

Breast Cancer Disparities Among American Indian Women

Marilyn A. Roubidoux, MD, Department of Radiology, University of Michigan Health Systems, TC 2910, Box 5326, 1500 E. Medical Center Drive, Ann Arbor, Mi 48109-5326,

Corresponding author email: roubidou@umich.edu

ABSTRACT

Health disparities in breast cancer among American Indian women include historically higher stage at diagnosis, younger age at diagnosis, higher ratios of rates of mortality vs incidence, geographic variability of incidence and mortality rates, more difficult access to breast imaging and cancer treatment, and racial misclassification in medical records resulting in underestimation of breast cancer data. This population is understudied as well as underserved and more research is needed to reveal specific causes and interventions for these breast cancer disparities. Proactive efforts may include improving access to regular screening, diagnosis and treatment, identifying high risk women for intervention, and continuing community based research and educational programs. After a cancer diagnosis, patient navigators and prompt access to up to date breast cancer therapy treatment may improve outcomes.

KEYWORDS: : Health Disparities, American Indians, Breast Cancer, Screening mammography, Breast Cancer Mortality

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The relative paucity of information about breast cancer in American Indian (AI) women compared to larger population racial groups makes assessment of this healthcare disparity among AI women more difficult. Breast cancer risk and outcomes information about this underserved population is limited or incomplete (Emerson et al., 2017; Martin et al., 2016). Studies of racial differences in breast cancer often do not include information about the AI population (Ahmed AT, 2017). Furthermore, information regarding breast cancer screening, incidence, and mortality rates in American Indian and Alaska Native women is commonly merged into a single group. However, looking at data from this merged single data group masks wide and unique variations in subgroups and regions. Since American Indian subgroups are heterogeneous by tribe, geographic location, and urban vs. rural residence, merging data into one mean value can obscure differences and disparities. As a result, evidence based breast cancer control in this population is more challenging. To address inequities in breast cancer screening, prevention, treatment and survivorship, accurate, timely, and specific data is needed. Community based participatory research among these women is a key method to obtain useful insight about breast cancer detection and treatment challenges, and from which to guide the design of interventions needed to address the inequities (Burhansstipanov L, 2010; Burhansstipanov et al., 2017).

Racial or ethnic minority patients are underrepresented in cancer registries due to racial misclassification occurring from missing or incorrect entries in medical records, and misclassification of American Indian patients is common. This misclassification results in underestimation of the breast cancer burden in AI

women (Haozous EA, 2014; Johnson et al., 2009; Roen et al., 2014; White et al., 2014b). Accuracy in medical records may be improved by matching records from different sources, i.e., linking cancer registries to tribal and Indian Health Service records. Data linkage changes breast cancer incidence rates substantially (Roen et al., 2014). Recently, linkages between Indian Health Service patient files and the national Death Index have improved accuracy in American Indian breast cancer mortality and incidence data (Espey DK, 2014; Roen et al., 2014; White et al., 2014b). In addition to problems of misclassification, 71% of American Indians reside in urban areas with medical care outside of the Indian Health Service (Emerson et al., 2017). Therefore Indian Health Service records represent only part of the entire population and data among urban American Indians is only recently emerging (Jacobs-Wingo JL, 2016).

In the United States there are medically underserved populations which have higher cancer burdens in incidence, mortality and/or outcomes. The national breast cancer incidence rate had a historic decrease 1998-2007, dropping 1.7% per year, with about 3% per year decrease between 1999-2004; in contrast, the overall incidence rates in American Indians and Alaska Natives were level during that time period (Krieger N, 2010). For American Indian women the overall incidence of breast cancer historically has been lower than that of the US population, but dramatic and persistent geographic differences in incidence rates among subgroups have been reported over many years (White et al., 2014b). Data from 1999-2009 demonstrated an overall incidence of breast cancer of 100/100,000, compared to 131/100,000 for white women (White et al., 2014b). However, the mean value masks the regional variability in

this population. The highest incidence rate was 141.3 in Alaska Native women, followed by 136.1/100,000 among women in the Southern Plains tribes; the lowest incidence was in AI women in the Southwest at 59.6 (White et al., 2014b). This regional variability of breast cancer incidence is unusual, as it is not found among other ethnicities or races (Wingo et al., 2008) and persists even when improving the accuracy of records by adjusting for racial misclassification (White et al., 2014b).

