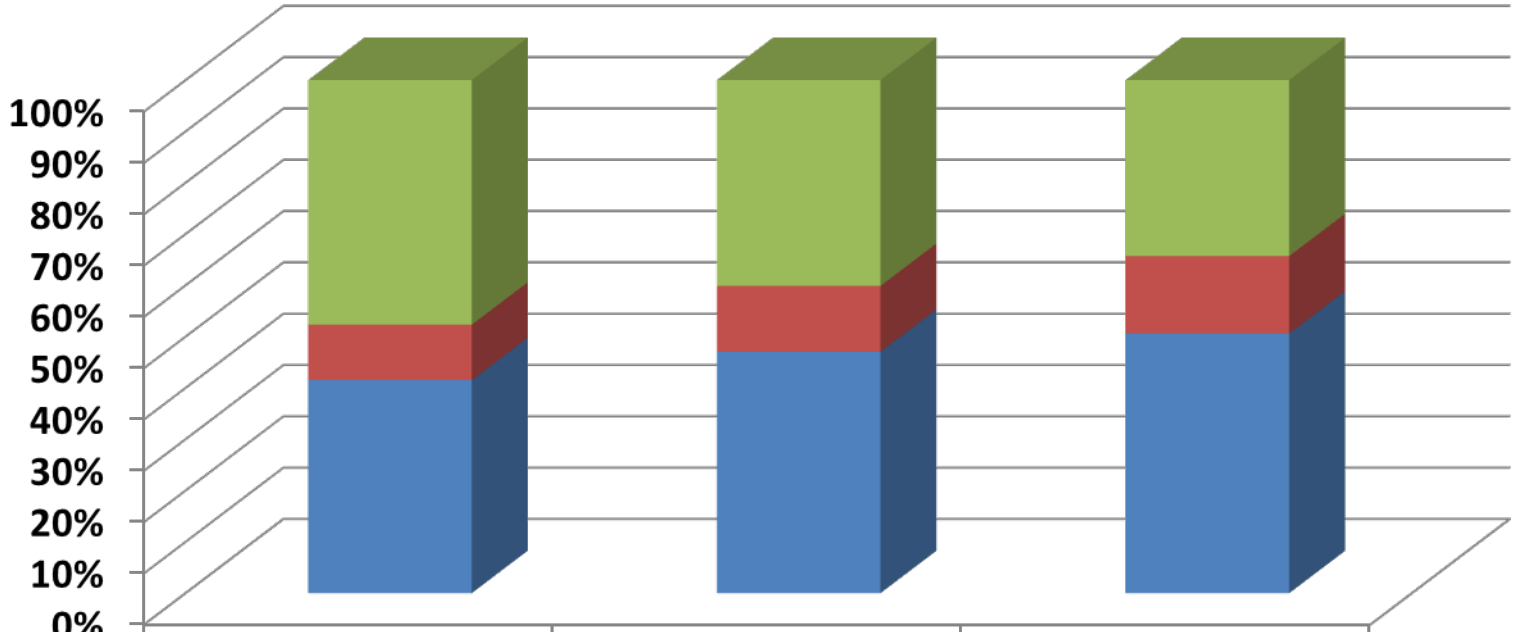
	20-39	40-49	50-59	60-69	70+
DK 41	40.7	35.3	32.9	41.8	53.4
No 12.9	4.4	12.8	11.4	12.6	15.8
Yes 46.1	51.8	51.9	55.7	45.6	30.8

Self-reported use of Oncotype DX by patients with ER+,N- cancer, by Race/ethnicity (N=1067) (p<.0001)



	Non-Hisp white	Hispanic	Black	Asian/ Other
DK	37.1	54.6	49.4	37.4
No	11.8	9.9	14.8	24.1
Yes	51	35.5	35.8	38.6

Self-reported use of Oncotype DX by patients with ER+,N- cancer, by Education (N=1067) (p<.06)

