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

# USING CANCER REGISTRY DATA TO EVALUATE BREAST CANCER INCIDENCE BY SUBTYPE

# 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)
- 4major 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)
- 31 (2010)  8 (2011) 7 (2012) US 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

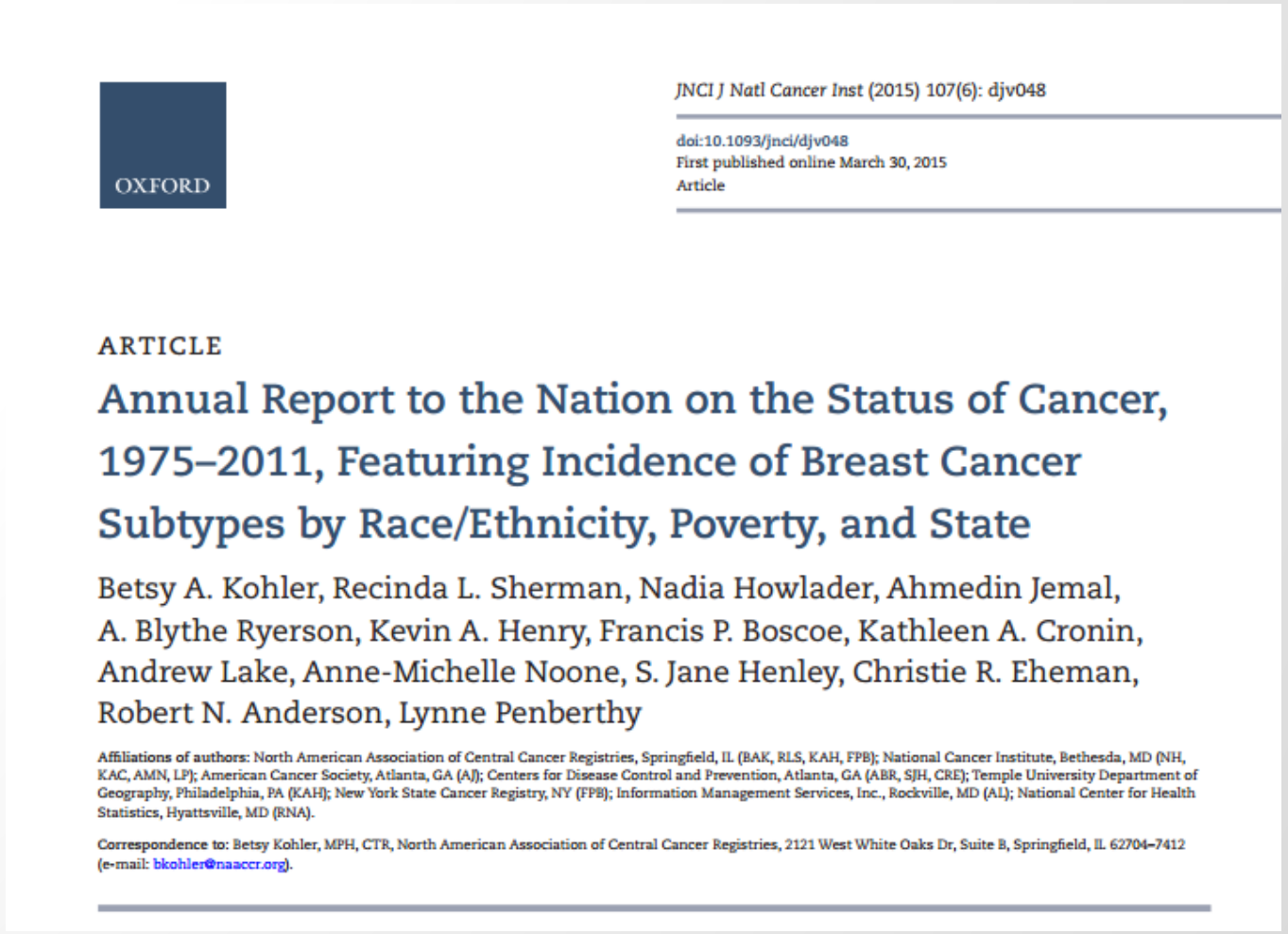
# CLASSIFICATION OF SUBTYPE FOR ANALYSIS

- 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 +
      - http://www.cap.org/apps/docs/committees/immunohistochemistry/summary_of_recommendations.pdf

