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Predictors of Healthcare Cost in a Wisconsin Acute Leukemia Population: Utilization of a State-Level All Payer Claims Database

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PREDICTORS OF HEALTHCARE COST IN A WISCONSIN ACUTE LEUKEMIA POPULATION: UTILIZATION OF A STATE-LEVEL ALL PAYER CLAIMS DATABASE

by

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ABSTRACT

PREDICTORS OF HEALTHCARE COST IN A WISCONSIN ACUTE LEUKEMIA POPULATION: UTILIZATION OF A STATE-LEVEL ALL PAYER CLAIMS DATABASE

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The University of Wisconsin-Milwaukee, 2012
Under the supervision of Ron Cisler, PhD

Understanding cost predictors of low incidence high cost cancers is increasingly important as the U.S. attempts to control health care costs. Acute myeloid and acute lymphoblastic leukemia are hematologic cancers requiring high cost care.

Using Anderson's model of health care utilization this study explores the influence of patient and community factors on health care costs. Insurance claims cost data obtained from the Wisconsin Health Information Organization provided a sample of 837 acute leukemia patients from April, 2009 and June, 2011. Total, ancillary, inpatient, outpatient, pharmacy and professional services costs were analyzed using a GLM gamma log link regression model to identify cost predictors. The added influence of patient and community enabling factors over patient characteristics and need for services was analyzed with hierarchical regression.

Study findings include: (1) Predisposing characteristics of acute leukemia patients may not follow the commonly reported direction of cost where higher cost was associated with older age and female gender. Instead their costs are expected to be higher in younger, male patients; (2) As expected, treatment with hematopoietic stem cell

transplant (HCT) and increased severity of disease represent significant cost drivers and strongly influence higher costs; (3) Community enabling resources influence cost where academic medical centers are associated with higher cost and providers located in areas of higher poverty are associated with lower cost; and (4) Costs related to different service types, i.e. inpatient, outpatient, etc., may not follow the same trends and result in important differences in findings. While this creates complexity in assessing cost drivers it can provide the opportunity for cost interpretation and decision making specific to service type.

Implications of study findings support the need for healthcare service research of rare diseases; further exploration of the relationship between treatment choice and cost as well as treatment disparities between providers and their locations; and the importance of clarity in service type cost.

Future research opportunities would include linking cost data to clinical outcomes data; expanding the cost dataset longitudinally to accommodate more patient records along with a longer timeline of data for each; and sub analyses of potential interactions between variables.

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LIST OF ABBREVIATIONS

ALL:	Acute Lymphoblastic Leukemia
AML:	Acute Myeloid Leukemia
Allogeneic:	Stem cell donor and recipient is not the same person
Autologous:	Stem cell donor and recipient is the same person
AWP:	Average wholesale price
AYA:	Adolescents and young adult
CIBMTR:	Center for International Blood and Marrow Transplant Research
CC:	Complications
CMS:	Centers for Medicare & Medicaid Services
CR1:	First clinical remission of disease
Cytogenetics:	The study of the structure and function of the cell, especially the chromosomes
DMV6:	Data Mart Version 6
ECM:	Exponential conditional mean
ETG:	Episode treatment group
GDP:	Gross domestic product
HCT:	Hematopoietic stem cell transplant

H-CUP:	Healthcare Cost and Utilization Project
HM:	Hierarchical model
HSC:	Hematopoietic stem cell
LOF:	Length of follow up
MCC:	Major complications
Member:	Insured patient
NACHC:	National Association of Community Health Centers
NCI:	National Cancer Institute
NDC:	National drug code
PHS:	Public Health Service
RVU:	Relative value unit
SEER:	Surveillance Epidemiology and End Results
WHIO:	Wisconsin Health Information Organization
WHAE:	Wisconsin Health Information Organization Health Analytics Exchange
WMS:	Wisconsin Medical Society

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Data used in this study was provided by the Wisconsin Health Information Organization, Inc., a Wisconsin nonprofit tax exempt corporation (WHIO) through an agreement with the Board of Regents of the University of Wisconsin System on behalf of the University of Wisconsin-Milwaukee Center for Urban Population Health. Data acquisition was funded through the Center for Urban and Population Health.

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CHAPTER 1: Introduction

1.1. Study Background.

Rapidly increasing health care costs are a significant concern in the United States. In 2009, the Federal Centers for Medicare and Medicaid reported the costs associated with the health care sector of the U.S. economy accounted for 17.3% of the gross domestic product (GDP). (www.cms.gov/National Health ExpendData) At the same time, the U.S. has been reported to have one of the highest worldwide growth rates in health care spending increasing from 9% of GDP in 1980 to 16% of GDP in 2008 (www.kff.org/insurance/snapshot).

While the majority of Americans have health insurance, the number covered by private health care insurance is decreasing and the number covered by government health insurance or uninsured is increasing. In September, 2011 the percentage of Americans with health insurance was reported at 256.2 million, 83.7% of the population. Private health insurance accounted for 64% of all insured with 55.3% attributed to employer based programs, a number that has been decreasing since 2001. The percentage of Americans covered by government health insurance programs increased to 31%; 15.9% Medicaid and 14.5% Medicare. The number of Americans without insurance increased to 49.9 million between 2010 and 2011, or 16.3 percent of the population (www.census.gov/hhes). The Bureau of Labor Statistics report a 6% increase in individual healthcare spending between 2008 and 2010; primarily driven by a 10.8% increase in the cost of health insurance (www.bls.gov/news.release/cesan).

Finding solutions for health care cost accountability, transparent reporting and a reduction of rapidly increasing health care costs is consistently noted as a high priority by many U.S. government leaders and agencies (www.acponline.org/advocacy; www.healthcare.gov; www.ahrq.gov/research). The Patient Protection and Affordable Care Act, signed into law on March 23, 2010 by President Obama, has been designed to expand health care coverage, control health care costs and to improve the health care delivery system (www.kff.org/healthreform). The new legislation is controversial and it is unknown if it will be effective in reducing the rate of growth in the health care market in the short or long term.

1.2. Leukemia Cost.

In *Facts 2012* the Leukemia and Lymphoma Society report new cases of leukemia, lymphoma and myeloma are expected to represent nine percent of the approximate 1.6 million new cancer cases diagnosed in 2011 with 12.5 percent of new cases attributed to leukemia alone. Diseases such as acute myeloid leukemia and acute lymphoblastic leukemia require high cost care in order to achieve long term, disease free survival. Use of prolonged hospital care, high levels of medical technology and specialized health care services contribute to the high cost of treatment (Yu, 2006). Expensive chemotherapy regimens along with the potential for hematopoietic stem cell transplant create a continuum of cost starting from initial diagnosis through disease remission. Ongoing oversight and maintenance treatments extend the use of health care services indefinitely.

1.3. Problem Statement.

As the U.S. health care system debates policies to control health care cost, it becomes increasingly important to understand the drivers of high cost care. Exploring cost predictors of low incidence, low prevalence but high cost cancers is important to both identify and better understand the underlying healthcare utilization and cost drivers. This study proposes to investigate both patient and community variables that may influence the cost of treatment of an acute leukemia population in Wisconsin.

1.4. Study Objective and Specific Aims.

The primary objective of this study is to explore the influence of certain patient demographic, provider demographic and socioeconomic variables on health care claims costs associated with a Wisconsin leukemia population identified within the State of Wisconsin all payer claims database and, through the utilization of this database, attempt to identify factors that are predictive of higher cost. The study examines patients with the diagnosis of acute lymphoblastic leukemia, acute myeloid leukemia, and are present in the Wisconsin Health Information Organization (WHIO) database from April 1, 2009 through June 6, 2011. WHIO is an all payer claims database representing residents of the State of Wisconsin. An underlying objective of the study is to assess the usefulness of the WHIO datamart for cost research.

In order to differentiate cost predictors related to service types, the study will examine claims costs associated with a the diagnosis of acute leukemia through six criterion variables: (1) Total claims cost; (2) Ancillary claims cost; (3) Inpatient claims cost; (4) Outpatient claims cost; (5) Pharmacy claims cost; and (6) Professional claims

cost. The study will investigate both by billed cost (i.e., what is charged to the patient) and standard cost (i.e., a WHIO defined standardization definition) in an effort to determine if the two costs are different. Diagnosis related claims costs are identified through WHIO defined episode treatment groups (ETG) and are the sum of all costs associated with the leukemia episode. Throughout this paper, the diagnosis-cause cost analyzed in this study is referred to simply as 'cost'. The definition of the WHIO defined episode treatment groups is outlined in Appendix B.

Whether cost is investigated using billed cost, standard cost or paid cost as a criterion variable is dependent on the perspective of the study. A study that is interested in the patient perspective may use billed cost. A study interested in using a closer definition to actual cost may choose standard cost. A study that has a business perspective may use paid cost. Billed cost, paid cost and standard cost is available in the WHIO datamart, but only billed cost and standard cost were available for use in this study. Standard cost is calculated to adjust for variations related to insurance contracting, region and disease severity and comorbidity. In a 1982 article, Finkler identifies the use of standard cost as best if the perspective of the study is real operational cost or resources used, but states that if the perspective of the study is the cost to the patient, billed cost is acceptable (Finkler, 1982). While the patient perspective is considered important overall, use of standard cost is more common in health cost studies.

The study has three specific aims:

Aim 1: To determine if patient predisposing characteristics of age and gender, the patient need factors of treatment type and treatment episode severity and the enabling

resources of county of residence socioeconomics, type of payer, are predictive of cost. In addition, to examine whether the type of health care provider, academic medical center or non-academic medical center, or its location socioeconomics are predictive of cost.

Aim 2: Using the optimal statistical model; to examine their influence on the cost criterions.

Aim 3: To investigate whether patient and community enabling resources; defined as provider type and location socioeconomics, patient enabling resources; defined as payer type and patient residence socioeconomics have added influence on cost over patient level predisposing characteristics: defined as age, gender and length of follow up and patient need; defined as episode treatment severity and treatment type.

1.5. Scientific Significance.

Prior theories of health care utilization identify patients need for care as a determining factor in use of health care services. In addition, people who use more health care have been shown to incur more health care costs (Andersen, 1995). An acute leukemia population will have a high need for healthcare, is expected to have high utilization of health care services and incur high cost. These factors create a financial burden to the patient, the provider and the community. Less understood are the patient and community factors associated with acute leukemia patients and their providers which may be predictive of higher cost. Knowledge of key factors that influence these costs will benefit decision making at the patient, provider, and policy making level.

Concern over increases in health care expenditures has created an immediate need to better understand costs and cost drivers in the health care system. This study of low

incidence, high cost patients will provide needed information about groups that may not be immediately assessed. Through the examination of factors that influence cost, this study will help identify if certain determinants can be used to better calculate the value of treatment for these diseases, allowing more informed resource allocation decision making.

1.6. Research Questions and Hypotheses.

This study uses data from an all payer claims database and multivariate regression modeling as a tool to identify whether patient characteristics, need and enabling factors and community factors are significant predictors of health care cost in a Wisconsin leukemia population. Specific research questions are:

1. Does the patient's age and gender, episode severity level, type of treatment and type of payer predict health care claims cost? Does where a patient lives and the socioeconomics of their U.S. County of residence predict health care claims cost? Do the type of provider and its location predict health care claims cost? Are any variables more useful in predicting the claims cost criterion?

Hypotheses: A patient's age, type of treatment, episode severity level is each expected to be significantly predictive of cost. Increases in each of these factors have been shown to increase cost. A public payer, lower patient socioeconomics and lower provider socioeconomics are also expected to be predictive of an increase in cost. Finally, an academic provider is expected to have higher costs when compared to a community provider.

2. How strong is the influence of each predictor on the cost criterion?

Hypotheses: While each is expected to be measurably predictive of the cost criterions, some variables, such as age, treatment, and disease severity level are expected to have a stronger influence when compared to others, such as payer type and gender. Provider type and location may have a slight influence on cost due to the differences in regional socioeconomics and organizational insurance contracting where higher costs are associated with academic medical centers and wealthier communities.

3. Does adding patient and community enabling resources, over and above patient predisposing characteristics and need for services predictors, significantly add to the predictability of the model, and if so, how strong is their influence?

Hypotheses: It is expected that, due to differences in patient's healthcare insurance and socioeconomics as well as regional socioeconomics and insurance contracting, the patient and community enabling resources predictors will significantly add value to the model.

Health care cost data can be difficult to obtain as well as organize for research purposes. An underlying intent of this study is to assess the usefulness of this type of administrative database to address health care cost research questions.

CHAPTER 2: Literature Review

Studies of economic evaluation and health services were identified in a search through PubMed and the Cochran Collaboration between years 2004 through 2011. (Key words: acute lymphoblastic leukemia, acute myeloid leukemia, hematopoietic stem cell transplant, chemotherapy, economic evaluation, health care cost, health services cost methodology, zip code socioeconomics).

2.1. Theoretical Framework.

Prior health determinants research is used as a theoretical basis for this study. While the theories may not directly address cost as an outcome, its presence is implicit in the areas of access, quality and resource allocation. Each theory supports the need to investigate and better understand the role of cost in health care utilization and decision making for the patient, provider and the community.

2.2. Behavioral Models of Health Care Utilization.

Aday proposed a comprehensive framework for health services research focusing on pathways that influence community and patient health outcomes (Aday, 2001). This conceptual model incorporates both a community and patient perspective with a goal of integrating health services and public health research. It integrates concepts of system structure and process, intermediate outcomes with a goal of an ultimate health outcome. In this model health policy, federal, state and local, is the highest level concept. Level two relates to structural areas and includes the health care delivery system (availability, organization, financing), population at risk (predisposing, enabling, need) and environment (physical, social, economic). Level three focuses on the process areas of

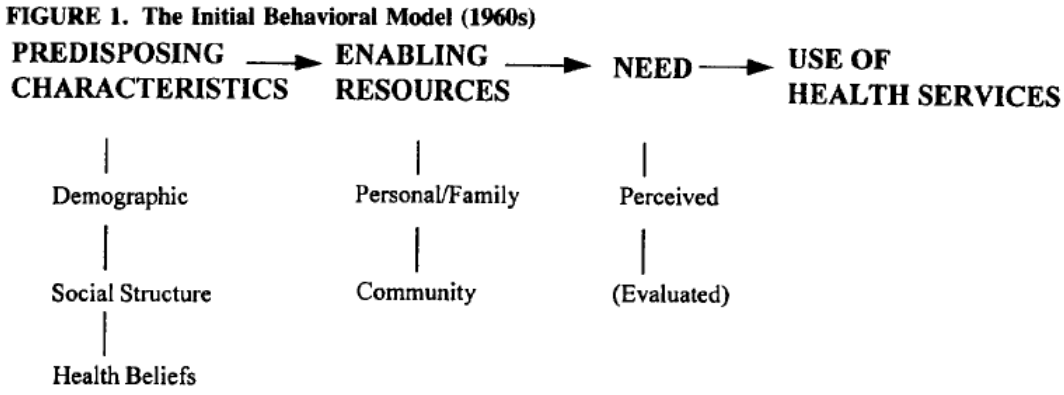
realized access to care (utilization, satisfaction) and health risk (environmental and behavioral). Level four identifies the first intermediate outcome of effectiveness (clinical and population). The second intermediate outcome level, five, is equity (procedural and substantive) and efficiency (production and allocative). Level six is the final, ultimate outcome of health for both the patient and the community. Each part of the conceptual model provides defined areas for health services research at both the patient and community level. By including micro and macro level concepts, the framework provides the ability to investigate both the detail of an area of interest and then link it to the public health focus of community health.

Aday used this conceptual base to create a framework for studying vulnerable populations. In this model, the areas of focus include; social and economic policy, community oriented health policy, medical care and public health policy along with ethical norms and values. Linkages between patient and community risk factors are illustrated along with variables that can be predictive of vulnerability for poor health outcomes. Health policy is identified as a mediator for the potential of positive versus negative health outcomes.

Aday's framework built on Anderson's 1960's Behavioral Model of Health Services Use which assessed determinants of health care utilization. (Anderson, 1968) With the intention of promoting equitable access to health services, Anderson (figure 2.1) investigated factors related to why families used health services. This behavior model proposes that an individual's use of health care can be attributed to certain individual and community or organizational predisposing factors that will either increase or decrease utilization. Predisposing factors are related to biology; such as age and gender, social

structure; such as education, occupation, ethnicity, environment and culture, and, health beliefs; such as attitudes, values and knowledge. In addition, both individual and community level resources are necessary to support the use of health care. These include factors such as income, health insurance, transportation, and availability of health care personnel and facilities. Finally, use of health care services will be influenced by the individual's perceived/evaluated need for services as well as their ability to access to health care resources, work within the health care system and effectively manage their clinical problem.

Figure 2.1 Anderson's behavioral model



Anderson, R.M. (1995). Revisiting the behavioral model and access to medical care: Does it matter? *Journal of Health and Social Behavior; Social Science Module,* Mar, 36, 1.

The models recognize that economic factors at both the individual and the community level, along with appropriate allocation of healthcare resources need to be addressed for improvement in population health. This study will further explore how patient, provider and community factors impact high utilization and costs of health services.

2.3. Health Services Utilization Database Research.

In 2003, Hay investigated cost hospital cost drivers using state-level data. Utilizing data from a representatively large U.S. health insurance plan, this article identifies a number of characteristics that contribute to inpatient costs; local area per capita wages and incomes, characteristics of the physician market, hospital technology, and hospital occupancy and case-mix severity. Other factors such as staff shortages and an economic slowing are noted to contribute to cost pressures.

Schneeweiss and Avorn reviewed the utility of large healthcare databases for epidemiologic health care research, focusing on pharmaceuticals (Schneeweiss and Avron, 2005). They conclude that electronic medical record systems have a great potential for research investigating comparisons, longitudinal data and clinical epidemiologic data. They note that care must be given to the design of studies to allow for the system limitations and potential sources of bias such as incomplete records, miscoding, incorrect record linkage, etc. As clinical detail and accountability increase, these systems are expected to become more useful to outcomes research.

Motheral and her colleagues provide a checklist for retrospective database studies (Motheral, Brooks, Clark, Crown, Davey, Hutchins, Martin & Stang, 2003). This article lists 27 questions that give guidance for designing a research study using a retrospective database specifically using medical claims or encounter databases. These questions help to guide and decision about the study data, study methods and conclusions. This study incorporated some of these conclusions into its study design, methods and conclusions.

2.4. U.S. Census Data and Socioeconomic Inequalities.

Geronimus and Bound in their 1998 article of using census-based aggregate variables as proxies for individual socioeconomics discuss the timing of census data, when it was collected, as well as the level of aggregation of the data (Geronimus and Bound, 1998). They found that while investigators can comfortably use census data that can be up to 20 years old, it is limited in use for individual level interpretation. They conclude that the aggregate variables available through geocoded data should not be viewed as proxies for the individual level construct because the aggregate variable will tend to be larger than the micro level variable due to biases related to correlation with other factors of the geographic region, i.e. income, race, etc. These variables need to be interpreted as an area-based, rather than an individual-based, constructs.

Kreiger and colleagues as part of the Public Health Disparities Geocoding Project published a series of articles related to the usefulness of US census data to investigate US socioeconomic inequalities. One of the articles investigated whether choice of area-based measurement or geographic level of measurement impact results of mortality and cancer incidence outcomes (Kreiger, Chen, Waterman, Soobader, Subramanian & Carson, 2002a). Choice of area-based measures should be related to the geographic areas socioeconomic position (SEP) and defined through variable that could meaningfully summarize the area's socioeconomic conditions and be robust over time and between regions. Variables included; occupational class, income, poverty, wealth, education and crowding. Geographic level was defined as census block, census tract and zip code. Results showed that measures of economic deprivation were most robust. The authors identify the usefulness of area-based socioeconomic measures when used with

meaningful geographic concepts but not as proxies for individual socioeconomic data. They identify the U.S. census measure of 'percentage of persons living below the US poverty line' as a variable that meets the criteria of economic deprivation, meaningful across regions and over time, and easily understood. In a separate 2002 article these authors discuss spatiotemporal difficulties associated with the use of zip code data and US census data. The authors caution researchers using geocoded data to clearly identify any spatiotemporal mismatches between the study dataset and the U.S. census variable (Kreiger, Chen, Waterman, Soobader, Subramanian & Carson, 2002b).

