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Melissa Riedel **Date**

Identifying Differences in Access to Care and Patient Outcomes of Pediatric and Adolescent Cancer Patients in the State of Georgia

by

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Abstract

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Intro: Children's Oncology Group (COG) facilities across the United States have established treatment protocols for pediatric and adolescent cancer patients to receive the best care. Previous studies have identified differences in access to care and patient outcomes among this population. Adolescents are less likely to receive treatment at COG facilities compared to children. Also, patients not treated at COG facilities are noted to have worse survival outcomes.

Objective: To identify differences in access to care and patient outcomes of pediatric and adolescent cancer patients treated at COG facilities compared to other treatment centers (non-COG facilities) in the state of Georgia.

Methods: Patients aged 0 to 19 years with a reportable neoplasm diagnosed from 2009 through 2018 were identified in Georgia Cancer Registry. Chi-Square analyses compared the distribution of demographic and clinical variables by type of facility where patient received treatment. Logistic regression analyses determined if a particular cancer type would be more likely treated at a COG facility. Survival rates were calculated via Kaplan-Meier method to compare survival rates of patients seen at COG versus non-COG facilities over 5 and 10 years. Cox Proportional Hazard calculated 5-year and 10-year Hazard Ratios (HRs) of patients treated at COG versus non-COG facilities by cancer type.

Results: There were 5972 new reportable diagnoses identified in the GCR. The COG patient population consisted of half of entire adolescent population and majority of the pediatric population (86.2%). Patients with pediatric cancer types were more likely to be treated at a COG facility. Adolescents with adult cancer types were more likely to be treated elsewhere. Kaplan-Meier curves show an overall slightly higher survival probability of patients treated at non-COG facilities compared to COG facilities. With the exception of Non-Hodgkin Lymphoma (5-Year HR 0.37; 10-Year HR 0.48), none of the observed HRs were statistically significant. In addition, 5-year and 10-year HRs were generally similar.

Conclusion: Access to COG facilities for both children and adolescents has continued to improve over the last 25 years for the state of Georgia. However, survival outcomes have remained similar during this time period based on where children and adolescents receive their treatment.

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Chapter 1: Introduction

Cancer consists of a set of diseases that affects every demographic group within the United States. Even though cancer can impact everyone's lives, a wide body of prior research has focused on cancer disparities and their influence on patient care and patient outcomes. Not only can the genetic biology of cancer influence these disparities, Social Determinants of Health can also influence care and outcomes (NCI, 2020). It is important that the pathways through which cancer disparities persist be thoroughly examined if one is to achieve the end goal of reducing and eliminating these cancer disparities.

Specifically, there have been previous studies identifying differences in access to care and patient outcomes for pediatric and adolescent cancer patients. There are accredited specialized cancer centers known as Children's Oncology Group (COG) facilities across the United States that have established treatment protocols for patients affected by childhood cancers (COG, 2022). However, due in part to Social Determinants of Health, not every child and adolescent receive their care at one of these specialized cancer centers.

A study by Gutierrez and colleagues described that patients receiving care at COG facilities have better patient outcomes than patients receiving care at non-COG facilities (Gutierrez, Cheung, Zhuge, Koniaris, & Sola, 2010). A separate study from Howell et al., also analyzed patient outcomes among the pediatric and adolescent patient population in the state of Georgia, in addition to examining access to care. Using population-based cancer registry data from 1998 to 2002, the retrospective analysis revealed that adolescents were less likely to be treated at a COG facility compared to children (Howell, Ward, Austin, Young, & Woods, 2007). In addition, there

was noted evidence that patients treated at COG facilities had better patient outcomes for cancers that are most common in the pediatric population.

The goal of this study is to perform a retrospective analysis with more recent population-based data to identify if there have been improvements to access to care and patient outcomes among pediatric and adolescent cancer patients in the state of Georgia since the previous study by Howell et al. Understanding the results of this analysis can better help public health researchers, pediatric oncologists, and other physicians recognize the value of pediatric and adolescent patient referral and patient care at COG facilities.

Chapter 2: Literature Review

Cancer continues to be one of the most prevalent and fatal diseases at both the global and national level. Using cancer incidence data from United States population-based cancer registries for the period 2003 through 2017, the American Cancer Society (ACS) estimates that around 1.9 million new cancers will be diagnosed in 2021 with approximately 16,000 new cases and 1,800 deaths projected among children and adolescents (R. L. Siegel, Miller, Fuchs, & Jemal, 2021). Unlike the adult population, cancer incidence rates have slightly increased in the pediatric and adolescent population throughout the past 40 years while mortality rates have declined but remain higher for adolescents compared to children.

While annual ACS estimates focus primarily on adult cancers, there have been multiple studies focused on pediatric and adolescent cancers. In one such analysis, D.A Siegel et al. utilized data from the National Program of Cancer Registries (NPCR) and the National Vital Statistic System where they observed 30,384 pediatric and adolescent deaths between 2002 and 2016 (D. A. Siegel et al., 2020). The overall mortality rate from the study was 24.5 deaths per 1 million (95% CI 24.3 to 24.8). Leukemia, brain/nervous system, and bone/joint were the three most common cancer types causing death among this population.

Similar to the ACS finding, mortality rates in this study were higher among adolescents compared to children. The mortality rate for adolescents aged 15 to 19 years old was 30.6 per 1 million (95% CI 30.0 to 31.2) compared a mortality rate of 22.5 per 1 million (95% CI 22.2 to 22.8) among children aged 0 to 14 years old. The authors noted these higher rates among adolescents could be due to several aspects. Common histology types among adolescents can have more adverse genetic and tumor biology. In addition, Children's Oncology Group (COG)

facilities do not treat as many adolescents as they do children. COG facilities typically have more clinical trials available compared to other facilities and thus not as many adolescents are enrolled in clinical trials. Mortality rates among this study population were also noted to be higher among patients living in areas of high poverty and among those with parents having lower educational levels.

In addition to mortality, D.A. Siegel et al. also examined cancer survival. Survival rates improved over time for pediatric and adolescent patients but were noted to be lowest for non-Hispanic blacks compared to other races and ethnicities. This study illustrates a commonality with other literature that race and ethnicity are core elements of cancer disparities regardless of age. Future research must focus on reducing these disparities through an examination of the pathways whereby they might present rather than just observing they exist.

Understanding reasons for cancer disparities has become a prominent area of cancer research in recent decades. According to the National Cancer Institute (NCI), unfavorable variations of epidemiological measures such as incidence, mortality, and stage at diagnosis, across subsets of a given population are examples of cancer disparities (NCI, 2020). Broadening the scope, Social Determinants of Health have been identified as a major influence of cancer and health disparities for individuals and particular population groups (Islami et al., 2021). Social Determinants of Health encompass the economic, physical, and social environments of individuals' lives. These factors can ultimately influence where children and adolescents receive their cancer care which may impact their survival.

More specifically, there are known cancer disparities within each of the Social Determinants of Health environments described above. As it relates to the economic environment, Beltrami and

colleagues showed that individuals of lower socioeconomic status (SES) and with lower income had associated higher mortality due to cancer, and that uninsured individuals or those who utilized public insurance (Medicaid) were more likely to have lower survival rates compared to those with private insurance (Beltrami, Hilliard, & Green, 2022). Logically, these population subgroups often overlap as individuals of lower SES and with lower income often do not have as many private insurance options. It should be noted that SES is typically measured at a community level whereas insurance status can be assessed individually (Tran, Coven, Park, & Mendonca, 2022). With this in mind, people that are either uninsured or utilize public insurance may have limited options on where they can receive their care. Not all hospitals and physicians accept public insurance or offer financial aid options for those that are uninsured.

Disparities in the physical environment include access to health care and transportation to facilities (NCI, 2020). Inadequate access to care can delay diagnosis and treatment for patients which thereby can affect survival. As an example, individuals living in rural areas may have limited access to nearby specialized care, which includes cancer treatment (Douthit, Kiv, Dwolatzky, & Biswas, 2015). They may have to travel far to a facility in order to receive proper care as their nearest community hospital may not have adequate resources to provide the same type of care. Transportation can also be an issue for many (NCI, 2020). This is likely especially true for pediatric and adolescent cancer patients. Children and adolescents have to rely on their caretakers to drive them to and from appointments. On top of this, transportation to and from facilities can be costly since cancer treatment and appointments can take place over a period of several months. Caretakers may not be able to afford to travel on a consistent basis, or they may not be able to take time off from their own jobs to provide transportation for their child

undergoing treatment. Again, these physical factors can impact where patients ultimately decide to receive their treatments.

Finally, the social environment includes social constructs such as race and ethnicity. Racial and ethnic disparities have been commonly researched as these are considered one of the most prominent types of cancer disparities for pediatric and adolescent cancer patients (D. A. Siegel et al., 2020). The social environment can also comprise of individual behaviors that can negatively impact one's health. Tobacco use, alcohol use, and poor diets are modifiable social behaviors associated with increased cancer risks (NCI, 2020). However, it is important to note that there may be people who do not have access to healthy food options. Others may have limited resources in order to properly quit smoking or excessive alcohol drinking. While social behaviors certainly play a significant role in health outcomes, it is important to consider that there are additional socioeconomic factors that can influence individual behaviors.

