

Molecular Subtypes of Female Breast Cancer: Their Associated Factors and Treatment

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Louisiana Tumor Registry

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Background

The background of the slide is a light pink color with a faint, stylized pink ribbon graphic on the right side, symbolizing breast cancer awareness.

- Breast cancer is now recognized as a heterogeneous disease with distinct biological molecular subtypes
- Most accepted classification based on molecular signatures: 4 “intrinsic” subtypes approximated by joint expression of hormonal receptors (ER/PR) and human epidermal growth factor 2 (HER2)
- These subtypes have different prognoses and treatment options.
- Variations in the distribution of these subtypes may explain partly the observed racial disparities in breast cancer survival in Louisiana, a racially and socioeconomically diverse population.

Objectives

- Describe the distributions and age-specific incidence rates of the four molecular subtypes of breast cancer among Louisiana women and their associated factors.
- Examine patterns of systemic treatment (mostly adjuvant) by subtypes of breast cancer, including use of target therapies.
- Explore factors associated with not receiving any systemic treatment

Methods

- Data sources:

- Routine Louisiana Tumor Registry data collection, including ER, PR and HER2
- CDC-funded special project of Enhancing Cancer Registry Data for Comparative Effectiveness Research (CER), part of the ARRA grant

Detailed information on treatment received within 12 months of diagnosis for breast, CRC cancers and CML



Methods

- Eligibility criteria
 - All ages (ranges from 23-101 yrs.)
 - Louisiana female residents
 - Diagnosed with invasive breast cancer in 2011
 - Microscopically confirmed cases only
 - No autopsy or death certificate cases
 - Paget's disease, mesothelioma, Kaposi's sarcoma, and lymphoma cases excluded



Methods

- Primary method of treatment data collection was medical record abstraction:
 - hospitals
 - non-hospital settings, including
 - free-standing ambulatory centers
 - radiation facilities
 - physician practice groups
 - medical oncologists
- Multiple visits to complete all treatment information in each patient



Methods

First course cancer-directed treatment included

- Surgery and Radiation
- Chemotherapy
 - Each chemo agent name
 - Chemo National Service Center (NSC) number
 - No. of chemo doses planned & received
 - total chemo dose planned & received
 - start and end date of chemotherapy
 - whether chemo was completed
- Hormonal therapy
- Biological response modifiers



Methods

- Using information on ER (SSF1), PR (SSF2) and HER2 Summary Result (SSF15), cases were classified into the following:
 - Luminal A (HR+/HER2-)
 - Luminal B (HR+/HER2+)
 - Triple Negative (HR-/HER2-)
 - HER2-enriched/amplified (HR-/HER2+)

Note: HR= '+' when ER+/PR+, ER+/PR-, or ER-/PR+



Methods

- 5-year age-specific incidence rates per 100,000 women were calculated by subtype for NHW & NHB.
- Univariate logistic regression analyses were used to identify factors associated with specific subtype and with not receiving systemic treatment.
- Multivariate logistic regression analyses were conducted to quantify adjusted associations.
- Analyses were carried out using SAS version 9.4.

Table 1. Distribution of Invasive Female Breast Cancer by Subtype. Louisiana versus SEER

	Louisiana (Diagnosis year: 2011)	SEER 18 (Diagnosis Year: 2010)
	N=3,818	N=57,483
HR+/HER2-	69.5%	72.7%
HR-/HER2-	15.1%	12.2%
HR+/HER2+	10.6%	10.3%
HR-/HER2+	4.8%	4.6%
Total	100%	100%
Unknown	(11.9%)	(12.0%)

The differences in the distributions is statistically significant ($p < 0.0001$)

Age-specific Incidence Rates by Molecular Subtype of Invasive Female Breast Cancer Diagnosed in Louisiana, 2011



Table 2A. Association of Breast Cancer Molecular Subtypes with Demographic and Clinical Factors: Odds Ratios of HR-/Her2- versus HR+/Her2-, Louisiana, 2011

