Using Enhanced Registry Data for Clinical Management and Cancer Care

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Louisiana Tumor Registry

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Background

- Historically population-based cancer registry data were used to describe cancer burden, trends and survival.

- In past 2 decades, registry data have been used for cancer control efforts and assessing the effectiveness of early detection programs.

- However, their use by clinical community has been limited despite increasing clinical data and biomarkers collected in recent years.

Background

- Enhanced cancer registry data, especially molecular data and biomarkers, offer an opportunity for collaboration with clinicians on patient care and clinical management

- We illustrated such collaboration using 2 LA projects

  - Lynch Syndrome (LS) screening among young colorectal cancer (CRC) patients ($\leq$ 50 yrs.)

  - Testing of biomarkers to classify breast cancer subtypes and assessing treatment.

Background

- CRC incidence rates are among the highest in the US in a region of S LA which has high % of French-speaking Cajuns, a founder population, suggesting a genetic predisposition or common environmental risk factor.
- Lynch Syndrome (LS) is the most common form of hereditary CRC, accounting about 5% of all CRC cases and 17% in early onset patients.
- CRC pts with LS have increased risk of subsequent CRC; thus recommended for more extensive colon resection (subtotal or total colectomy)
- LS can be tested by microsatellite instability (MSI) and/or immunohistochemtry (IHC) for mismatch repair proteins
- Results can be used to guide surgical planning

Background

- Breast cancer is now recognized as a heterogeneous disease with distinct biological molecular subtypes which have different prognoses and treatment options.
- Prevalence of biomarkers (ER,PR and HER2 receptors) testing and distribution of breast cancer subtypes in large populations have been available in recent years (SEER and NAACCR).
- Less known is whether the test results facilitate treatment decision and impact clinical practice at the population level.

Objectives

- Illustrate how enhanced clinical cancer registry data (molecular & biomarkers) can be used to assess treatment and clinical practice
- Demonstrate collaboration between cancer surveillance program and clinical community is feasible
- Show how enhanced registry data offer opportunity to increase awareness of guideline-concordant care among clinicians

Methods

- Data sources
  - Routine Louisiana Tumor Registry (LTR) data collection, including ER, PR and HER2
  - CDC-funded special project of Enhancing Cancer Registry Data for Comparative Effectiveness Research (CER)
    - Microsatellite Instability (MSI)
    - Detailed information on 1st course of treatment received within 12 months of diagnosis, including type of surgery, radiation, chemotherapy (drug & dosage), hormonal therapy and targeted therapy.

Methods

- 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

- For the CRC project, additional records were reviewed centrally by registry researchers and physicians with expertise in management of hereditary CRC syndromes, including:
  - colonoscopy report
  - operative report
  - pathology report
  - MSI/IHC testing results
  - NAACCR abstract

- Path reports available for 93% of cases who had colonoscopy with biopsy and 99% who had surgical resection

Methods

- Eligibility criteria for colorectal cancer (CRC) Lynch Syndrome screening project
  - Louisiana residents
  - *Ages 50 and younger*
  - Diagnosed with colorectal cancer in 2011
  - Microscopically confirmed cases only
  - No autopsy or death certificate cases
  - Exclude *non-adenocarcinomas* and histologies not included in the AJCC 7th ed. staging

Methods

- Eligibility criteria for breast cancer molecular subtypes
  - *All ages*
  - Louisiana residents, *female*
  - Diagnosed with *invasive* breast cancer in 2011
  - Microscopically confirmed cases only
  - No autopsy or death certificate cases
  - Histology groupings included in the AJCC 7th ed. staging scheme for breast; exclude *sarcomas* and *lymphomas*

Methods

- Using information on ER, PR and HER2, breast cancer cases were classified into the following groups approximate the 4 molecular “intrinsic” subtypes:
  - HR+/HER-
  - HR+/HER2+
  - Triple Negative (HR-/HER2-)
  - HR-/HER2+

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

Methods

- Pearson Chi-Square tests was used to determine statistical difference between bivariate.
- Univariate logistic regression analyses were used to identify factors associated with ordering MSI/IHC testing for CRC and for not receiving systemic treatment for breast.
- Multivariate logistic regression analyses were conducted to quantify adjusted associations.
- Analyses were carried out using SAS version 9.4.