Cancer disparities, such as the examples previously mentioned, are reflected among the pediatric, adolescent, and young adult patient populations. A systematic review completed by researchers at the Indiana University School of Public Health and School of Medicine identified commonly linked Social Determinants of Health with pediatric cancer outcomes. The review analyzed 25 studies out of over 800 initially identified from PubMed (Tran et al., 2022). As suspected, the Social Determinants of Health most commonly associated with poorer survival outcomes were low SES and uninsured or public insurance. Other Social Determinants of Health such as urban versus rural residence and driving distances to treatment facilities produced varied results. A second review by Beltrami and colleagues showed that inadequate access to care for both pediatric and adolescents can also lead to an increase in cancer mortality (Beltrami et al., 2022). Other aspects like treatment non-compliance, communication difficulties between physicians and

patients/caretakers, and implicit racial bias have also been considered causes for cancer disparities among pediatric and adolescent cancer patients. It is important to conduct further analyses in these areas that have not been studied as extensively or that have produced mixed results in order to better understand the significance of their impact on outcomes for pediatric and adolescent patients.

One important consideration for pediatric and adolescent cancer patient outcomes is where patients receive their cancer care. Children's Oncology Group (COG) facilities, supported by NCI, are accredited pediatric and adolescent cancer treatment centers. Currently, there are over 200 COG facilities that are located within children's hospitals and academic teaching hospitals across the nation and overseas (COG, 2022). These facilities strive to promote clinical trials for potential new cancer treatments, partake in research to better understand the diseases, and engage in supportive care and survivorship of patients.

As previously noted, COG facilities are less likely to treat adolescent and young adult patients than pediatric patients (D. A. Siegel et al., 2020). There have been several studies that highlight this finding. In Utah, researchers utilized the state registry data from 1994 to 2000 to identify where patients aged 0 to 24 years received their cancer treatment (Albritton, Wiggins, Nelson, & Weeks, 2007). During the time of the analysis, there was only one pediatric cancer center for the state that was located in Salt Lake City. Results revealed that 34 percent of patients aged 15 to 19 years received some sort of treatment at this facility. This percentage was overwhelming low compared to the over 80 percent of children aged 0 to 14 years that received care at this same facility. This study only identified this discrepancy between children and adolescents and did not further investigate if outcomes were affected by location of cancer care.

Another study compared patient outcomes for children and adolescents treated for neuroblastoma and Wilms tumor at COG facilities versus non-COG facilities in Florida between 1981 and 2004 (Gutierrez, Cheung, Zhuge, Koniaris, & Sola, 2010). Five and ten year survival rates were higher for patients treated at COG facilities compared to non-COG facilities for both cancers. The researchers observed that patients seen at COG facilities were more likely to receive chemotherapy secondary to surgical interventions. In addition and similar to the Utah study, older adolescent patients were more likely to receive treatment at non-COG facilities than COG facilities.

As previously mentioned, adolescent cancer patients have been noted to have higher mortality rates compared to pediatric patients (D. A. Siegel et al., 2020). Higher mortality rates among adolescent patients could be partially attributed to where adolescent cancer patients receive their treatments. Wolfson et al., used the Los Angeles County Cancer Surveillance Program to analyze the impact on cancer treatment location for adolescents and young adults with Acute Lymphoblastic Leukemia (ALL) and Acute Myeloid Leukemia (AML). Cases diagnosed between 1998 to 2008 revealed that adolescents (15 to 21 years old) had lower survival when not treated at either comprehensive cancer centers or COG facilities compared to adolescents that were treated at these specialized medical facilities (Wolfson, Sun, Wyatt, Stock, & Bhatia, 2017). Again, adolescents analyzed in this study were less likely to receive treatment at COG facilities compared to patients aged 14 years and younger.

A final study by Howell et al. analyzed survival outcomes for patients diagnosed from 1998 to 2002 in the state of Georgia (Howell, Ward, Austin, Young, & Woods, 2007). Using data from the Georgia Cancer Registry (GCR), researchers identified and compared the distribution of pediatric and adolescent patient characteristics who received treatment at COG facilities versus

those that received treatment at non-COG facilities in Georgia. Demographics that were analyzed using logistic regression were: age, sex, race, cancer site, and cancer stage. Kaplan-Meier analyses were performed to assess five-year survival rates and Cox Proportional Hazard ratios were estimated to compare outcomes based on location of cancer treatment (COG versus non-COG facilities) and by race.

In this study, 70 percent of all identified patients were treated at COG facilities; however, only slightly more than a third of adolescents in the study were treated at these facilities. Children and adolescents treated at COG facilities tended to have lower mortality risk for common pediatric cancer types than those treated elsewhere, although results were generally not statistically significant. Surprisingly, adolescents that were treated for adult cancer types such as carcinomas and melanoma tended to have lower mortality risk at non-COG facilities, although again, results were not significant. Black children and adolescents had higher mortality compared to white children and adolescents. This key finding was true regardless of where they received their cancer treatment.

From these several studies, there is a clear indication that receiving cancer treatment at COG facilities can positively impact patient outcomes for both pediatric and adolescent patients. However, the distinction that adolescents are less likely to be treated at COG facilities creates a unique cancer disparity for this particular age group.

There are well-documented patient outcome disparities among pediatric and adolescents in the United States when treated at different facilities. It is evident from prior analyses that children and adolescents have overall better patient outcomes when treated at a COG facility compared to non-COG facility. COG facilities are more equipped to provide standard cancer care for

childhood cancer types and have access to the latest clinical trials. However, many factors related to a patients' Social Determinants of Health can affect where a child or adolescent goes to receive their treatment and prior studies have highlighted that a large percentage of adolescents are not being treated at COG facilities.

The purpose of this research is to provide an updated landscape on receipt of cancer care and corresponding outcomes among pediatric and adolescent cancer patients in the state of Georgia using the most current data from the Georgia Cancer Registry. Longer term outcomes will also be examined to add to current knowledge on this issue.

Chapter 3: Methods

Cancer is a notifiable disease in the United States and its reporting is mandated by state government. Cancer reporting is HIPAA exempt as it is a public health surveillance activity. Secondary retrospective data for this study were obtained from the Georgia Cancer Registry (GCR). GCR is a population-based registry responsible for capturing all cancer cases diagnosed in the state of Georgia since 1995 (Georgia Department of Public Health, n.d.). Cancer registries are critical public health surveillance systems for policymakers and researchers to monitor trends in cancer incidence, mortality, and survival and to monitor patterns of cancer care within the state.

Cancer registries have strict reporting requirements. Identifying and reporting cancer cases can be a complex and comprehensive process. Dedicated specialists known as Certified Tumor Registrars (CTRs) are responsible for identifying and abstracting cancer cases from medical records and then reporting those data to registries. CTRs utilize multiple coding manuals and guidebooks to accomplish reporting requirements. For example, the International Classification of Diseases for Oncology, Third Edition (ICD-O-3), contains the topography (primary site) and morphology (histology and behavior) codes of all known neoplasms. Cancer stage, as another example, is determined by both the SEER Summary Stage manual as well as the American Joint Committee on Cancer Staging Manual. It is important to recognize the significant role CTRs have in ascertaining surveillance data for public health research.

Children and adolescents aged 0 to 19 years who were diagnosed with a reportable neoplasm from 2009 through 2018 were identified in GCR's database. Reportable neoplasms for GCR include all invasive and in-situ cancer types as well as benign and borderline central nervous

system (CNS) tumors. In order to capture as many cases as possible for analysis, all reportable neoplasms over a patient's lifetime were included. Since the previous study by Howell et al., analyzed only five years of GCR data, ten years of data were included in this study to provide a better understanding of long-term outcomes in these patients. Once eligible patients were identified by GCR, the following data elements were pulled for each case: age at diagnosis, gender, race, ethnicity, primary insurance payer, census-based poverty level derived from the address of the patient at the time of diagnosis, cancer type, cancer stage, vital status, cause of death, date of diagnosis, date of last contact, and location of treatment (COG versus non-COG facility).

Age at diagnosis was defined in 5 categories (<1, 1-4, 5-9, 10-14, 15-19 years) but was further dichotomized into pediatric (0-14 years) and adolescent (15-19 years) for specific analyses. Race and ethnicity were combined into one data field for simplicity. The new field 'Ethnicity/Race' was defined as: Non-Hispanic White, Non-Hispanic Black, Non-Hispanic Other, and Hispanic. Primary insurance payer included the groups: Not Insured, Private Insurance, Public Insurance, Tricare/Military, Insurance NOS, and Unknown. Public insurance consisted of both Medicaid and Medicare. Cancer stage was determined using the SEER Summary Stage 2000 and 2018 manuals. Summary Stage categorizes cancer stage by: In-situ, Localized, Regional, Distant, Benign/Borderline, and Unknown. The SEER Summary 2018 Manual was used in place of the 2000 manual for patients diagnosed January 1, 2018, and later. Summary Stage classifications for pediatric cancers did not change substantively across this time period and were thus combined into a single field for analyses.

Date of last contact is defined as the most recent follow-up date of a patient that is recorded in the GCR registry. For patients that are no longer alive, the last date of contact is their date of

death. Survival time was calculated from the date of diagnosis to the date of last contact or the study endpoint of 12/31/2019, whichever came first. Survival time was further censored at 5 or 10 years depending on the analyses. Cause of death was analyzed by all causes of death using International Classification of Diseases 10th Edition, with the inclusion of cancer-specific deaths which comprised the majority of all deaths in this young population.

Currently, there are four COG facilities in the state of Georgia: Children's Hospital of Atlanta – Egleston, Augusta University Medical Center, Medical Center of Central Georgia located in Macon, and Memorial Health University Medical Center in Savannah. Piedmont Columbus Regional Midtown Hospital was a former COG facility until 2017. If a patient received any type of treatment at a Georgia COG facility, they were recorded as having treatment at a COG facility for the purpose of these analyses.