In 2005 Kreiger and colleagues investigated a method of routine monitoring of socioeconomic health disparities using census tract poverty data (Kreiger, Chen, Waterman, Rehkopf & Subramanian, 2005). The percentage of persons living below the U.S. poverty line variable was used in census tract groups and provided a cost-efficient method of assessment that can be applied to health outcomes within the region and across the US. The authors argue if the US public health surveillance data were geocoded, this method would provide a good mechanism for routine assessment of socioeconomic-based health disparities.

2.5. Cancer: Epidemiology and Cost.

Cancer is the second most common cause of death in the U.S.; with an estimated 577,000 deaths expected in 2012 (www.cancer.org/acs/groups). Cancer impacts the lives of over 11 million Americans; it does not discriminate by age, ethnicity, income or region (www.srab.cancer.gov).

Since the beginning of this century, the overall incidence and death rates of cancer have been decreasing; a result related to early detection, cancer prevention and better treatment options. In The Annual Report to the Nation on the Status of Cancer, 1975-2007, Kohler and colleagues found a decrease in the overall incidence of cancer in the U.S. population, but noted that due to the expected increase in life expectation the absolute number of individuals diagnosed with cancer is expected to increase creating an increase in demand for cancer related health care services (Kohler, Ward, McCarthy, Schymura, Ries, Eheman, Jemal, Anderson, Ajani & Edwards, 2011). The authors point out the need for effective management of these diseases through not only prevention, detection treatment and survivorship but also the protection of resources necessary to provide good quality care. They conclude that utilization of quality population-based data systems and translation of evidence-based clinical and basic research findings are critical to sound public policy decisions for cancer.

Using patient-reported demographic and socioeconomic data from the Social and Economic Supplement to the Census Bureau's Current Population Survey, Clegg and colleagues reported cancer-related disparities linked to individual-level socioeconomic status for all combined cancers as well as the specific cancers of lung, breast, prostate, cervix and melanoma (Clegg, Reichman, Miller, Hanky, Singh, Lin, Goodman, Lynch, Schwartz & Chen, 2009). Results showed, for each of the major cancer diagnoses, significant differences in incidence rates from self-reported data of education level, family income and poverty status. The authors note the importance of differentiating between patient level characteristics and community level characteristics, particularly if measuring a similar construct such as socioeconomic status. They conclude that social

disparities in cancer incidence may be related to socioeconomic and demographic differences in cancer-related risk factors and behaviors, that disparities in health care access may contribute to different types and stages of care and individuals with lower SES and educational level are more likely to have higher rates of cancer risk factors.

The American Society of Clinical Oncology, Meropol and colleagues issued a guidance statement regarding the cost of cancer care (Meropol, Schrag, Smith, Mulvey, Langdon, Blum, Ubel & Schnipper, 2009). The statement recognizes that while better prevention, detection and treatment have reduced the cancer death rate, costs of cancer treatment have steadily risen and continue to grow rapidly creating an unsustainable financial burden to all levels of cancer care. The guidance statement makes the following recommendations: recognizes that physician-patient discussions regarding cost of care are an important, a need for communication support tools for oncology providers related to cost of care, the development of educational resources about the high cost of cancer care. This article identifies the need for a clear understanding of cost drivers in the cancer care system so that all patients can get access to, and are able to afford, high-quality cancer care.

In countries with centralized government managed health care, such as Canada, the Netherlands, Europe, there are studies that address the cost of diseases directed at the appropriate use of health care resources. However, the decentralized U.S. health care delivery system has made it challenging to assess health related costs for patients, organizations and populations. The National Cancer Institute website reports a steady increase in U.S. spending for cancer care (www.cancer.gov). A January, 2011 study from the Division of Cancer Control and Population Sciences projects the continued

increase in cancer care cost with the adoption of new, more advanced treatments as standards of care (http://progressreport.cancer.gov).

Chang and colleagues estimated the cost of cancer for patients diagnosed with seven of the major types of cancer (Chang, Long, Kutikova, Bowman, Finley, Crown & Bennet, 2004). This study found significant financial burden for cancer patients. Within the groups studied, mean monthly cost of treatment ranged from $2,187 to $7,616 with cost driven by hospitalization and an average monthly loss of 2 work days. In contrast, a non-cancer control was shown to have an average monthly cost of $329. They note the viable use of administrative databases to estimate both direct and indirect costs.

The most common forms of cancers are prostate, breast, lung, and colorectal cancer. Logically, they receive both higher levels of attention and, ultimately, funding. Cancers such as leukemia are as deadly to the patient and require expensive treatment. Health services research for cancers with lower incidence rates is important both to understand the financial burden of these diseases and to protect appropriate allocation of resources. In 2010, the National Cancer Institute reported the direct cost of cancer care in the U.S. as $124.57 billion and the direct cost of care for leukemia was equal to $5.44 billion, roughly 4.3% of total direct cost (www.cancer.gov/aboutnci/serving-people/cancer-statistics).

2.6. Epidemiology of Acute Lymphoblastic Leukemia and Acute Myeloid Leukemia.

Acute Lymphoblastic Leukemia (ALL) and Acute Myeloid Leukemia (AML) are cancers of the hematopoietic system, the system of the body which produces blood cells. These cancers are considered acute due to the rapid spread of disease; left untreated, they

will be fatal. Common treatments for both diseases include chemotherapy, radiation and hematopoietic stem cell transplantation.

Acute lymphoblastic leukemia (ALL) is a common hematopoietic cancer with an estimated 5000 cases diagnosed each year. The Surveillance Epidemiology and End Results (SEER) website of the National Cancer Institute (NCI) reports the prevalence of ALL in the U.S. as of January 1, 2008 to be approximately 62,193 alive, 34,306 female and 27,887 male. An estimated 20,300 individuals will be diagnosed with ALL in 2011; 8,460 female and 11,840 male, with an estimated number of deaths equal to 5,800. Between the years 2004-2008 the overall median age at diagnosis for ALL was 13 years; approximately 60% of individuals diagnosed with the disease are under the age of 20 years. In children, the annual incidence of ALL is approximately 9-10 cases per 100,000 with a median age at diagnosis between 2-5 years. ALL accounts for 25% of all diagnosed childhood cancer and 75% of childhood leukemia. The overall reported 5-year survival for 2001-2007 was 64.4% with a median age at death between 2003-2007 being 49 years of age (www.seer.cancer.gov/statistics). Treatment of ALL includes chemotherapy, radiation and hematopoietic stem cell transplantation with all patients initially treated with chemotherapy. Hematopoietic stem cell transplant is considered when disease recurs or when disease characteristics at diagnosis are such that the patient is unlikely to be cured with chemotherapy alone. Type and level of treatment is determined by factors such as patient age, white blood cell count at diagnosis, cytogenetics and disease status (i.e. whether in remission or with persistent leukemia despite chemotherapy). In 2008 in the U.S., approximately 1000 allogeneic transplants were performed for patients diagnosed with ALL, roughly 430 for pediatric patients,

representing approximately 6% of all transplants performed (www.cibmtr.org/summaryslides).

Acute myeloid leukemia is a hematopoietic cancer that begins in the bone marrow and impacts cells that would develop into white blood cells. It is one of the most common forms of leukemia in adults with average onset around 60 years of age (www.seer.cancer.gov/statistics). In 2011, 18,100 new cases were estimated to be diagnosed. Of those diagnosed, 9,830 are men and 8,270 are women. The number of deaths from AML in 2011 is estimated to be 9,320. Between the years 2004-2008, SEER data report the median age at diagnosis of AML to be 67 years of age, with roughly 70% of all patients over the age of 55 with a 4.3/3.0 ratio of males to females. The median age at death was 72 years of age with a male/female ratio of 3.6/2.2 per 100,000. The years 2001-2004 and 2004-2008 a slightly increasing trend was reported for both incidence (1.8% increase) and death (0.3% increase) in the AML population.

Treatment of AML includes chemotherapy, radiation and the hematopoietic stem cell transplant. Standard treatment of adult AML is dependent on the disease subtype but may include combination chemotherapy, high dose chemotherapy and stem cell transplant using either the patients cells (autologous transplant) or donor cells (allogeneic transplant). As with ALL, type and level of treatment is determined by factors such as patient age, white blood cell count at diagnosis, cytogenetics and disease status, whether in remission or with persistent leukemia despite chemotherapy. In the U.S. approximately 2500 transplants were performed for patients diagnosed with AML, slightly over 400 for pediatric patients, representing approximately 15% of all transplants performed (www.cibmtr.org/summaryslides).

2.6.1. Acute lymphoblastic leukemia treatment, survival and cost.

Acute lymphoblastic leukemia is diagnosed more commonly in children versus adults. Pui and Evans indicate that of the number of ALL cases diagnosed annually, roughly two thirds are from the pediatric population (Pui and Evans, 2006). In children, the rate of 5 year survival is high, currently over 80%. Assignment to the best therapy follows a strict assessment of relapse risk with a goal of avoiding high levels of toxicity but attaining a high cure rate. Pediatric patients are grouped into the risk categories of standard, high and very high risk.

ALL in adults is a challenging disease with a significantly lower rate of survival of less than 40% (Narayanan and Sami, 2011; Paulson, Szwajcer & Steftel, 2011; and Fielding, Richards & Chopra, 2007). While most patients are able to achieve remission through treatment, most will eventually relapse. Survival after relapse is reported to be 10-20%. Adult treatment options tend to follow the basic structure of the pediatric program; however, due to the poor survival rate after relapse, there is a current debate about the value of more aggressive treatment prior to relapse in the form of hematopoietic stem cell transplant (HCT).

Schafer and Hunger compare the survival rate of adolescents and young adults (AYA) to both the pediatric and the adult population indicating that the AYA survival rate fall somewhere in the middle (Schafer and Hunger, 2011). While there has been steady improvement in survival over the last few decades, they cite trials that show better survival for AYA's following pediatric treatment regimens. They conclude that future research should focus on socio-political and biological factors that may impact this

group. Stock and colleagues discuss clinical and demographic differences between the AYA and the pediatric population which may account for differences in survival between the groups (Stock, La, Sanford, Bloomfield, Vardiman, Ganyon, Larson & Nachman, 2008). In a letter to the editor, Kantarjian and O'Brien suggest that an analysis of patterns of insurance coverage may be of interest in this group (Kantarjian and O'Brien, 2009). AYA's may go through timeframes with no insurance coverage, affecting access and consistency of health care utilization.

VanLitsenburg and colleagues provide a cost-effectiveness investigation of pediatric ALL in chemotherapy only regimens concluding that treatment was cost effective for patients in standard risk and medium risk groups (VanLitsenburg, Uyl-de Groot, Raat, Kaspers & Gempke, 2011). Risk is mainly determined through levels of minimal residual disease. However, high risk patients were excluded from the study due to their eligibility for hematopoietic stem cell transplant and represented approximately 10% of the group.

2.6.2. Acute myeloid leukemia treatment, survival and cost.

Acute myeloid leukemia is the most common type of leukemia in adults. Deschler and Lubbert describe the epidemiology and etiology and identify it as a significant contributor to the number of cancer related deaths in the U.S. (Deschler and Lubbert, 2006). For most patients the cause of disease is unknown, however age, genetic disorders and other hematologic disease have been reported as having a link to higher rates of mortality. AML's incidence rate is higher for males and occurs predominantly in adults, with over 80-85% of all cases reported in patients >15 years of age. In adults,

AML tends to impact those >65 years of age, with over 42% reported cases. Survival is reported to be 23% at five years if <55 and 11% if >55. Untreated disease is always fatal. The improvement in supportive care options possibly has impacted the higher rates of survival over the years. One conclusion of the authors identifies the ability to use population level databases as instrumental in the ability to detect differences because of the rarity of the disease

Redaelli and colleagues provide a literature review of the economic burden of AML showing it to be a disease with a high cost of care affecting older adults (Redaelli, Botteman, Stephens, Brandt & Pashos, 2004). With the aging population, incidence rates are expected to increase. The review of the literature resulted in a selection of twenty nine studies that met the author's inclusion criteria. The studies offered a range of cost type, both indirect and direct, as well as cost comparison between different treatment regimens. They note the lack of studies from a societal perspective and state this as a clear direction for future research.

In an article investigating the cost–effectiveness of aggressive therapy after relapse in AML patients, Yu and colleagues compare a chemotherapy based treatment regimen to a hematopoietic stem cell transplant (HCT) based treatment regimen (Yu, Gau, You, Chern, Chau, Tzeng, Ho & Tsu, 2007). AML is expensive to treat due to high rates of hospitalization and high cost treatments. They conclude, that in patients <60, high dose chemotherapy only regimens estimated five year survival was higher than five year survival in the allogeneic transplant group. In addition, it was more cost-effective in the chemotherapy only group with medium risk or lower. However, they note that their

study is based on costs of care in Taiwan and results may not be transferable to Europe or the U.S., given the different cost structures between countries.

2.7. Leukemia in Wisconsin.

The Wisconsin Department of Health Services reports on leukemia but is not specific to AML and ALL. Annually, approximately 832 Wisconsin residents were reported to be diagnosed with leukemia from 2002-2006 according to the National Center for Health Statistic's Public Use Mortality file. In Wisconsin, leukemia is the most commonly diagnosed cancer under the age of 15. Leukemia's incidence rate was higher in males than in females (19.0 per 100,000 versus 11.0 per 100,000). An average of 485 deaths from leukemia was reported each year from 2002-2006; it is the leading cause of diseased based death in children under the age of 15, with higher mortality rates reported in males versus females (http://www.dhs.wisconsin.gov/wcrs/pdf/cancerwi0206.pdf).

2.8. Chemotherapy.

Chemotherapy is a treatment that uses chemical components to stop the growth of cancer cells. Some leukemia's are treated only with chemotherapy regimens designed using multiple factors such as type of disease, severity of disease, patient age, etc. In AML, most patients begin treatment in induction chemotherapy with a goal of bringing the disease into remission. If remission (CR1) is successful, most leukemia cells will be destroyed. If it is unsuccessful additional chemotherapy treatment or hematopoietic stem cell transplant (HCT) may be necessary (www.marrow.org/patient/disease_and_treatment).

In ALL, chemotherapy is the standard treatment for pediatric patients prior to first remission (CR1); however at first remission HCT becomes a viable treatment option. Adult ALL has not followed the same treatment guidelines as the pediatric group and HCT is an option at diagnosis. In prior ALL studies reviewed, cost of chemotherapy was contrasted to cost of HCT. The results of a 2007 study Orsi and colleagues concluded that allogeneic HCT for ALL patients in CR1 improved both event-free survival when compared to chemotherapy or autologous transplant and showed an acceptable level of cost-effectiveness (Orsi, Bartolozzi, Messori & Bosi, 2007). However, Yu and colleagues in a cost analysis with an acute myeloid population concluded that the cost-effectiveness of high dose chemotherapy treatment was comparable to allogeneic HCT in high risk patients, but in medium risk patients, high dose chemotherapy proved to be more cost-effective (Yu, Gau, You, Chern, Chau, Tzeng, Ho & Tsu, 2007). In their conclusion, they identified the need for further research in the area given their sample size and cost differentiation. VanLitsenburg and colleagues studied the influence of new medication and technology in a cost-effectiveness analysis of a pediatric ALL population treated with chemotherapy only regimens (VanLitsenburg, Uyl-de Groot, Raat, Kaspers & Gempke, 2011). This study found treatment to be cost-effective in standard and medium risk patients. Other chemotherapy cost studies compare newer drugs entering the market to those historically available. (Hann, Stevens, & Goldstone, 1997; Kattan, Inoue, Giles, Talpaz, Olzer, Guilhot, Zuffa, Huber & Beck, 1996)

2.9. Hematopoietic Stem Cell Transplant.

Currently, hematopoietic stem cell transplant (HCT) is the only approved use of stem cells for disease treatment. A hematopoietic stem cell (HSC) is a cell that has the

ability to produce new blood and immune cells and is found in the bone marrow, peripheral blood and umbilical cord blood. Like normal HSC's, malignant hematopoietic stem cells also have the capacity for self-renewal and are the cause of various leukemia's. While chemotherapy can successfully treat, and eliminate cancer, in some cases more intensive treatment is required for a cure. HCT is more intensive than chemotherapy; this treatment involves high-dose chemotherapy and irradiation followed by infusion of hematopoietic stem cells from a suitable related or unrelated donor. Both normal and malignant stem cells are destroyed and the infusion of hematopoietic stem cells restores the content of the bone marrow in the person with ALL. Despite the aggressive treatment, leukemic cells can persist or recur after HCT requiring further therapy, which may or may not be successful at disease eradication.

The Healthcare Cost and Utilization Project (H-CUP) identified bone marrow transplant as the procedure with the most rapidly growing cost with aggregate costs growth of 84.9 percent between 2004 and 2007. (Stranges, Russo & Friedman, 2009) Prior research of cost and cost-effectiveness in hematopoietic stem cell transplant has investigated; the disease treatment (inpatient and outpatient); comparatively assessed the introduction of a new drug or therapy option (cord blood); and the ability to identify pre-transplant characteristics that impact cost. (Jacobs, Hailey, Turner & Maclean,2000; Lee, Klar, Weeks & Antin, 2000; Lin, Lairson, Chan, Du, Leung, Kennedy-Nassar, Martinez, Gottschalk, Bollard, Heslop, Brenner & Krance, 2010; Majhail, Mothukuri & MacMillian, 2010; Saito, Cutler, Zahrieh, Soiffer, Ho, Alyea, Koreth, Antin & Lee, 2008) In a 2004 article, Gajewski and colleagues reviewed the relationship between providers and payers of HCT concluding that providers need to understand the true cost of care as

well as be able to identify predictable and unpredictable outlier risks (Gajewski, Foote, Tietjen, Melson, Simmons & Champlin, 2004). Ashfaq and colleagues recognized that detailed information available regarding HCT cost exists along with some cost effectiveness research, however, they state that there is limited evidence available related to adults and children with acute leukemia, noting the small size of the studies and their limited use for policy decision making (Ashfaq, Yahaya, Hyde, Andronis, Barton, Bayliss & Chen, 2010). Other HCT cost studies have been limited to direct cost of treatment within a single center, some extending cost to 1 year or 2 years post treatment. Researchers have indicated a need for additional economic and quality of life studies. (Stephens, Gramegna, Laskin, Botteman & Pashos, 2005).

During the 1990's changes to clinical practice in HCT included the increased use of autologous transplantation, peripheral blood transplantation, outpatient treatment as well as the use of cord blood for donor cells. Studies conducted during this timeframe investigated cost comparisons of these treatment related changes, concluding an overall reduction in cost with the new treatment options. In a review of the literature, Pickard and colleagues provided a comprehensive review of studies relating to health related quality of life and economic evaluation in pediatric ALL (Pickard, Topfer & Feeny, 2004). While some studies address disease specific economic burden and cost comparisons, most conclude that actual cost effectiveness analysis in the U.S. health care sector continues to be a challenge (Majhail, Mothukuri, Brunstein & Weisdorf, 2009; Redaelli, Botteman, Stephens, Brandt & Pashos, 2004).

There have been significant advances in the clinical outcomes of hematopoietic stem cell transplant with a relatively large body of research investigating transplant

outcomes and new treatment cost effectiveness. Bennett and colleagues showed decreasing cost related to the introduction of new donor options (Bennett, Waters, Stinson, Almagor, Pavletic, Tarantolo & Bishop, 1999). Other studies have provided detail of how to cost and overall cost of the procedure itself. (Majhail, Mothurkuri, Brunstein & Weisdorf, 2009; Westerman and Bennett, 1996; Waters, Bennett & Pajeau, 1998). Cordonnier and colleagues studied whether the use of reduced intensity treatment regimens were less costly (Cordonnier, Maury, & Esperou, 2005). They found no significant reduction in cost due to the higher rates of infection and graft versus host disease in patients on the reduced intensity regimens.

