Acta Scientific MEDICAL SCIENCES (ISSN: 2582-0931)

Volume 5 Issue 9 September 2021

Research Article

Colon Cancer: The Exclusion of Native Americans and Hispanics from Clinical Trials in the United States

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Received: August 08, 2021

Published: August 19, 2021

Abstract

Introduction: Each year there are 150,000 new cases of colon cancer in the United States. The chance of death for Hispanics and Native Americans who get colon cancer is much higher than whites even though both groups are much less likely to get colon cancer than whites. In this study, we look at the inclusion or exclusion of Hispanics and Native Americans from colon cancer clinical trials.

Methods: In this retrospective study, 48 colon cancer clinical trials in the United States with an aggregate of 421,530 participants performed within the last ten years were selected at random. These clinical trials were evaluated for the inclusion and exclusion of minorities.

Results: Though whites make up only 60.1% of the population they make up 89% of the colon cancer clinical trial participants. African Americans, and Hispanics who make up 13.4% and 18.5% of the population only made up 5.6% and 0.6% of the colon cancer clinical trial participants. Only two native Americans out of 421,530 colon cancer clinical trial participants could be identified.

Conclusion: Colon Cancer Clinical trials have systematically excluded Hispanics and Native Americans while minimizing the participation of African Americans. This may be directly related to the increased death rates seen in these groups and provides evidence for the non-generalizability of colon cancer clinical trials.

Keywords: Colon Cancer; Clinical Trials; Native Americans; Hispanics; African Americans; Health Care Disparities; Racism; Pharmacogenetics

Introduction

It is estimated that there will be 149,500 new cases of colon cancer in 2021 with 52,980 deaths representing 8.7% of all cancer deaths in the United States [1]. The annual health care cost for colon cancer is about 18 billion dollars with about 300 million dollars being spent on research for this disease [2,3]. The incidence per 100,000 of colon cancer for Whites is 38.8%, African Americans 43.7%, Asians 31.8%, Hispanics 34.4%, and Native Americans 38.6%. The death rates are Whites 13.6%, African Americans 18.7%, Asians 9.6%, Hispanics 11.3%, and Native Americans 15.5%. It is of interest to note that though Native Americans are less likely to get colon cancer than whites they are more likely to die from colon cancer. What perhaps is most telling is that the chances of dying once diagnosed with colon cancer is for Whites 35.1%, African

Americans 42.8%, Hispanics 38.7%, and Native Americans 40.5%. Among the factors that may be responsible for these findings are racist attitudes towards minorities by healthcare providers [4], poorer services available in minority areas [5], inadequate health insurance [6] and lack of adequate health care information provided to minority communities [7]. Yet, the problem may even be more fundamental than this in that the therapeutic interventions may be less efficacious and more toxic in minority populations due to their exclusion from clinical trials. This may in turn limit the generalizability of therapeutic interventions. Here we look at the inclusion or exclusion of ethnic minorities in colon cancer clinical trials.

Methods

In this study, colon cancer clinical trials performed within the United States within the past ten years were selected by searching PubMed and using the terms colon cancer and clinical trial. Sixty-two 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 was clearly defined, and 4) published within the past ten years. Forty-eight peer reviewed papers met the inclusion criteria [8-54]. These papers were then evaluated for the inclusion of ethnic minorities in the methods and reporting of results and had an aggregate of 421,530 participants.

Results

In this retrospective study, 48 clinical trials met the inclusion criteria with an aggregate of 421,530 participants. It was found that during the evaluation of the methodology of these papers that 19 of the 50 clinical trials reported the ethnicity of the participants or roughly a third. Only one trial reported the results by ethnic group. In terms of participation, 89.1 % were white, 5.6% African American, 5.1% Asian, 0.61% Hispanic and 0% Native Americans. This compares to the expected by extant population in the United States of 60.1% white, 13.4 % African American, Asian 5.9%, Hispanic 18.5% and Native American 1.5% (see Figure 1). All ethnic groups were underrepresented except for white who were over-represented in these clinical trials. Yet, the underrepresentation may be worse as only 36% of the clinical trials even reported the ethnicity of the participants implying that minority participation may be much lower than reported. In either case, the inclusion rate of Hispanics and Native Americans was already almost non - existent. The inclusion rate of African Americans was at best only 41% of expected number by their population in the United States.