All quantitative analyses were performed via SAS Enterprise Guide statistical analysis software (SAS Enterprise Guide Version 8.3.2.140, 2020). Chi-Square analyses were performed to compare the distribution of different demographic and clinical variables by the type of facility at which a patient received treatment. Variables analyzed included age, gender, race/ethnicity, primary payer, cancer stage, diagnosis year, and vital status. To note, there were patients that identified as 'Other' gender which consisted of Transgender and Non-Binary gender identifications; but, due to the small cell size, they were omitted from the chi-square analysis distribution.

Next, the distribution of patients treated at a COG versus non-COG facility based on cancer type was compared, stratified by age (pediatric versus adolescent). Logistic regression analyses, controlling for age, race/ethnicity, and gender were used to determine if a particular cancer type

would be more likely treated at a COG facility than a non-COG facility among pediatric and adolescent patients. Odds ratios and 95 percent confidence intervals were generated to show the odds of being treated at a COG versus a non-COG institution for the various cancer types.

Following the logistic regression analyses, survival proportions were calculated using the Kaplan-Meier life-table method to compare patients treated at COG versus non-COG facilities at 5 years and 10 years. Survival proportions at 5 years and 10 years were also compared separately for pediatric and adolescent patients. Finally, Cox Proportional Hazard models were utilized to calculate 5-year and 10-year Hazard Ratios and 95 percent confidence intervals among patients treated at COG versus Non-COG hospitals by cancer type, controlling for race/ethnicity, age, gender, and for solid tumor cancer types, stage. This study was submitted for determination through Emory's electronic IRB system and was deemed exempt.

Chapter 4: Results

There were 5972 new reportable diagnoses in the GCR between 2009 and 2018 for patients aged 0 to 19 years old. 74.4% of all patients were treated at a COG facility. Table 1 contains the overall distribution of patient demographics and clinical characteristics by hospital type. Age was evenly distributed for those treated at a COG facility while the majority (63.7%) of patients treated at Non-COG facilities were patients aged 15-19 years old. Only 50.5% of the entire adolescent population was treated at a COG facility compared to 86.2% for the childhood population.

Among the total adolescent population of the study sample, a large proportion of adolescents treated at COG facilities were treated for common pediatric cancer types such as ALL (77.8% of all adolescents with ALL), AML (67.6%), lymphoma (63.0%), and bone cancers (76.6%). At non-COG facilities, there was a larger proportion of adolescents treated at these facilities for adult cancer types, including carcinomas (59.3%) and melanoma (93.0%).

53.2% of the COG patient population consisted of males while there was a higher proportion of females treated (54.8%) within the non-COG patient population. 50.1% of patients seen at COG facilities were Non-Hispanic White, followed by 30.6% patients being Non-Hispanic Black and 15.2% patients that identified as Hispanic. In comparison, 59.4% of the non-COG patient population consisted of Non-Hispanic White patients followed by a smaller proportion of Non-Hispanic Blacks (24.0%) and Hispanic (11.0%) patients treated at these facilities.

Public insurance was most common among patients treated at COG facilities (43.3%). Non-COG facilities' most common insurance status was private insurance (41.5%). To compare, 37.7% of COG patients had private insurance whereas 41.5% of non-COG patients had private insurance.

There were a staggering smaller number of patients (18.9%) with public insurance seen at non-COG facilities. It should be noted that there was a large amount of patients that were classified as patients with either Insurance NOS or unknown insurance status. Unknown insurance status was especially prominent for patients seen at a non-COG facility as that made up 21.6% of the non-COG facility patient distribution. Insurance status findings cannot be definitive due to the large proportion of patients with unknown insurance and Insurance, NOS statuses.

39.2% of the COG patient population had distant stage which made up the largest proportion of all COG patients. However, it should be noted that systemic diseases, such as ALL and AML, are classified as distant according to the SEER Summary Stage Manual instructions. 32.8% of COG patients were staged as in-situ/local which consisted of the second largest proportion of COG patients. The largest proportion of non-COG patients were staged as in-situ/localized stage (36.2%), followed by a large proportion of with benign or borderline tumors (23.4%). Patients with distant stage only made up 20.6% of non-COG patient population. Overall, there were 176 patients that were classified with unknown stage which makes up 2.9% of all patients. Out of 176 patients, 114 patients with unknown stage were seen at non-COG facility (7.5%).

Throughout the years, there has been an increase in number of diagnoses for both COG and non-COG facilities. Table 1 shows that there were 366 diagnoses and 145 diagnoses from COG and non-COG facilities respectively in 2009. In 2018, the number of diagnoses increased to 496 and 202 for COG and non-COG facilities respectively. This is in line with previous literature that has also shown an overall increase in cancer diagnoses among pediatric and adolescent patients over the years. However, the increase in number of diagnoses is not statistically different for this COG versus non-COG distribution.

Out of 4445 patients seen at a COG facility, 83.4% of patients were considered ‘Alive’ as of their last date of contact; 87.4% of the 1527 non-COG patients were considered ‘Alive’ as of their last date of contact as well. COG facilities are likely to see more complex and complicated cancer cases, which would likely attribute to slightly lower percentage of patients alive compared to non-COG facilities in these bivariate results.

Table 2 shows the distribution patients treated at COG versus non-COG facilities by cancer site, stratified by age, with calculated odds ratios (OR) and their 95% confidence intervals (CI). OR calculations include adjustment for ethnicity/race, gender, and age. For the blood cancers, ALL patients of both pediatric (OR 2.17; 95% CI 1.61 to 2.97) and adolescent (OR 3.39; 95% CI 2.09 to 5.66) aged groups were more likely to be treated at a COG facility than a non-COG facility. The same held true for patients with AML. Myelodysplastic Syndrome (MDS) and other myeloproliferative disorders showed an opposite pattern where both pediatric and adolescent patients were less likely to be treated at a COG facility (Peds OR 0.63; 95% CI 0.37 to 1.12; Adol OR 0.48; 95% CI 0.26 to 0.85).

In line with systemic disease types, pediatric and adolescent Hodgkin’s Lymphoma (HL) and Non-Hodgkin’s patients were more likely to be treated at a COG facility than non-COG facility. For example, Pediatric HL cases were 2.4 times more likely to be treated at a COG facility than non-COG facility (95% CI 1.26 to 5.19).

As expected, other common pediatric cancer types such as neuroblastoma, retinoblastoma, and rhabdomyosarcoma were more likely to be treated at COG facilities for pediatric patients. It should be noted while these cancer types are more common in pediatric patients, they can present in adolescent patients as well. However, due to low case numbers for these particular cancer

sites, many of these sites were omitted from the OR analysis for adolescent patients. Interestingly, pediatric patients with germ cell tumor diagnoses were more likely to be treated at a COG facility (OR 1.67; 95% CI 0.98 to 3.05) whereas adolescent patients with germ cell tumors were less likely to be treated at a COG facility (OR 0.65; 95% CI 0.44 to 0.94).

For adult cancer types, pediatric patients with melanoma were much less likely to be seen at COG facilities (OR 0.28; 95% CI 0.14 to 0.57). Adolescent patients with both carcinomas and melanomas were less likely to be seen at COG facilities. The ORs for adolescent patients with carcinomas and melanoma was 0.76 (95% CI 0.57 to 1.01) and 0.08 (95% CI 0.03 to 0.19) respectively. Lastly, there were 298 cases that were classified as 'Other/Unknown' cancer types. These cancer types were less likely to be seen at a COG facility for both pediatric (OR 0.25; 95% CI 0.43 to 0.94) and adolescent (OR 0.48' 95% CI 0.32 to 0.73) patients.

Figures 1 and 2 show the Kaplan-Meier curves of 5-year and 10-year survival estimates for patients treated at COG versus non-COG facilities, respectively, all ages combined (0-19). Both figures convey that patients treated at non-COG facilities had slightly higher survival probabilities compared to patients treated at COG facilities (non-COG: 5-Year: 87.8%; 10-Year: 84.5%; COG: 5-Year: 84.3%; 10-Year: 80.4%). Figures 3 and 4 show the Kaplan-Meier curves of 5-year and 10-year survival estimates of pediatric patients treated at COG versus non-COG facilities. Both figures show very similar 5-year and 10-year survival probabilities of pediatric patients treated at COG versus non-COG facilities (non-COG 5-Year: 86.0%; 10-Year: 80.9%; COG: 5-Year: 85.4%. 10-Year: 80.8%). Figures 5 and 6 show the Kaplan-Meier curves of 5-year and 10-year survival estimates of adolescent patients treated at COG versus non-COG facilities. These figures show notable differences in survival probabilities of adolescent. Adolescents treated at non-COG facilities had overall higher survival probability compared to adolescents

treated at COG facilities (non-COG 5-Year: 89.1%; 10-Year: 86.3%; COG: 5-Year: 83.6%. 10-Year: 79.5%). These survival probabilities are considered statistically different (5-Year P-Value: 0.0004; 10-Year P-Value: 0.0001).

Table 3 shows the 5-year and 10-year Hazard Ratios (HR), and CIs of patients treated at a COG facility versus non-COG facility based on cancer types. HR calculations includes adjustments for ethnicity/race, gender, and age as well as stage for solid tumor cancer types. With the exception of NHL, none of the observed hazard ratios were statistically significant and the 5-year and 10-year ratios were generally similar. Across all cancer types, the HR at 5 years was 0.91 (95% CI 0.76 to 1.10) and the HR at 10-years was 0.93 (95% CI 0.78 to 1.11) for those treated at a COG facility compared to non-COG facility. Some general patterns in the data were observed with patients treated at COG vs non-COG facilities tending to have a lower risk of death for cancer types most common in the pediatric population and higher risk of death for traditional adult cancer types.

