

The Underrepresentation of Minorities and Non-Generalizability of Breast Cancer Clinical Trials?

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Received date: August 20, 2021; **Accepted date:** September 03, 2021; **Published date:** September,10 2021

Abstract

Introduction: This year 43,000 women will die from breast cancer in the United States. African Americans and Native Americans though less likely to get breast cancer, once diagnosed they are much more likely to die from breast cancer. This increased death rate may in part be due to the non-generalizability of breast cancer clinical trials. In this study, we evaluate the participation of ethnic minorities from breast cancer clinical trials.

Methodology: In this study, fifty-six breast cancer clinical trials completed in the last ten years in the United States were evaluated for the inclusion of ethnic minorities in the breast cancer clinical trials.

Results: Only 21% of breast cancer clinical trials include information on ethnicity in the methodology while only 7% provided any information on the effect or toxicity of the therapeutic intervention in minority groups while 100% report the results for Whites. Though Whites only make up 60.1% of the population, they were 87.5% of the clinical trial participants while African Americans were 6.2%, Hispanics 3.1%, Asians 2.9% and Native Americans were 0.2% of the participants.

Conclusion: Racial minorities have been underrepresented in breast cancer clinical trials which may contribute to unnecessarily high death rates in these groups while suggesting limited generalizability of breast cancer clinical trials.

Keywords: Breast cancer • Clinical trials • Native Americans • Health care disparities • Racism • Pharmacogenetics • Non-generalizability • Exclusion

Introduction

One out of 8 women will get breast cancer in her lifetime. Each year in the United States 282,000 women will be diagnosed with breast cancer representing 14.8% of the new cancers. Forty-three thousand women will die this year of breast cancer [1]. Whites have the highest incidence of breast cancer at 131.8 per 100,000 females per year. This is in part due to White women having a higher statistical rate of alcoholism, drug usage, and a later age of first child than women of other ethnic groups [2-4]. All of which increase breast cancer rates. These facts become important later. African Americans, who have a lower incidence of breast cancer than Whites, have a higher death rate than Whites [5]. Once a person is diagnosed with breast cancer their chance of dying if white is 15%, African Americans 21.9%, Hispanics 13.7%, Asians 11.1%, and Native Americans 18.1%. Thus, African and Native Americans are at increased risk of death when they get breast cancer though both groups having a lower incidence of breast cancer. Breast cancer is treated depending on the type of breast

cancer it is whether estrogen receptor positive or negative, progesterone receptor positive or negative, and her2/neu positive or negative along with the stage of the cancer I, II, III or IV [5]. These standard treatments have been derived from clinical trials which are funded by the National Institutes of Health (NIH) and/or the Pharmaceutical Industry with the Food and Drug Administration approving or not approving the therapeutic intervention.

Due to molecular differences in the cell cycle, cell differentiation, genetic and epigenetics factors the type of breast cancer plays a heavy role in determining the outlook for the disease. For instance, African American women tend to have a higher rate of the most aggressive type of breast cancer, triple negative that presents with the absence of the estrogen, progesterone and her2/neu receptors [6]. The presentation of a higher risk type of breast cancer has been used to explain away the higher risk of death among African American women from breast cancer. Yet, Native American women who also have a higher risk of death once they have breast cancer do not present with the higher risk forms of breast cancer yet have a higher death rate. It can even be argued that they present with a more benign form of breast cancer than Whites. Thus, perhaps part of the problem is how therapeutic interventions are determined and approved in the United States. In this retrospective study we look at the inclusion and exclusion of ethnic minorities in breast cancer clinical trials.

Methodology

In this study, breast cancer clinical trials performed within the United States within the past ten years were selected by searching PubMed and using the terms breast cancer, clinical trials, and study. Seventy-five papers were then screened to ensure that 1) they were clinical trials; 2) they were performed in the United States; 3) that the number or participants were clearly defined; and 4) published within the past ten years. Fifty-seven peer reviewed papers met the inclusion criteria [7-62]. These papers were then evaluated for the inclusion of ethnic minorities in the methods and results sections of the paper. These fifty-six clinical trials had an aggregate of 196,662 participants.