Results

Colorectal Cancer

Results: Summary CRC Findings

- 274 CRC pts ≤ 50 years from 61 facilities were eligible for analysis
- 63 pts (23%) had MSI/IHC tests ordered; results were available for 60 cases (95%)
- Of those tested, 21.7% had abnormal MSI and/or IHC
- Of those with abnormal IHC, staining patterns were consistent with LS in 87.5%
- Only 17% of the MSI/IHC results were available pre-operatively.

Table 1A. Patient Socio-demographic Factors Associated with Ordering MSI/IHC Testing, Colorectal Cancer, Louisiana, 2011*

Variable	No (N=475)	Yes (N=63)	Unadjusted OR (95% CI)	Adjusted [1] OR (95% CI)
Age at diagnosis				
≤40	67.9%	32.1%	2.11 (0.95, 4.71)	
41-45	76.9%	23.1%	1.31 (0.57, 3.00)	
46-50	80.1%	19.9%	Ref	
Health Insurance				
Not insured	84.6%	15.4%	0.56 (0.18, 1.44)	
Insured	75.3%	24.2%	ref	
Unknown	87.5%	12.5%	0.44 (0.01, 3.53)	
CRC 1st degree relatives				
No	76.4%	23.6%	Ref	Ref
Yes	52.0%	48.0%	**2.98 (1.21, 7.33)**	**2.76 (1.03,7.40)**
Unknown	82.0%	18.0%	0.71 (0.38, 1.31)	0.84 (0.40, 1.73)

*Karlitz et al. Am J Gastroenterol, 2015

[1] Adjusted for urban-rural, MSI features, CRC in first degree relatives & hospital type, Firth Method due to small #

Table 1B. Patient Socio-demographic Factors Associated with Ordering (Y/N) MSI/IHC Testing, Colorectal Cancer, Louisiana, 2011*

Variable	No (N=475)	Yes (N=63)	Unadjusted OR (95% CI)	Adjusted [1] OR (95% CI)
Urban-rural Residence				
Urban (Metro)	74.1%	25.9%	Ref	Ref
Rural (non-Metro)	87.7%	12.3%	**0.40 (0.19, 0.87)**	0.49 (0.21, 1.11)
Non-Louisiana	62.5%	37.5%	1.71 (0.59, 4.96)	1.91 (0.53, 6.86)
Hospital type				
THCP	83.3%	16.7%	**0.30 (0.11, 0.77)**	0.55 (0.18, 1.63)
COMP	59.6%	40.4%	Ref	Ref
CHCP	83.0%	17.0%	**0.31 (0.10, 0.83)**	0.62 (0.20, 1.88)
Public	93.5%	6.5%	**0.10 (0.01, 0.48)**	**0.17 (0.04, 0.77)**
Non-CoC/ Non-public	75.3%	24.7%	0.49 (0.22, 1.07)	0.92 (0.39, 2.17)

THCP=Teaching hos Cancer Program, COMP=Community hosp comprehensive CP; CHCP; Community hosp CP.
[1]Adjusted for urban-rural, MSI features, CRC in first degree relatives & hospital type; Firth Methods due to small #

Table 1C. Tumor Characteristics Associated with Ordering (Y/N) MSI/IHC Testing, Colorectal Cancer, Louisiana, 2011*

Variable	No (N=475)	Yes (N=63)	Unadjusted OR (95% CI)	Adjusted [1] OR (95% CI)
MSI feature seen on histology				
No	60.0%	40.0%	1.30 (0.50,3.41)	0.94 (0.32, 2.77)
Yes	66.1%	33.9%	Ref	Ref
Unknown	82.6%	17.4%	**0.41 (0.21, 0.79)**	0.56 (0.27, 1.16)
AJCC 7th Ed Stage				
Stages 0 and I	82.3%	17.7%	0.44 (0.16, 1.12)	
Stage II	66.7%	33.3%	Ref	
Stages III and IV	78.5%	21.5%	0.55 (0.26, 1.18)	
Unknown stage	66.7%	33.3%	1.00 (0.02, 20.50)	