NHL/Other Lymphomas was the only cancer type with statistically significant HR. Patients treated for NHL/Other Lymphomas had a much lower risk of death when treated at a COG facility (5-Year HR 0.37; 10-Year HR 0.48). Other pediatric cancer types such as neuroblastoma, nephroblastoma, and germ cell tumors produced HRs less than 1.0, but had wider confidence intervals that included 1.0. Both carcinomas and melanomas had a higher risk of death when treated at COG facilities. For carcinomas, there was a 1.4 times higher likelihood of death at 5 years, and 1.5 times likelihood of death at 10 years when treated at a COG facility. Patients with melanoma had over 3 times likelihood of death when seen at a COG facility.

Overall, the number of observed deaths was small. Out of 5972 patients, 832 patients (660 COG, 172 non-COG) passed away during the first 5 years of the study period. At the end of the 10-year study period, 918 patients (726 COG, 192 non-COG) passed away. It is important to consider that this is a relatively small proportion of deaths, which when analyzed by individual cancer types, which can influence calculated HRs and their precision.

Chapter 5: Discussion

Results from this study reveal an improvement in access to care at Children Oncology Group's (COG) facilities for adolescents in comparison to Howell et. al 2007's study. Only a third of adolescents were seen at a COG facility between 1998 and 2002 (Howell et al., 2007). From 2009 to 2018, about half of all adolescents were seen at a COG facility at some point during their care. This was especially true for common pediatric disease types like ALL, AML, lymphoma, and bone cancers.

However, adolescents continue to be more likely treated at a non-COG facility for adult cancer types such as carcinomas and melanomas. There are several possible explanations for this finding. First, there are currently only four COG facilities in the state of Georgia, located in Atlanta, Augusta, Macon, and Savannah. The four pediatric cancer centers are all located in major urban areas in Georgia, which may negatively impact those that live in rural regions of Georgia and neighboring states. In addition, these few pediatric cancer centers are vastly outnumbered by the number of adult cancer centers across the state. It may be that the distance of the four pediatric cancer centers is too far for adolescents to travel to and from for treatment. This analysis did not include patients' county of residence within Georgia due to PHI constraints; therefore, it is not possible from this analysis to truly understand if proximity to treatment centers played a major role in where adolescents received cancer treatment, especially for rural residents.

As Howell et al. also mentioned in their study, patient bias may also play a role in where adolescents choose to receive their treatment. While there has been an obvious improvement in number of adolescents seen at a COG facility over the past twenty years, many adolescents may still uphold a certain social mentality that they prefer to be treated as an adult patient over a

pediatric patient (Howell et al., 2007). It is ultimately the patient's or guardian's decision where they want to be treated, even if their decision is against the medical advice and recommendations of medical professionals.

Another noteworthy result is that more female patients are treated at non-COG facilities compared to male patients. One reason this may be is that there may be specific cancer types more common among females that are best treated at a non-COG facility. It would be interesting to perform a more in-depth analysis on female patients' diagnosis types that are seen at a non-COG facility compared to COG facility to better understand this association.

While the majority of both COG patients and non-COG patients identify as Non-Hispanic White, COG facilities had a larger proportion of Non-Hispanic Blacks and Hispanics treated at these facilities compared to the proportion of these population groups treated at non-COG facilities. This is similar to the results seen with the Howell et al., study that minority racial and ethnic groups do have adequate access to COG facilities for treatment. However, further analysis will need to be conducted to identify if there is still the presence of racial and ethnic disparities when comparing outcomes between different races and ethnicities seen at COG facilities and non-COG facilities.

COG facilities treat a higher prevalence of patients with public insurance compared to non-COG facilities. Pediatric and adolescent patients with public insurances make up 43.3% of the total COG patient population, while only 18.9% of the non-COG patient population utilize public insurance. One potential reason for this result may be that COG facilities are more likely to accept patients regardless of insurance status compared to non-COG facilities. Private facilities may be less inclined to accept patients with public insurance and prefer to accept patients with

private insurance. Patient insurance status can provide significant information on where patients may choose to receive treatment, but caution should be taken when using this particular distribution as this demographic distribution may not be truly representative of this particular population. In addition, most pediatric and adolescent patients are dependent on their parent or guardians' insurance – therefore, it should be noted this distribution is likely showing the parents/guardians' insurance statuses.

A major limitation of reported insurance status from this dataset is the high percentage of patients with unknown insurance status. Over 600 of the 5972 records were reported with unknown insurance status. Insurance status is typically reported from patients' electronic medical records (EMR). If the EMR does not have an insurance card on file when cancer registry abstraction occurs, then the CTR will report the patient with having unknown insurance status. However, insurance status may be updated at a later time in a patient's EMR thereby establishing an inconsistency in the registry record. Another limitation with insurance status is the potential inaccurate reporting of one's insurance status. For example, 'Insurance, NOS' is a generic option that may be used when those reporting the cases are unfamiliar if the insurance for a particular patient is considered to be public or private insurance. Another potential inaccurate discrepancy is the presence of few records reported to have Medicare insurance, a form of public insurance mainly available to those aged 65 years and older. It would be very unlikely that pediatric and adolescent patients have access to Medicare insurance unless they have a co-existing condition such as End-Stage Renal Disease.

As expected with the previous study, COG facilities were more likely to treat patients with advanced stages of cancer compared to non-COG facilities. This is likely because COG facilities are more equipped with their established pediatric oncology protocols to treat patients who have

complex and high risk disease types. COG facilities also have extensive availability of pediatric and adolescent clinical trials (D. A. Siegel et al., 2020). Clinical trials at COG facilities are at the forefront of treatment protocols for these facilities and are encouraged by providers for patients to enroll if patients are eligible. Lastly, when standard treatment protocol is not enough, clinical trials may be the only treatment options for those that have more complex disease types and advanced stage diseases.

One drawback that should be noted for the 'Distant' stage category is that systemic diseases such as ALL and AML are coded to 'Distant' per SEER coding rules. Aside from staging, systemic cancers are typically categorized within different risk categories based on prognostic factors such as histology subtype and genetic biology (ACS, 2019). Cancer registries are not required to collect risk categorization as part of case abstraction, but it would be interesting for a future study to further analyze and identify if there are any statistical differences of the likelihood of being seen at a COG facility among patients with low risk and high risk systemic diseases as well as differences in survival outcomes among different risk groups.

The Cox Proportional Hazard model results reveal that patients with pediatric disease types have better survival rates when treated at a COG facility over both five years and ten years after initial diagnosis. This is similar to the results of the previous study that patients have overall better survival outcomes at COG facilities compared to non-COG facilities (Howell et. al, 2007). The very low HR results reveal that patients with neuroblastoma, nephroblastoma, and hepatoblastoma are shown to have a protective factor when treated at a COG facility compared to non-COG facility. This is similar to the results from Gutierrez et al.'s study that noted improved survival outcomes for patients treated at COG facilities in Florida for both Wilms Tumor and neuroblastoma (Gutierrez et al., 2010).

Unfortunately, there seems to be a continued presence of lower survival rates of pediatric type cancers among both pediatric and adolescent patients treated at non-COG facilities since Howell et al.'s study. This could be that non-COG facilities do not have the same treatment protocol standards as COG facilities. Non-COG facilities likely rely more on adult cancer type treatment protocols which could be different from pediatric treatment protocol.

Interestingly, children and adolescents that are seen at COG facilities for adult cancer types like carcinomas and melanomas have a higher likelihood of death than those treated at non-COG facilities. It is possible that children and adolescents seen at COG facilities with these cancer types may have more advanced stages, beyond what we are able to control for with the stage variable in our analyses, which is why they may have been to a COG facility in the first place. In-situ and localized melanomas can typically be treated at a dermatology office, making it unnecessary for patients to seek further treatment at a COG facility. The same applies for in-situ and localized carcinomas such as thyroid carcinomas. As another example, localized thyroid carcinoma treatment normally involves either partial or total surgical removal of the thyroid gland followed by an oral hormonal medication that can be prescribed by an endocrinologist. Nevertheless, it may be that children and adolescents with adult cancer types are best suited to receive treatment at non-COG facilities over COG facilities.

Another interesting result is the high likelihood of death for patients of 'Other and Unknown' cancer types treated at COG facilities. This high likelihood is especially true within the first five years of diagnosis. More patients were likely to be treated at non-COG facilities for these cancer types based on the low OR results; nonetheless, the high HRs could likely be due to the late presentation and advanced stages of these unique cases at COG facilities. It is a possibility that these particular patients were referred to COG facilities too late in their disease course. This

thereby impacts the timeliness of further work-up to determine a specified histology and therefore appropriate treatment plan.

It was important to include analysis of ten year survival outcomes to better understand if outcomes at COG and non-COG facilities changed over time be. Cancer incidence may have increased over the years, but more and more patients are surviving from their cancer diagnoses over longer periods of time. By only including analysis of five year survival outcomes, this may not reveal the true picture of the current pediatric and adolescent patient population in Georgia. Overall, the results show that the outcomes at COG and non-COG facilities do not change considerably over time. There are relatively minor differences when comparing five year and ten year hazard ratios for most cancer sites in this analysis. Nevertheless, survivorship and supportive care after cancer treatment should continue to be a necessity for pediatric and adolescent patients through young and middle adulthood.

There are several limitations that are worth mentioning for transparency and clarity. Similar to Howell et al., study's, it is unclear the extent of patients' treatment administration. In other words, based on the reported data, it cannot be determined if patients received their full or partial treatment at a COG facility or non-COG facility. Many patients may be referred to a different facility throughout their initial treatment course; therefore, this limitation may affect the survival outcomes compiled for this study.

Another noted limitation of the study is the follow-up of this particular patient population. Follow-up for pediatric and adolescent patients can be a challenging endeavor for cancer registries compared to adult patients due to several reasons. Children and adolescents are more likely to move out of their parents' or guardians' residence when reaching adulthood (NCI, n.d.).

