

RACIAL DISPARITIES IN ACUTE MYELOID LEUKEMIA SURVIVAL RATES: A MIXED METHOD ANALYSIS OF CONTRIBUTING FACTORS

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ABSTRACT: In the United States leukemia cancer patients of color continue to have lower overall survival outcomes compared to Caucasian leukemia patients, yet existing research does not detail what factors are contributing to a disparity in survival. This proposal aims to explore the impact variables such as transportation access, insurance status, and stage of cancer at diagnosis have in various populations ability to survive the cancer. Using a mixed method longitudinal study design with online survey elements, the proposal asks demographic questions, patient behaviors questions, along with socioeconomic status assessment, and utilizes qualitative narrative interviewing. The patients receiving active care for leukemia will be selected randomly from four chosen cancer treatment centers in the Greater Seattle area, those who agree to participate will continue with the study for five years. The results of the proposed study are expected to yield a greater understanding of factors that decrease the rates of leukemia survival in populations of color, with the intent of influencing better care and outcomes for those populations. It is imperative that we continue to investigate the underlying factors that lead to disparities in survival and we believe this proposal is an important step in advocating for equitable care.

Introduction

The prevalence of leukemia related cancers is on the rise, along with the death rates. The United States' annual estimated leukemia related death toll in 2015 was 22,840 people (LaRussaA, 2015). An estimated 60,300 new cases occurred in 2018, with the resulting death toll of 24,370 (Kandola, 2018). Leukemia is a progressive type of blood cancer in which the bone marrow produces abnormal platelets, white and red blood cells. The disease limits the patient's ability to fight and recover from infections. There are four common types of leukemia: acute myeloid leukemia (AML), chronic myeloid leukemia (CML), acute lymphocytic leukemia (ALL), and chronic lymphocytic leukemia. This study will be focusing on acute myeloid leukemia (AML), though background research referenced may include leukemia subtypes. The general survival rates for leukemia patients are not always favorable, and further review of survival rates shows that some demographics are less likely to survive than others for reasons not yet fully

understood. The proposed study aims to research and answer questions regarding the underlying factors that may be contributing to lower rates of survival for leukemia patients of color compared to their Caucasian counterparts. The research hypothesizes that if a leukemia patient is a person of color, then they will have a lower survival rate than that of a Caucasian leukemia patient. Such contributing factors this research will consider are the stage of diagnosis, family structure, and distance from treatment centers.

To understand the depth of these survival disparities, peer-reviewed studies were referenced in the development of this proposal. Much of the literature reviewed contained similar results, supporting that people of color statistically have lower blood cancer survival rates than Caucasian populations. According to the American Association of Cancer Research, African Americans have a seventeen percent increased risk of cancer-related death when compared to Caucasians, and Hispanics have a twelve percent increased risk

(AACR, 2011). Many of the studies referenced pulled data from the SEER database (Surveillance, Epidemiology, and End Results), a program of the National Cancer Institute (NCI) and a repository source of epidemiologic information on incidence and survival rates of cancer in the United States. This research has the potential to reshape how professionals approach treatment plans, health interventions, and attempts in promoting health equity with the goal of improving the survival outcomes for marginalized communities.

In looking specifically at how AML patient survival outcomes can change over time, a Plos One journal article, which studied the United States population between the years of 1973 to 2014, was referenced to get a baseline understanding of the disparities in the survival of adult leukemia patients (Utuama, et al., 2019). The longitudinal study collected data from the SEER database with the results stratified by the race, age, and sex of the patients. The outcome of this study showed that African Americans had the lowest rate of leukemia survival among races (Utuama, et al., 2019). The data also concluded that Asian populations had the greatest improvement in survival over the course of the study. This data prompted further questions into why African American populations have not had the same level of improvements in overall survival despite medical advancements.

Additional longitudinal research that provided perspective included a cohort study which tracked the trends in survival and incident rates of leukemia patients. The study reported: 66,404 cases from 1972 to 1998 found that African Americans had a lower prevalence of leukemia diagnosis than Caucasians (Xie, et al., 2003). A study published in *Clinical Lymphoma Myeloma and Leukemia* also concluded lower survival rates among racial minorities but looked at patients specifically with hairy cell leukemia, a slowly progressing blood-borne cancer (Giri, et al., 2015). Findings from these studies support the idea that survival rates vary by race, with each study acknowledging a lack of understanding into why. This is an opportunity to explore contributing factors that have likely been overlooked.