# 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



OXFORD

*JNCI J Natl Cancer Inst* (2015) 107(6): djv048

doi:10.1093/jnci/djv048
First published online March 30, 2015
Article

ARTICLE

## Annual Report to the Nation on the Status of Cancer, 1975–2011, Featuring Incidence of Breast Cancer Subtypes by Race/Ethnicity, Poverty, and State

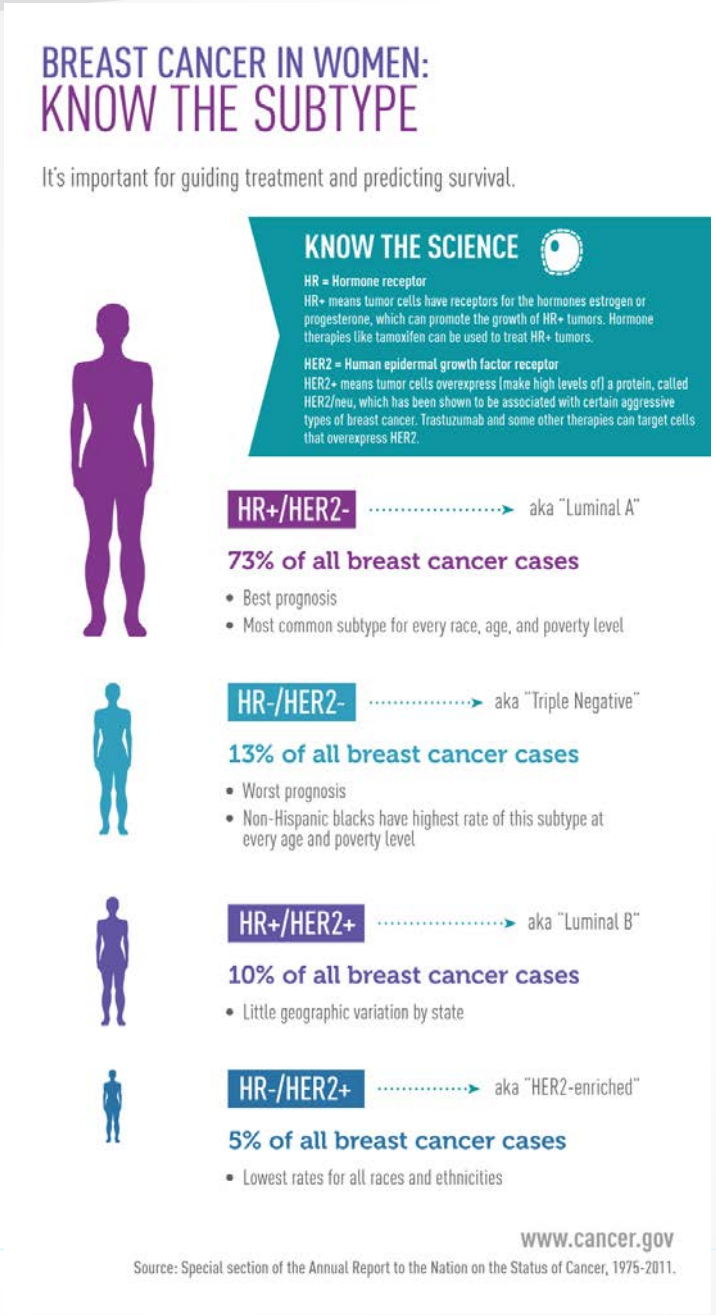
Betsy A. Kohler, Recinda L. Sherman, Nadia Howlader, Ahmedin Jemal, A. Blythe Ryerson, Kevin A. Henry, Francis P. Boscoe, Kathleen A. Cronin, Andrew Lake, Anne-Michelle Noone, S. Jane Henley, Christie R. Eheman, Robert N. Anderson, Lynne Penberthy

**Affiliations of authors:** North American Association of Central Cancer Registries, Springfield, IL (BAK, RLS, KAH, FPB); National Cancer Institute, Bethesda, MD (NH, KAC, AMN, LP); American Cancer Society, Atlanta, GA (AJ); Centers for Disease Control and Prevention, Atlanta, GA (ABR, SJH, CRE); Temple University Department of Geography, Philadelphia, PA (KAH); New York State Cancer Registry, NY (FPB); Information Management Services, Inc., Rockville, MD (AL); National Center for Health Statistics, Hyattsville, MD (RNA).