This makes it difficult for cancer registries to keep track of pediatric and adolescent patients future residences and ultimately, their disease status. In addition, it is possible that adolescent patients may be receiving treatment closer to a facility where they are attending university that is different from their permanent residence (NCI, n.d.). These loss-to-follow-up challenges thereby may impact the survival outcomes of this analysis.

A final limitation of this analysis is that for calculated Kaplan-Meier lifetables and HRs, cause of death was not limited to cancer specific deaths. Analyses included all causes of death using ICD-10 cause of death codes. It is expected that most deaths in this patient population are cancer-related due to the young age demographics of this population. However, there were causes of deaths recorded that may have been an attributable cause due to the cancer diagnosis rather than the true cause of death. For example, a patient may have been diagnosed with cancer, and the patient passed away due to acute respiratory failure. The primary cause of death in the patient's record may have been recorded as acute respiratory failure rather than cancer (which is the true cause). It is likely that the young patient would have not passed away from acute respiratory failure had the patient not been diagnosed with cancer. There is the potential of improper coding of the true cause of death. A future study could be to look at the survival outcomes and HRs of patients that passed away from cancer-specific deaths.

From this analysis, access to COG facilities for both children and adolescents has continued to improve over the last 25 years for the state of Georgia. However, survival outcomes between COG and non-COG facilities have shown similar results as presented in Howell et al.'s study from 15 years ago. It is evident that for most pediatric cancer types, COG facilities continue to play a central role in providing the gold-standard care for children and adolescents. It is also evident that children and adolescents with adult cancer types may fare better at a non-COG

facility. Conversations about these associations are essential among public health researchers and providers in order to better understand the importance of proper patient referral to the appropriate facility type when considering pediatric and adolescent patients' cancer types. This consideration can potentially guide children and adolescents towards receiving the best possible care and outcome.

Table 1: Distribution of Patient Demographics by Hospital Type					
Demographics	**COG Institution Count / % Total: 4445 / 74.4**		**Non-COG Institution Count / % Total: 1527 / 25.6**		**Chi-Square (p-value)**
Age, years					
< 1	341	7.7	43	2.8	< 0.001
1 – 4	1128	25.4	154	10.1	
5 – 9	927	20.8	155	10.2	
10 – 14	1057	23.8	202	13.2	
15 - 19	992	22.3	973	63.7	
Gender[1]					
Male	2360	53.2	690	45.2	< 0.001
Female	2080	46.8	837	54.8	
Ethnicity/Race					
Non-Hispanic White	2229	50.1	907	59.4	< 0.001
Non-Hispanic Black	1360	30.6	366	24.0	
Non-Hispanic Other	182	4.1	86	5.6	
Hispanic	674	15.2	168	11.0	
Primary Payer					
Not Insured	155	3.5	101	6.6	< 0.001
Private Insurance	1675	37.7	634	41.5	
Public Insurance	1926	43.3	289	18.9	
Tricare/Military	140	3.1	68	4.5	
Insurance, NOS	249	5.6	105	6.9	
Unknown	300	6.8	330	21.6	
Stage					
In-situ/Local	1457	32.8	553	36.2	< 0.001
Regional	662	14.9	188	12.3	
Distant	1742	39.2	315	20.6	
Benign/Borderline	522	11.7	357	23.4	
Unknown	62	1.4	114	7.5	
Diagnosis Year					
2009	366	8.2	145	9.5	0.14
2010	399	9.0	139	9.1	
2011	438	10.0	134	8.8	
2012	410	9.2	155	10.1	
2013	444	10.0	150	9.8	
2014	451	10.1	143	9.4	
2015	467	10.5	163	10.7	
2016	491	10.9	157	10.3	
2017	483	10.9	139	9.1	
2018	496	11.2	202	13.2	
Vital Status					
Alive	3707	83.4	1335	87.4	0.0002
Dead	738	16.6	192	12.6	

[1] 'Other' Gender count/percentage were omitted due to small cell size

Table 2: Distribution of Patients Treated at COG versus Non-COG facility by Cancer Type, Stratified by Age Groups with Odds Ratios/Confidence Intervals

Diagnosis Type[1]	Ages 0-14 years old						Ages 15-19 years old					
	COG Institution Count / %		Non-COG Institution Count / %		Odds Ratio[2]	95 % Confidence Intervals[2]	COG Institution Count / %		Non-COG Institution Count / %		Odds Ratio[2]	95 % Confidence Intervals[2]
ALL	634	91.1	62	8.9	2.17	(1.61, 2.97)	84	77.8	24	22.2	3.39	(2.09, 5.66)
AML	163	89.1	20	10.9	1.67	(1.04, 2.80)	48	67.6	23	32.4	2.17	(1.28, 3.76)
MDS/Other Myeloproliferative Diseases	54	75.0	18	25.0	0.63	(0.37, 1.12)	20	36.4	35	63.6	0.48	(0.26, 0.85)
Leukemia, NOS	25	83.3	5	16.7	1.03	(0.42, 3.11)	-	-	-	-	-	-
Hodgkin's Lymphoma	105	92.1	9	7.9	2.40	(1.26, 5.19)	122	58.1	88	41.9	1.35	(0.97, 1.88)
Non-Hodgkin's Lymphoma/Other Lymphomas	331	88.5	43	11.5	1.61	(1.14, 2.33)	102	63.0	60	37.0	1.48	(1.02, 2.17)
CNS/PNS	900	82.5	191	17.5	1.0	(1.0, 1.0)	222	48.9	232	51.1	1.0	(1.0, 1.0)
Neuroblastoma	199	89.2	24	10.8	1.75	(1.13, 2.81)	-	-	-	-	-	-
Retinoblastoma	87	89.7	10	10.3	1.79	(0.95, 3.73)	-	-	-	-	-	-
Nephroblastoma/Renal	172	90.0	19	10.0	1.78	(1.11, 3.03)	-	-	-	-	-	-
Hepatoblastoma/Liver	47	90.4	5	9.6	2.02	(0.87, 5.90)	-	-	-	-	-	-
Bone	146	88.0	20	12.0	1.55	(0.97, 2.61)	72	76.6	22	23.4	3.11	(1.88, 5.33)
Rhabdomyosarcoma	91	92.0	8	8.0	2.42	(1.23, 5.50)	-	-	-	-	-	-
Other Sarcomas	109	81.3	25	18.7	0.90	(0.57, 1.46)	40	48.8	42	51.2	0.87	(0.54, 1.41)
Germ Cell Tumors	120	88.9	15	11.1	1.67	(0.98, 3.05)	68	41.7	95	58.3	0.65	(0.44, 0.94)
Carcinomas	126	84.6	23	15.4	1.20	(0.76, 1.97)	132	40.7	192	59.3	0.76	(0.57, 1.01)
Melanoma	18	54.5	15	45.5	0.28	(0.14, 0.57)	5	7.0	66	93.0	0.08	(0.03, 0.19)
Other/Unknown	126	0.75	42	0.25	0.63	(0.43, 0.94)	41	31.5	89	68.5	0.48	(0.32, 0.73)

[1]Diagnosis Types with 25 total cases or less were omitted from table and OR analysis

[2]Odds Ratios/Confidence Intervals includes adjustment for ethnicity/race, gender, and age

Abbreviations: Children's Oncology Group (COG), Acute Lymphoblastic Leukemia (ALL), Acute Myelogenous Leukemia (AML), Myelodysplastic Syndrome (MDS), Central Nervous System/Peripheral Nervous System (CNS/PNS)

The odds ratio calculated in this table is the odds of patients with a cancer type were treated at COG facility over a non-COG facility

Table 3: 5-year and 10-year Hazard Ratios/Confidence Intervals of Patients Treated at COG Versus Non-COG Hospitals by Diagnosis Type

Diagnosis Type	5-year Hazard Ratio[1]	95 % Confidence Intervals	10-year Hazard Ratio[1]	95 % Confidence Intervals
All Cancer[2]	0.91	(0.76, 1.10)	0.93	(0.78, 1.11)
ALL	0.62	(0.34, 1.12)	0.64	(0.36, 1.13)
AML	0.83	(0.47, 1.46)	0.83	(0.47, 1.46)
MDS/Other Myeloproliferative Diseases	1.46	(0.57, 3.75)	1.48	(0.62, 3.53)
Leukemia, NOS	2.55	(0.29, 22.57)	2.55	(0.29, 22.57)
Hodgkin's Lymphoma[2]	1.04	(0.30, 3.56)	0.80	(0.26, 2.48)
Non-Hodgkin's Lymphoma/Other Lymphomas[2]	0.37	(0.18, 0.75)	0.48	(0.24, 0.95)
CNS/PNS[2]	0.78	(0.54, 1.12)	0.80	(0.57, 1.13)
Neuroblastoma[2]	0.75	(0.28, 2.00)	0.77	(0.29, 2.05)
Retinoblastoma[3]	-	-	-	-
Nephroblastoma/Renal[2]	0.19	(0.01, 3.36)	0.19	(0.01, 3.36)
Hepatoblastoma/Liver[2]	0.00	(0.00, -)	0.00	(0.00, -)
Bone[2]	1.37	(0.60, 3.15)	1.57	(0.69, 3.56)
Rhabdomyosarcoma[2]	1.03	(0.21, 5.17)	1.03	(0.21, 5.17)
Other Sarcomas[2]	0.86	(0.29, 2.53)	1.06	(0.38, 2.99)
Germ Cell Tumors[2]	0.49	(0.16, 1.50)	0.49	(0.16, 1.50)
Carcinomas[2]	1.40	(0.64, 3.09)	1.50	(0.71, 3.20)
Melanoma	3.41	(0.38, 30.82)	3.12	(0.46, 21.45)
Other/Unknown[2]	3.76	(0.41, 34.20)	1.27	(0.29, 5.62)