Variable	HR+/HER2- (N=1,900)	HR-/HER2- (N=412)	Adjusted ¹ OR (95% CI)
Age at diagnosis (yrs.)			
<50	16.5%	31.6%	1.46 (1.08-1.99)
50-64	37.3%	38.1%	1.00
65-74	26.1%	16.0%	0.66 (0.47-0.94)
75/+	20.1%	14.3%	0.97 (0.67-1.39)
Race/Ethnicity			
Non-Hispanic White	72.0%	51.5%	1.00
Non-Hispanic Black	24.8%	46.6%	1.80 (1.40-2.32)
Hispanic and Others	3.2%	1.9%	0.59 (0.26-1.34)

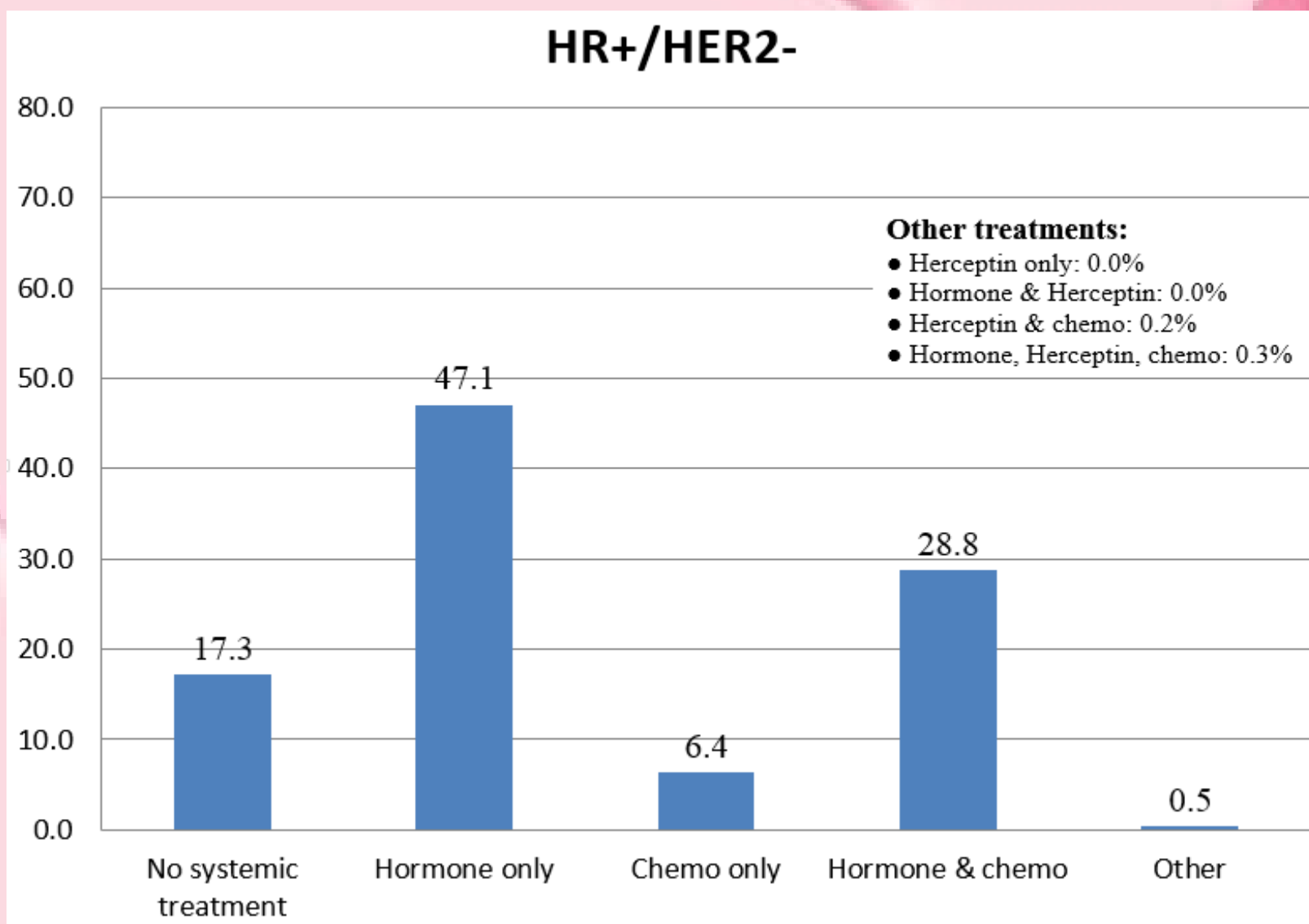
¹ Adjusted for age, race, AJCC stage, and Bloom-Richardson grade.