**Correspondence to:** Betsy Kohler, MPH, CTR, North American Association of Central Cancer Registries, 2121 West White Oaks Dr, Suite B, Springfield, IL 62704–7412 (e-mail: bkohler@naaccr.org).

# IMPUTATION OF SUBTYPE (HER2)

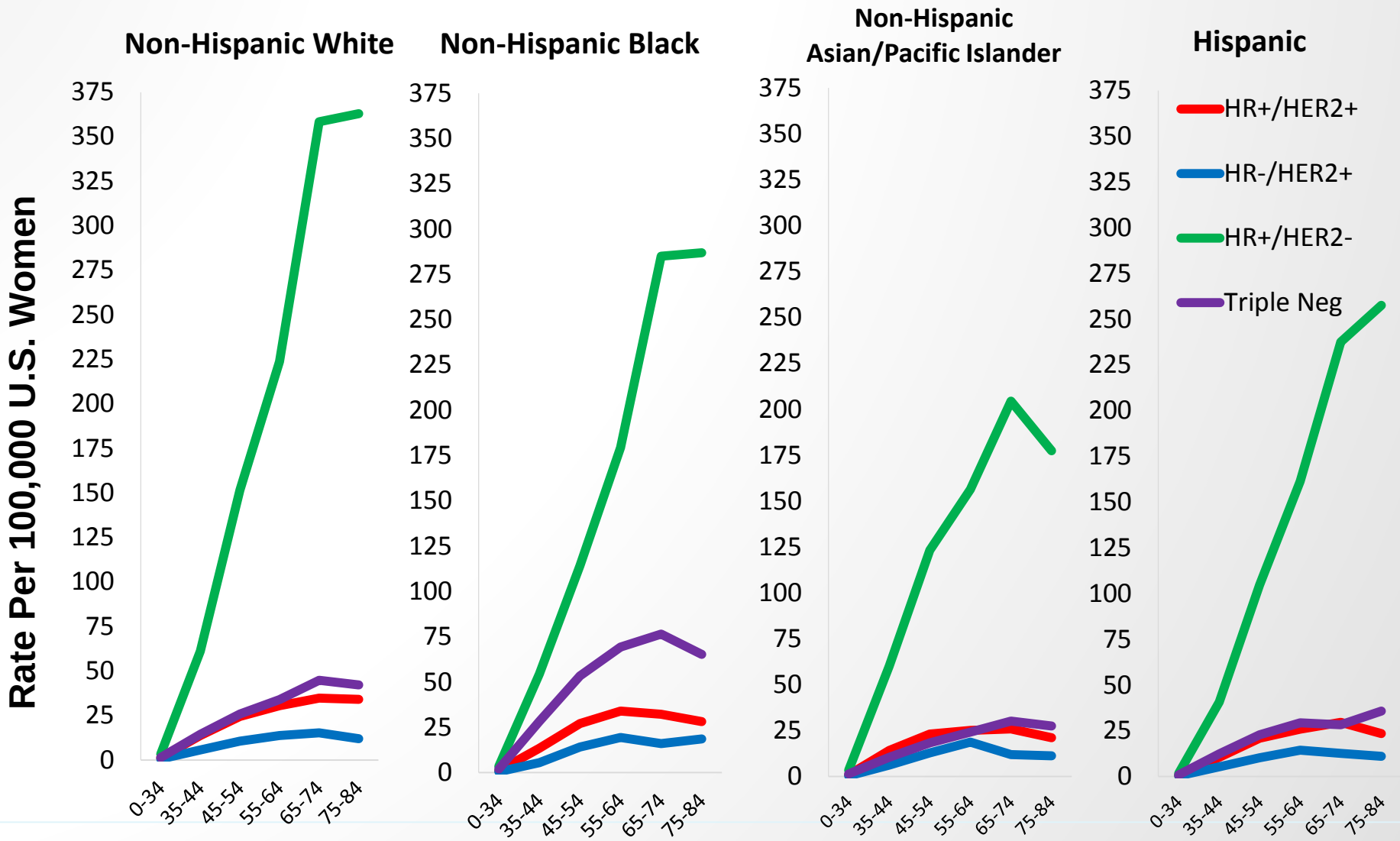
- Sequential Regression Multiple Imputation (aka Multiple imputation with chain equation)
- Imputed missing HER2 Status and all other breast cancer covariates with missing information
- Covariates in imputation model include
  - Age, race, ethnicity, registry, reporting source, ER status, PR status, tumor grade, tumor size, tumor histology, surgery, county-based poverty and urban/non-urban indicator