Although the average breast cancer mortality rate in American Indian and Alaska Native women (22.2/100,000) has been lower than white women (24.1/100,000) (White et al., 2014a), it is not as low as would be expected when comparing incidence rates. Similar to the incidence rates, the mortality rates vary regionally, with higher death rates from breast cancer among American Indian women compared to white women in the Northern Plains, Alaska, and the Southern plains (White et al., 2014b). Since the *ratios* of mortality to incidence were reported higher for the years 1990 to 2009 among American Indian women than among white women, American women had a comparatively higher risk of death from breast cancer (White et al., 2014b). Breast cancer mortality rates nationally decreased 39% after screening mammography became commonly used, beginning in 1989- to 2015. This improvement is attributed to a combination of better and earlier detection with screening mammography and improved therapies, with 50-80% of the mortality rate decline due to screening mammography (DeSantis et al., 2017; Vervoort MM, 2004). The mortality rate decline occurred for white women and African American women but was comparatively unchanged among AI/AN in the years up to 2009 (White et al., 2014b). In more

recent years, death rates for AI/AN women were reported to have decreased although, the decline in death rates among AI/AN women began in 2005, more than a decade later than other racial and ethnic groups (DeSantis et al., 2017). Additionally that same recent data indicated that AI/AN women continue to have a lower proportion of localized stage and a higher proportion of regional stage disease than white women (DeSantis et al., 2017). Survival from breast cancer was poorer among urban American Indian women who were Northern California Kaiser Permanente enrollees compared to non-Hispanic white women, with mortality rates from breast cancer that were 47% higher (Emerson et al., 2017). Survival from breast cancer in this study was lower even when controlling for income and comorbid conditions (Emerson et al., 2017). Although not proven, it was presumed in this study that these California AI women had approximately equal access to cancer care services, suggesting that the survival differences were not due to differences in cancer screening or treatment. Further studies like these are needed to study factors that influence breast cancer mortality in American Indian women, including cancer stage and histology, screening, treatment, and social-behavioral-cultural factors. For example, differences in breast cancer by hormone receptor and HER2 status have been reported for American Indian/Alaska Native women who were found to have had a 3.9 fold higher risk of stage IV triple negative breast cancer, an aggressive subtype (Chen and Li, 2015).

Breast cancer incidence varies by age, among all races and ethnicities, with many more cancers occurring in older women than younger women. The older the woman, the more likely she will be diagnosed with breast cancer, and although more

attention has been given to breast cancer among young women, women ages 60 years or older are at the highest risk for breast cancer. It has been reported that more American Indian women are diagnosed with breast cancer at a younger age, mean age of 53.5 years, compared to non-Hispanic White (NHW) women, who are diagnosed at a mean of 63.4 years (Wingo et al., 2008). Although the overall average breast cancer incidence rate is lower compared to NHW, the incidence rate among American Indian women less than 50 years of age (2007) is not lower than the national incidence rate for this age group (National Cancer Institute, 2010). Prior studies reported that 30% of AI/AN women with breast cancer are diagnosed before they reach 50 years of age, a substantially higher proportion than for NHW women, of whom only 19% are diagnosed before age 50 years (Wingo et al., 2008). Similar findings were reported in a Michigan study, with a mean age of breast cancer diagnosis for AI women younger than that of white women, and a greater percentage diagnosed under 50 years compared to white women (Roen et al., 2014). Younger age of breast cancer diagnosis confers a higher mortality because the tumors are larger and higher grade cancers than occur in younger women. Thus, if screening in American Indian women does not occur until age 50 years, a substantial proportion of women with breast cancer will miss a chance for early detection (Arleo et al., 2017).