Table 2B. Association of Breast Cancer Molecular Subtypes with Demographic and Clinical Factors: Odds Ratios of HR-/Her2- versus HR+/Her2-, Louisiana, 2011

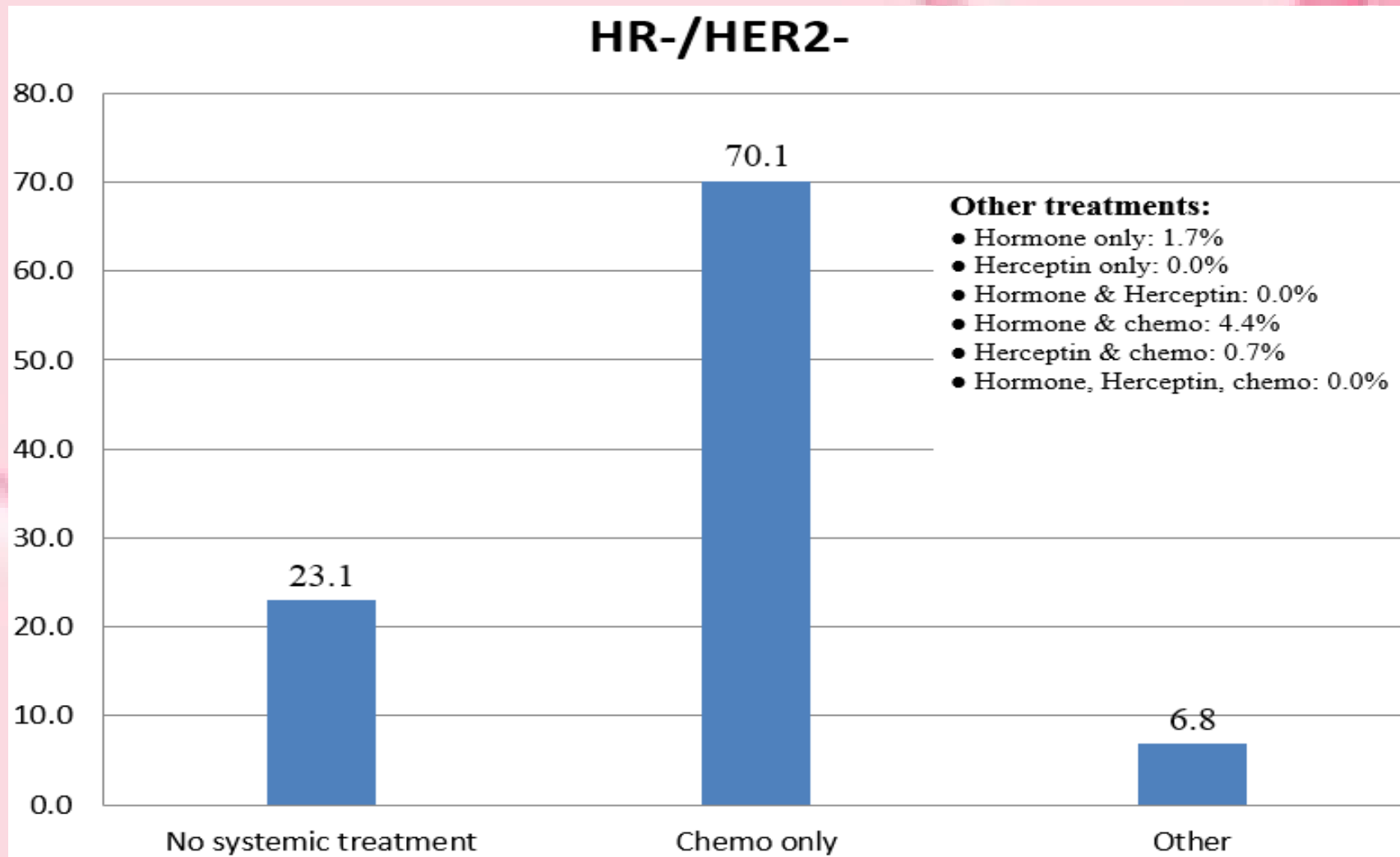
Variable	HR+/HER2- (N=1,900)	HR-/HER2- (N=412)	Adjusted ¹ OR (95% CI)
AJCC 7 th stage			
I	53.1%	37.6%	1.00
II	30.6%	38.3%	1.01 (0.76-1.33)
III	10.9%	16.0%	1.10 (0.76-1.60)
IV	5.5%	8.0%	1.10 (0.68-1.79)
Bloom-Richardson grade			
Low	27.4%	3.6%	1.00
Medium	46.3%	19.7%	2.98 (1.69-5.24)
High	16.6%	67.7%	25.35 (14.65-43.86)
Unknown	9.6%	9.0%	6.01 (3.18-11.36)