Results and Discussion

Fifty-seven clinical trials were evaluated for the inclusion or exclusion of racial minorities in breast cancer clinical trials. Of the 56 clinical trials only 21 reported the ethnic characteristics of the participants in the methodology while, only 5 provided the results of the therapeutic intervention on ethnic minorities. These 5 clinical trials who reported the result of the therapeutic information were only two trials which had sufficient numbers of ethnic minorities to provide useful information on these populations of the intervention. Whites who make up 60.1 of the population were 87.5% of the population. Hispanics who make up the largest ethnic minority in the United States are 18.5% of the population but only 3.1% of the breast cancer clinical trial participants. African Americans who are 13.4% of the population made up only 6.2% of the clinical trial participants. Asians and Native Americans who make up 5.9% and 1.5% of the population had a representation of only 3.1% and 0.2% of the breast cancer trial participants (Figures 1a and 1b). The participation of ethnic minorities may actually be lower than reported as 63% of the breast cancer clinical trials did not report the ethnic break-down of the participants. The actual participation in clinical trials by Hispanics may be as low as 1.6%, African Americans 3.2%, Asians 1.5%, and Native Americans 0.14%.

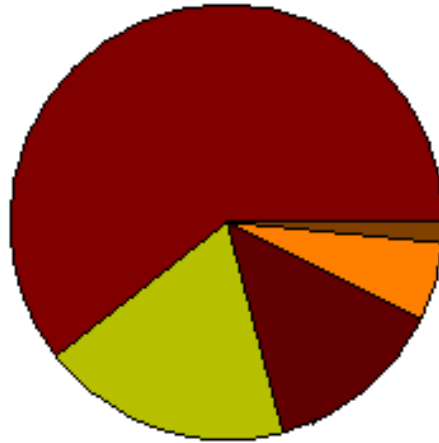


Figure 1a. Breast cancer clinical trial participation rate among population by ethnic group.
Note: () whites 60.1%, () Hispanics 18.5%, () African American 13.4%, () Asian 5.8%, () Native American 1.5%.

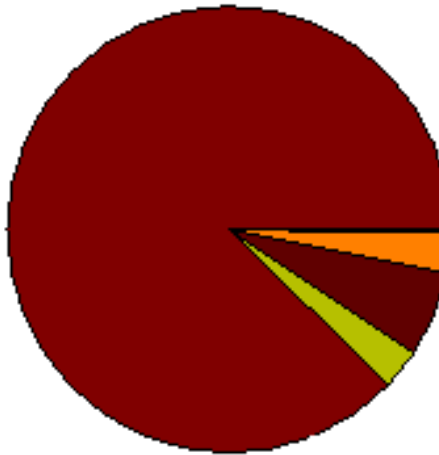


Figure 1b. Breast cancer clinical trial participation rate among participation by ethnic group.
Note: () whites 87.5%, () African American 6.2%, () Asian 2.9%, () Hispanics 2.9%, () Native American 0.2%.

In order to have clinical trials that are generalizable to the population as a whole they must include not only representatives from ethnic minorities in significant numbers in the trial but, report on how the therapeutic intervention acted on different ethnic groups. Here we see that the overwhelming number of breast cancer clinical trials did not even bother to report the ethnic background of the participants and even fewer reported how the intervention affects ethnic minorities. Though ethnic minorities make up 40% of the population they only represent 13% of the breast cancer clinical trial participants with perhaps less than 2% providing any useful information of the therapeutic intervention efficacy or toxicity on minority populations. In a country where we speak of women's rights apparently in health care and research it only applies to White Women as Hispanic, Native American, and African women are underrepresented and seem not to count as they are deemed irrelevant in clinical trials and as shown in this paper this applies to breast cancer as well.

In a country where the myth is that hard work and good conduct are rewarded, we see that this is not true as White women tend to get breast cancer at the highest rates due to lifestyle choices especially those in the earlier years of life recalling that cancers develop over decades [63,64]. Thus, what one did twenty years ago or more determine today's cancer due to the eventual overcoming of the individuals DNA repair mechanisms that preserve genomic integrity [65]. On the other hand, ethnic minorities die at higher rates of breast cancer in part due to exclusion from medical research based on skin color! To change this minority community must step up and provide their own doctors, scientists, and researchers to address this health care disparity and to change the future for the better. This will also help the minority community regain trust in health care providers and researchers and improve community engagement [66].

Conclusion

There is a total disregard for the life's, well-being, and health of ethnic minorities by the pharmaceutical industry, the federal government, and medical researchers in the United States. Racial minorities have been underrepresented in breast cancer clinical trials which may contribute to unnecessarily high death rates in these groups suggesting limited generalizability of breast cancer clinical trials. The lack of representation of minorities in breast cancer clinical trials represents an easily solvable problem resulting from systematic racism against non-whites in the United States. Hispanics and Native Americans are clearly the most discriminated against groups in clinical research followed by African Americans in breast cancer clinical trials and research. In breast cancer trials, racial minorities have been provided with insufficient or inadequate representation which has led to more number of death rates which is unnecessary. While they managed to limit the general ability for the same.

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