*Karlitz et al. Am J Gastroenterol, 2015

[1] Adjusted for urban-rural, MSI features, CRC in first degree relatives & hospital type, Firth Methods due to small #

Breast Cancer Subtypes

Table 2. Distribution of Invasive Female Breast Cancer by Subtype. Louisiana, SEER & NAACCR, 2011

	Louisiana	SEER 18#	NAACCR*
	N=2,953	N=54,529	N=178,125
HR+/HER2-	69.8%	73.5%	72.6%
HR-/HER2-	14.8%	12.1%	13%
HR+/HER2+	10.6%	9.9%	10%
HR-/HER2+	4.8%	4.5%	5%
Total	100%	100%	100%
Unknown	(7.3%)	(9.2%)	(11%)

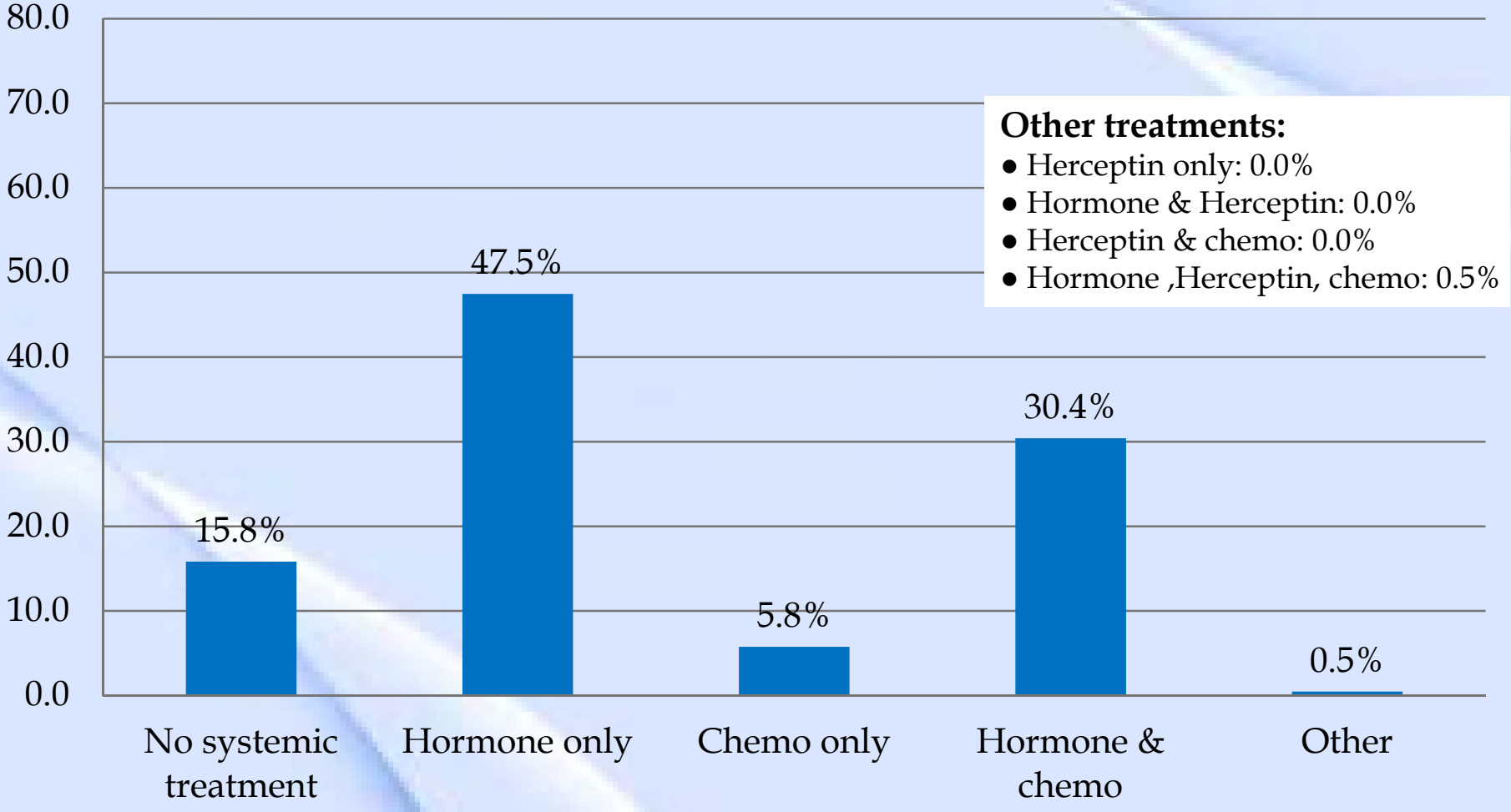
#p<0.0001 (LA vs. SEER)