¹ Adjusted for age, race, AJCC stage, and Bloom-Richardson grade.

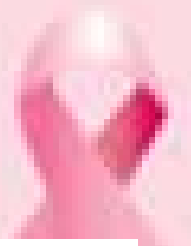
Treatment Distribution for Invasive Female Breast Cancer Diagnosed in Louisiana, 2011



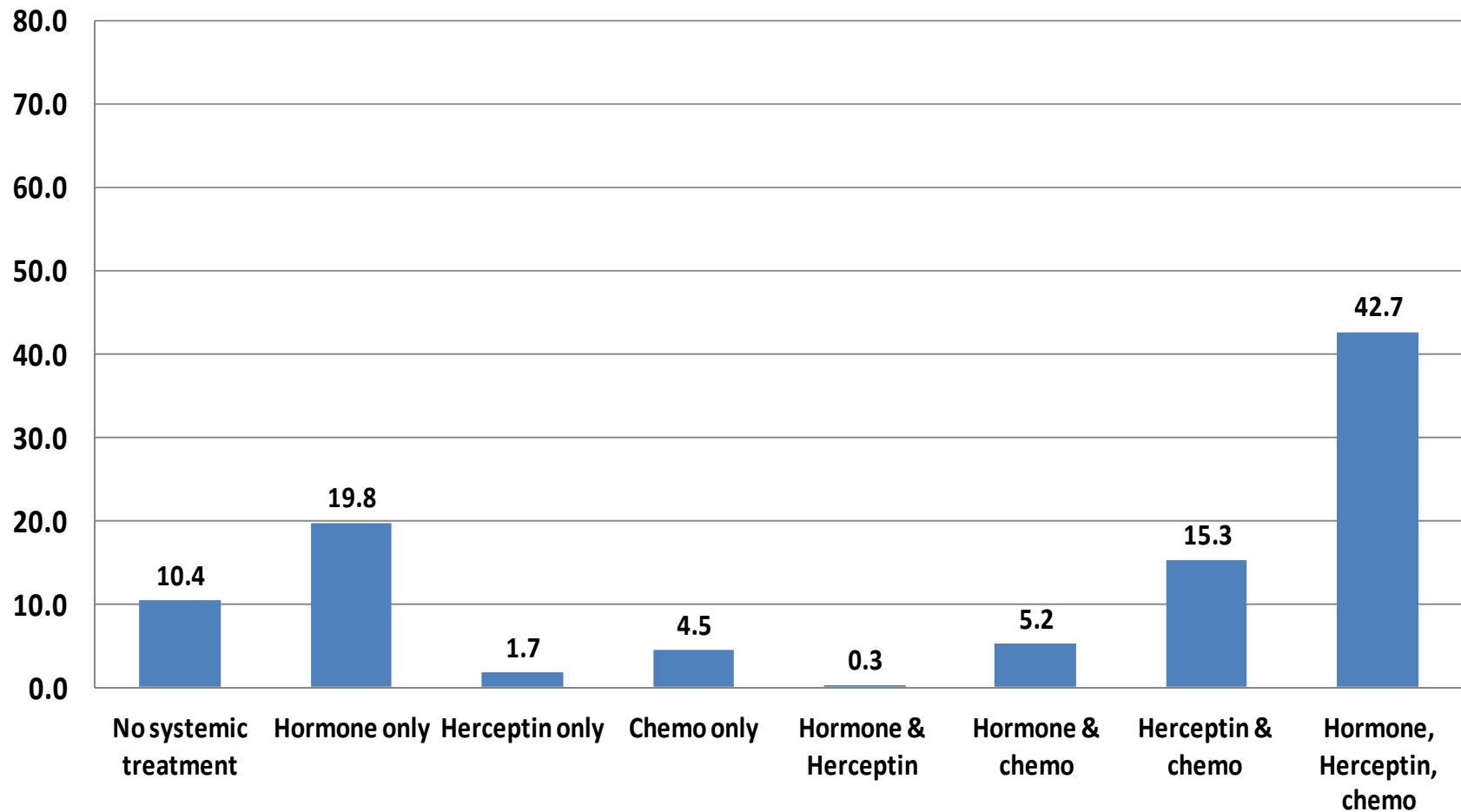
Treatment Distribution for Invasive Female Breast Cancer Diagnosed in Louisiana, 2011