Decision models for predicting long term outcomes and costs were reported by Costa and colleagues (Costa, McGregor, Laneuville & Brophy, 2007). The study used a Markov decision analysis model in an adult population with acute leukemia and concluded that although initial transplant cost are high, the long term benefits of the transplant when compared to a non-transplant alternative, provided incremental cost effectiveness ratio (ICER) values that were both socially and financially acceptable. Saito and colleagues investigated costs of allogeneic HCT with high dose regimens (Saito, Cutler, Zahrieh, Soiffer, Ho, Alyea, Koreth, Antin & Lee, 2008). This study provided detailed single institution cost of treatment, cost estimates for complicated and uncomplicated HCT procedures and costs for management of specific transplant related complications.

In a 2010 study Lin and colleagues evaluated the cost and cost effectiveness of allogeneic peripheral blood stem cell transplantation compared to bone marrow transplantation in pediatric patients with acute leukemia (Lin, Lairson, Chan, Du, Leung,

Kennedy-Nassar, Martinez, Gottschalk, Bollard, Heslop, Brenner & Krance, 2010). This study concluded that comparative economic evaluation supported bone marrow transplant for standard-risk patients but indicated at lack of certainty for high-risk patients. The ability to predict overall cost using pre-transplant patient characteristics was investigated by Lee and colleagues (Lee, Klar, Weeks & Antin, 2000). Their study was unable to identify pre-transplant characteristics; however it concluded that preventing clinical complications could significantly impact overall cost.

CHAPTER 3: Methods

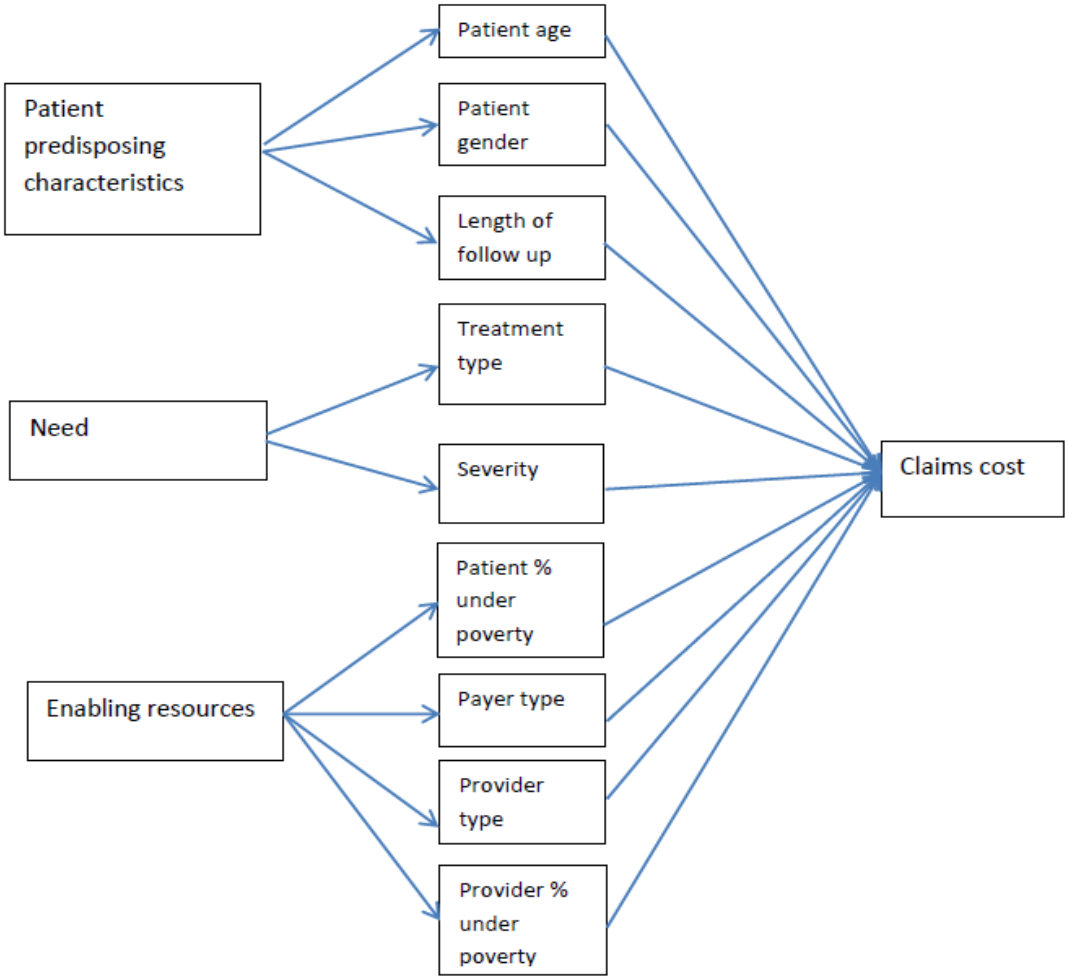
3.1. Design.

This study is a cross-sectional secondary analysis of insurance claims data from the Wisconsin Health Information Organization for patients diagnosed with acute leukemia. The active WHIO data mart contains 24 months of insurance claims data, collected over 27 months for completeness and refreshed approximately every 6 months. The study's conceptual models are constructed using Anderson's healthcare utilization model assumptions regarding the influence of patient predisposing characteristics, enabling resources and need (Figure 3.1). Concept model 1 fits each predictor variable into the Anderson model and its relationship to each cost criterion. Concept model 2 presents the hierarchical relationship between the grouped variables and the cost criterion. A quantitative analysis of the data is performed using multivariate regression methods, specifically generalized linear modeling (GLM). Predictor variables have been identified and assessed in terms of their potential effect on the cost criterion variable

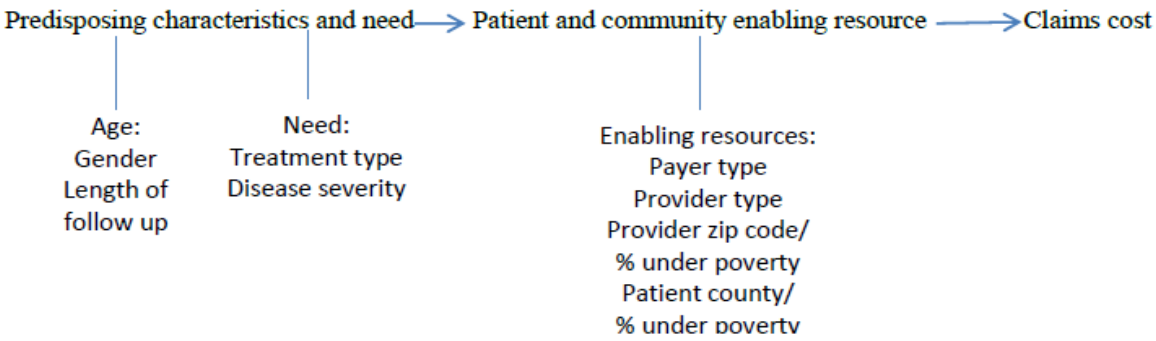
Figure 3.1.Concept Models.

Concept model 1: Predictive model of claims cost; specific aims 1 and 2

The model will be repeated for each cost criterion



Concept model 2: Differential influence on claims cost of patient and community resources over and above patient predisposing characteristics and need for services; specific aim 3



3.2. Data.

The Wisconsin Health Information Organization (WHIO) is a state-wide collaboration of insurance companies, health care providers, large employers and public agencies (www.wisconsinhealthinfo.org). Starting in 2005, this group developed a State-level database of health insurance claims in order to provide data useful for examining health care issues related to quality, efficiency and safety within the State of Wisconsin. Access to the data is available through the *Wisconsin Health Information Organization Health Analytics Exchange* (WHAE), a data base reporting system covering more than 247.6 million insurance claims for care to roughly 3.8 million Wisconsin residents. The exchange began collecting data in 2008 and provides access to a rolling 27 months of data; a total of 23.1 million episodes of care. Version 6 of the data mart (DMV6) contains information for approximately 64.9% of the Wisconsin population. Commercial claims represent 42% of the total, 25% are Medicaid FFS claims, 20% are Medicaid HMO claims and 13% are Medicare claims. Additional detail regarding the DMV6 data is provided in Appendix A.

The WHIO Health Analytics Exchange reporting system is designed for health care organization use, not specific to research, therefore limiting the types of research possible. For the purposes of this study, the Wisconsin Medical Society (WMS) provided a core data set of all insurance claims for all patients with a diagnosis code of leukemia and lymphoma, DRG 200-208, in the DMV6 data. Due to its size, the WMS data file was filtered to include only acute leukemia diagnoses. Additional variables were obtained directly from the WHAE reporting system. A relational database was created in Microsoft® Access 2010 and all variables were merged by patient ID to create the final

study dataset. The study dataset was transferred to SAS 9.3, © SAS Institute, Inc., for data analysis.

3.3. Sample.

The study sample consists of WHIO database patients with a diagnosis of acute myeloid leukemia (AML) or acute lymphoblastic leukemia (ALL) coded at any time within the DMV6 data base. The WHIO-DMV6 datamart includes a population of patients with claims submitted between the dates 4/1/2009 and 6/30/2011. The initial dataset contained patients with any leukemia or lymphoma diagnosis which was further filtered to the specific diagnosis of acute AML and ALL. Table 3.1 provides the description and diagnosis codes for this sample.

Table 3.1. Lymphoma and Leukemia Diagnosis Codes.

DRG code description	Surgical code	Medical code
Lymphoma and leukemia without major O.R. procedure with mcc	820	
Lymphoma and leukemia with major O.R. procedure with cc	821	
Lymphoma and leukemia with major O.R procedure without cc/mcc	822	
Lymphoma and leukemia without major O.R. procedure with mcc		834
Lymphoma and leukemia without major O.R. procedure with cc		835
Lymphoma and leukemia without major O.R. procedure without cc/mcc		836

CC-complications
MCC-major complications

The datamart tracks patients by claims received and uses episode treatment groups or ETG's (Table 3.2) that assign claims to both a specific diagnosis as well as a specific time of the event. Patients can be assigned up to three diagnoses in each episode of care and are included in the study if an acute leukemia diagnosis was present. Service types are used to identify where the cost was generated, i.e. inpatient, outpatient, ancillary, professional or pharmacy.

Table 3.2.Episode Treatment Group-ID; Leukemia Episode Treatment Group.

ETG type	ETG-ID
Leukemia without surgery	85
Leukemia with surgery	86
Leukemia with active management without surgery	87
Leukemia with active management with surgery	88

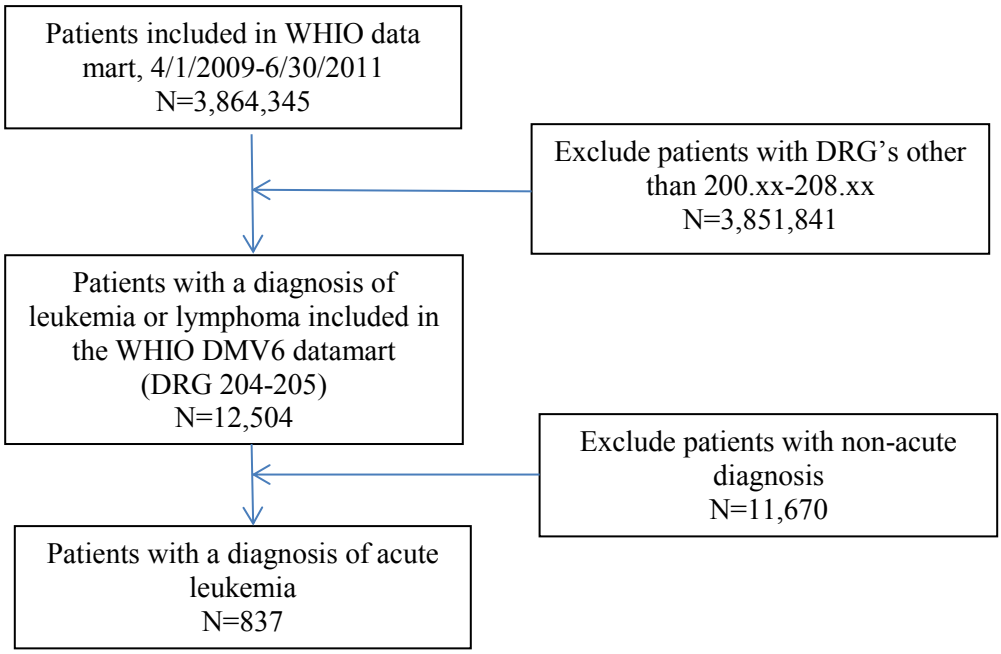
The DMV6 data set provided claims for 12,504 unique patients with a lymphoma or leukemia DRG as the primary, secondary or tertiary diagnosis. A further filter for the acute leukemia ICD-9 codes identified a sample of 837 unique patients with a diagnosis of acute lymphoblastic or acute myeloid leukemia. (Table 3.3)

Table 3.3.ICD-9 CM Code for Acute Leukemia

Diagnosis	ICD-9 CM code
Acute lymphoblastic leukemia	204.xx
Acute myeloid leukemia	205.xx

The flow chart identifying datamart patients with acute leukemia is provided in Figure 3.2.

Figure 3.2. Flow Chart of Acute Leukemia.



3.4. Variables.

Variables that were reviewed for inclusion into the study models are listed in Table 3.4. Model variables are included based on their potential influences on healthcare cost on the patient and community level as well as their availability in the datamart. Healthcare outcomes are known to be influenced by patient and disease related along with treatment related factors. However, a limitation of the WHIO datamart is that it does not provide data specifically related to clinical outcome and the variables used in this study are limited to those available within the datamart. Patient age and gender are included; unfortunately race is not available in the data base and cannot be included in

the analysis. All study variables are assessed for their potential influence on healthcare cost through a review of prior literature. Each variable has been reviewed for definition within the database, availability and redundancy. Overall availability and completeness of a variable has been assessed for its impact and usefulness for the study.

3.5. Measurement.

3.5.1. Criterion variable: cost.

The criterion variable, cost, is defined by total cost, ancillary cost, inpatient cost, outpatient cost, pharmacy cost and professional cost. Cost data for the study is available in two ways: (1) Cost of service billed, defined as provider charges; and (2) Standard cost, defined through a standard pricing methodology that attempts to smooth out cost differences caused by factors such as contractual agreements and region. Because this study is interested in both patient and community perspective the cost of services billed and the standard cost will be modeled in the analysis. The claims cost criterion is defined as a diagnosis-specific cost and represents all claims received for a patient where an acute leukemia diagnosis code has been used for any of the three diagnoses codes in the WHIO datamart. All costs used in the study are associated with insurance claims and will be referred to simply as 'cost'.

3.5.2. Predictor variables.

3.5.2.1. Predisposing characteristics

Patient predisposing characteristics predictor variables of cost are defined as (1). Patient age (i.e., age recorded in the datamart); (2) Patient gender (i.e., gender recorded in

the datamart); and (3) Length of follow up (i.e., calculated as the difference in the number of days between the start of service date and end of service date).

Age has been linked to better outcomes in a number of studies. (Deschler and Lubbert, 2006; Lee, et.al, 2000, Saito, Zahrieh, Cutler, Ho, Soiffer, Alyea & Lee, 2007) It has also been attributed to higher healthcare costs, with increasing age is associated with increasing costs, particularly in diseases prevalent in an older population. Other studies have shown a gender difference in use of health care services, with females having a higher utilization rate, and subsequently, higher cost. (Bertakis, Azari, Helms, Callahan & Robbins, 2000)

Because this is a point in time sample, length of follow up variable is included in the regression model to control for differences in patient follow up within the datamart. Datamart differences in follow up may occur due to a variety of unrelated causes, for example, death, loss of insurance, movement out of the region or a late occurrence in the datamart. (Diehr, Yanez, Ash, Hornbrook & Lin, 1999) This is not a patient characteristic but the variable is grouped as a predisposing characteristic in order to control for the inherent differences in follow up present in the data. A relationship to the need for resources group was explored but rejected due to the sample's unknown underlying differences in cause.

3.5.2.2. Patient Need.

Patient need level predictor variables include: (1) Treatment type (i.e., defined as chemotherapy only or chemotherapy plus HCT; and (2). Episode severity level (i.e.,

ranked from 1-4 with 1=low severity, 2=low/medium severity, 3=medium/high severity and, 4=high severity).

Treatment of disease as well as disease severity level has the potential for significant influence on both clinical outcome and cost and is well documented in the literature. (Ashfaq, et.al, 2010, Cordonnier, et.al, 2005, Jacobs et.al, 2000, Yu, et.al, 2006) Treatment type will be defined as chemotherapy plus allogeneic and autologous HCT or chemotherapy only. Severity is calculated per episode of treatment and utilizes the patient's comorbidities, prior healthcare use and prior types of services known in the datamart. Calculations for severity level are provided in Appendix E.

3.5.2.3. Enabling resources

Enabling resources predictor variables include: (1) Patient county percent under poverty (i.e., defined by the ZIP code of patient's County and the corresponding U.S. census reported % of residents from that county with income below poverty line and the US census reported % below poverty line); (2) Payer type (i.e., defined by public payer or private payer); (3) Provider type (i.e., defined by academic medical center or non-academic medical center); and (5) Provider percent under poverty (i.e., defined by the ZIP code of provider location and the corresponding U.S. census reported % below poverty line).

The percent under poverty variable is used to assess individual level socioeconomic effects. Clegg and colleagues reported a higher rate of late-stage cancer diagnoses with lower socioeconomic status (Clegg, et.al, 2009). In 2009 study of HCT outcomes, Baker and colleagues found low income patients , i.e. <$36,400, had lower

probability of overall survival and higher probability of treatment related mortality when compared to higher income patients , i.e >$56,000, (Baker, Davies, Majhail, Hassebroek, Klein, Ballen, Bigelow, Frangoul, Hardy, Bredeson, Dehn, Friedman, Hahn, Hale, Lazarus, LeMaistre, Lobreiza, Maharaj, McCarthy, Setterholm, Spellman, Trigg, Maziarz, Switzer, Lee, Rizzo, 2009). While Geronimus and Bound state that U.S. census-based aggregate variables are not appropriate proxies for individual socioeconomic status, Krieger and colleagues conclude that they are meaningful measurements of area-based socioeconomics (Geonimus and Bound, 1998; Krieger, et.al, 2005). The percentage of persons living below the U.S. poverty line variable was identified as meeting the criteria for as a valid and useful socioeconomic measurement. In this study, all socioeconomic measures are area-based.

In prior behavioral health studies, payer type has been shown to impact cost through differences in hospital length of stay. (Sclar, et.al, 2008) Because HCT is generally reimbursed as a bundled payment by insurance companies, public versus private sources of reimbursement may have an impact on initial treatment cost and may impact treatment costs over time. Meropol and colleagues discuss the payer's role in reducing health care expenditures and the need to use evidence-based decision making while determining cost efficiencies (Meropol, et.al, 2009). In 2009, Kantarjian and O'Brien commented on the need to investigate the role of insurance policies in the young adolescent age group, noting the lack of coverage lending to lack of care over prolonged timeframes in this group (Kantarjian, et.al, 2009). Specific to HCT, Gajewski and colleagues identify the need for consistent provider/payer dialogue to insure payer support for and patient access to this treatment option (Gajewski, et.al, 2004).

A 2003 article of hospital cost drivers, J. Hay identifies overall economic activity of the community, price-level variation, hospital technology, hospital market and healthcare labor force as some of the factors associated with inpatient cost growth. In this study, provider type is defined as academic medical center versus not academic medical center because of the expectation that academic medical centers will have a different cost structure than community hospitals (Hayes, 2003). Yuan and colleagues conclude that while teaching not-for-profit hospitals had better clinical performance than other hospitals, they also had significantly longer length of stay (Yuan, Cooper, Einstadter, Cebul & Rimm, 2000).

Provider ZIP code and % below poverty line is included to assess a community level geographic and socioeconomic effect. Anderson's behavioral model would predict a community socioeconomic influence on the cost outcome due to access to higher levels and quantity of health care services in more affluent socioeconomic locations. The community SES measurement is based upon the location of the provider, its reported US census % of persons below the US poverty line. The provider location is determined by the reported address of the provider in the WHIO database. The study variables are listed in Table 3.4.

Table 3.4 Description of Study Variables.