*p=0.0105 (LA vs. NAACCR)

Sources: Howlader N et al. JNCI, 2014
Kohlar BA et al. JNCI, 2015

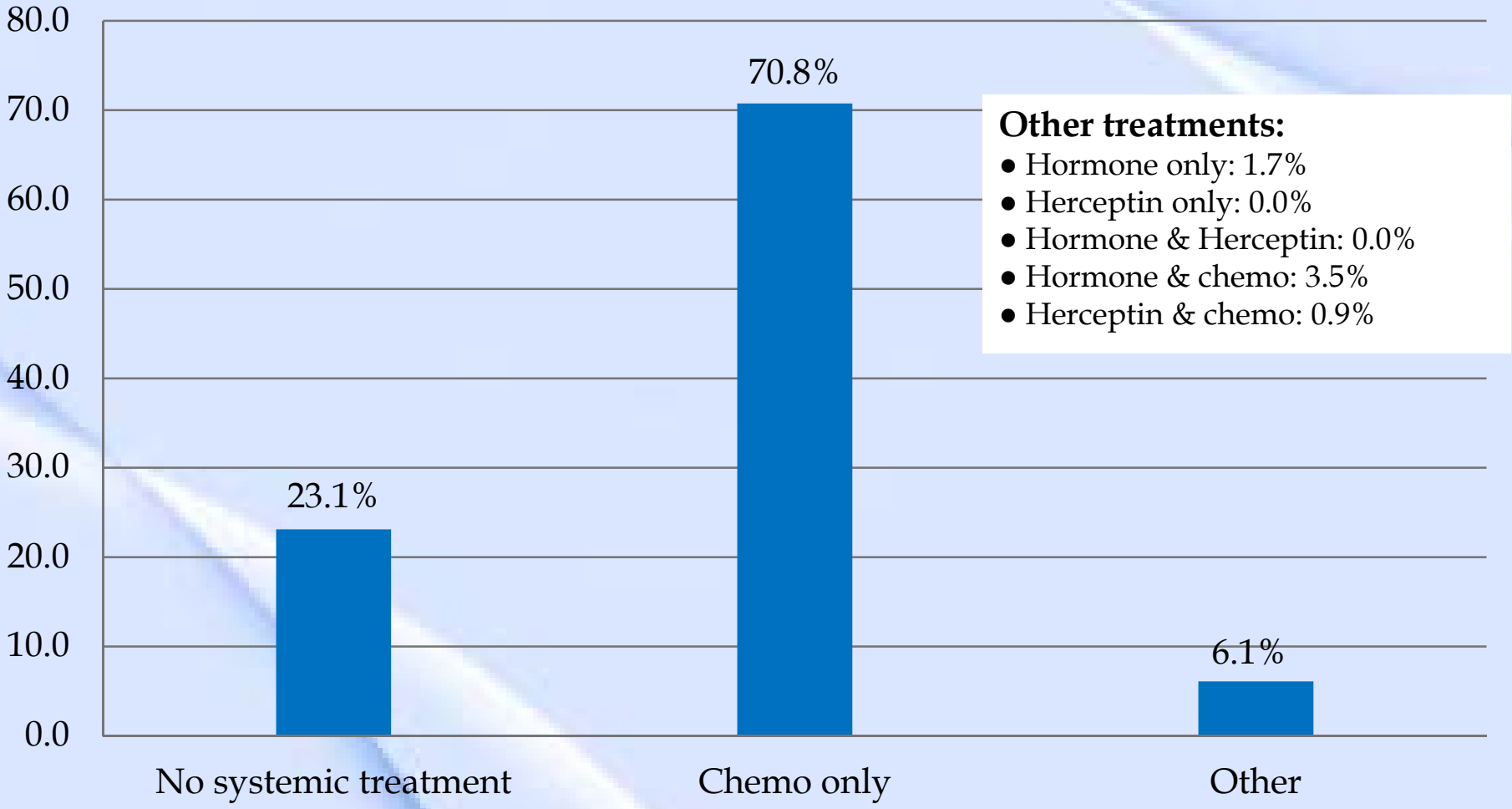
Systemic Treatment for Invasive Female Breast Cancer Louisiana, 2011 (All Cases)

