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**Molecular, treatment and behavioral factors in breast cancer race disparities**

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**Public Abstract:**

Background: African American (AA) women with breast cancer have more recurrences and lower survival rates compared to their white counterparts. The racial survival gap is largest among women with hormone receptor-positive (HR+) breast cancer, meaning that their cancer expresses estrogen and progesterone receptors, but not HER2 receptors, and is responsive to estrogen-blocking medications as part of treatment. Hypothesized but understudied reasons for HR+ outcome disparities include: differences in obesity rates, biological difference between HR+ tumors in AA women and white women, and underuse of endocrine therapy (estrogen-blocking medications taken for 5-10 years after diagnosis) among AA women.

Methods: This study will use the broad and deep data resources of the Carolina Breast Cancer Study Phase III (CBCS III) to better understand the contributions of obesity, biological differences, and endocrine therapy (ET) underuse to racial disparities in HR+ breast cancer outcomes. The CBCS III study is a large prospective cohort study focused on understanding racial differences in breast cancer. CBCS III has already reached its enrollment target of 1500 white and 1500 AA women with newly diagnosed breast cancer, of whom approximately 1700 are expected to have ER or PR+/HER2- disease and to be eligible for inclusion in the study proposed in this application. First, molecular subtyping data from previously collected tumor samples in women with ER+/PR+/HER2 negative receptor profile will be
analyzed for racial differences in the patterns of gene expression in their tumors, commonly called the molecular subtype. Next, molecular subtype data along with detailed data regarding income and education, tumor characteristics, initial treatments, baseline obesity and ET use will be used in a series of statistical models to measure which factors have the most influence on outcome disparities. Finally, in depth case analysis using medical records and patient survey data will be conducted to identify ET non-initiators and early discontinuers, to identify racial differences in ET taking behavior, and to understand reasons for non-initiation and early discontinuation.

Expected results: This study is expected to identify the key drivers of racial variation in HR+ breast cancer outcomes, to improve our understanding of why women underutilize highly effective and non-toxic ET, and to prioritize targets for a future intervention study to improve outcomes for AA women.

Expected impact: This study will provide an unprecedented opportunity to comprehensively examine biologic, socio-demographic, and treatment contributions to racial disparities in HR+ breast cancer outcomes. The results are expected to lead within 3 years to the proposal of a rational, targeted intervention to reduce racial disparities in HR+ breast cancer.