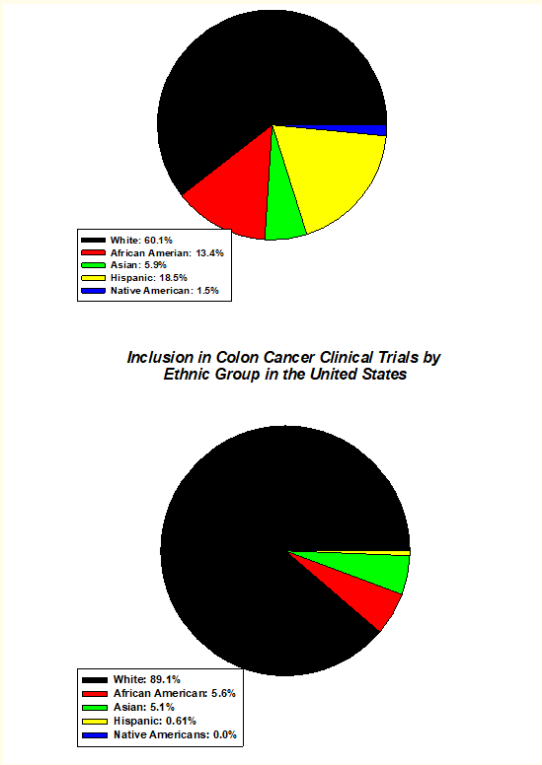

Figure 1: Comparative Inclusion in Colon Cancer Clinical Trials.

Discussion

In the United States for a therapeutic intervention to be approved it must undergo phase I clinical, phase II clinical and phase III clinical trials and the treatment have a good therapeutic index for a particular disease. The therapeutic index is the effective dose for half the population divided by the toxic dose for half the population ($TI = ED^{50}/TD^{50}$). Even under the best circumstance in a homogeneous population with a good therapeutic index there will be some people who do not have a response to a drug or intervention at normal doses and others who will undergo to toxicity at normal doses [55]. The more deadly or serious the disease the narrower the therapeutic index is allowed to be. The "normal dose" itself which is generated during the clinical trials represents the population that was included within the clinical trial. Thus, due to variances in environment, genetics, and epigenetics the pharmacogenetics may vary considerably among different ethnic popula-

tions. Thus, the results of the clinical trials may not be generalizable to populations excluded from the clinical trials. This may lead to ineffective treatment and/or an inordinate amount of toxicity in excluded groups.

Colon Cancer trials have been heavily biased in the inclusion of whites. African Americans who have a higher risk or colon cancer and a higher death rate surprisingly have been underrepresented when one would think they might be a primary focus of these trials. Indeed, Hispanics and Native Americans have been completely excluded as if their lives don't matter. Both groups though less likely than whites to get colon cancer once they get colon cancer have a much higher death rate. In otherwards their genetics, epigenetics and environment seem to be better in limiting colon cancer but, once they get it their death rates are high. The treatment of colon cancer is primarily determined by the stage of the colon cancer in a one size fits all manner [56]. This implies that the therapeutic intervention in minorities is lacking due to their exclusion from clinical trials. The National Institutes of Health and Big Pharma who fund clinical trials and carry them out often with major medical centers share responsibility in the racist approach of clinical trials with the Food and Drug Administration who approve the medications and therapeutics. Out of 48 colon cancer clinical trials only one had useful results for non-whites or < 2%. All the colon cancer clinical trials included an overwhelming number of whites, and all included useful information for whites. One may ask is it reasonable that out of 421, 530 colon cancer clinical trial participants only 265 Hispanics and 2 native Americans could be identified?

Conclusion

Colon Cancer Clinical trials have systematically excluded Hispanics and Native Americans while minimizing the participation of African Americans. This may be directly related to the increased death rates seen in these groups and provides evidence for the non-generalizability of colon cancer clinical trials. The Federal Government, Big Pharma and major medical centers in the United States share responsibility for this racism which has led to the unnecessary and tragic death of minorities in the United States.

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