Variable name	Variable type	Variable measurement	WHIO datamart variable
Leukemia diagnosis cost: 204.xx 205.xx	Criterion variable	Total Inpatient Outpatient Pharmaceutical Ancillary Professional	Cost=billed Cost=standard Service type: Ancillary=1 Inpatient=2 Outpatient=3 Professional=4 Pharmacy=7 (does not include retail pharmacy claims)
Age	Predictor variable	0-99	Age
Gender	Predictor variable	0=Male 1=Female	Gender
Length of follow up	Predictor variable	0-xxx	End date of service – Start date of service
Episode severity level	Predictor variable	1=low 2=low/medium 3=high/medium 4=high	Severity: highest level of severity coded
Treatment type	Predictor variable	0=Chemotherapy only 1=Chemotherapy and HCT	CPT code
County zip code/ county % poverty level	Predictor variable	ZIP: 5 digit character Member county % poverty: continuous ratio	ZIP code US census all people % poverty level
Payer type	Predictor variable	0=Commercial 1=Public	Payer type: public payer coded when present
Provider type	Predictor variable	0=Community provider 1=Academic medical center	Provider affiliation: academic center coded when present
Provider ZIP code/ Provider zip % poverty level	Predictor variable	ZIP: 5 digit character Provider zip code % poverty level	ZIP code US census all people % poverty level

3.6. Statistical Analyses.

Use of administrative data bases to assess questions relating to health care cost can create data analysis challenges. Because these databases are created for reimbursement rather than research, they generally have limited scope regarding detailed patient demographics, disruption in coverage, clinical outcomes and generally contain censored data.

In a 1999 article, Diehr describes methods of analysis for health care cost and utilization (Diehr, et.al, 1999). Multivariate regression is often used to identify cost predictors within groups. The authors discuss the one part model as most efficient when attempting to understand the effect of covariates on total cost because it creates a single regression coefficient for each variable and results are easily interpreted. The article provides additional detail regarding skewed cost data, differences in types of cost, adjusting for different lengths of follow up and, death and censoring. Barber and Thompson in a 2004 article discuss the use of generalized linear models (GLM) for the analyses of cost data rather than ordinary least squares (OLS) and identify the gamma, log link model as providing the best result. They identify challenges inherent in the analysis of cost data because of a typical skewed distribution and the need to use estimates of mean costs. Dodd and colleagues compared different multivariable regression models for analyzing cost data and found gamma with log link modeling provided the best result (Dodd, Bassi, Bodger & Williamson, 2006) .

This study uses recommendations from these articles to fit the best method to the sample in order to analyze the study specific aims. The final decision of the GLM

gamma log link model was made after an initial review of the study data and assessment of its fit with model assumptions. SAS 9.3 software is used to analyze the multivariate regression models all tests will be considered significant at the 0.05 level.

3.7. Complexity of Cost Data Analyses.

Analysis of cost data is complex due to the tendency of being right-skewed with long, right tails, due to; (1) The presence of large numbers of low cost events in addition to a few very high cost events; (2) The lack of negative events; (3) The higher utilization of services due to more severe diagnosis; (4) The high cost of certain types of treatment; (5) Differences in follow up; and (6) Some patients utilize health services at a greater rate and are responsible for a higher proportion of heath care cost (Dodd, Bassi, Bodger, Williamson, 2006; Barber & Thompson, 2004; Basu & Manning, 2009; Lin, 2000).

Estimates that are meaningful and easy to interpret are preferred by decision makers. In economic or policy evaluation they will often rely on the differences in mean costs and whether the differences in the means between groups are statistically significant. However, the use of arithmetic mean healthcare costs can be misleading due to the underlying nature of the data. Highly skewed data will have medians that greatly differ from the means. Barber and Thompson, 2004, describe the generalized linear models (GLMs) as useful for regression of cost models due to their flexible methods for the analysis of mean costs, the allowances for non-normal data distributions and the ease of interpretation of the results.

3.8. Generalized Linear Model (GLM).

Using Ordinary Least Squares (OLS) regression with cost data is problematic due to the non-normality of the data's distribution which can result in a bias that may predict negative costs. The calculation of a log transformed outcome variable can solve the non-normal distribution problem but provides a result that is difficult to interpret given that log transformed OLS estimates are differences in the transformed log cost, an outcome that is not of interest. Generalized Linear Models (GLM) have been recommended for the analysis of cost data because they allow the advantages of a log link in the model but the differences in the mean outcome is estimated directly and statistical inferences are easier to interpret (Neal & Simons, 2007; Manning & Mullahy, 2001; Dodd, et.al, 2006; Basu, 2005; Manning & Mullahy, 2002).

GLM's are extensions of traditional linear models but characterize data through a link function (g) and a distribution family (F). In a GLM the mean of the sample relates to a linear predictor through a nonlinear link function and the criterion probability distribution conforms to an exponential family of distributions. A GLM link function, such as log, logit, identity and inverse, characterizes the relationship of the raw untransformed criterion scale to the predictors, i.e. the relationship between the predictors and the mean criterion response variable. The GLM family specifies the criterion distribution that reflects the mean-variance relationship where:

Gaussian = constant variance

Poisson = variance is proportional to the mean

Gamma = variance is proportional to the square of the mean

Inverse Gaussian or Wald = variance is proportional to the cube of the mean

GLM's can have a variety of forms but the general form is:

$$g(\mu_i) = x_i\beta_i + e,\ y_i \sim F,$$

where μ_i is the expected mean value from the model, β_i, are the regression coefficients, *e* is the error and F represents the models distribution function. The criterion variable (Y_i) is independent and has a probability distribution from an exponential family. GLM accommodates skewed data through variance weighting of the criterion variable rather than transformation. The variance of the criterion depends on the mean through a variance function V:

$$var(Y_i) = \phi V(u_i)/w_i,$$

where ϕ is a constant and *w* is a known weight for each observation. If the weight is unknown, it is estimated. Fitted generalized linear models are summarized through parameter estimates, standard errors, goodness-of-fit statistics, confidence intervals and hypothesis tests (Basu, 2005; Manning & Mullahy, 2001).

3.8.1. GLM gamma log link model.

GLM's fit the needs of health care cost analysis because of a focus on criterion means and flexibility in the selection of the distribution family. Literature comparing the best GLM for use in health economic analysis routinely selects the gamma log link model as a candidate for providing the best fit for health care cost data. (Dodd et.al, 2006; Barber & Thompson, 2004) The gamma model is generally used with continuous and

non-negative response variables and assumes the constant coefficient of variation that is often found in cost data.

Log transformation can be sometimes used to normalize cost data. The GLM log link model assumes:

$ln(E(y/x)) = X\beta;$ the relationship of the predictors to the log of the estimated criterion mean cost.

The gamma family of distribution assumes variance, V, is proportional to the square of the mean, μ^2:

$$V(\mu) = \mu^2, \text{ or } V(y/x) \text{proportional to } [E(y/x)]^2, \text{ or}$$

$$V[y/x] = \alpha[E(y/x)]^{\lambda},$$

where α is the shape of the parameter and λ is the specific distribution model (family) used in the GLM.

The λ gives the family distribution:

$\lambda = 0$ Gaussian

$\lambda = 1$ Poisson

$\lambda = 2$ Gamma

$\lambda = 3$ Inverse Gaussian or Wald

The appropriate use of the gamma model in this study is tested through the modified Park's test for the variance of each cost outcome. (Manning & Mullahy, 2001) The modified Park's test is defined as:

$$ln(Y_i - \hat{Y}_i) = \lambda_0 + \lambda_1 ln(\hat{Y}_i) + e_i,$$

where ln(Yi – Ŷi) is the natural log of the raw residuals squared, ln(Ŷi) is the natural log of the predicted Y_i, λ_0 is a constant and λ_1 is the coefficient that gives the family.

The final GLM gamma log link model can be represented as:

$$ln[E(Y_i)] = \beta_0+\beta_1X_1+\beta_2X_2+ \beta_3X_3+\ldots+\beta_kX_k; \text{ or}$$

$$E(Y_i) = exp(\beta_0+\beta_1X_1+\beta_2X_2+ \beta_3X_3+\ldots+\beta_kX_k),$$

where Y_i is the criterion variable, $E(Y_i)$ is the expected value of the criterion variable, X_k are the predictor variables and β_k are the estimated coefficients. Maximum likelihood estimation is used to calculate the parameters (β) of the model. The appropriate use of the log link in this study is assessed through the distribution curves of the raw scale variables, their residuals and the log scale variables and residuals.

3.8.2. Interpretation of the GLM gamma log link model.

In a GLM gamma log link model the relationship between the mean of the criterion variable (Y_i) and the predictor is defined as:

$$ln[E(Y_i)] = \beta_0+\beta_1X_1+\beta_2X_2+ \beta_3X_3+\ldots+\beta_kX_k; \text{ or}$$

$$E(Y_i) = exp(\beta_0+\beta_1X_1+\beta_2X_2+ \beta_3X_3+\ldots+\beta_kX_k);$$

where a change in the criterion variable is considered to be proportional to a change in the predictor variable. Interpretations can be described as:

> A 1 unit change in X_1 would change the mean of Y_i by a factor of $\exp(\beta_1)$ or e^{β}_1 or changing X_2 from 0 to 1 would change the mean of Y_i by a factor of $\exp(\beta_2)$ or e^{β}_2.

The model does not hold the other variables fixed and variable changes adjust for the contributions of all other variables in the model.

In this study,

> $e^{\beta} > 1$ when $\beta > 0$ and indicates increasing cost,
>
> $e^{\beta} < 1$ when $\beta < 0$ and indicates decreasing cost and,
>
> $e^{\beta} = 1$ when $\beta = 0$ and indicates no change in cost

The hypothesis being tested is:

> H_0: $e^{\beta} = 1$
>
> H_1: $e^{\beta} \neq 1$,

and tested with a Wald chi-squared statistic at $\alpha = 0.05$ level of significance.

3.9. Study Regression Models.

Two types of regression models will be tests: (1) An overall predictive model of study variables; and (2) A hierarchical model.

1. Predictive model of study variables:

1. $Y_{Totalcost}=\beta_0+\beta_1 length\ of\ follow\ up+\beta_2 age+\beta_3 gender+\beta_4 treatmenttype+\beta_5 severity+\beta_6 cty\%bp+\beta_7 payertype+\beta_8 providertype+\beta_9 pro\%bp+e$

2. $Y_{Ancillarycost}=\beta_0+\beta_1 length\ of\ follow\ up+\beta_2 age+\beta_3 gender+\beta_4 treatmenttype+\beta_5 severity+\beta_6 cty\%bp+\beta_7 payertype+\beta_8 providertype+\beta_9 pro\%bp+e$

3. $Y_{Inpatientcost}=\beta_0+\beta_1 length\ of\ follow\ up+\beta_2 age+\beta_3 gender+\beta_4 treatmenttype+\beta_5 severity+\beta_6 cty\%bp+\beta_7 payertype+\beta_8 providertype+\beta_9 pro\%bp+e$

4. $Y_{Outpatientcost}=\beta_0+\beta_1 length\ of\ follow\ up+\beta_2 age+\beta_3 gender+\beta_4 treatmenttype+\beta_5 severity+\beta_6 cty\%bp+\beta_7 payertype+\beta_8 providertype+\beta_9 pro\%bp+e$

5. $Y_{Pharmacycost}=\beta_0+\beta_1 length\ of\ follow\ up+\beta_2 age+\beta_3 gender+\beta_4 treatmenttype+\beta_5 severity+\beta_6 cty\%bp+\beta_7 payertype+\beta_8 providertype+\beta_9 pro\%bp+e$

6. $Y_{Professionalcost}=\beta_0+\beta_1 length\ of\ follow\ up+\beta_2 age+\beta_3 gender+\beta_4 treatmenttype+\beta_5 severity+\beta_6 cty\%bp+\beta_7 payertype+\beta_8 providertype+\beta_9 pro\%bp+e$

2. A two-step hierarchical regression model will test the effect of community and patient enabling variables above and beyond the effect of patient predisposing characteristics and need variables.

Hierarchical entry 1: Cost ~ length of follow up, age, gender, treatment type, severity.
Hierarchical entry 2: Cost ~ length of follow up, age, gender, treatment type, severity, cty%belowpoverty, payer type, provider type, pro%belowpoverty.

3.10. Study Power and Sample Size.

In the 4th edition of *Using Multivariate Statistics*, Tabachnick and Fidell advise to attain the best result through the use of the fewest variables (Tabachnick and Fidell, 2001). Their list of consideration for variable use include cost, availability, meaning and theoretical relationships. This study primarily relies on theoretical relationships identified in prior research to select the variables. Given the economic perspective of the study and the expected small sample size due to the rarity of the disease, the number of variables identified for the analysis has been kept to a minimum.

An online sample size and power calculator was used and a calculated sample size of 113 was identified as necessary to provide power of 0.80, assuming an alpha of .05, anticipated effect of 0.15 (medium effect, Cohen, 1982).

(http://danielsoper.com/statcalc3/calc.aspx?id=1)

Multivariate regression also requires that the ratio of the number of subjects to predictor variable to be substantial enough for the solution to be meaningful. Again, Tabachnick and Fidell provide a simple rule of thumb equation: $N \geq 50 + 8m$, where m=the number of independent variables. In this study the number of independent variables, m=9, resulting also in $N \geq 122$ and expected power to be > 80% (Tabachnick and Fidell, 2001).

The initial study dataset of identified an overall sample of 837 patients; however, due to more limited availability of provider data, the analysis sample reduced to 638. In addition, each cost criterion analysis utilizes only the data, and a corresponding sample size, associated with that stated cost. All sample sizes were reviewed and determined to

be greater than the minimum required N ≥ 122; sufficient to meet the requirement for >80% power for the analysis. (Table 3.5)

Table 3.5. Sample Size by Cost Criterion.

Criterion variable	Sample size
Total	638
Ancillary	138
Inpatient	201
Outpatient	497
Pharmacy	325
Professional	618

3.11. Study Sample Flow Charts.

The initial sample of 837 eligible patient records from the WHIO data mart is described in chapter 3 and is depicted in Figure 3.1. The sample size available for statistical analysis was dependent upon the number of patient records that were present within each cost criterion and is subsequently different for each. Power was assessed for all samples and was found to meet the minimum requirement of 80%. Statistical analysis with Generalized Linear Modeling was performed for each cost criterion. Hierarchical modeling of patient and community enabling variables over and above patient predisposing and need variables was performed for the total cost criterion only.

Figures 3.3-3.8 depict the selection flow charts for each cost. The total cost sample (Figure 3.3) loses only those patients where provider data was unavailable and includes the largest sample of 638. The professional cost sample of 618 (Figure 3.8), the

outpatient cost sample of 497, (Figure 3.6), the pharmacy cost sample of 325 (Figure 3.7) and the inpatient cost sample of 201, (Figure3.5) solidly meet the minimum sample size power requirements. The ancillary cost sample, (Figure 3.4) has the smallest group of 138.

Figure 3.3.Total Cost Sample Flow Chart.

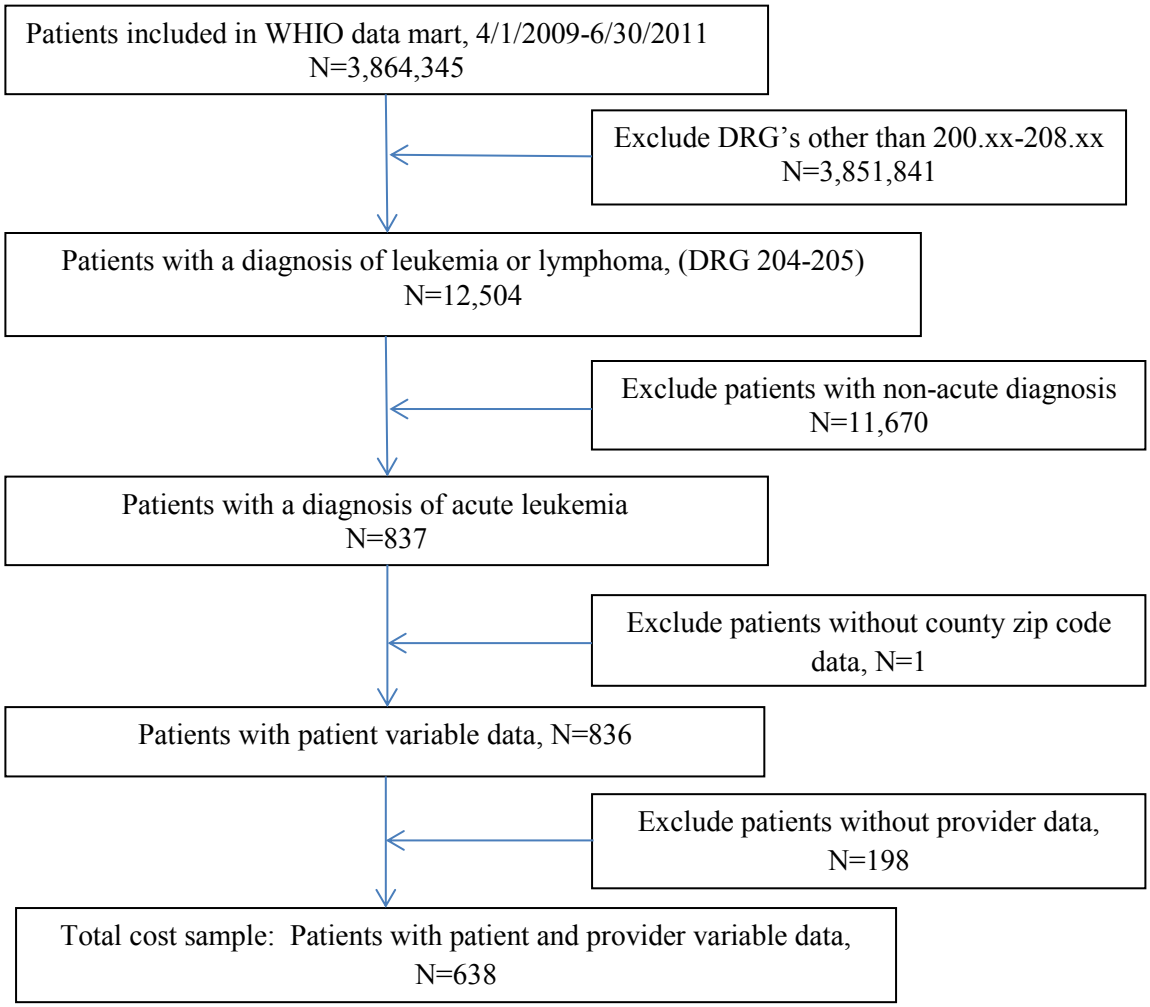


Figure 3.4.Ancillary Cost Sample Flow Chart.