Research Question and Hypothesis

“The cancer death rate for African-Americans is 25 percent higher than Caucasians, and Hispanics and Latinos are more likely to be diagnosed with cancer at a later, and more dangerous, stage of the disease” (Blakemore, 2018). The question this study aims to ask is: what factors are leading to racial disparities in acute myeloid leukemia patient survival? The research hypothesis is: if a leukemia patient is a person of color, then they will have a lower survival rate than that of a Caucasian leukemia patient, with the independent variable being race, and the dependent being survival. The present study examines possible contributing factors such as socioeconomic status, stage of diagnosis, age, race, and transportation barriers that could affect the survival gap.

Background

The stage of diagnosis and the age of patients at the time of diagnosis are variables of great interest due to the impact diagnosis timing has on overall survival. The SEER database was used in a study published in *Scientific Reports* journal which looked at the stage and age of diagnosis among races with leukemia subtype cancers. The study reviewed data from predominant United States races (African American, Native American, Asian/Pacific Islander, Hispanic, Caucasian) and showed that significant differences existed between race and age of the patients at the time of diagnosis (Zhao, et al., 2018). African Americans were more likely to be diagnosed at a later age and stage of cancer, with associated lower overall survival rates. An additional peer-reviewed study researching diagnosis in races presented alternative outcomes, stating that African American patients with a leukemia diagnosis at a younger age had worse survival rates when compared to that of Caucasian patients (Shenoy, et al., 2011). Upon reviewing this supplemental research, it appears that confounding factors and additional variables need to be studied to further understand the causes of survival disparities. The proposed research will examine the association between diagnosis time frame and survival outcomes.

Transportation is a contributing factor that may also have significance in survival outcomes by affecting the number of treatments a patient can attend. In a review of articles about healthcare accessibility and utilization, a qualitative study of reported attitudes and behavior trends with a population of 1,059 households in North Carolina was considered. This study presented by the Journal of Rural Health addressed concerns of patients having little transportation access to utilize healthcare in rural areas (Arcury, et al., 2006). The results found that patients who used public transportation or had access to a vehicle had a higher chance of using the healthcare provided in that area. This information was taken into consideration since cancer patients receiving active treatment are typically very weak and may need to rely on others to get them to their appointments. An opportunity exists to review the relationship between transportation accessibility and survival.

The role of insurance in impacting survival rates for AML is another relationship of interest. A population-based study published in the Cancer scientific journal describes how a patient's insurance status at the time they were diagnosed affected the overall survival of that individual (Perry et al., 2017). The five-year-long longitudinal study involving 5,784 patients concluded that patients 65 years old and on Medicaid had a significantly lower survival rate than those who had private insurance. Patients who were younger than 65 or who did not have insurance also had a lower survival rate when compared to those with insurance. With the costs of insurance rising and wages stagnating, it is important to consider how those that are in a lower socioeconomic status may have different health outcomes; "80% of the racial life expectancy gap between Black and Caucasian men could be attributed to socioeconomic factors" (Carlson, 2019). The study population will be reviewed to see which racial groups may have a higher likelihood of being uninsured, or in low socioeconomic status.

The supplemental and background research used in the development of this study supports the existence of race-based disparities in leukemia survival. The proposed research will expand the lens

by which practitioners view diagnosis, treatment, and survival outcomes in different populations, and promote equitable care solutions. This proposal will go through a methodology of how the study will be conducted safely and ethically. Peer-reviewed journals have assisted in establishing a general understanding and direction for the research to focus on, as well as significant gaps that need addressing.

Method

Study Design

A mixed method study design shall be used incorporating cross-sectional, longitudinal, quantitative, and narrative approaches. A cross-sectional design is most appropriate for this proposal since the aim of the study is to record and track patient behaviors and attitudes concerning health outcomes annually over a five-year extended period. This design allows the research to address both qualitative and quantitative data. Utilizing a convergent mixed method approach, this study will allow researchers to establish a patient baseline regarding the stage of diagnosis, prognosis, access to transportation, insurance status, socioeconomic status, and immigration status using a survey. The quantitative patient-reported data will be analyzed and then used to generate more targeted questionnaires and research directions. Qualitative narrative interviews with individually selected patients from a smaller sample of the larger population will also be conducted to discuss their experience with cancer treatment, progression, and survival.