HR+/HER2- (Luminal A)



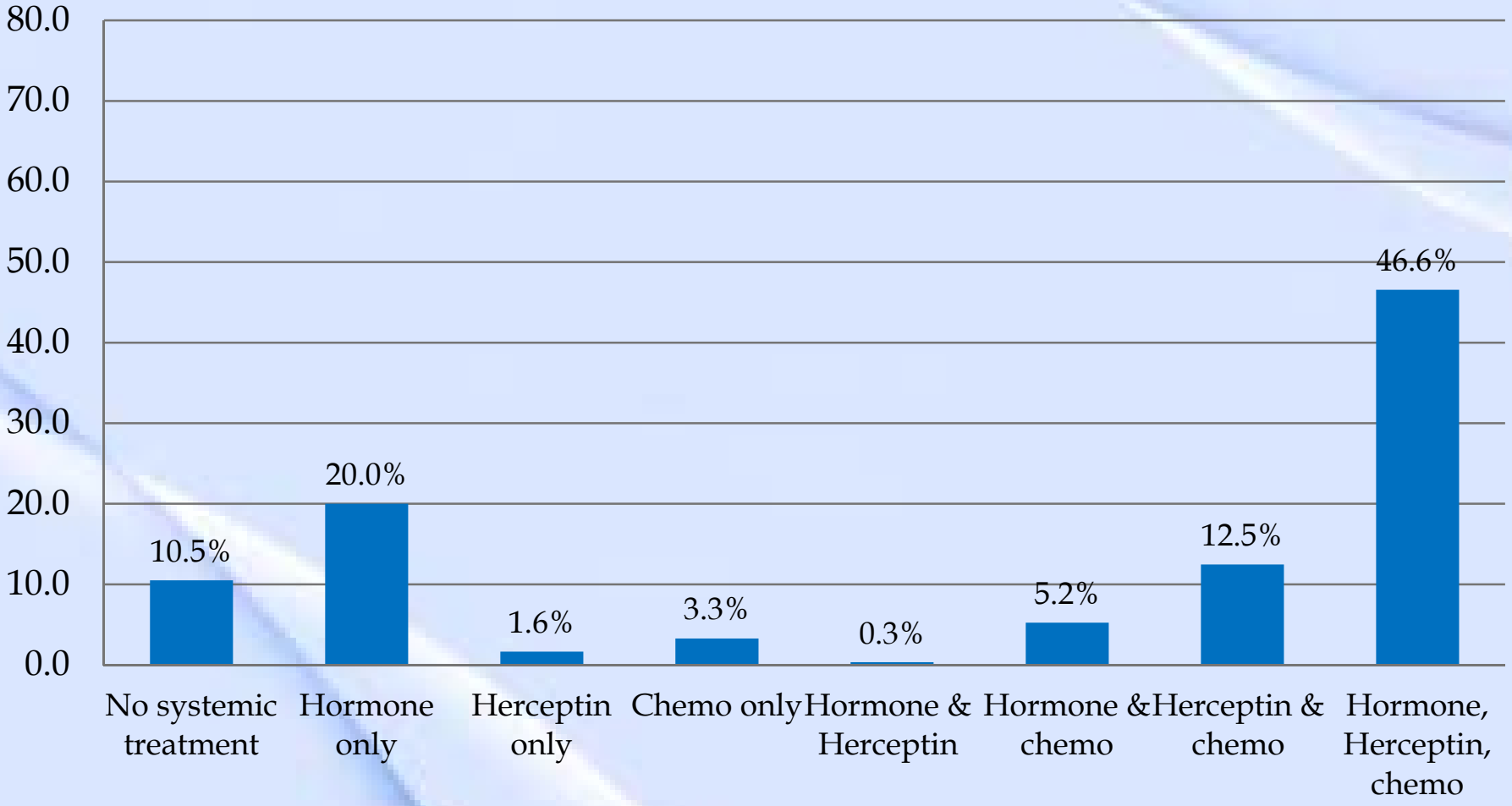
Systemic Treatment for Invasive Female Breast Cancer
Louisiana, 2011 (All Cases)