Treatment Distribution for Invasive Female Breast Cancer Diagnosed in Louisiana, 2011



HR+/HER2+



Treatment Distribution for Invasive Female Breast Cancer Diagnosed in Louisiana, 2011

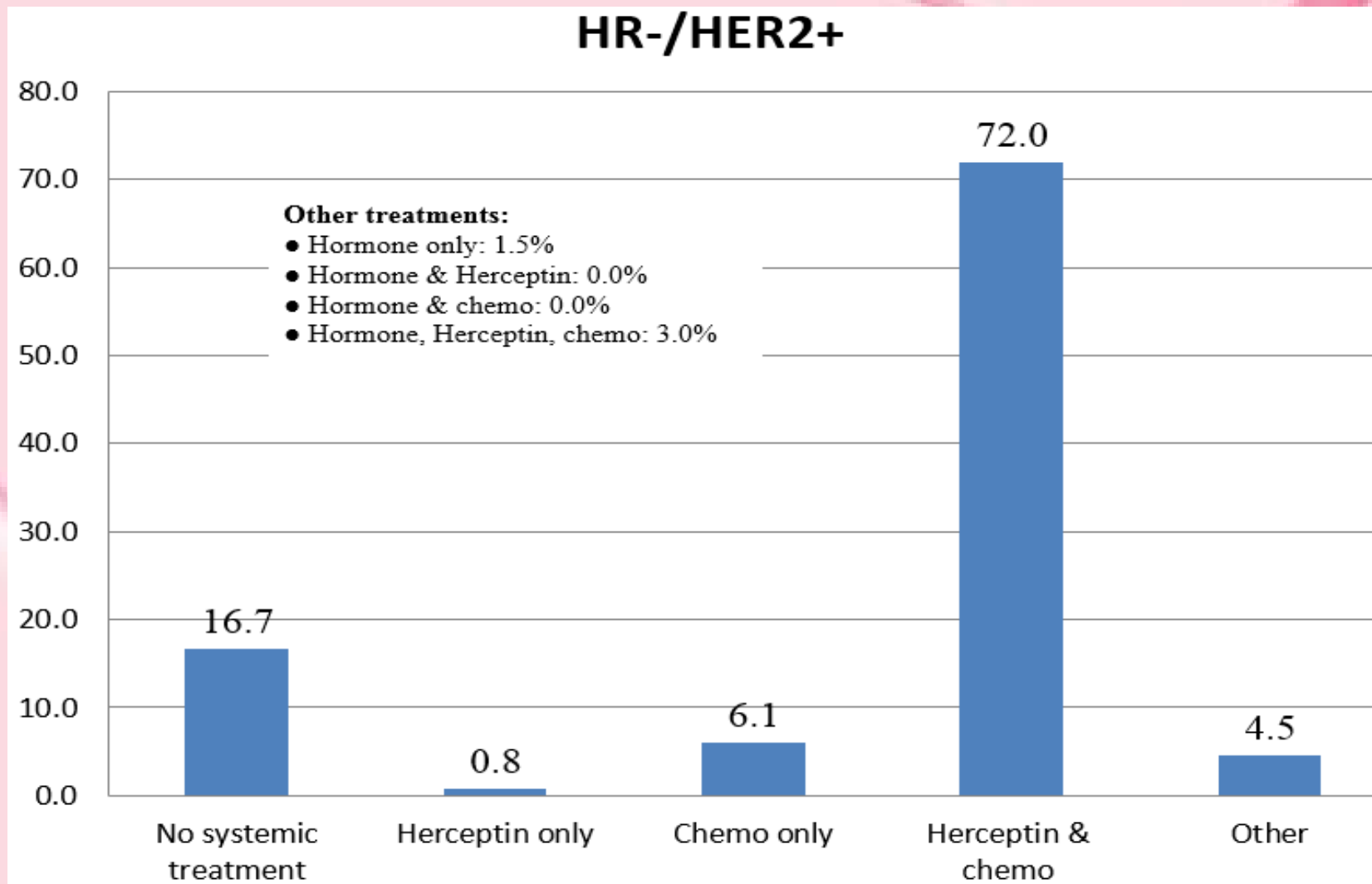


Table 3A. Molecular Subtypes of Invasive Female Breast Cancer Associated with Not Receiving Systemic Treatment Louisiana, 2011

Variable	No Treatment (N=475)	Unadjusted OR (95% CI)	Adjusted ¹ OR (95% CI)
Subtypes			
HR+/HER2-	17.3%	1.00	1.00
HR-/HER2-	23.1%	1.44 (1.11-1.86)	2.15 (1.57-2.94)
HR+/HER2+	10.4%	0.56 (0.38-0.83)	0.60 (0.40-0.92)
HR-/HER2+	16.7%	0.96 (0.60-1.54)	1.45 (0.87-2.42)

¹ Adjusted for age, race, AJCC stage, Bloom-Richardson grade, lymph node involvement, and comorbidity.

Table 3B. Demographic Factors of Invasive Female Breast Cancer Associated with Not Receiving Systemic Treatment in Louisiana, 2011

Variable	No Treatment (N=475)	Unadjusted OR (95% CI)	Adjusted ¹ OR (95% CI)
Age at diagnosis (yrs.)			
<50	9.1%	0.66 (0.47-0.93)	0.67 (0.47-0.96)
50-64	13.2%	1.00	1.00
65-74	17.4%	1.38 (1.06-1.82)	1.41 (1.07-1.87)
75/+	35.1%	3.56 (2.75-4.60)	3.49 (2.65-4.59)
Race/Ethnicity			
Non-Hispanic White	18.3%	1.00	1.00
Non-Hispanic Black	15.6%	0.83 (0.66-1.04)	0.92 (0.72-1.17)
Hispanic and Others	13.1%	0.67 (0.35-1.28)	0.71 (0.36-1.41)

¹ Adjusted for subtype, age, race, AJCC stage, Bloom-Richardson grade, lymph node involvement, and comorbidity.