The longitudinal approach is needed for this study to accurately assess disparities in survival among racial groups. The relative rate for cancer survival is set at five years from the time of diagnosis (NCI, 2019), which makes the longitudinal method most appropriate for the research purposed. For the collection of quantitative data using the total population of participants, a survey will be utilized due to the cost-effective nature, standardization, and convenience for both participants and researchers to discuss the behaviors and assign a numeric value to the trends. The survey will be multiple choice and contain structured questions that are open and

closed-ended. A website will be created to house the survey and permission gathered to collect the response data. Researchers will follow participants for five years after collecting the initial baseline data. Baseline questions will be asked again annually along with annual narrative interviews of the patient experience.

Sampling and Population

This convergent mixed-method study will have 3000 adult participants between the ages of 20-50, whom all are currently diagnosed with acute myeloid leukemia (AML). The participant racial backgrounds will be a mix of persons of color and Caucasian people. Additionally, the participants will all be in active treatment at one of the four following Greater Seattle cancer treatment centers/hospitals: Lifespring Cancer Center, Seattle Cancer Care Alliance, UW Medical Cancer Center, Swedish Medical Oncology. The research sampling will include subgroups representative of the predominant United States racial groups which include African/African American, Native American, Hispanic, Asian/Pacific Islander, Caucasian, the sex of participants and socioeconomic status.

Proposed Sample & Sampling Techniques

In the selection of participants, a combination of cluster sampling and quota sampling techniques will be utilized. Researchers will be targeting the group of acute myeloid leukemia patient populations within the chosen oncology centers databases. Recruiting will take place within the treatment centers via advertisements on posters and the clinic websites that contain the study information and objectives. Clinic support groups, promotions from physicians, and an email campaign for those subscribed to the clinic's mailing list will also be utilized to reach potential participants. The pool of individuals willing to participate will not include anyone who has previously had any other form of cancer. The participants will be broken into clustered groups distributed by race (African/African American, Native American, Hispanic, Asian/Pacific Islander, Caucasian). Additional quota sampling will be applied second to ensure the cluster samples include each sex (male, female), and economic

status variation; those above 2018 Seattle median income of \$93,500, and those below (Guy, 2019). The outcome will be population groups of different races that contain both sex groups and levels of economic status. Random selection will take place from these clustered groups, and confidentiality applied to those selected. The clustered quota sampling will allow for equal opportunity among the larger available population while ensuring researchers have enough diversity to represent the larger population with just 3000 participants. For the selection of participants who will take part in the narrative interview, judgment-based sampling will be done so that researchers can identify patients who can answer interview questions with reduced risk of traumatization or distress.

Operationalization and Measurement

For this study, the independent variable is the race of the participants; defined as African/African American, Native American, Hispanic, Asian/Pacific Islander, and Caucasian. The dependent variable is survival (the continued state of living or existing by medical standards) after five years from the original diagnosis; while death may occur, it cannot be attributed to another disease. Other possible variables being considered include immigrant status, stage of cancer, stage and age of diagnosis, insurance status, family type, and distance from treatment centers. This study will define acute myeloid leukemia as a type of rapidly progressing cancer that results from the bone marrow producing abnormal white blood cells, red blood cells, and platelets.

The participants will be asked to complete an annual survey over the course of 5 years that will contain multiple-choice close-ended and open-ended questions. The survey will ask self-identifying demographic data such as participant age, family status, race, insurance status, and immigration status, in addition to diagnosis-related questions like the age and stage of the acute myeloid leukemia diagnosis, and prognosis. The multiple-choice questions will ask about access to transportation and socioeconomic status. The initial survey will be used to establish a baseline for each patient and

assess current health status, accessibility, and any further confounding variables to consider.