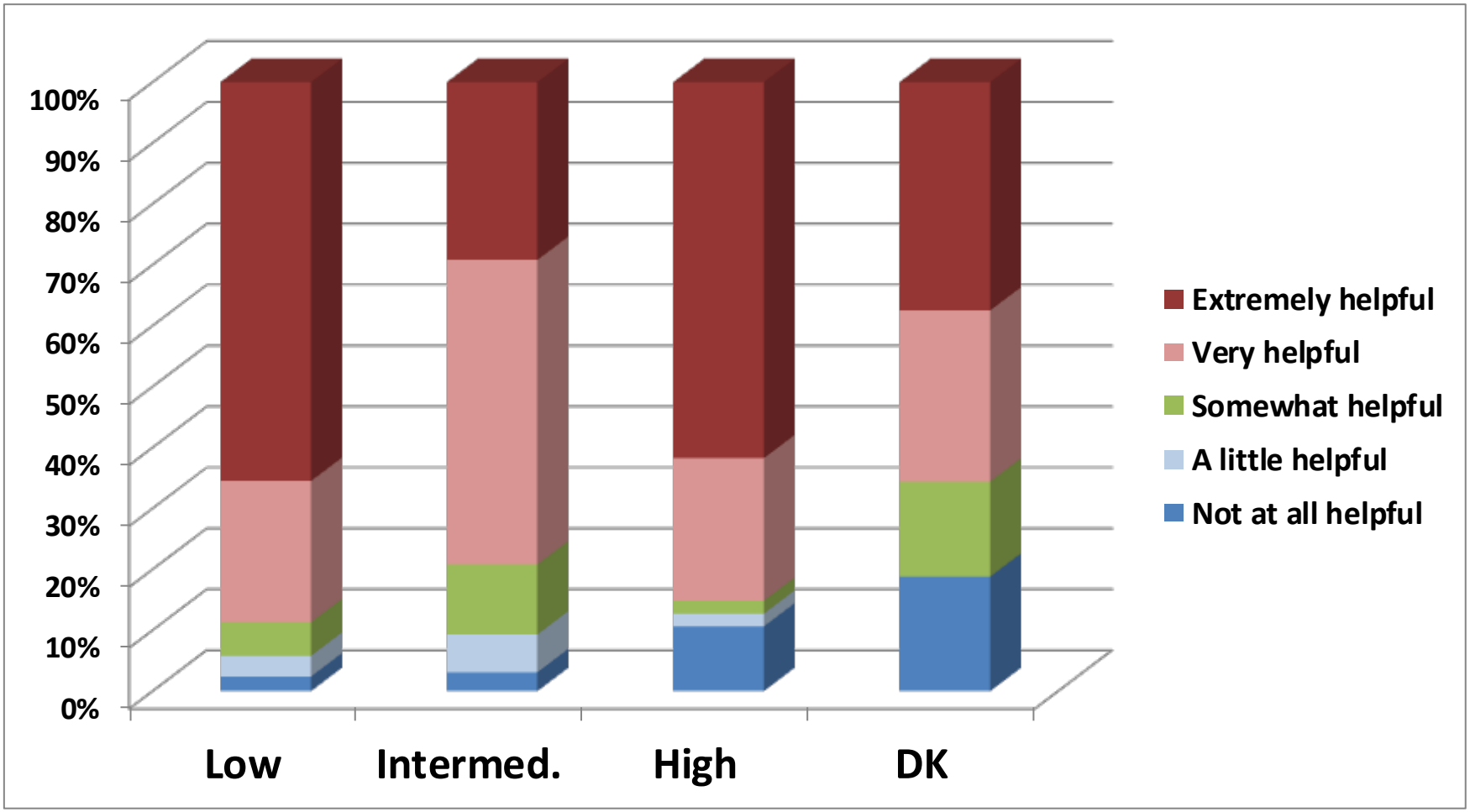


	HS grad or less	College grad or some college	Grad degree +
DK	47.7	40.1	34.3
No	10.8	12.8	15.1
Yes	41.5	47	50.6

