USING CANCER REGISTRY DATA TO EVALUATE BREAST CANCER INCIDENCE BY SUBTYPE

HR/HER2 variables in CINA

Recinda Sherman, Nadia Howlader, Xiao-Cheng Wu, Manxia Wu, Bin Huang, Carol Kruchko

Data Assessment Workgroup
NAACCR 2015, Charlotte, NC
Tuesday June 16, 2015
PRESENTATION OVERVIEW

- HR/HER2 variables
- 2010-2012 Assessment
- Annual Report to the Nation
- Conclusions
BREAST CANCER SUBTYPES

• Bimodal age distribution
  • Mortality
  • 2 subtypes, hormone dependent

• Gene-expression profiling
  • Confirmed 2 main groups
    • 4 molecular subtypes
      • Luminal A, Luminal B, human growth factor neu (HER2) enriched, basal like
BREAST CANCER SUBTYPES

- Etiologically different
- Documented differences in incidence by subtype and race
  - Potentially driving black/white disparities
  - Important public health implications
- Significant differences in prognosis by subtype
  - Critical component of clinical treatment decisions
- Recent study indicates most women are unaware of their subtype
  - This may impact treatment compliance
BREAST CANCER SUBTYPES

- 4 molecular subtypes of breast cancer are approximated by tumor expression of 3 markers
  - Human Epidermal Growth Factor Receptor 2 (HER2)
  - Estrogen Receptor (ER)
  - Progesterone Receptor status (PR)

- 4 major breast cancer molecular subtypes

- ER and PR jointly defined as Hormone Receptor status (HR)
  - HR+/HER2- (approximates Luminal A)
  - HR+/HER2+ (approximates Luminal B)
  - HR-/HER2+ (HER2 enriched)
  - HR-/HER2- (Triple Negative)
CINA VARIABLES

- New directions in cancer surveillance reporting
  - Presenting data in more clinically & analytically relevant categories

- Nationally required data items
  - SSF1 ER Assay
  - SSF2 PR Assay
  - SSF15 HER2 Summary Result
    - Required nationally beginning in 2010
CINA VARIABLES

• Breast schema
  • http://web2.facs.org/cstage0205/breast/Breastschema.html

• 3 digit codes

• ER/PR
  • +, -, borderline, results not interpretable, test ordered results not in chart, no test ordered, unknown, obsolete data, NA

• HER2
  • +, -, borderline, test ordered results not in chart, no test ordered, unknown, NA

• Extend of Disease – CS Folder in SEER*Stat
  • Create own groupings
CINA DATA ASSESSMENT

• 84 Registries
  • US & Canada
  • Regardless of fitness for use on other data

• 2010-2012 diagnosis years
  • ER/PR collected prior
  • HER2 required 2010
**ESTROGEN RECEPTOR STATUS (ER)**

- “Unknowns” Range 0 – 80%; Average 7%—slight decrease over time
  - 2 US (+1 in 2012); 2 Canadian registries >20% (not fit for use)
- Ordered, Not Interpretable
  - Range 0 –<1%; Average 0%
- Ordered, Not in Chart
  - Range 0 –5%; Average 1%
- Not Ordered
  - Range 0 –18%; Average 1%
- Blank/Invalid
  - Range 0 –80%; Average 2%
- Unknown
  - Range 0 –36%; Average 4%
- NA
  - 153 of 788,838—should not occur—slight increase over time
PROGESTERONE RECEPTOR STATUS (PR)

- "Unknowns" Range 0 – 80%; Average 8%--slight decrease over time
  - 2 US (+1 in 2011 & 2012); 2 Canadian registries >20% (not fit for use)
- Ordered, Not Interpretable
  - Range 0 – 1%; Average 0%
- Ordered, Not in Chart
  - Range 0 – 5; Average 1%
- Not Ordered
  - Range 0 – 18%; Average 2%
- Blank/Invalid
  - Range 0 – 80%; Average 2%
- Unknown
  - Range 0 – 36%; Average 4%
- NA
  - 152 of 788,838—should not occur
HUMAN GROWTH FACTOR-NEU RECEPTOR STATUS (HER2)

- “Unknowns” Range 0-100%; Average 28% 2010; 15% 2011; 12% 2012
- 2 Canadian registries >20% (not fit for use)
  - Ordered, Not Interpretable – not a category
  - Borderline Range 0-11%; Average 2% (+?)
  - Ordered, Not in Chart
    - Range 0–28%; Average 1%
- Not Ordered
  - Range 0–28%; Average 5%; decrease over time
- Blank/Invalid
  - Range 0–100%; Average 2%; slight decrease over time
- Unknown
  - Range 0–66%; Average 5%; slight decrease over time
- NA
  - 39,273 of 788,838—should not occur
CLASSIFICATION OF SUBTYPE FOR ANALYSIS

• HR
  • ER+, or PR+, or borderline ER or PR = HR+
  • Aligns with recent clinical guidelines that use lower cutoffs to determine +
  • ER- and PR- = HR-

• HER2
  • HER Borderline HER2 = “unknown” HER2
    • 2013 Guidelines changes
      • Lowered threshold for +
ANNUAL REPORT TO THE NATION

- J Natl Cancer Inst
- Breast cancer by subtype & race/ethnicity
  - Age, stage, grade, area-based poverty
- Breast cancer by subtype
  - Map by State
- 2011 data only
- Imputed
  - <20% missing HR/HER2
- Open Access

http://jnci.oxfordjournals.org/content/107/6/djv048.full.pdf+html
IMPUTATION OF SUBTYPE (HER2)

• Sequential Regression Multiple Imputation (aka Multiple imputation with chain equation)

• Imputed missing HER2 Status and all other breast cancer covariates with missing information

• Covariates in imputation model include
  • Age, race, ethnicity, registry, reporting source, ER status, PR status, tumor grade, tumor size, tumor histology, surgery, county-based poverty and urban/non-urban indicator
Triple-Negative
- Non-Hispanic White 11%
- Non-Hispanic Black 23%
- Non-Hispanic Asia/Pacific Islander 11%
- Hispanic 13%
INCIDENCE RATES OF BREAST CANCER MOLECULAR SUBTYPES BY RACE/ETHNICITY, 2011

Age at Diagnosis (Years)

- Non-Hispanic White
- Non-Hispanic Black
- Non-Hispanic Asian/Pacific Islander
- Hispanic

Rate Per 100,000 U.S. Women

HR+/HER2+
HR-/HER2+
HR+/HER2-
Triple Neg
SUMMARY OF ARN SPECIAL TOPIC

• Rates of HR+/HER2-, the least aggressive breast cancer subtype, were highest among non-Hispanic whites and highest in low poverty areas

• Non-Hispanic blacks had highest rates of triple negative breast cancer, the highest rates of late-stage disease, and the highest rates of poorly/undifferentiated pathology among all the subtypes
  • all of which are associated with lower survival, and correspond with NHBlacks having the highest rates of breast cancer deaths
NEXT STEPS

- Trends over time
- HER2 change in clinical definition
- Mortality data by subtype
- Subtype specific public health interventions
- Database available
  - Approved research/researchers
Questions?