In addition to an annual survey given over five years, judgment selected patients from the cluster samples will be allowed to provide a narrative interview with researchers. These interviews should help provide qualitative data on participant attitudes and behavior trends. Example questions that might be asked in the interviews include, “how likely are participants to miss a treatment/appointment?”, “how reliable is patient transportation to appointments?”, “Is the cost of treatment concerning or challenging?”, etc. The narrative interview answers will be measured using a 4-point rating system, with secondary questions as needed. An example of the rating will go as follows: How likely are you to miss an appointment due to transportation challenges? Answers: very likely (1 point), somewhat likely (2 points), somewhat unlikely (3 points), not likely (4 points). Score data will be charted and assessed whether the participant has more positive or negative health behaviors that may influence survival; scores <50 will indicate more positive behaviors, while >50 will indicate more negative behaviors. Data from the selected treatment centers will also be collected and reviewed to record the annual status of the patient’s survival, in addition to any changes in prognosis or diagnosis. Clinical data such as progression/regression of the disease, treatment plan, and missed appointments will also be recorded for review.

Data Collection

The data for this research will include collections from the cancer treatment centers databases, self-reported surveys, and narrative interviews. The data will be collected for the duration of five years from an initial patient cancer diagnosis. Participants will be given full disclosure of the research project, the data that will be collected, the purpose and benefits of the research, and the future use. Participants will also be given a full informed consent form, and they will reserve the right to leave the research study at any time. Once researchers have obtained consent forms, participants will be given annual self-reported surveys that speak to diagnosis, status, and

access challenges. Researcher selected participants from cluster groups will be interviewed in-person to provide personal experiences. The narrative interviews will assess patient behaviors, attitudes, and trends concerning acute myeloid leukemia treatment and survival. The narrative interview answers will be measured using a 4-point rating system using the following example guideline: very likely (1 point), somewhat likely (2 points), somewhat unlikely (3 points), not likely (4 points). Data will be scored and reviewed alongside survey data and treatment centers data collected to see if relationships between self-reported behaviors and attitudes, diagnosis progress, access, and overall survival correlate.

Analysis

In this study, we will be using multivariate analysis to look at underlying factors such as transportation, socioeconomic status, and insurance to the survival of acute myeloid leukemia in different race populations. A combination of self-reported interview data such as behaviors, understanding, attitudes, and trends, alongside surveys and clinical data on attendance, treatment progress, and cancer stage, will also be analyzed. Qualitative data will be analyzed using applied coding. Researchers will use coding categories such as emotion, frequency, money, family, choices, causes, and sequence, to organize narrative interview responses. The coding will allow for organization and a better understanding of the trends and attitudes. Researchers will be assessing if there are stand-out factors among racial groups that may be influencing the survival of acute myeloid leukemia. With this combination of qualitative and quantitative data, we expect to find factors such as lower socioeconomic status, which statistically impacts people of color in higher numbers (Williams, 2016), influencing a patient’s ability to surpass the 5-year survival mark. We expect to find patients with self-reported survey scores of 50 points or greater to have more factors impacting their ability to survive the diagnosis than those with lower scores; those scores should also represent the impact among racial groups.

Ethical Considerations

For the cross-sectional study, ethical considerations will be accounted for. Full informed consent will be obtained from participants and educational material distributed regarding what researchers will be collecting, how we will protect their data (secure databases with limited access, clinical records, confidentiality agreements, privacy clauses), and what we plan to use the data for along with why. HIPPA regulations will be followed for the storage and protection of all health data of participants, along with any additional rules in place at the cancer treatment facilities. Institutional Review Board approval will also be sought in terms of research plan approval and survey questions for participants to ensure the rights of participants involved during the study are protected. This study will also consider the potential for the emotional distress of participants during the narrative interviews. Therefore judgment-based selection will occur so that researchers who have established trust with the participants can gauge which individuals would be best to include. Interview participants will also be given the freedom to stop the interview at any time. While participants will not be encouraged by researchers to change their behaviors, precautions shall be taken regarding the wellbeing of the patient's health. If researchers and medical staff at treatment centers notice a trend in health decline and associated behavior, there will be an intervention and full disclosure of findings. In addition, the study will not continue with the participant.