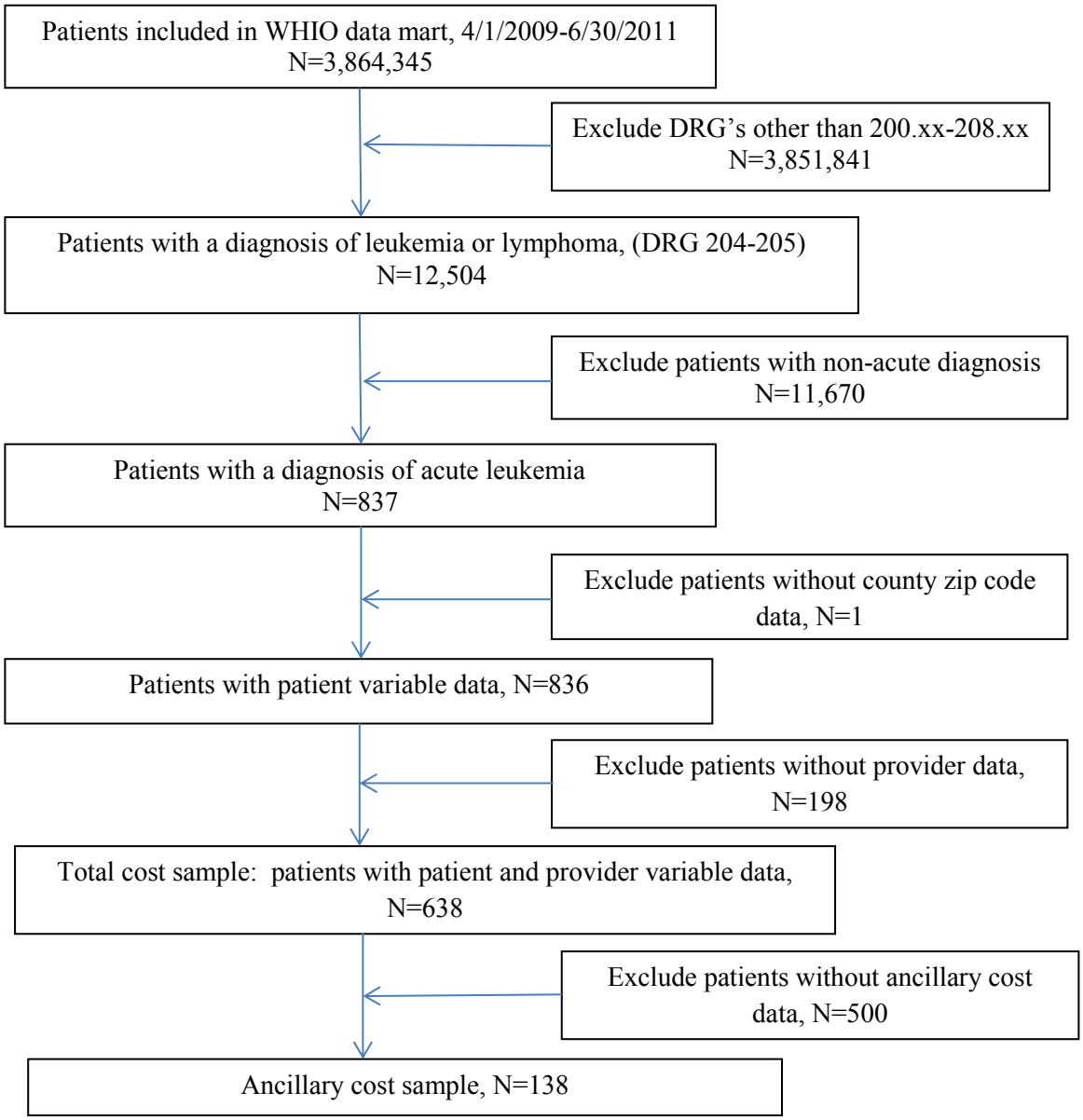


Figure 3.5.Inpatient Cost Sample Flow Chart.

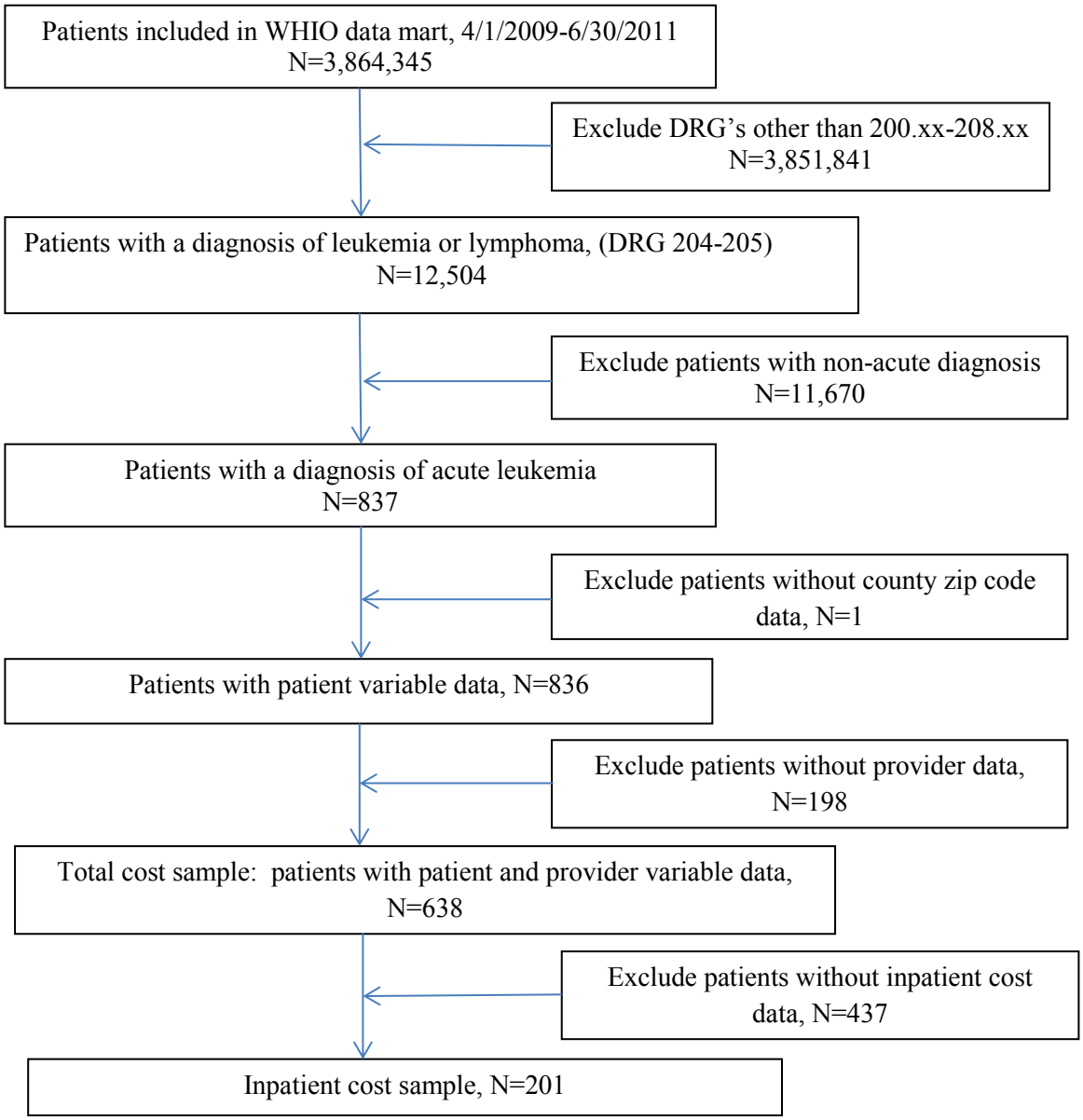


Figure 3.6.Outpatient Cost Sample Flow Chart.

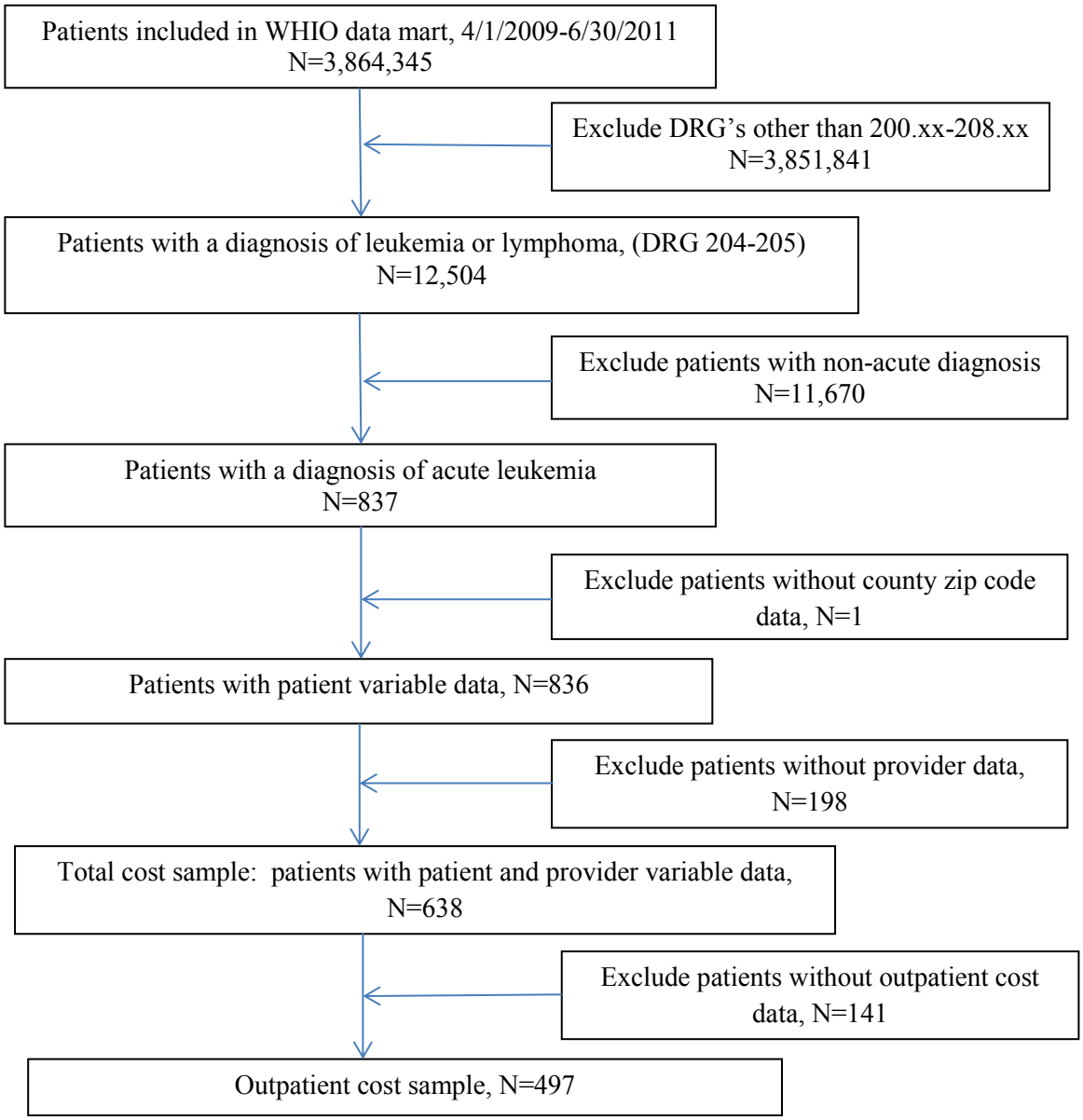


Figure 3.7.Pharmacy Cost Sample Flow Chart.

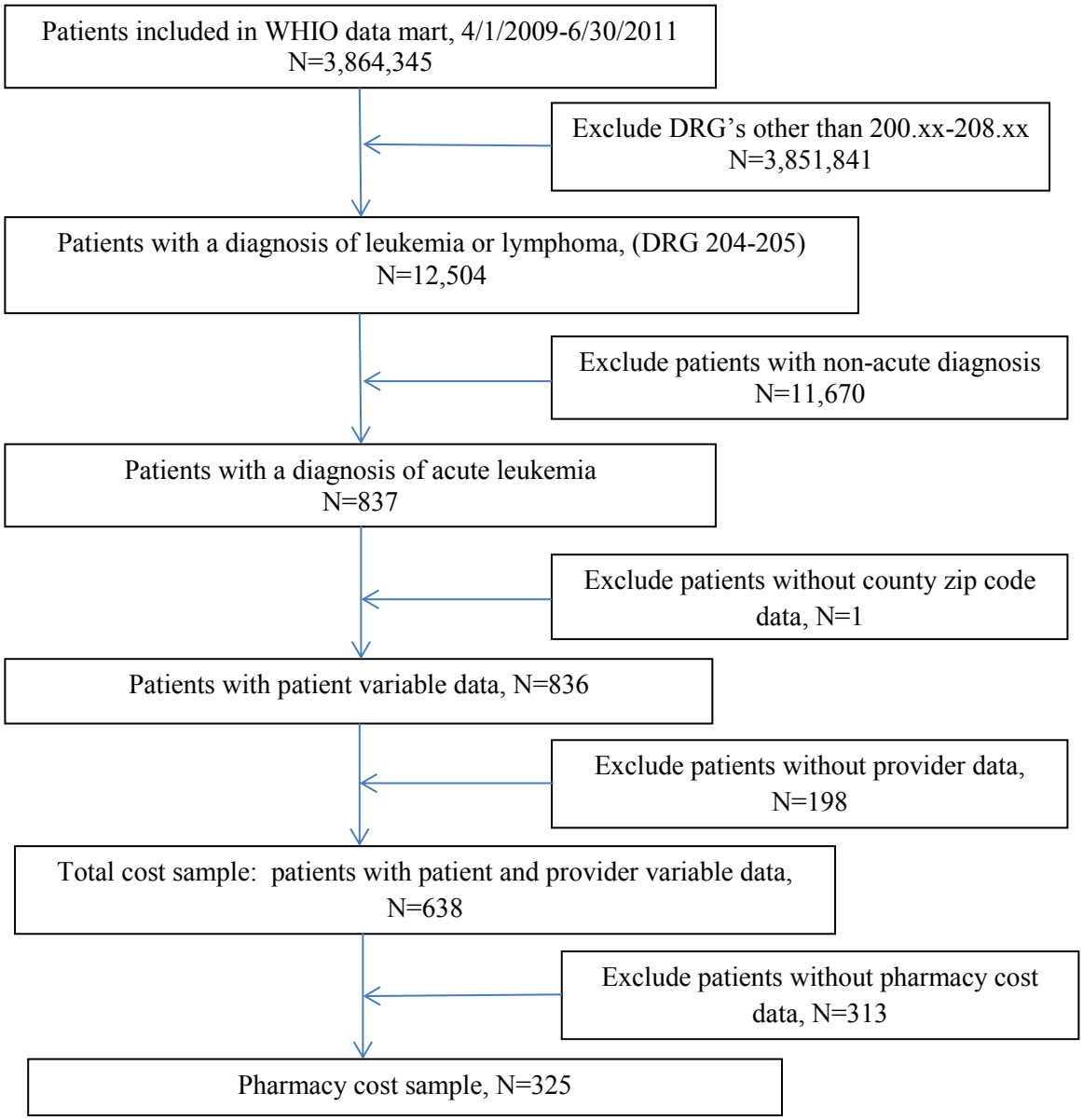
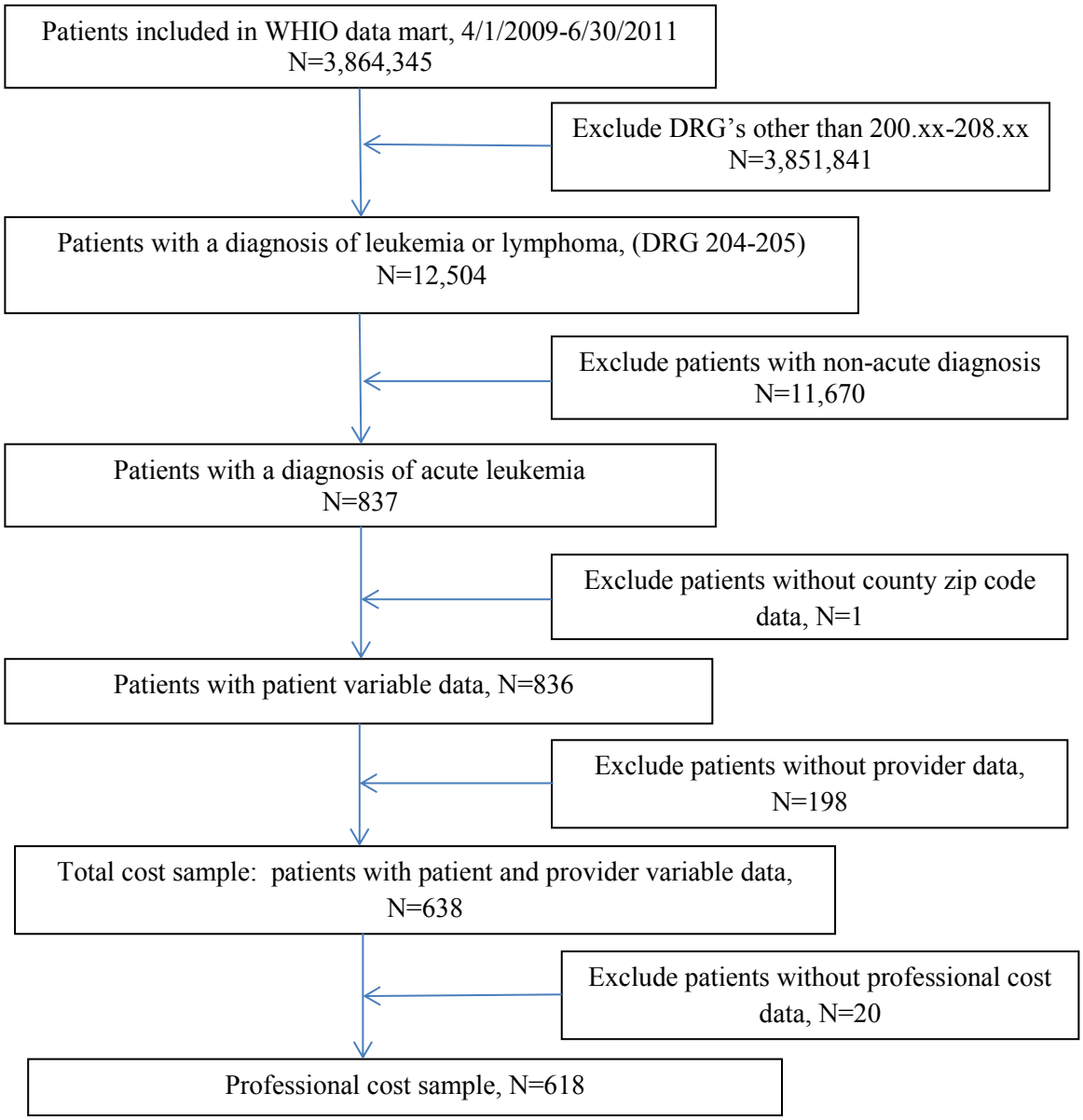


Figure 3.8.Professional Cost Sample Flow Chart.



3.12. Model Selection With Study Data.

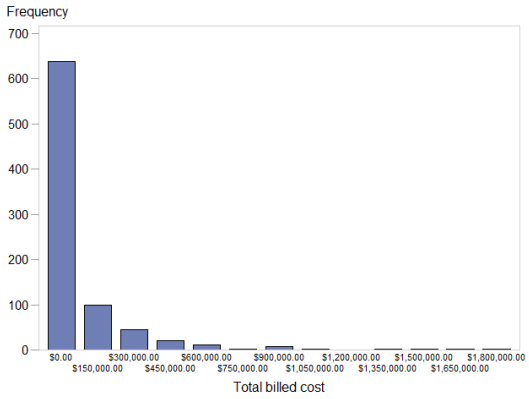
An assessment of the study data for use with a GLM gamma log link model was handled in two ways: (1) Visual inspection of both raw scale and residual scale data for use of the log link; and (2) The modified Park's test to identify the family. Prior cost research was also used to guide the decision of the best choice of model.

3.12.1. Distribution of criterion variables.

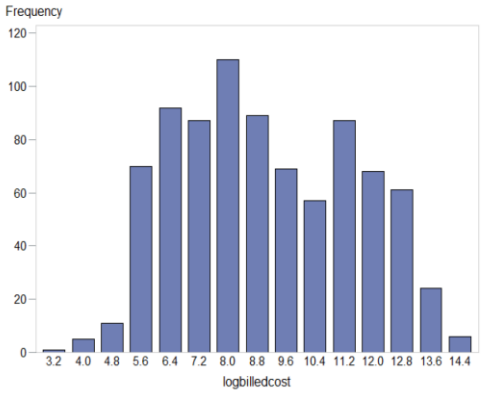
Graphical representation of the distribution of each criterion variable, for billed cost and standard cost data, are presented in Figures 3.9-3.20. The distribution of the raw scale, log raw scale, residual and log residual is provided. In each of the distributions, the raw scale and residual scale distributions indicate non-normal, positively skewed distributions that may display high kurtosis. Each of the variables maintained a consistent distribution when comparing billed cost data to standard cost data. When transformed to the log scale, some variables displayed a more normal distribution when compare to others; inpatient cost (Figure 3.13-3.14) versus pharmacy cost (Figure 3.17-3.18). In general, transformation to the log scale resulted in a closer to normal distribution and provides support for the use of the log link method.

Figure 3.9. Distribution of Total Billed Cost.