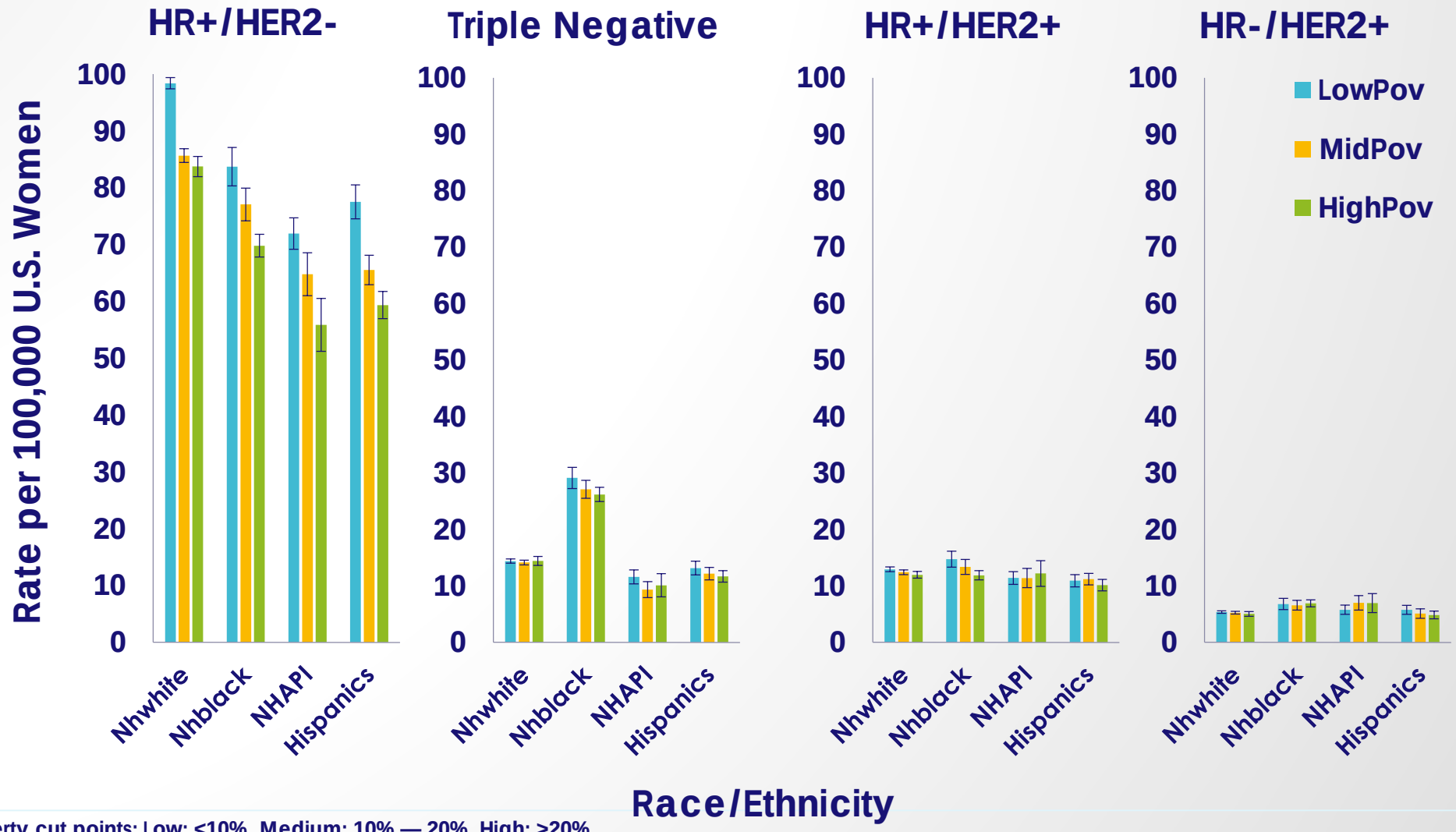

Triple-Negative

- 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



# INCIDENCE RATES OF BREAST CANCER MOLECULAR SUBTYPES BY POVERTY AND BY RACE/ETHNICITY, 2011




Poverty cut points: Low: <10%. Medium: 10% — 20%. High: >20%

# 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?