Discussion

Significance

Acute myeloid leukemia (AML) is a broad category of cancers that affect white blood cells, with the survival rate depending on several factors. An estimate of 60,300 new cases occurred in 2018, with a resulting death rate of 24,370 (Kandola, 2018). These numbers are significant because they demonstrate that almost half of these new cases of AML resulted in death. The racial disparities in acute myeloid leukemia survivors in the greater Seattle area between the age groups of 20 to 50 years old were chosen as the target study

population for the study. The sample population consists of 3000 people with an equal set of males and females from each major American race group (African American/ African, Native American, Asian American Pacific Islander, Hispanic, and Caucasian). Participants sampled will contain diverse income levels and access to healthcare services. Different race groups with factors impacting survival such as stages of AML, socioeconomic statuses, the distance from treatment centers, and access to transportation to their treatment centers will be examined. This proposal holds significance due to documented differences in acute myeloid leukemia survival rates between people of color and Caucasian people. Existing studies have looked at the racial differences and survival rates amongst groups of patients, however, this study attempts to fill in persistent knowledge gaps by looking further into possible contributing factors.

The findings from this study will benefit society by adding to awareness of the racial disparities that are affecting the outcome of acute myeloid leukemia patients. Increased awareness may help address the disparity by providing steps for action and bringing additional preparedness in the treatment process. This would ideally contribute to the prevention of low survival rates in identified racial groups. Additional awareness and understanding of contributing factors may help in the development of population targeted public health programs aimed to assess and educate early-on. For example, a policy implementing education programs that provide resources such as insurance, immunization, childcare, screenings, and other health opportunities for disadvantaged people. Such a program could help medical professionals catch diseases earlier, educate patients about risks and behaviors, and have treatment plans with better overall health outcomes.

One of the main factors discussed in this proposal that has historically received little consideration is the effects of unreliable transportation on health outcomes. One study found that "Transportation barriers are often cited as barriers to healthcare access. Transportation barriers lead to rescheduled or missed appointments, delayed care, and missed or delayed medication use" (Syed, et al., 2014).

Improvement in transportation availability, especially in low-income areas at a lower cost may help patients attend their treatment sessions on time and regularly at their treatment centers. Applying similar research methods to other types of cancers or chronic illness with a lens that includes contributing factors such as transportation and access barriers could assist in understanding survival disparities for those illnesses as well.

Limitations

Some possible limitations for this proposed study would be the loss of follow-ups. Participants that are no longer reachable could cause a gap of data in our research from a certain population of people. If 500 or more out of the people that were enrolled for this study choose to opt-out, there would be an impact in data collection. A patient's death before the five-year mark may also lead to insufficient data collected. This may result in the research not having enough well-rounded data to support the contributing factors for the racial disparity in acute myeloid leukemia survivors. Recall bias is also a possible limitation, due to participants not being able to remember information or past experiences accurately. This could result in false information being submitted on surveys or interviews. Additionally, there may be language barriers or challenges in obtaining correct diagnosis dates and experiences if the patients have been diagnosed in other countries. A lack of interpreters would limit researchers from recording data and shared stories from participants who do not speak English as a first language, therefore resulting in misinformation being recorded.

Immigration status could also be an issue, due to the detainment and deportation practices of the United States. Undocumented patients may be too afraid to get diagnosed when they know they are sick due to this barrier. An article from Health Affairs mentions that undocumented immigrants can apply for Medicaid coverage, however, the benefits are not as generous as they would be for a U.S. citizen. The article goes on to say that the immigrant's coverage is restricted to emergencies such as labor and long-term care (Goldman et al., 2005). We may

not be able to follow up with patients due to these coverage restrictions, which can result in data not being collected as thoroughly. The patient's stage of diagnosis could also be a limitation if a person is diagnosed in a later stage, their assessment of their health behaviors and attitudes going forward might not have an impact due to the advance spread of the disease. There is a chance that the participants of this study may not complete surveys annually which limits our data analysis. The patient's death before the five-year mark can lead to insufficient data collected. Lastly, generalization could be a limitation because the results we find within the Seattle area may not apply to a different city or state.

Future Directions

Future research can be done to look more into the causes of racial disparities in Leukemia survivors. We focused on factors such as patients missing their appointments or treatments due to transportation barriers, stage of diagnosis, and age of diagnosis when compared with the race of patients to determine if those variables had an impact on Leukemia survival rates. Research in the future could investigate immigration status and how that affects Leukemia patients who are afraid or have limitations to access health treatments. Future studies can also focus on early Leukemia diagnosis at younger ages and compare their survival rates. Finally, larger sample size can be used for future studies to get more information as to why there are racial disparities from a wider range of people in various regions. Research from this study can be used as secondary information to help solve unanswered questions.

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