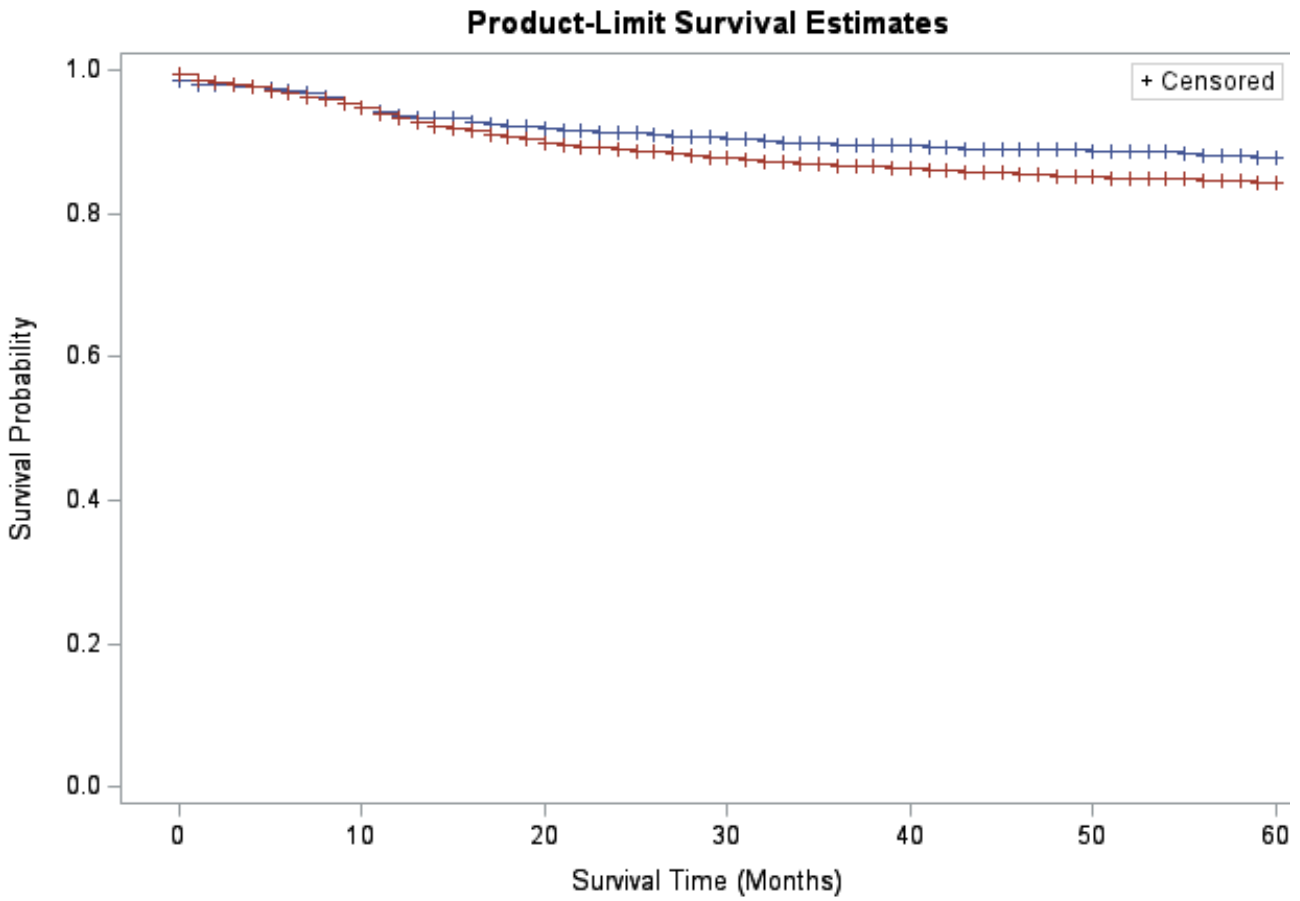
[1]Hazard Ratios/Confidence Intervals includes adjustment for ethnicity/race, gender, and age

[2]Hazard Ratios/Confidence Intervals includes adjustments for stage

[3]Due to small number of deaths, HR analysis was omitted

Abbreviations: Children's Oncology Group (COG), Acute Lymphoblastic Leukemia (ALL), Acute Myelogenous Leukemia (AML), Myelodysplastic Syndrome (MDS), Central Nervous System/Peripheral Nervous System (CNS/PNS)

Figure 1: 5-Year Kaplan-Meier Curve of All Patients Treated at COG versus Non-COG facilities



Survival Probabilities after 5 years:

Non-COG facilities: 87.8%

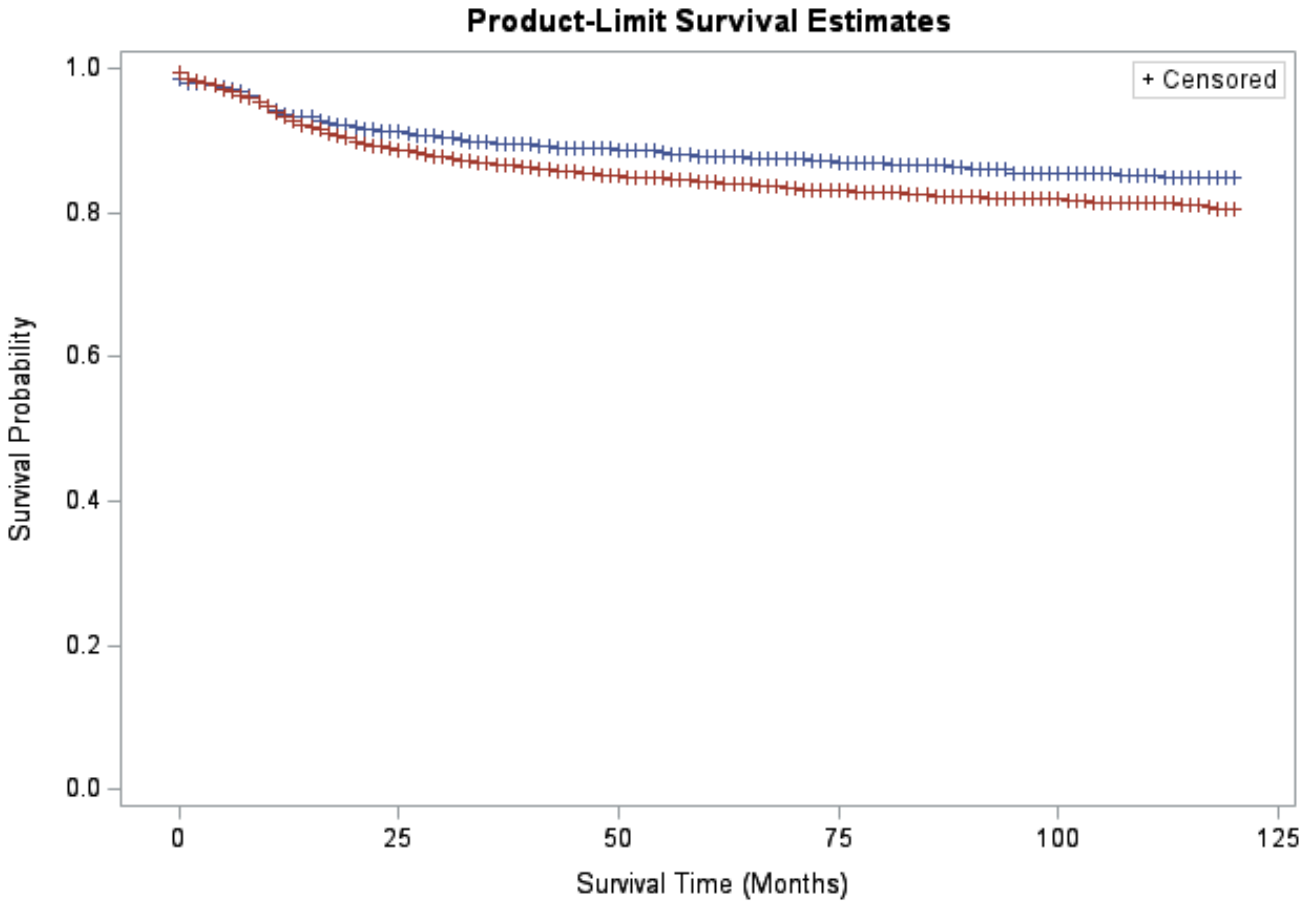
COG facilities: 84.3%

Log-Rank P-Value: 0.0019

Legend:

non-COG facilities: COG facilities:

Figure 2: 10-Year Kaplan-Meier Curve of All Patients Treated at COG versus Non-COG facilities



Survival Probabilities after 10 years:

Non-COG facilities: 84.8%

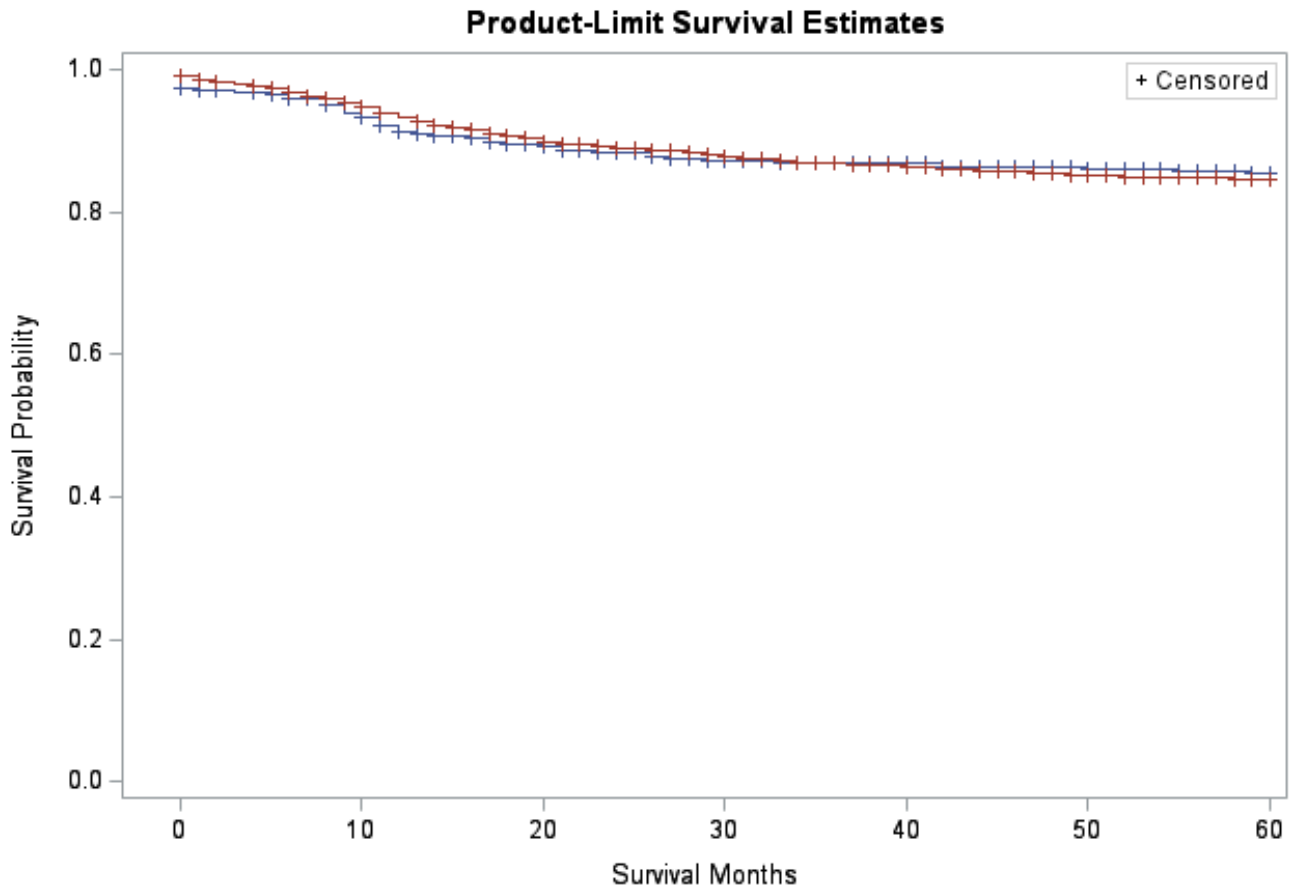
COG facilities: 80.5%

Log-Rank P-Value: 0.0013

Legend:

non-COG facilities: COG facilities:

Figure 3: 5-Year Kaplan-Meier Curve of Pediatric Patients Treated at COG versus Non-COG facilities



Survival Probabilities after 5 years:

Non-COG facilities: 86.0%

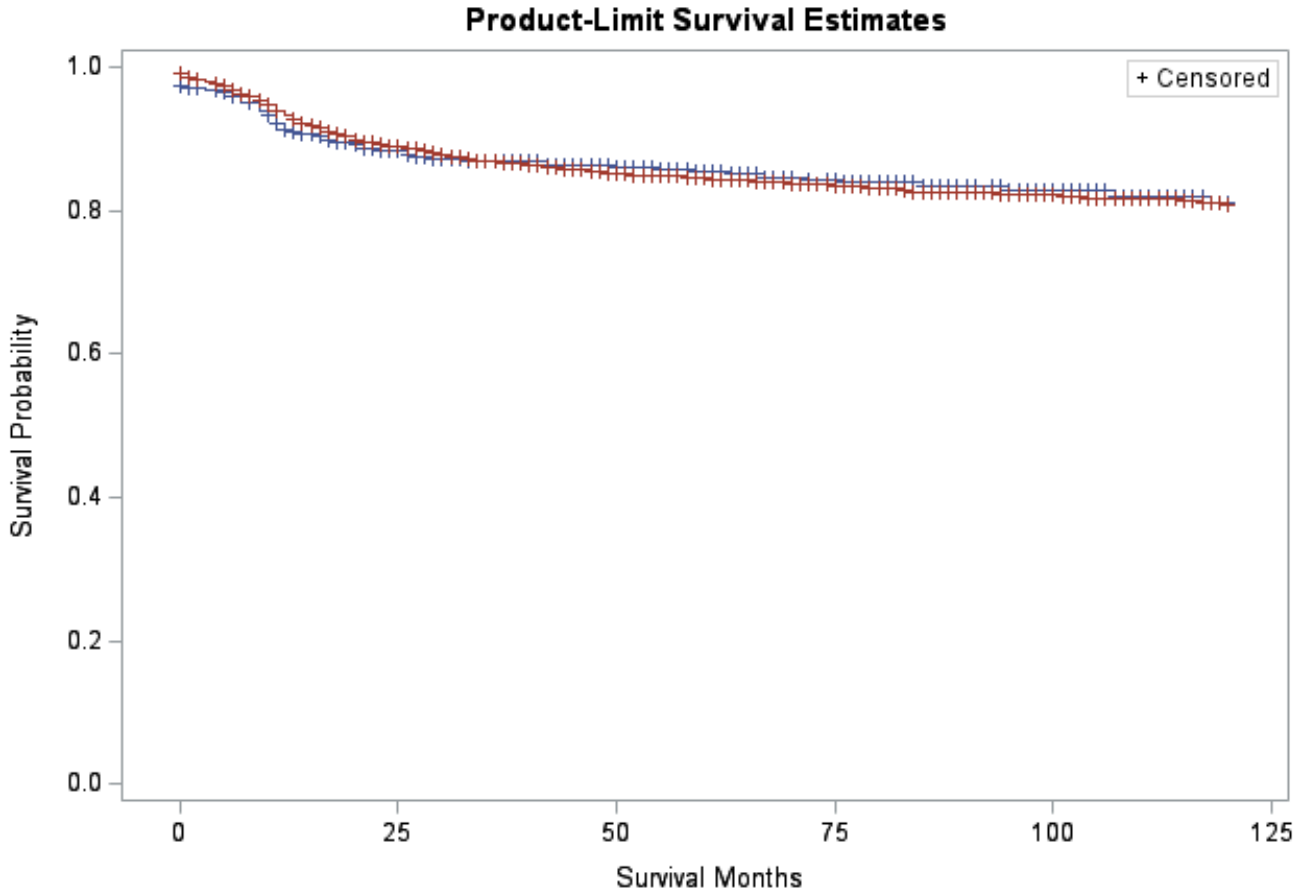
COG facilities: 85.4%

Log-Rank P-value: 0.842

Legend:

non-COG facilities: COG facilities:

Figure 4: 10-Year Kaplan-Meier Curve of Pediatric Patients Treated at COG versus Non-COG facilities



Survival Probabilities after 10 years:

Non-COG facilities: 80.9%

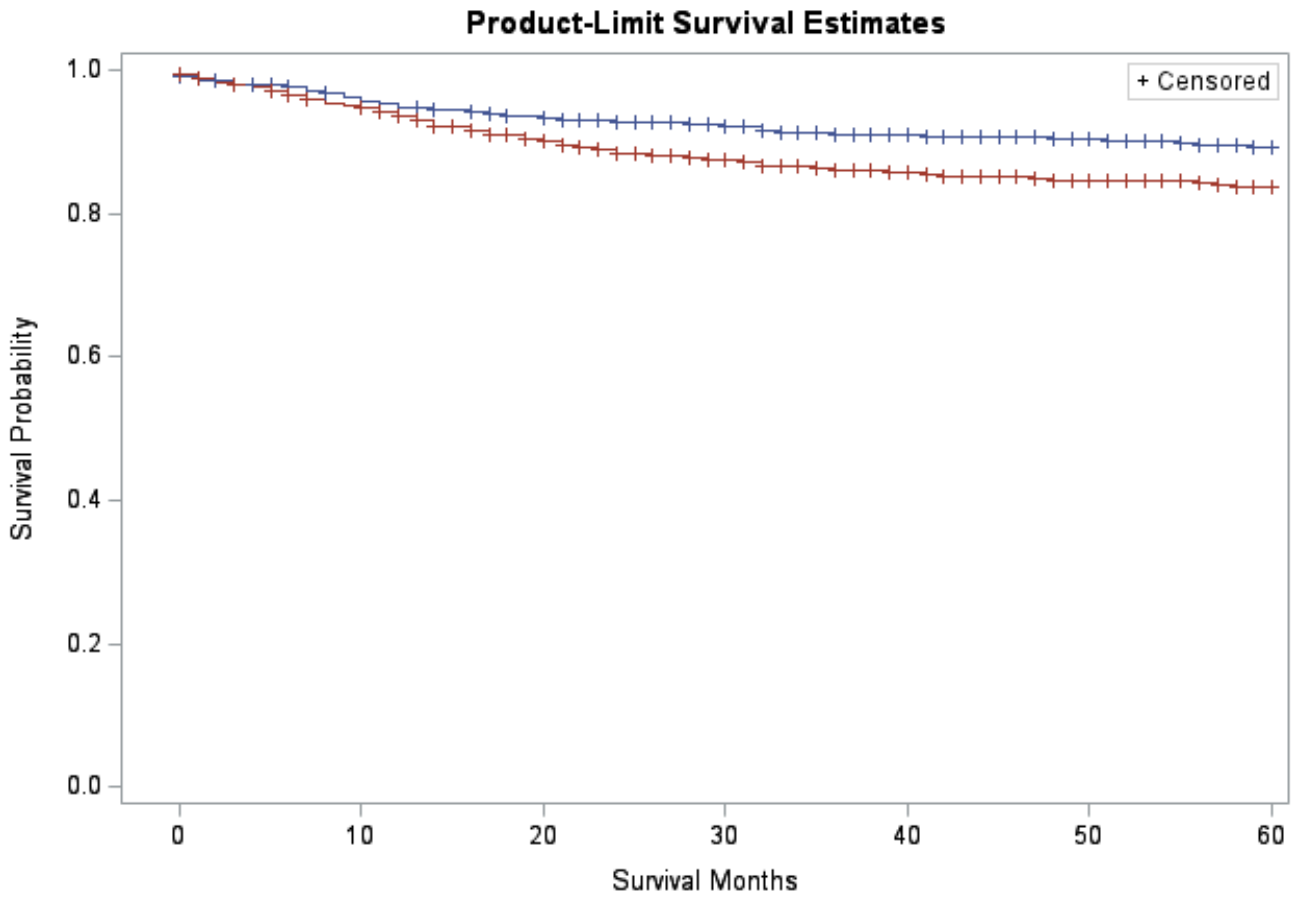
COG facilities: 80.8%

Log-Rank P-Value: 0.915

Legend:

non-COG facilities: COG facilities:

Figure 5: 5-Year Kaplan-Meier Curve of Adolescent Patients Treated at COG versus Non-COG facilities



Survival Probabilities after 5 years:

Non-COG facilities: 89.1%

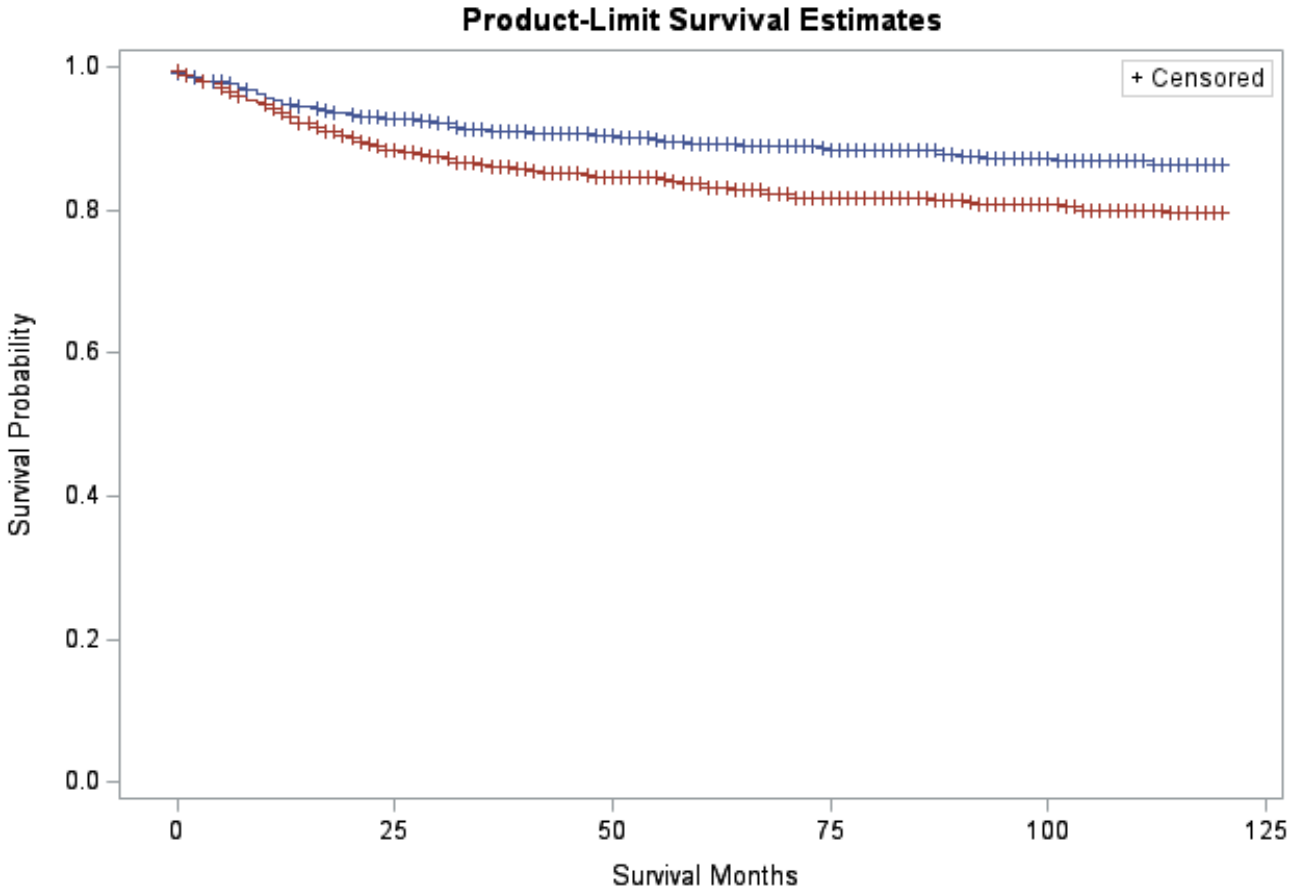
COG facilities: 83.6%

Log-Rank P-Value: 0.0004

Legend:

non-COG facilities: COG facilities:

Figure 6: 10-Year Kaplan-Meier Curve of Adolescent Patients Treated at COG versus Non-COG facilities



Survival Probabilities after 10 years:

Non-COG facilities: 86.3%

COG facilities: 79.5%

Log-Rank P-Value: 0.0001

Legend:

non-COG facilities: COG facilities:

References

1. ACS. (2019, February 12 2019). Prognostic Factors in Childhood Leukemia (ALL or AML). Retrieved from https://www.cancer.org/cancer/leukemia-in-children/detection-diagnosis-staging/prognostic-factors.html

2. Albritton, K. H., Wiggins, C. H., Nelson, H. E., & Weeks, J. C. (2007). Site of Oncologic Specialty Care for Older Adolescents in Utah. *Journal of Clinical Oncology, 25*(29), 4616-4621. doi:10.1200/jco.2006.08.4103

3. COG. (2022). Children's Oncology Group: About Us. Retrieved from https://childrensoncologygroup.org/about

4. Douthit, N. K., Sakal; Dwolatzky, Tzvi; Biswas, Seema. (2015). Exposing some important barriers to health care access in the rural USA. *Public Health, 129*(6), 611-620. doi:https://doi.org/10.1016/j.puhe.2015.04.001

5. GDPH. (n.d.). Georgia Comprehensive Cancer Registry. Retrieved from https://dph.georgia.gov/chronic-disease-prevention/georgia-comprehensive-cancer-registry

6. Gutierrez, J. C., Cheung, M. C., Zhuge, Y., Koniaris, L. G., & Sola, J. E. (2010). Does Children's Oncology Group hospital membership improve survival for patients with neuroblastoma or Wilms tumor? *Pediatric Blood & Cancer, 55*(4), 621-628. doi:https://doi.org/10.1002/pbc.22631

7. Howell, D. L., Ward, K. C., Austin, H. D., Young, J. L., & Woods, W. G. (2007). Access to Pediatric Cancer Care by Age, Race, and Diagnosis, and Outcomes of Cancer Treatment in Pediatric and Adolescent Patients in the State of Georgia. *Journal of Clinical Oncology, 25*(29), 4610-4615. doi:10.1200/jco.2006.07.6992

8. Islami, F., Guerra, C. E., Minihan, A., Yabroff, K. R., Fedewa, S. A., Sloan, K., . . . Jemal, A. (2021). American Cancer Society's report on the status of cancer disparities in the United States, 2021. *CA: A Cancer Journal for Clinicians, n/a*(n/a). doi:https://doi.org/10.3322/caac.21703

9. NCI. (2020, November 17, 2020). Cancer Disparities. Retrieved from https://www.cancer.gov/about-cancer/understanding/disparities

10. NCI. (n.d.). Best Practices: Follow-up for Patients Under 20 Years of Age. Retrieved from https://seer.cancer.gov/seerdms/portal/news/best-practices-follow-up-for-patients-under-20-years-of-age

11. SAS. (2020). SAS Enterprise Guide Software (Version 8.3.2.140).

12. Siegel, D. A., Richardson, L. C., Henley, S. J., Wilson, R. J., Dowling, N. F., Weir, H. K., . . . Buchanan Lunsford, N. (2020). Pediatric cancer mortality and survival in the United States, 2001-2016. *Cancer, 126*(19), 4379-4389. doi:https://doi.org/10.1002/cncr.33080

13. Siegel, R. L., Miller, K. D., Fuchs, H. E., & Jemal, A. (2021). Cancer Statistics, 2021. *CA: A Cancer Journal for Clinicians, 71*(1), 7-33. doi:https://doi.org/10.3322/caac.21654

14. Tran, Y. H., Coven, S. L., Park, S., & Mendonca, E. A. (2022). Social determinants of health and pediatric cancer survival: A systematic review. *Pediatric Blood & Cancer*, e29546. doi:https://doi.org/10.1002/pbc.29546

15. Wolfson, J., Sun, C.-L., Wyatt, L., Stock, W., & Bhatia, S. (2017). Adolescents and Young Adults with Acute Lymphoblastic Leukemia and Acute Myeloid Leukemia: Impact of Care at Specialized Cancer Centers on Survival Outcome. *Cancer Epidemiology, Biomarkers & Prevention, 26*(3), 312-320. doi:10.1158/1055-9965.Epi-16-0722