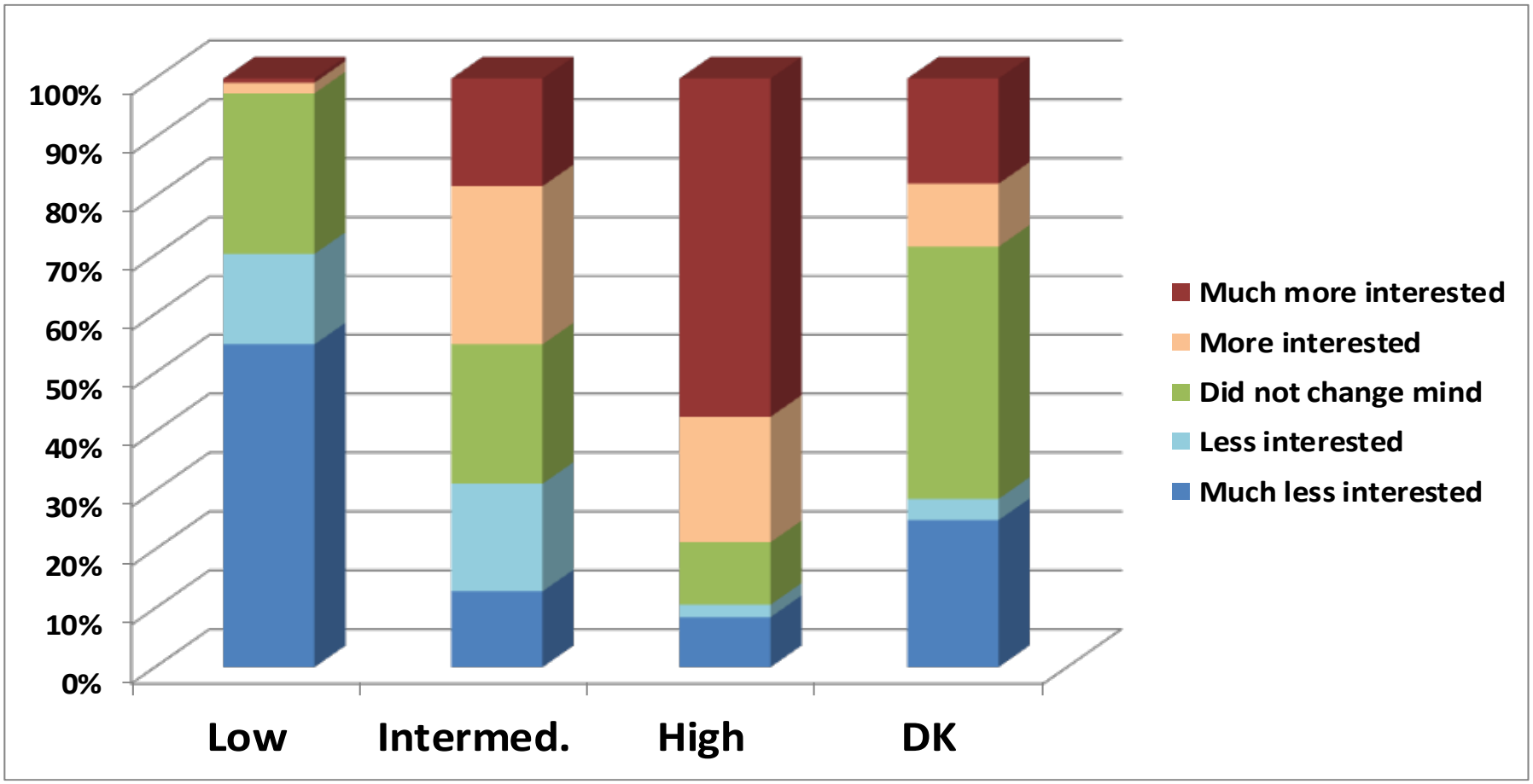
Percent Receiving Chemotherapy (self-report) by Oncotype DX Risk Score group by Clinical subtype

	Low	Inter-med.	High	DK	Total
ER+,N-	4	55.7	86.4	28.2	24
ER+,N+ (1-3)	15.2	77.8	90	62.5	46.5
ER- , N- or +	--	--	--	--	59.1