HR-/HER2- (TNBC)



Systemic Treatment for Invasive Female Breast Cancer
Louisiana, 2011 (All Cases)

HR+/HER2+ (Luminal B)



Systemic Treatment for Invasive Female Breast Cancer
Louisiana, 2011 (All Cases)

HR-/HER2+ (HER2 Enriched)

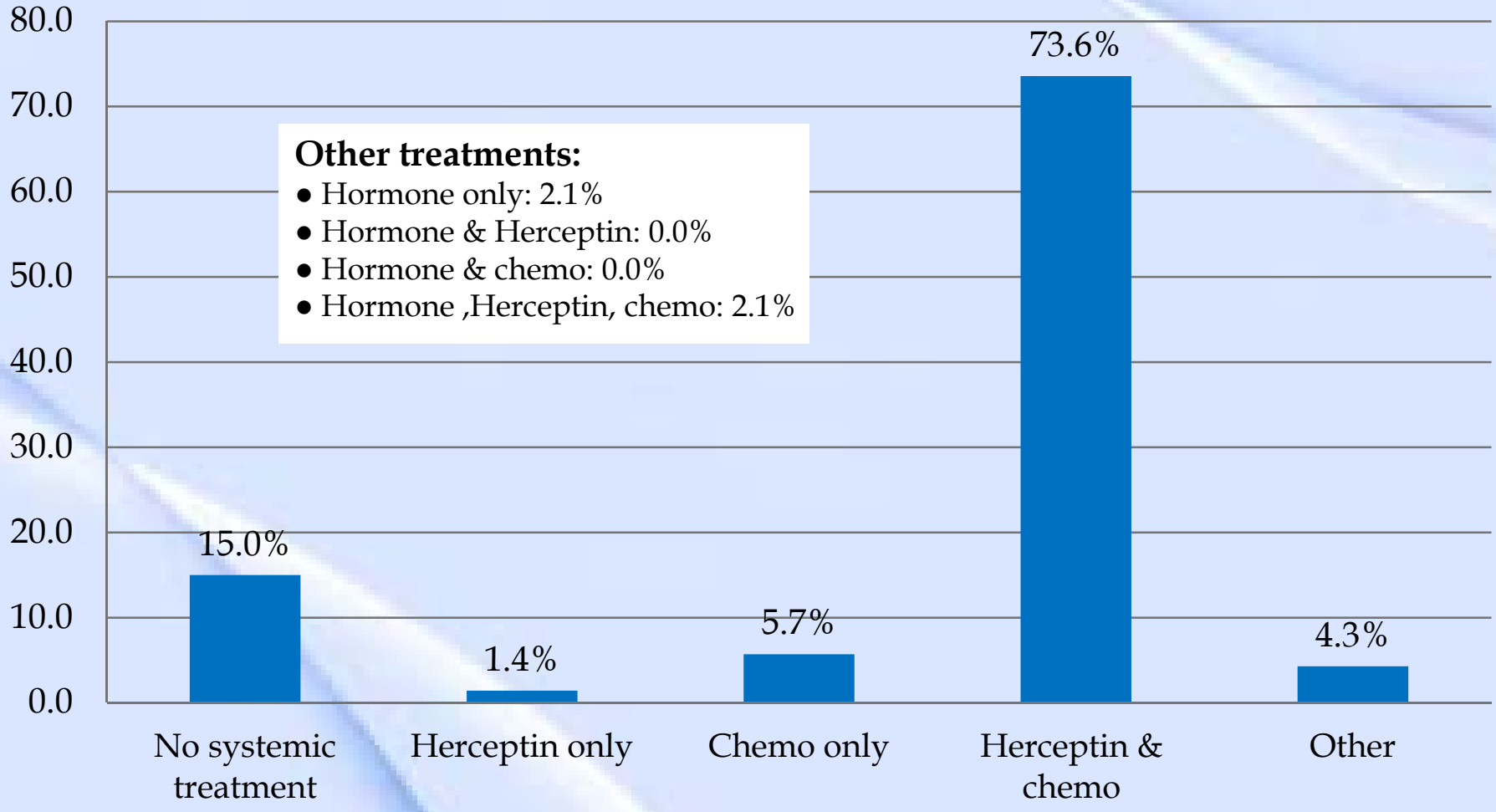


Table 3A. Molecular Subtypes of Invasive Female Breast Cancer Associated with Not Receiving Systemic Treatment Louisiana, 2011

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)

*Cases with known stage

[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, 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, Louisiana, 2011

Variable	No Treatment (N=475)	Unadjusted OR (95% CI)	Adjusted [1] OR (95% CI)
AJCC 7th Ed 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, 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.

Table 4. Reasons for Not Receiving Systemic Treatment Breast Cancer, Louisiana, 2011

Reasons	# of patients	%
Died prior to planned or recommended TX	14	2.8%
Refused TX by patient or family	102	20.2%
Tumor size: ≤ 0.5 cm	60	11.9%
Tumor size: >0.5 cm – 1 cm	233	46.0%
Advanced age: 70-74	12	2.4%
75-79	18	3.6%
80/+	19	3.7%
Stage IV tumors	2	0.4%
No documented reasons	46	9.1%
Total	506	100%

Summary Breast Findings

- 72% - 78% of invasive breast cancer patients with HR+ tumor had hormonal therapy
- 61% - 75% with HER2+ tumor received Herceptin
- About 0.5% to 6.1% were given therapies contraindicated to their HR and HER2 tumor status
- 11% - 23% of invasive breast cancer patients with known molecular subtype did not receive any systemic treatment
- Factors associated with not receiving systemic include triple negative subtype and advanced age (65/+)

Conclusions

- Enhanced clinical registry data offered opportunities for collaborations with clinical community
- Findings of these 2 projects were presented by clinicians at professional conferences. One paper was published at clinical journal and another was submitted for review
- Not only did they promote use of registry data but also increase the awareness of guideline concordant care among clinicians.
- With the changing practice of personalized and precision medicine, registries can position themselves with additional relevant clinical & biomarkers data (via special studies) for expanded use in managing cancer care

Strengths & Challenges

- The collaboration with clinical community provides visibility of population-based registry. Justify sustained or expanded funding for cancer surveillance programs.
- Allow assessment of cancer care practice in the community setting, beyond cancer centers and major facilities.
- Increase the awareness of guideline concordant care among clinicians.

Require additional registry resources and staff time to verify data and follow back as well as data analysis – special study

- There is a learning curve for clinicians to understand registry data and appropriate use
- Clinician's competing responsibilities of patient care and research

Acknowledgement

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Thank You!

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