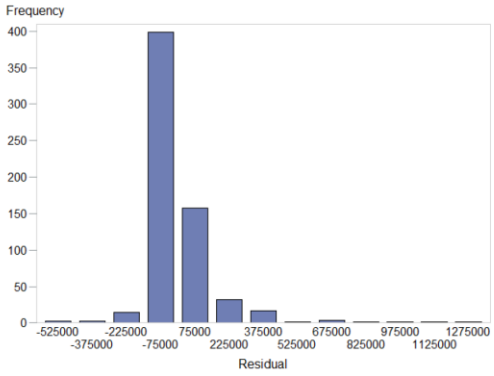
Distribution of totla billed cost



Distribution of log total billed cost



Distribution of total billed cost residual



Distribution of log total billed cost residual

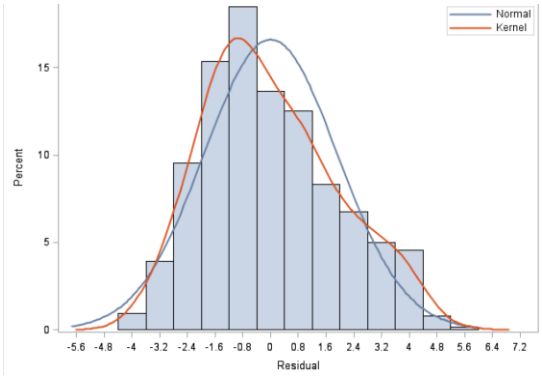
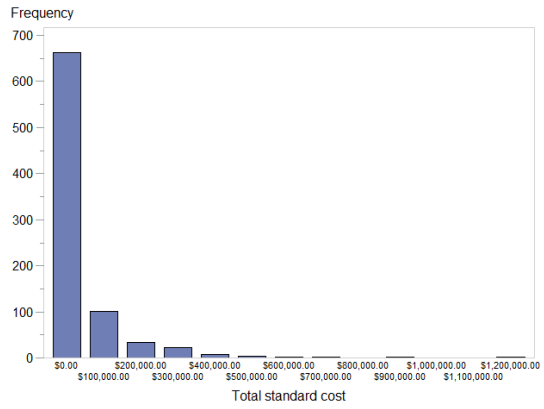
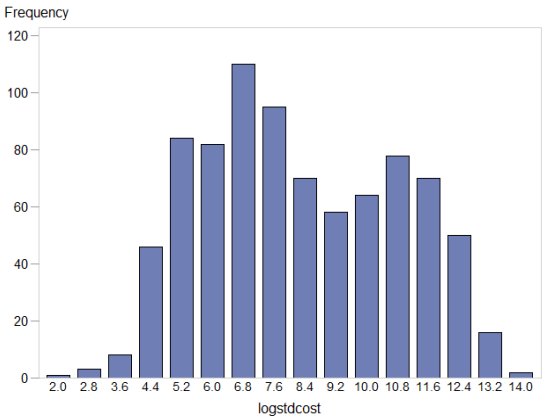


Figure 3.10. Distribution of Total Standard Cost.

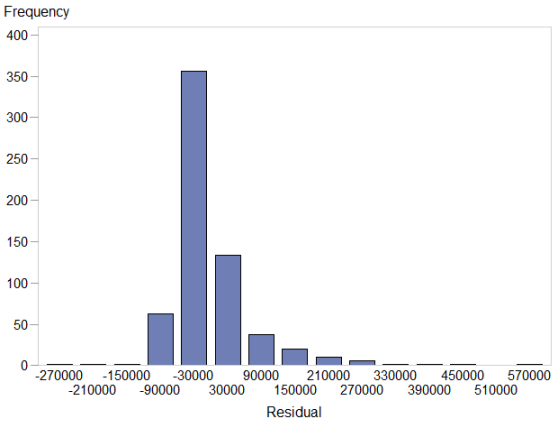
Distribution of total standard cost



Distribution of log total standard cost



Distribution of total standard cost residual



Distribution of log total standard cost residual

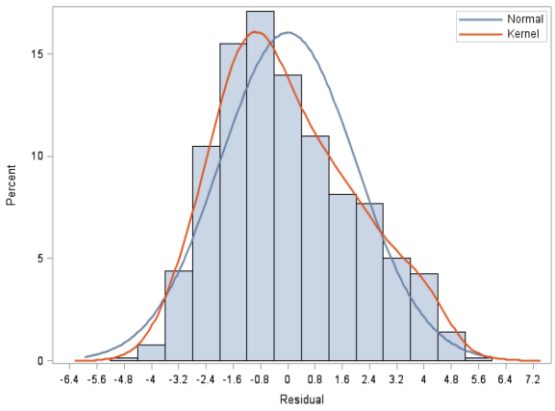
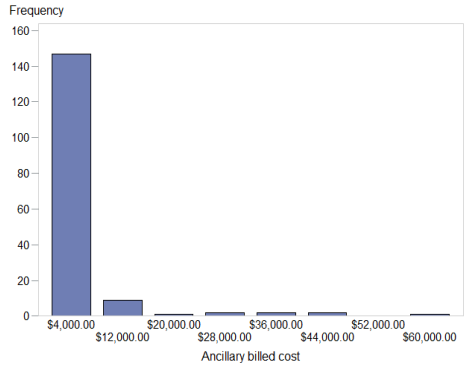
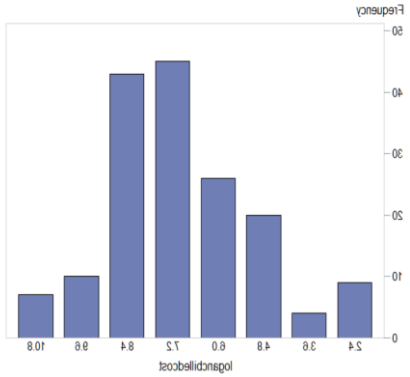


Figure 3.11 Distribution of Ancillary Billed Cost.

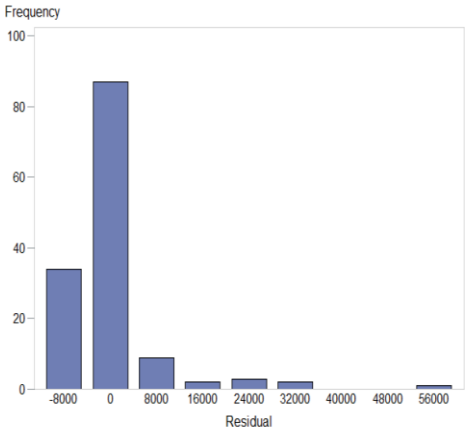
Distribution of ancillary billed cost



Distribution of log ancillary billed cost



Distribution ancillary billed cost residual



Distribution of log ancillary billed cost residual

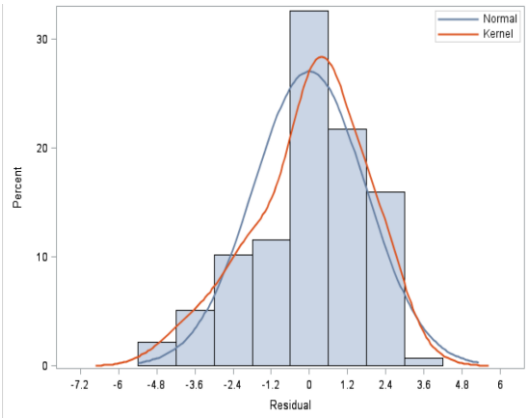
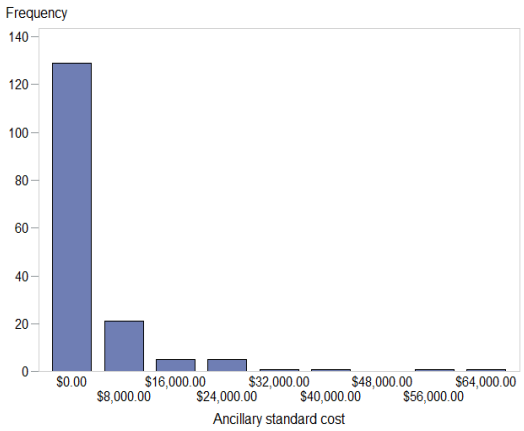
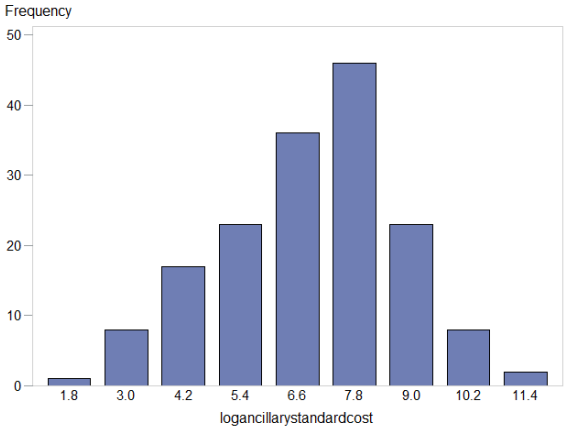


Figure 3.12. Distribution of Ancillary Standard Cost.

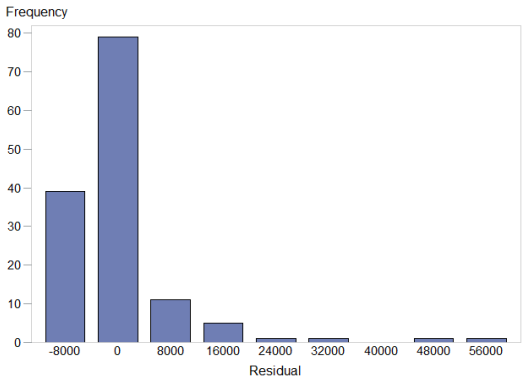
Distribution of ancillary standard cost



Distribution of log ancillary standard cost



Distribution of ancillary standard cost residual



Distribution of log ancillary std cost residual

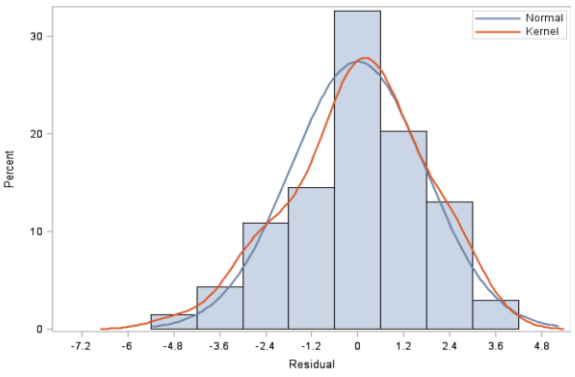
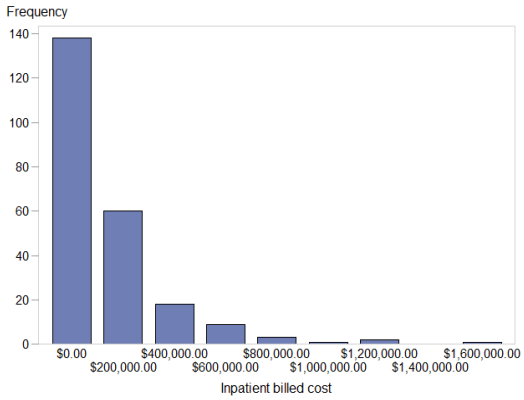
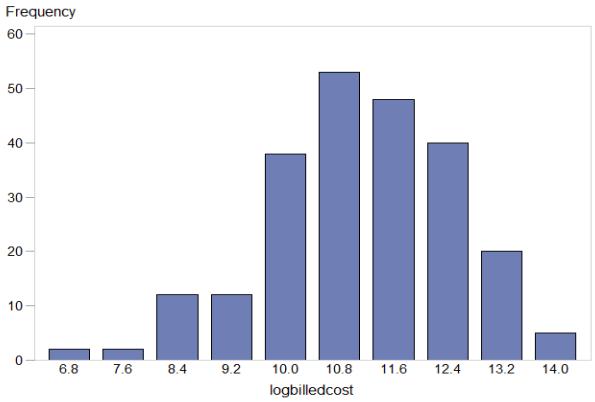


Figure 3.13. Distribution of Inpatient Billed Cost.

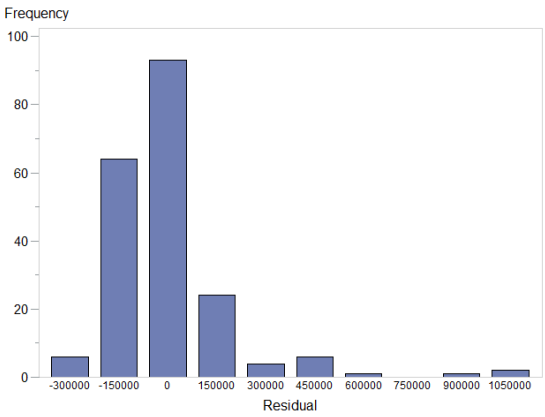
Distribution of inpatient billed cost



Distribution of log inpatient billed cost



Distribution of inpatient billed cost residual



Distribution of log inpatient billed cost residual

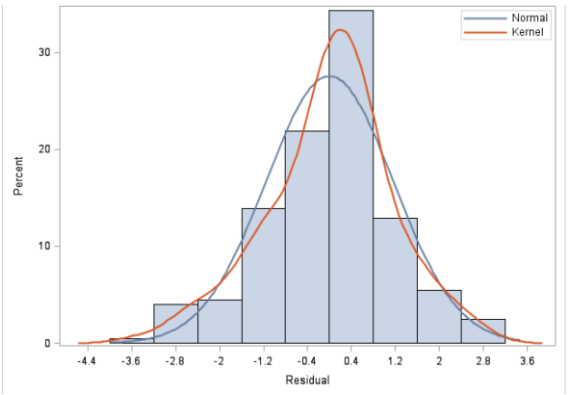
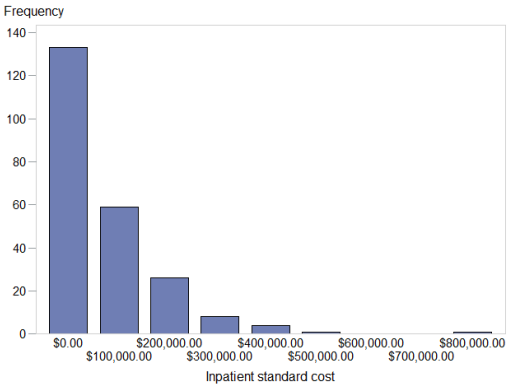
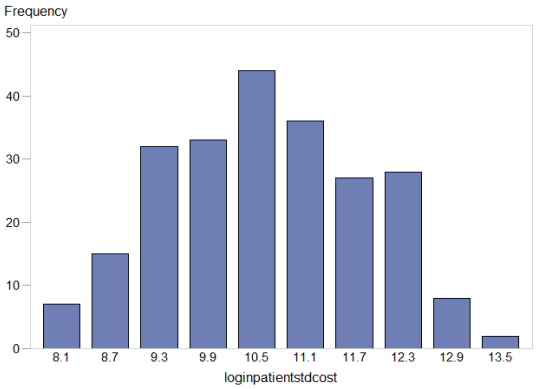


Figure 3.14.Distribution of Inpatient Standard Cost.

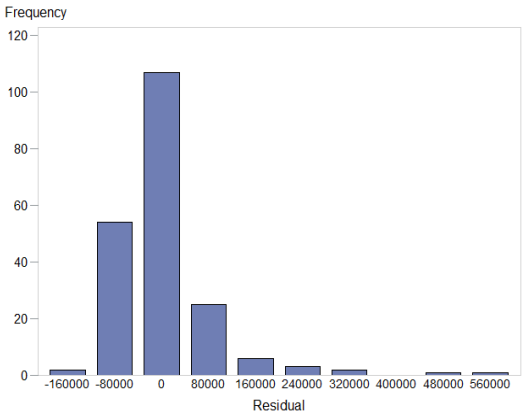
Distribution of inpatient standard cost



Distribution of log inpatient standard cost



Distribution of inpatient standard cost residual



Distribution of log inpatient std cost residual

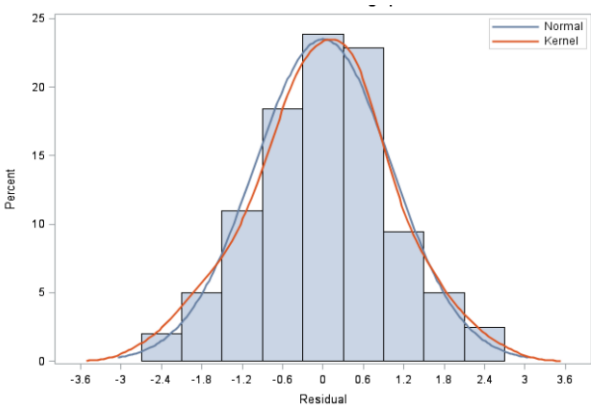
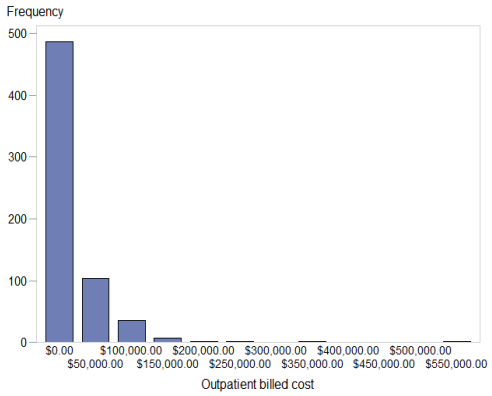
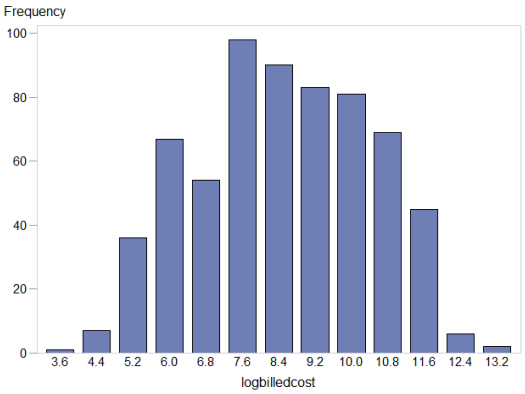


Figure 3.15. Distribution of Outpatient Billed Cost.

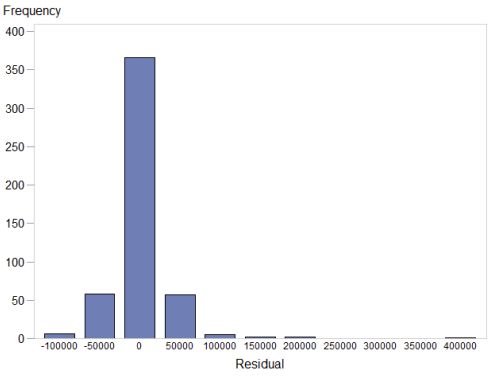
Distribution of outpatient billed cost



Distribution of log outpatient billed cost



Distribution of outpatient billed cost residual



Distribution of log outpatient billed cost residual

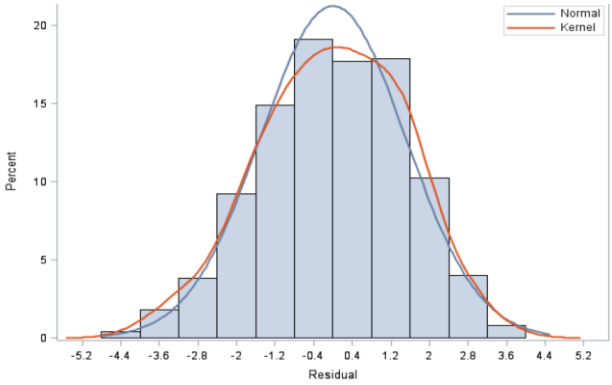
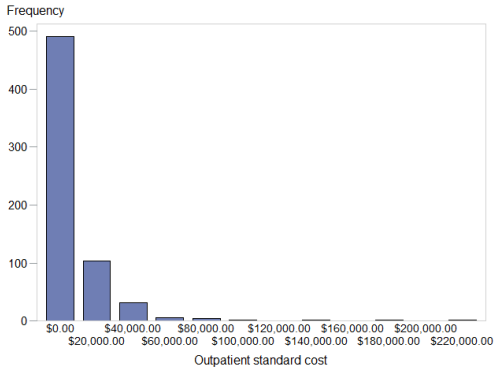
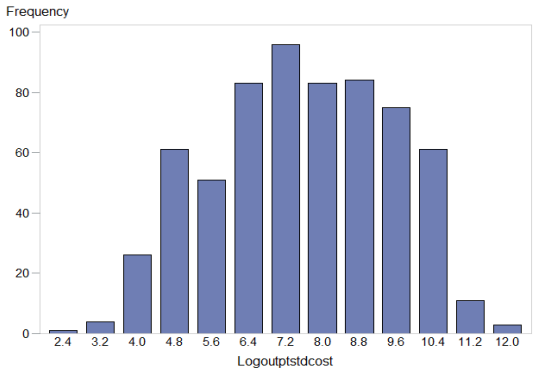


Figure 3.16. Distribution of Outpatient Standard Cost.