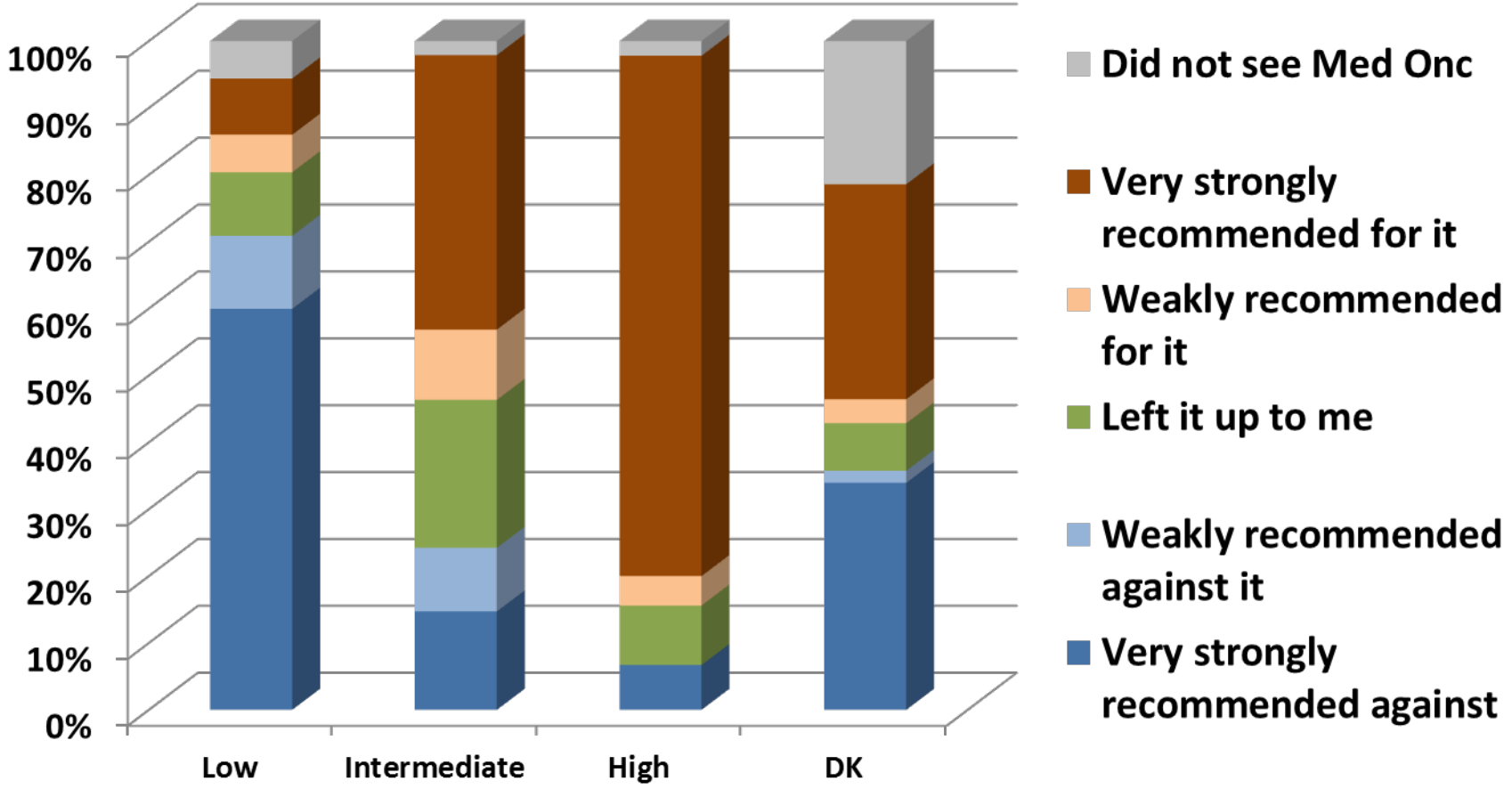
How helpful was the Oncotype DX test by Risk Group Score for patients with ER+,N- cancer (N=468) (p<.0001)



How did the Oncotype DX test results change your mind about getting chemotherapy by Risk Group Score For patients with ER+,N- cancer (N=454) (p<.0001)



How strongly did first medical oncologist recommend Chemotherapy by Risk Score group Group Score for patients with ER+,N- cancer (N=480) (p<.0001)



Summary and Conclusions

- A high percentage of women with early breast cancer don't know if they received Oncotype DX
- SEER has recently conducted a linkage with Genomic Health for the diagnosis years up to 2012.
- These results indicate that this linkage is crucial because the routinely collected SEER variables on use and Risk Score for Oncotype DX show little agreement with the self-reported data.

Summary and Conclusions

- Women have indicated that the test is very helpful in making their decision about use of chemotherapy, especially among those with a low risk score, giving them confidence in the option to forgo chemotherapy.

- Medical oncologists appear to appropriately recommend use or non use of chemotherapy based on the risk score level.

- Additional results will be available on the reliability of the self-reported data once the linkage of these cases with Genomic Health is completed.