Annual screening mammography increases the rate of early detection of localized disease and improves patient health. Screening mammography detects breast cancer several years before the cancer is palpable (Rosenberg et al., 2006), increases patient survival (Kopans, 2007) and allows women the option of breast preservation

treatments such as lumpectomy and radiation therapy. Screening mammography could improve the health disparity among American Indians by detecting breast cancer at an earlier stage (DeSantis et al., 2017). The minimal 'risks' of mammography, including false positive biopsies and anxiety from the need for additional views, are minor, far outweighed by a diagnosis of a later stage of breast cancer. Mammography is the lowest cost, most widely available, standardized, and evidence-based method to detect breast cancer. There is a strong consensus that mammography screening for women 50 to 69 years of age reduces breast cancer mortality. Unfortunately, screening women 40 to 49 years of age has been controversial (Arleo et al., 2017). However, since 40% of the years of life that are lost by women due to breast cancer are among women 40 to 49 years of age (Arleo et al., 2017; Kopans, 2007; Kopans, 2010; Wingo et al., 2008) screening mammography beginning at age 40 years is recommended by the American Cancer Society, and is a definite recommendation by the National Comprehensive Cancer Network (NCCN), the American College of Obstetrician and Gynecologists, and the American College of Radiology (Arleo et al., 2017). Results from clinical trials suggest that the mortality rate from breast cancer can be reduced by 30% when recommendations for screening are followed (Arleo et al., 2017; de Gelder R1, 2015; Kopans, 2007; Kopans, 2010). Since the vast majority of women who get breast cancer have no family history of the disease (Neal CH et al., 2018), it is not appropriate to limit mammogram screening to high risk women in the 40 to 49 years age group. Targeted screening for specific subgroups of young women at higher risk is indicated, including genetic testing and supplementary screening at an

early age with breast MRI examinations (Expert Panel on Breast et al., 2017; Samphao et al., 2009). In addition to screening high risk women in this younger age group, elderly women can also benefit from screening mammography, preventing breast cancer morbidity and death 5-10 years later (Arleo et al., 2017).

Racial minorities are less likely than white women to receive adequate mammogram screening, and of all racial minorities, American Indians have historically had the least breast cancer mammogram screening (Peek and Han, 2004; Roen et al., 2013; Smith-Bindman R, 2006). Historically, use of screening mammography can vary by region, such that the average national screening rates for American Indian women can obscure regional disparities (Peek and Han, 2004; Schumacher et al., 2008). Data regarding the prevalence of any method of screening (mammography, clinical breast exam, or breast self-examination) in minority populations is scarce. Self-reported mammography use from the Behavioral Risk Factor Surveillance System (BRFSS) has typically shown less use of mammography among AI/AN than other racial groups (Centers for Disease Control and Prevention, 2010). In the Northern Plains, an area of elevated breast cancer prevalence among AI women, only 51% of women reported “ever” having had breast cancer screening (Pandhi et al., 2010). The percentage of AI women in the Southwest reporting “never” was 30.1% (Schumacher et al., 2008). Self-reported estimates of adherence to screening mammography are not accurate and are commonly higher than medical records (Peek and Han, 2004), and self-reported mammography use among minority and low income women is over estimated because of under sampling. Using medical records to assess mammogram screening,

the Indian Health Service GPRA report of 2009 indicated that only 45% (40-55% by region) of AI women had screening mammograms (Service, 2010). In a study with screening mammogram data obtained directly from mobile mammography records, the majority (60.14 %) of women in the Northern Plains who presented to the mobile mammogram unit reported not having had a screening mammogram in the previous 2 years, which is lower screening adherence than found nationally, and screening rates were lowest among women ages 41-49 years (Roen et al., 2013).

The recommendations for the interval between screening mammograms vary from one to two years. In computer models, more frequent mammogram screening dramatically reduces the mortality rate of breast cancer (Arleo et al., 2017; Michaelson et al., 1999). The likelihood of metastatic disease is decreased by 51% when mammography is performed annually (Michaelson et al., 1999). Increasing the compliance with annual screening mammography is the most evidence-based intervention to decrease the mortality rate of American Indian women since adherence to recommended screening intervals may reduce breast cancer mortality rates (de Gelder R1, 2015; Smith-Bindman et al., 2006). Historically, adherence to screening intervals has substantial variation by race/ethnicity, age, insurance status, and family history (Strzelczyk and Dignan, 2002). There is minimal data about adherence to screening mammography among AI/AN women. Wampler et al. found that American Indian women in Colorado were less likely than non-Hispanic White women to adhere to recommendations for screening mammography, both annually and biennially, with the chief predictor being economic status (Wampler et al., 2006). Among Northern Plains AI women presenting to a mobile