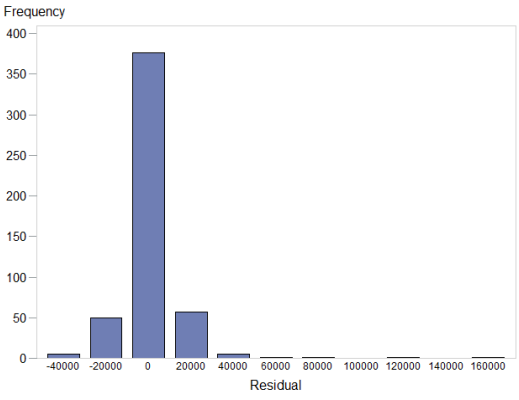
Distribution of outpatient standard cost



Distribution of log outpatient standard cost



Distribution of outpatient cost std residual



Distribution of log outpatient std cost residual

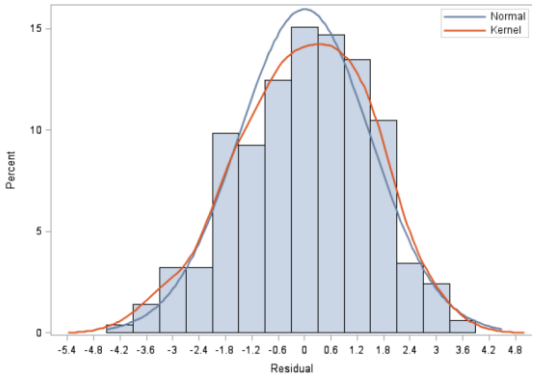
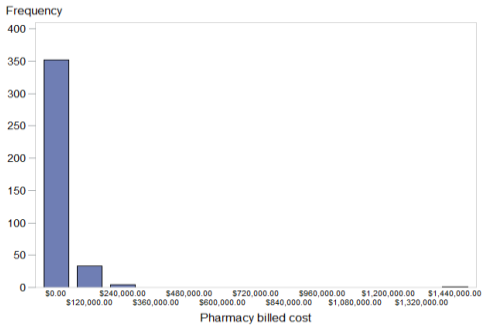
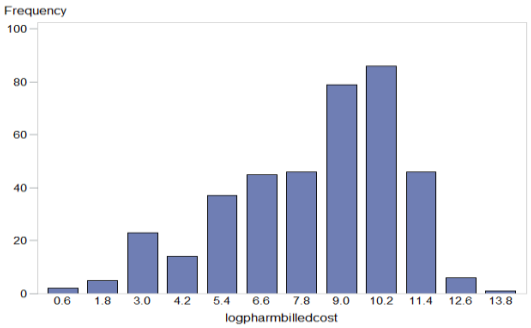


Figure 3.17. Distribution of Pharmacy Billed Cost.

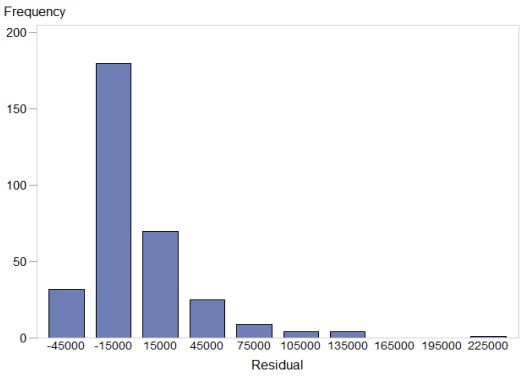
Distribution of pharmacy billed cost



Distribution of log pharmacy billed cost



Distribution of pharmacy billed cost residual



Distribution of log pharmacy billed cost residual

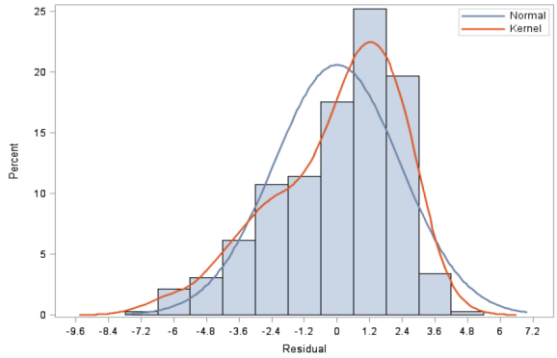
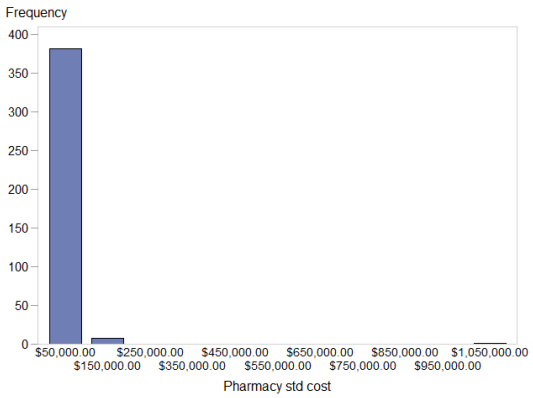
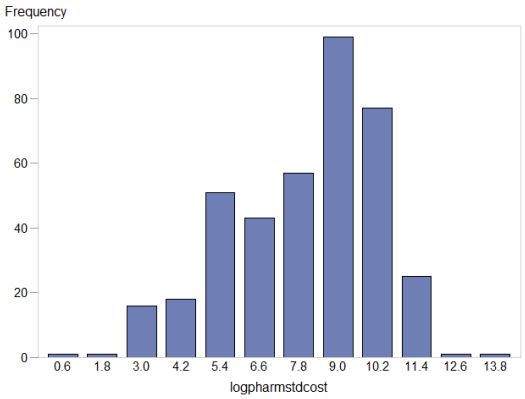


Figure 3.18. Distribution of Pharmacy Standard Cost.

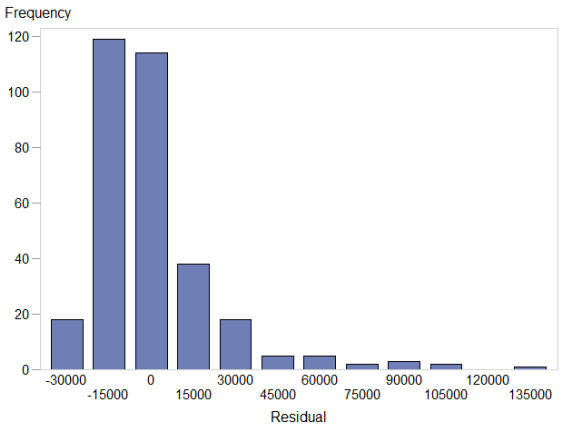
Distribution of pharmacy standard cost



Distribution of log pharmacy standard cost



Distribution of pharmacy std cost residual



Distribution of log pharmacy std cost residual

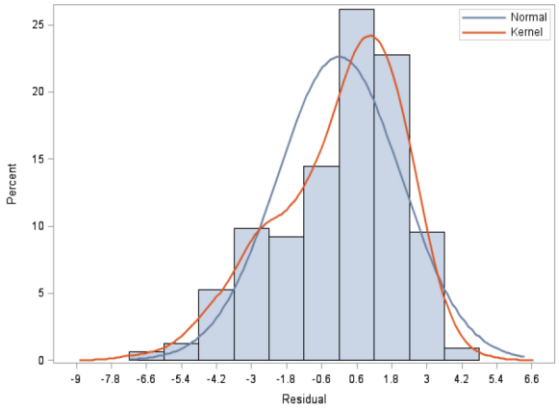
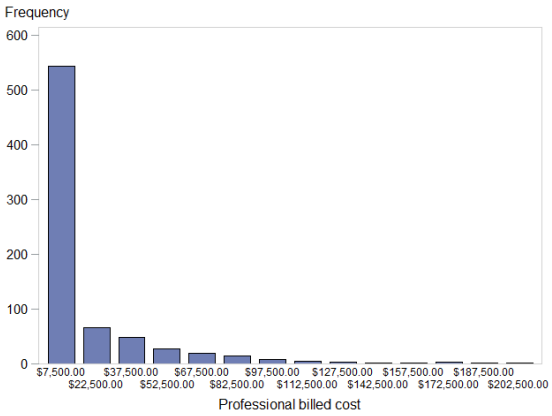
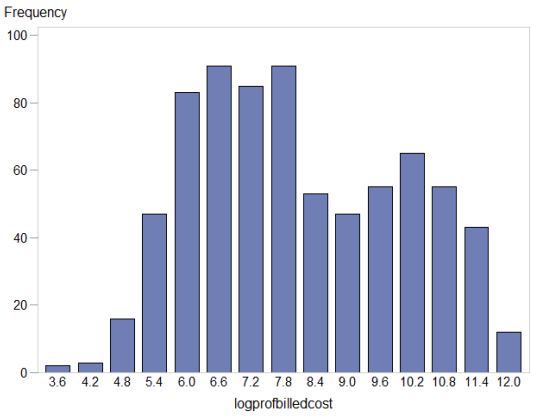


Figure 3.19. Distribution of Professional Billed Cost.

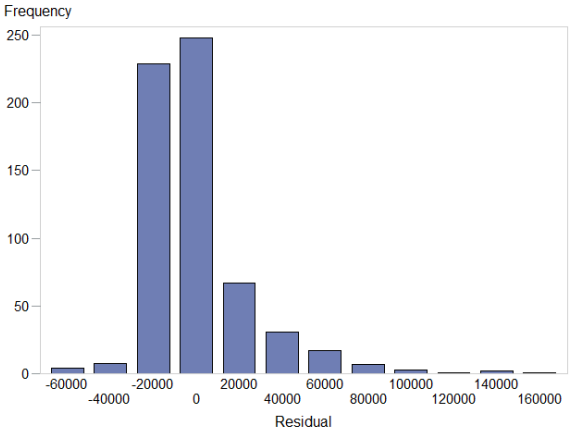
Distribution of professional billed cost



Distribution of log professional billed cost



Distribution of professional billed cost residual



Distribution of log professional billed residual

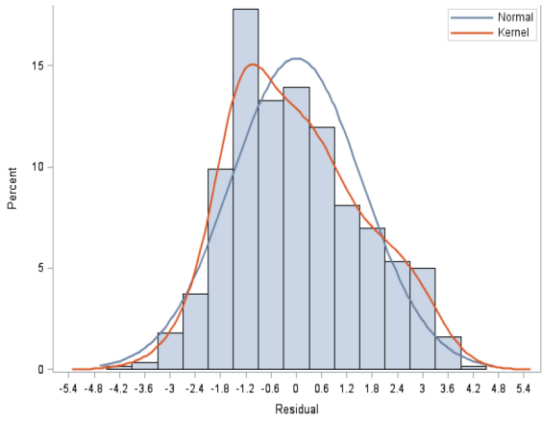
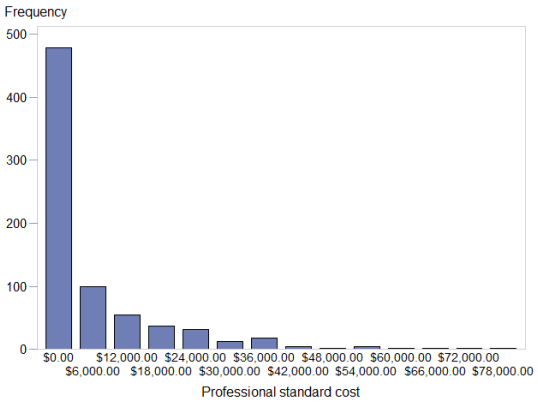
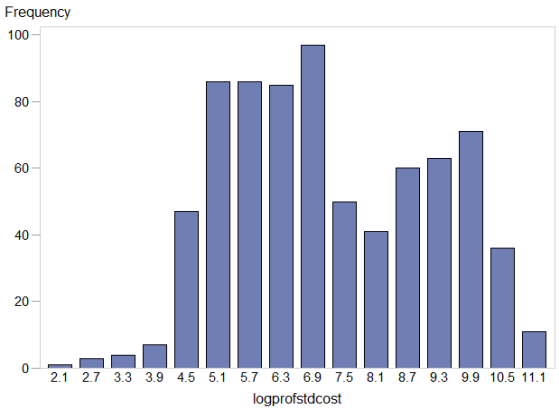


Figure 3.20. Distribution of Professional Standard Cost.

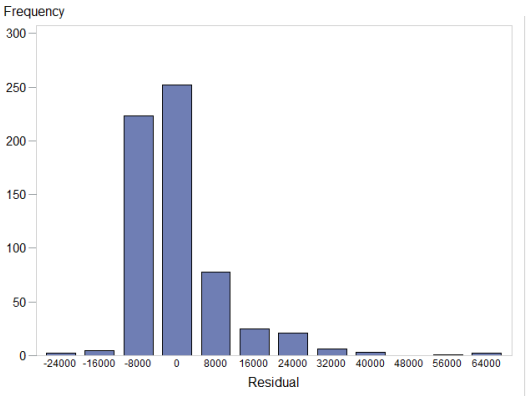
Distribution of professional standard cost



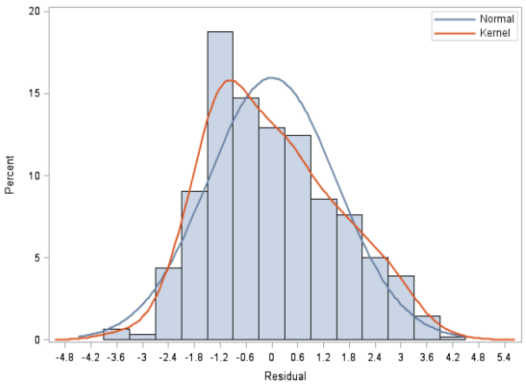
Distribution of log professional standard cost



Distribution of professional std cost residual



Distribution of log professional std cost residual



3.12.2. Results of the Modified Park's Test for Family Distribution of Criterion Variables.

Results from the modified Park's test to determine the family distribution of the criterion variables are presented in Table 3.6. The test results were somewhat inconclusive, with a λ ranging between 1.2 for standard outpatient cost and 2.0 for billed ancillary cost. With these results either a gamma distribution or a Poisson distribution would seem to be the most appropriate choice. Prior health economics research consistently selects the gamma family as the choice for cost data distributions. Given the range of results and relying on the prior studies, this study will use the gamma family model.

Table 3.6. Results of Modified Park's Test.

Cost Outcome		λ	s.e.	95% CI	p-value
Total cost					
	Billed	1.5	0.0698	1.3 – 1.6	<0.0001
	Standard	1.4	0.0694	1.3 – 1.6	<0.0001
Inpatient cost					
	Billed	1.3	0.2044	0.9 – 1.7	<0.0001
	Standard	1.3	0.8251	0.8 – 1.8	<0.0001
Outpatient cost					
	Billed	1.4	0.1087	1.2 – 1.6	<0.0001
	Standard	1.2	0.1001	0.9 – 1.3	<0.0001
Ancillary cost					
	Billed	2.0	0.2707	1.5 – 2.5	<0.0001
	Standard	1.9	0.2326	1.5 – 2.4	<0.0001
Professional cost					
	Billed	1.3	0.0869	1.1 – 1.5	<0.0001
	Standard	1.6	0.1056	1.4 – 1.8	<0.0001
Pharmacy cost					
	Billed	1.3	0.1399	1.0 – 1.6	<0.0001
	Standard	1.8	0.1653	1.4 – 2.1	<0.0001

3.13. Protection of Human Participants and the Health Insurance Portability and Accountability Act

In accordance with the Health Insurance Portability and Accountability Act (HIPPA) requirements, all patient identifiers were removed prior to receipt of study data. According to Public Health Information regulations this is considered a limited data set because of the presence of ZIP code data.

The University of Wisconsin-Milwaukee Institutional Review Board granted Exempt Status under Category 4 as governed by 45 CFR 46.101 on April 13, 2012. Appendix F contains a copy of the New Study-Notice of IRB Exempt Status letter.

CHAPTER 4: Results

Results of the data analyses presented in this chapter are separated into three sections: (1) Descriptive statistics of the analysis variables for cost criterions; (2) Results of the predictive model by cost criterion and cost type; and (3) Results of the hierarchical model of patient and community enabling resources over patient predisposing characteristics and need for services.

4.1. Descriptive Statistics of Analysis Variables.

Predictor variable characteristics are presented for each criterion in Tables 4.1-4.6: Total cost (Table 4.1); Ancillary cost (Table 4.2); Inpatient cost (Table 4.3); Outpatient cost (Table 4.4); Pharmacy cost (Table 4.5); and Professional cost (Table 4.6). Descriptive statistics of each criterion variable are presented for the billed cost (Table 4.7) and the standard cost (Table 4.8).

4.1.1. Descriptive statistics of predictor variables

In the WHIO datamart, patient claims are associated with type of services rendered. A patient may not have used all service types within the 24 month timeframe of this study causing the sample sizes between the six cost criterions to vary as seen in the chapter 3 flow charts. Predictor variable descriptive statistics show similarities between the samples for age, gender, patient % under poverty, payer type and provider % under poverty but do show some differences in the percentages of: (1) Treatment type, where there was a slightly higher percentage of treatment with HCT in ancillary cost and inpatient cost (11-12% versus 3-6% respectively); (2) Levels of severity, where total cost and professional cost had a low to medium/low range of severity; inpatient cost, outpatient cost and pharmacy cost showed higher levels of severity in the low/medium to

high/medium range and; ancillary costs showed medium/high to high levels of severity and; (3) The mean length of follow up for patients ranged from a low of 330 days in the total cost to a high of 445 days in the pharmacy cost and may be attributed to the differences in the sample size as well as differences in the complexity of the total cost claim (comprised of many types of services) versus the single services of the other costs.

4.1.1.1. Total cost.

The predictor variables descriptive characteristics of total cost are presented in Table 4.1. This sample contained 837 patients but was reduced to 638 patients due to the limited amount of provider data. Mean age was 27 years with a range of 0-90 with slightly more males (56%) present. Mean length of follow up in the datamart was 330 days with a range from 0-729. The mean of the patient socioeconomic measure county % under poverty is 12.36 and ranged from 4.6% – 26%. Most patients were treated with chemotherapy only (97%) and had a severity score that was either low or medium/low (64%). Payer types were fairly evenly distributed; 48% commercial versus 52% public. Community providers exclusively treated 49% of patients, 27% were treated at least once at an academic medical center and 24% of the providers were undetermined. The mean of the provider socioeconomic variable % under poverty was 6.35% and ranged from 0.5% - 39.6%.

Table 4.1. Descriptive Statistics of Predictor Variables for Total Cost.