Table 3C. Clinical Factors of Invasive Female Breast Cancer Associated with Not Receiving Systemic Treatment in Louisiana, 2011

Variable	No Treatment (N=475)	Unadjusted OR (95% CI)	Adjusted ¹ OR (95% CI)
AJCC 7th stage			
I	22.4%	1.00	1.00
II	13.7%	0.55 (0.44-0.69)	0.57 (0.44-0.75)
III	9.7%	0.37 (0.25-0.55)	0.37 (0.23-0.60)
IV	13.0%	0.52 (0.33-0.82)	0.31 (0.18-0.52)
Bloom Richardson grade			
Low	20.0%	1.00	1.00
Medium	16.9%	0.81 (0.63-1.05)	0.94 (0.71-1.24)
High	14.9%	0.70 (0.53-0.93)	0.85 (0.60-1.20)
Unknown	21.2%	1.08 (0.75-1.54)	1.07 (0.72-1.61)

¹ Adjusted for subtype, age, race, AJCC stage, Bloom-Richardson grade, lymph node involvement, and comorbidity.

Table 3D. Clinical Factors of Invasive Female Breast Cancer Associated with Not Receiving Systemic Treatment in Louisiana, 2011

Variable	No Treatment (N=475)	Unadjusted OR (95% CI)	Adjusted ¹ OR (95% CI)
Lymph node involvement			
Negative	18.1%	1.00	1.00
Positive	10.5%	0.53 (0.41-0.69)	0.98 (0.71-1.35)
Unknown	32.6%	2.19 (1.68-2.87)	2.98 (2.15-4.12)
Comorbidity			
0	17.1%	1.00	1.00
1	17.1%	1.00 (0.77-1.30)	0.79 (0.60-1.06)
2/+	23.7%	1.51 (0.97-2.43)	0.98 (0.61-1.58)

¹ Adjusted for subtype ,age, race, AJCC stage, Bloom-Richardson grade, lymph node involvement, and comorbidity.

Conclusions

- The 4 molecular subtypes of breast cancer show very distinct patterns and age-specific incidence rates especially for the triple negative
- Relative to the most common subtype (HR+/HER2-), TN is more likely to
 - occurs among NHB women
 - be diagnosed at younger ages (<50)
 - has high Bloom-Richardson grade
- May explain partly the survival disparity in breast cancer among NHB women in Louisiana.

Conclusions

- Among invasive breast cancer patients with known HR and HER2 status
 - 68% - 76% with HR+ had hormonal therapy
 - 60% - 76% with HER2+ had Herceptin
 - Higher % among those with single receptor expressed
- About 0.5% to 6.8% were given therapies contradict to their HR and HER2 tumor status (“inappropriate” use)



Conclusions

- About 10% - 23% of invasive breast cancer patients with known HR and HER2 status did not receive any systemic treatment
- Factors significantly associated with not receiving systemic include:
 - triple negative subtype
 - older age (65/+)
- Patients of younger age (<50) and more advanced stage disease were more likely to receive systemic treatment.
- Race/ethnicity BR grade, lymph node involvement and comorbidity were not associated with receiving systemic treatment, after adjusted for other factors.

Strengths & Limitations

- This is the first statewide, population-based study to examine systemic treatment among invasive breast cancer patients by molecular subtype
- Include patients diagnosed and treated outside large cancer centers and major facilities, allowing the assessment of treatment guideline dissemination
- Despite extensive effort in collecting systemic treatment, information on all therapies may not be available to abstractors.
- Preliminary, broad examination of treatment by subtype, did not assess therapy by stage or treatment guideline

Acknowledgements

The data used for this presentation came from support of:

- CDC-funded CER Project
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- NCI's SEER Program
- CDC's NPCR

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A pink ribbon symbol, a common icon for breast cancer awareness, is located in the upper right corner of the slide. The background of the slide is a light pink color with a subtle, wavy pattern.

Thank You!

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