mammography unit, adherence to screening mammography guidelines (defined as a prior mammogram within the past two years) occurred in 39.86 % of the AI women, lower than adherence to screening reported in the same time period where 74.34 % of white women complied with screening mammography guidelines in a national mammography database (Roen et al., 2013). Disparities in screening mammography are improving among medically underserved populations but still persist among racial/ethnic minorities and low income women (Peek and Han, 2004). While regular compliance with screening mammography is important for early detection, many factors affect compliance such as local availability of mammographic facilities, physician recommendations, financial issues (insurance, low cost programs), and patient attitudes. The EARTH study found that predictors for mammography compliance included higher educational status, higher income, older age, positive family history, and urban location (Schumacher et al., 2008). Pandhi found that the strongest predictor for compliance with cancer screening in the Northern Plains was the provider recommendation (Pandhi et al., 2010).

In 1990 the National Breast and Cervical Cancer Early Detection Program (NBCCEDP) was initiated to improve the access of medically underserved women to screening mammography and subsequent diagnostic procedures. This program provides support to women in all 50 states and to 12 tribal programs among 6 states. Published data from the NBCCEDP indicate that while first round screening in AI/AN women yields fewer cancers than screenings in white women, subsequent round screening detections and positive predictive values are similar to that of other racial/ethnic groups (Eheman et al., 2006). This indicates that

mammography is equally effective and accurate in AI/AN and NHW women. It is estimated that approximately 49% of eligible AI/AN women in NBCCDP programs have been screened, which is a higher rate than any other racial/ethnic group and demonstrates the importance of this CDC program to native women (Tangka et al., 2006).

Difficult access to breast screening and diagnosis may contribute to the disparity in American Indian women in breast cancer mortality to incidence ratios. A recent study of geographic access to breast imaging services reported marked differences among population subgroups (Onega et al., 2014). Travel time to mammography and ultrasound for 85% of US women was less than 20 minutes, with Black and Asian women having the shortest median travel times. Travel times greater than 30 minutes for mammography and ultrasound were found for 39.6% of Native American women compared to only 12.6% of white women and 6% of black women. Access to MR imaging is even worse. Long travel times (>30 min) for breast MRI were found in 85% of American Indian women, as compared to only 46.5% of white women and 26.1% of black women. These disparities in American Indian women persisted despite rural or urban locations. The authors concluded that American Indian women are disadvantaged in geographic access to breast imaging as measured by travel times. Potential interventions could be designed to reduce these transportation inequities, improve racial disparity in early breast cancer diagnosis and mortality from this malignancy (DeSantis et al., 2017; Onega et al., 2014). Rural women in general have lower screening mammography rates than urban women, a finding seen in the EARTH study (Schumacher et al., 2008). A contributing factor is the lack of convenient mammography facilities.

One countermeasure taken to improve mammography access in this region, was a mobile screening mammography unit taken to 18 rural and urban clinics in this rural IHS area in 2006-2017 (Roen et al., 2013; Roubidoux et al., 2006).

In addition to mobile mammography, telemedicine is another way to encourage screening and to assess breast cancer risk among women who live in remote areas, for whom regular screening is more challenging. Through telemedicine, Alaska Native and American Indian women may meet with providers or patient navigators to discuss their breast cancer risk and to learn life style modifications to which can reduce breast cancer risk. Using telemedicine, high risk women in remote areas can be identified and targeted for screening, and for preventive therapy with risk reducing strategies and medications. A previous pilot study showed that telemedicine risk counseling, enabled by technology and a patient navigator, is feasible and has high patient satisfaction. (Pruthi et al., 2013)

To effectively advise American Indian patients about breast cancer screening, individual risk needs to be determined because screening recommendations are based upon assessing a patient's risk for breast cancer (Expert Panel on Breast et al., 2017). When a woman's risk is determined to be average, screening mammography and/or digital breast tomosynthesis is recommended beginning at age 40 years. Thereafter, annual repeat mammogram screening confers the greatest years of life saved from detecting a breast cancer. (Arleo et al., 2017) When a woman has dense breasts, breast ultrasound may be an adjunct to mammography for incremental cancer detection, although ultrasound may result in increased false positive

results. For women at very high risk due to prior mantle irradiation between the ages of 10 to 30 years, mammography is recommended starting 8 years after radiation therapy but not before age 25 years. In these patients, screening with breast MRI should also be done. For women with a genetic risk, such as women with BRCA gene mutations, or a 20% lifetime risk of breast cancer, annual screening mammography is recommended beginning 10 years earlier than the affected relative's age of onset, but not before age 30. Additionally, breast MRI is recommended for this group of women because MRI has greater sensitivity than screening mammography. (Expert Panel on Breast et al., 2017)

In order to determine patient risk, providers and patient navigators may use one of a few available breast cancer risk prediction models. Commonly used models are The International Breast Intervention Study (IBIS), or Tyrer-Cuzick, model and the Gail model. (Millstine et al., 2014) The Tyrer-Cuzick model is based on data from the International Breast Intervention Study (IBIS) from the United Kingdom. This model can be employed to determine whether a woman is a candidate for annual screening MRI in conjunction with annual mammograms. The need for screening MRI should be based on 2007 American Cancer Society Guidelines, which indicate that a lifetime risk of greater than 20 percent merits supplemental MRI screening. The Gail model, which uses age, race, menarche, age at first live birth, history of cancer in first degree relatives, history of breast biopsy, and history of atypical ductal hyperplasia to predict 5-year and lifetime risks is used only in women age 35 years or older and cannot be applied to those with a history of breast cancer, lobular carcinoma in situ, or ductal carcinoma in situ. However, it is well suited to determine

whether chemoprevention is indicated for breast cancer risk reduction. When a woman is identified to be at high risk, chemoprevention may also be prescribed, using tamoxifen, raloxifene, or exemestane, each of which has been shown to lower lifetime risk of breast cancer. (Burns et al., 2016; Millstine et al., 2014; Visvanathan et al., 2013)

Historically, racial/ethnic minorities and low income women have been less likely to receive physician recommendations for mammography, and this variability in physician recommendations must be addressed (Peek and Han, 2004). Native American women are strongly influenced by their relationship with their provider, their experiences and their degree of trust in the health care system (Canales and Geller, 2004). However, lack of consistency in provider from one year to the next, and frequent moves between urban and reservation domiciles undermines a good provider relationship (Burhansstipanov L, 2010). Lay health advisers in the communities can also be effective in improving compliance of Native American women to screening mammography, especially since barriers to participation can be complex (Burhansstipanov L, 2010).

Although breast cancer is the most common malignancy among American Indian women, it is second to lung cancer as a cause of death. This is because survival of women with breast cancer is much higher than survival of women with lung cancer. Therefore, breast cancer is less likely to threaten the life of a smoker than are smoking related diseases such as chronic obstructive pulmonary disease and cardiovascular disease. As screening mammography becomes better established in native American communities, mammogram screenings become opportunities for teachable moments to encourage other

healthy behaviors such as smoking cessation and colorectal cancer screening (Carlos and Fendrick, 2004).

Aside from risk reducing chemoprevention medications, American Indian women may decrease their risk of breast cancer with exercise, minimizing alcohol intake, and practicing breast feeding for durations as long as feasible. Other actions that may decrease the risk of breast cancer include increasing the intake of omega 3 fatty acids (fish oil), citrus fruits, and vegetables of the cabbage family. Further positive steps include reducing dietary omega 6 fatty acid (vegetable oils) by substituting extra virgin olive oil, reducing the intake of red meat, high fat and hormone containing dairy products, and by using vitamin D supplements. (Ronco et al., 2010) They may decrease their risk of death from breast cancer by engaging in annual screening mammography and for supplemental screening with magnetic resonance imaging when genetic risk is evident. Finally, guideline concordant breast cancer care and treatment needs to be more universally received by this population. (Javid SH, 2014)

Disparities in breast cancer among American Indian women may be addressed through a variety of activities. First, the heterogeneity of American Indian populations must be recognized and health information examined by local group rather than being lumped into one large group. Furthermore, the accuracy of the information must be improved by reducing racial misclassification. In addition to analyzing data among geographic subgroups, differences between rural and urban women must be recognized. Access to breast cancer screening and treatment must be improved for all Native American women, and continuing community needs assessments and educational

interventions and needed for this understudied population.

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Conflict of interest

The authors declare that no competing or conflict of interests exists. The funders had no role in study design, writing of the manuscript, or decision to publish.

Authors' contributions

MAR designed and conceived the study and wrote the manuscript.

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