Predisposing characteristic	
Age, *n*	837
Mean ± s.d.	27 ± 23.64
Median	17.0
Range	0-90
Gender, *n (%)*	837
Female	367 (44)
Male	470 (56)
Length of follow up, n	837
Mean ± s.d.	330 ± 265
Median	363
Need	
Treatment type, *n (%)*	837
Chemotherapy only	810 (97)
Chemotherapy and HCT	27 (3)
Severity, *n (%)*	837
Low	95 (11)
Low/medium	445 (53)
High/medium	152 (18)
High	145 (17)
Enabling resources	
Patient county zip code % under poverty, *n*	837
Mean ± s.d	12.36 ± 4.47
Median	12.2
Range	4.6 – 26.0
Payer type, *n (%)*	837
Commercial	400 (48)
Public	437 (52)
Provider type, *n (%)*	837
Community	410 (49)
Academic medical center	228 (27)
Not determined	199 (24)
Provider zip code % under poverty, *n*	638
Mean ± s.d.	6.35 ± 5.9
Median	3.3
Range	0.5-39.6

4.1.1.2. Ancillary cost.

The predictor variables descriptive characteristics of ancillary cost are presented in Table 4.2. This sample contained 164 patients but was reduced to 138 patients due to the limited amount of provider data. Mean age is 28 years with a range of 0-88 and more males (62%) were present. Mean length of follow up in the datamart was 439 days with a range from 0-729. The mean of the patient socioeconomic measure county % under poverty is 12.43% with a range of 4.6% – 20.1%. Most patients were treated with chemotherapy only (88%) and this sample had the highest severity scores of either medium/high or high (61% combined). The majority of payer types are public (56%). Community providers exclusively treated 45% of patients, 39% were treated at least once at an academic medical center and 16% of the providers were undetermined. The mean of the provider socioeconomic variable % under poverty was 5.97% and ranged from 1.10% - 39.6%.

Table 4.2. Descriptive Statistics of Predictor Variables for Ancillary Cost.

Predisposing characteristics	
Age, *n*	164
Mean ± s.d.	28 ± 25
Median	17
Range	0 – 88
Gender, *n (%)*	164
Female	62 (38)
Male	102 (62)
Length of follow up, days, *n*	164
Mean ± s.d.	439 ± 235
Median	461
Range	0 – 729
Need	
Treatment type, *n (%)*	164
Chemotherapy only	145 (88)
Chemotherapy and HCT	19 (12)
Severity, *n (%)*	164
Low	10 (6)
Low/medium	53 (33)
High/medium	40 (24)
High	61 (37)
Enabling resources	
Patient county zip code % under poverty, *n*	164
Mean ± s.d	12.43 ± 4.44
Median	12.20
Range	4.60 – 20.10
Payer type, *n (%)*	164
Commercial	72 (44)
Public	92 (56)
Provider type, *n (%)*	164
Community	74 (45)
Academic medical center	64 (39)
Not determined	26 (16)
Provider zip code % under poverty, *n*	138
Mean ± s.d.	5.97 ± 5.39
Median	3.55
Range	1.10 – 39.60

4.1.1.3. Inpatient cost.

The predictor variables descriptive characteristics of inpatient cost are presented in Table 4.3. This sample contained 232 patients but was reduced to 201 patients due to the limited amount of provider data. Mean age is 27 years with a range of 0-90 and a higher percentage of males (66%) are present. Mean length of follow up in the datamart was 420 days with a range from 0-729. The mean of the patient socioeconomic measure county % under poverty is 11.98 and had a range of 4.6% – 20.1%. Most patients were treated with chemotherapy only (89%) and had severity scores of either medium/low or medium/high (63% combined). The majority of payer types were public (56%). Community providers exclusively treated 48% of patients, 39% were treated at least once at an academic medical center and 13% of the providers were undetermined. The mean of the provider socioeconomic variable % under poverty was 6.10% and ranged from 1.2% - 39.6%.

Table 4.3. Descriptive Statistics of Predictor Variables for Inpatient Cost.

Predisposing characteristics	
Age, *n*	232
Mean ± s.d.	27 ± 25
Median	16
Range	0 – 90
Gender, *n (%)*	232
Female	79 (34)
Male	153 (66)
Length of follow up, days, *n*	232
Mean ± s.d.	420 ± 243
Median	449
Range	0 - 729
Need	
Treatment type, *n (%)*	232
Chemotherapy only	206 (89)
Chemotherapy and HCT	26 (11)
Severity, *n (%)*	232
Low	19 (12)
Low/medium	92 (39)
High/medium	60 (24)
High	61 (25)
Enabling resources	
Patient county zip code % under poverty, *n*	232
Mean ± s.d	11.98 ± 4.19
Median	12.2
Range	4.60 – 20.10
Payer type, *n (%)*	232
Commercial	102 (44)
Public	130 (56)
Provider type, *n (%)*	232
Community	111 (48)
Academic medical center	90 (39)
Not determined	31 (13)
Provider zip code % under poverty, *n*	201
Mean ± s.d.	6.10 ± 5.61
Median	3.20
Range	1.20 – 39.60

4.1.1.4 Outpatient cost.

The predictor variables descriptive characteristics of outpatient cost are presented in Table 4.4. This sample contains 639 patients but is reduced to 497 patients due to the limited amount of provider data. Mean age is 27 years with a range of 0-90 and with more males (57%) present. Mean length of follow up in the datamart was 388 days with a range from 0-729. The mean of the patient socioeconomic measure county % under poverty is 12.23% with a range of 4.6% – 21.1%. Most patients were treated with chemotherapy only (96%) and severity scores ranged from medium/low or medium/high (74% combined). The majority of payer types were public (52%). Community providers exclusively treated 47% of patients, 30% were treated at least once at an academic medical center and 23% of the providers were undetermined. The mean of the provider socioeconomic variable % under poverty was 6.41% and ranged from 0.5% - 39.6%.

Table 4.4. Descriptive Statistics of Predictor Variables for Outpatient Cost.

Predisposing characteristics	
Age, years, *n*	639
Mean ± s.d.	27 ± 24
Median	17
Range	0 - 90
Gender, *n (%)*	639
Female	274 (43)
Male	365 (57)
Length of follow up, days, *n*	639
Mean ± s.d.	388 ± 252
Median	413
Range	0 – 729
Need	
Treatment type, *n (%)*	639
Chemotherapy only	612 (96)
Chemotherapy and HCT	27 (4)
Severity, *n (%)*	639
Low	71 (11)
Low/medium	338 (53)
High/medium	131 (21)
High	99 (15)
Enabling resources	
Patient county zip code % under poverty, *n*	639
Mean ± s.d	12.23 ± 4.47
Median	12.20
Range	4.60 – 21.10
Payer type, *n (%)*	639
Commercial	309 (48)
Public	330 (52)
Provider type, *n (%)*	639
Community	303 (47)
Academic medical center	194 (30)
Not determined	142 (23)
Provider zip code % under poverty, *n*	497
Mean ± s.d.	6.41 ± 5.95
Median	3.20
Range	0.50 – 39.60

4.1.1.5. Pharmacy cost.

The predictor variables descriptive characteristics of pharmacy cost are presented in Table 4.5. This sample contains 390 patients but is reduced to 325 patients due to the limited amount of provider data. Mean age is 27 years with a range of 0-90 and has slightly more males (59%) present. Mean length of follow up in the datamart was 445 days with a range from 0-729. The mean of the patient socioeconomic measure county % under poverty of 12.4% and had a range of 4.6% – 20.1%. Most patients were treated with chemotherapy only (94%) with slightly higher severity scores of either medium/low or medium/high (69% combined). The majority of payer types were public (56%). Community providers exclusively treated 47% of patients were treated, 36% were treated at least once at an academic medical center and 17% of the providers were undetermined. The mean of the provider socioeconomic variable % under poverty was 6.7% and ranged from 1.1% - 39.6%.

Table 4.5 Descriptive Statistics of Predictor Variables for Pharmacy Cost

Predisposing characteristics	
Age, years, *n*	390
Mean ± s.d.	27 ± 25
Median	16
Range	0 – 90
Gender, *n (%)*	390
Female	158 (41)
Male	232 (59)
Length of follow up, days, *n*	390
Mean ± s.d.	445 ± 240
Median	488
Range	0 – 729
Need	
Treatment type, *n (%)*	390
Chemotherapy only	365 (94)
Chemotherapy and HCT	25 (6)
Severity, *n (%)*	390
Low	38 (10)
Low/medium	185 (47)
High/medium	84 (22)
High	83 (21)
Enabling resources	
Patient county zip code % under poverty, *n*	390
Mean ± s.d	12.40 ± 4.28
Median	12.20
Range	4.60 – 20.10
Payer type, *n (%)*	390
Commercial	173 (44)
Public	217 (56)
Provider type, *n (%)*	390
Community	185 (47)
Academic medical center	140 (36)
Not determined	65 (17)
Provider zip code % under poverty, *n*	325
Mean ± s.d.	6.70 ± 5,73
Median	4.30
Range	1.10 – 39.60

4.1.1.6. Professional cost.

The predictor variables descriptive characteristics of professional cost are presented in Table 4.6. This sample contains 748 patients but is reduced to 618 patients due to the limited amount of available provider data. Mean age is 27 years with a range of 0-90 with slightly more males (56%) present. Mean length of follow up in the datamart was 350 days with a range from 0-729. The mean of the patient socioeconomic measure county % under poverty is 12.41% with a range of 4.6% - 26%. Most patients were treated with chemotherapy only (97%) and had a severity score ranging from low to low/medium (65% combined). The majority of payer types were public (53%). Community providers exclusively treated 52% of all patients, 31% were treated at least once at an academic medical center and 17% of the providers were undetermined. The mean of the provider socioeconomic variable % under poverty was 6.4% and ranged from 0.5% - 39.6%.

Table 4.6. Descriptive Statistics of Predictor Variables for Professional Cost.

Predisposing characteristics	
Age, years, *n*	748
Mean ± s.d.	27 ± 23
Median	17
Range	0 – 90
Gender, *n (%)*	748
Female	329 (44)
Male	419 (56)
Length of follow up, days, *n*	748
Mean ± s.d.	354 ± 261
Median	375
Range	0 – 729
Need	
Treatment type, *n (%)*	748
Chemotherapy only	722 (97)
Chemotherapy and HCT	26 (3)
Severity, *n (%)*	748
Low	84 (11)
Low/medium	405 (54)
High/medium	138 (18)
High	121 (16)
Enabling resources	
Patient county zip code % under poverty, *n*	747
Mean ± s.d	12.41 ± 4.55
Median	12.20
Range	4.60 – 26.00
Payer type, *n (%)*	748
Commercial	352 (47)
Public	396 (53)
Provider type, *n (%)*	748
Community	390 (52)
Academic medical center	228 (31)
Not determined	130 (17)
Provider zip code % under poverty, *n*	618
Mean ± s.d.	6.44 ± 5.98
Median	3.60
Range	0.50 – 39.60

4.1.2. Descriptive statistics of criterion variables.

This study uses six cost criterion variables: (1) Total cost; (2) Ancillary cost; (3) Inpatient cost; (4) Outpatient cost; (5) Pharmacy cost; and (6) Professional cost. Each cost criterion is analyzed by both billed cost, presented in Table 4.7 and standard cost, presented in Table 4.8.

4.1.2.1. Billed cost.

Billed cost criterion descriptive statistics are presented in Table 4.7. Mean billed costs varied greatly between criterion variables with inpatient cost having the highest mean cost of $15435 ± $221,790 with range $790-$1,671,326, followed by total cost mean $86,309 ± $206,913 with range of $29-$1,866,606, the pharmacy cost mean $25,108 ± $80,850 with range $1-$1,447,914, the outpatient cost mean $21,424 ± $43,720 with range $29-$571,594, the professional cost mean $16,077 ± $80,85 with range $38-$203,272 and the ancillary cost mean $4,101 ± $8,475 with range $7-$63,360.

The median and quartile range of the data additionally provides useful distribution measures of each criterion variable and indicate the presence of extreme values at both low and high data points. There were large differences in value between the medians and the means however, the medians showed a similar trend when comparing between the criterion variables with an inpatient median cost $71,277 with quartile range $2,116-$187,595, a median total cost $6,034 with quartile range $1,198-$66,093, a median pharmacy cost $6,716 with quartile range $647-$26,652, a median outpatient cost $4,972 with quartile range $1,280-$23,915, a median professional cost $2,451 with quartile range of $676-$17,748 and a median ancillary cost $1,262 with quartile range $373-$3,878.

Table 4.7. Descriptive Statistics for Billed Cost.

Criterion variable ($)	Mean	Median	S.D.	Range	25% quartile	75% quartile
Total cost	86,309	6,034	206,913	29 - 1,866,606	1,198	66,093
Ancillary cost	4,101	1,262	8,475	7 – 63,360	373	3,878
Inpatient cost	155,435	71,377	221,790	790 – 1,671,326	26,116	187,595
Outpatient cost	21,424	4,972	43,720	29 – 571,594	1,280	23,915
Pharmacy cost	25,108	6,716	80,850	1 – 1,447,914	647	26,652
Professional cost	16,077	2,451	80,850	38 – 203,272	676	17,748

4.1.2.2. Standard cost.

The descriptive statistics of standard cost is presented in Table 4.8. The standard costs are consistently lower in value for all criterion variables when compared to billed cost. Taking the lower value into account, the standard costs follow the same general trend as the billed cost with a high mean, large standard deviation and wide range of data. The inpatient cost has the highest mean cost $80,786 ± $104,001 with range $2,680-$836,656, followed by the total cost mean $43,379 ± $102,703 with range $10-$1,229,960 , the pharmacy cost mean $17,078 ± $60,011 with range $1-$1,097,438, the outpatient cost of $8,410 ± $17,589 with range $10-$227,957, the professional cost mean $6,490 ± 11,378 with range $7-$80,867 and, the ancillary cost mean $4,123 ± 8,833 with range $5-$64,248. The median, combined with the 25%-75% quartile range provide a more comprehensive description of the data. Inpatient cost has the highest median cost

$40,908 and a 25%-75% quartile range $16,855 - $108,750, followed by the median pharmacy cost $5,070 with a 25% - 75% quartile range $483 - $17,434, the median total cost $2,723 with a 25% - 75% quartile range $539 - $35,471, the median outpatient cost $1,953 with a 25% - 75% quartile range $493 - $9,208, the median ancillary cost $1,230 with a 25% - 75% quartile range $296 - $3,248 and, the median professional cost $1,002 with a 25% - 75% quartile range $298 to $7448. The professional cost had the greatest reduction in value because of the standardization of cost and resulted in the lowest median cost. Standard ancillary cost moved from the lowest median in the billed cost to the second lowest median in the standard cost. All other costs remained in the same high to low position.

Table 4.8. Descriptive Statistics for Standard Cost.

Criterion variable ($)	Mean	Median	S.D.	Range	25% quartile	75% quartile
Total cost	43,379	2,723	102,703	10 – 1,228,960	539	35,471
Ancillary cost	4,123	1,230	8,834	5 – 64,248	296	3,248
Inpatient cost	80,787	40,908	104,001	2,680 – 836,656	16,855	107,750
Outpatient cost	8,410	1,953	17,590	10 – 227,957	493	9208
Pharmacy cost	17,078	5,070	60,012	1 – 1,097,437	483	17,434
Professional cost	6,491	1,002	11,379	7 – 80,867	298	7,448

4.2. Results of the Predictors of Cost Model.

Multivariate methods were used to model the cost criterion variables related to: (1) Whether a patients predisposing characteristics (i.e., age, gender and length of follow

up), their need for service factors (i.e., treatment type and episode severity) and the patient and community enabling resources (i.e., patient county of residence % under poverty, payer type, provider type and its location % under poverty) are predictive of cost; and (2) An examination of the magnitude of predictor variable influence on cost criterion variables. The underlying hypothesis is each predictor variable will have a significant effect on the cost criterion with varying degrees of magnitude. Generalized linear model (GLM) gamma log link models were run for each cost criterion and each cost type, billed and standard. Significance is assessed at the $p \leq 0.05$ level.

Analysis results of the full and reduced models are presented by cost criterion and cost type. The exponential conditional mean is reported as the e^{β} coefficient and represents the proportional change factor; a one unit change in the predictor variable will result in a proportional change of e^{β} in the criterion variable. The full model included all predictor variables and was run separately for total billed cost and total standard cost. Reduced model variables were identified in the GLM through a Type 3 analysis which used a chi-square test of the likelihood ratio with, $\alpha=0.05$. A second GLM analysis was run using only the variables that tested as significant. Results for both the full model and reduced model variables are presented.

4.2.1. Total cost.

The estimated results for the total cost are presented in Table 4.9. The full model predictor variable estimates resulting in a significant increase to total cost included: (1) Gender, where male gender is 1.69 times total billed cost of female gender ([CI=1.29-2.2], p<.0001) and a 1.59 times total standard cost of female gender ([CI=1.22-2.09], p=.0007) and; (2) Length of follow up, where a per day increase in length of follow up is

1.001 times the total billed cost ([CI=1.001-1.002], p<.0001) and with the same result in total standard cost.

The significant variable estimates that resulted in a reduction to the cost criterion variables included; (1) Treatment type, where the cost of chemotherapy only treatment is 0.12 times the cost of chemotherapy and HCT treatment ([CI=0.06-0.22], p<.0001); (2) Severity level, where cost for lower levels of severity resulted in a reduction in cost when compared to higher levels of severity. Severity level 1, low level, was 0.36 times the cost of severity level 4, high level, ([CI=0.21-0.006), p<.0001) for total billed cost and 0.35 times the cost of severity level 4 for total standard cost ([CI=0.21-0.59], p<.0001) and, severity level 2, medium/low severity, was 0.39 times the cost of severity level 4 in total billed cost ([CI=0.27- 1.08], p=<.0001) and 0.41 times the cost of severity level 4 in total standard cost ([CI=0.28-0.6], p<.0001; (3) Age, where a one year increase in age was 0.99 times the cost of the prior year in total billed cost, ([CI=0.98-0.99], p=0.0002) and was similar, 0.99 times, in total standard cost, ([CI=0.99-0.99], p=0.002) and; (4) Provider type, where the cost of claims from a community provider was 0.77 times the cost of claims from an academic provider in total billed cost ([CI=0.51-0.89], p=0.007) and 0.67 times the cost from an academic provider in total standard cost ([CI=0.5-0.88], p=0.006).

Variable estimate results not significant in the models include: (1) Patient county % under poverty, where a 1% increase in the percentage under poverty rate was 0.99 times total billed cost when compared to lower % under poverty ([CI=0.97-1.02], p=0.79) with a similar result in total standard cost, 0.99, ([CI=0.97-1.22], p=0.77); (2). Payer type, where a commercial payer was 0.77 times the cost of a public payer in total billed

cost ([CI=0.59-1.02], p=0.06) and .79 times the cost of a public payer in total standard cost ([0.59-1.04], p=0.1); (3) Severity level 3, was 0.96 times the cost of severity level 4 in total billed cost ([CI=0.47-1.08], p=0.12) and 0.77 times the cost of severity level 4 in total standard cost ([CI=0.5-1.18], p=0.24) and; (4) Provider % under poverty where a 1% increase in the % under poverty rate was 0.99 times the total billed cost of the lower poverty rate ([CI=0.98-1.02], p=0.65) and 0.99 times the total standard cost of the lower poverty rate ([CI=0.97-1.16], p=0.49).

In the reduced model, severity level 3 and 4 were combined. The variable estimates that resulted in a significant increase to the cost criterion variables include: (1) Gender, where the cost of total billed for males was 1.75 times the cost of females ([CI=1.36-2.27], p=<0.0001), and 1.66 times the cost of females in total standard ([CI=1.28-2.15], p=0.0001); and (2) Length of follow up, where a one day increase in the length of follow up was 1.001 times the cost of the shorter timeframe in total billed cost and total standard cost, ([CI=0.001-0.002, p<0.0001).

Costs were significantly reduced by: (1) Treatment type, where chemotherapy only cost was 0.13 times the cost of chemotherapy and HCT in total billed cost ([CI=0.06-0.23, p<0.0001) and 0.14 times the cost of chemotherapy and HCT in total standard cost ([CI=0.06-0.26], p<0.0001); (2) Severity level, where severity level 1 was 0.44 times the cost of severity levels 3 and 4 in total billed cost, ([CI=0.28-0.7], p=0.0003) and 0.41 times the cost of severity levels 3 and 4 in total standard cost, ([CI=0.26-0.61], p=0.0002) and severity level 2 was 0.44 times the cost of severity levels 3 and 4 in total billed cost ([CI=0.33-0.58], p<0.0001), and 0.45 times the cost of severity levels 3 and 4 in total standard cost ([CI=0.34-0.61], p<0.0001); (3) Community

providers resulted in 0.73 times the cost of academic providers in total billed cost ([CI=0.57-0.96], p=0.02), and 0.71 times the cost of academic providers in total standard cost ([CI=0.54-0.94], p=0.01); and (4) A per year increase in age had 0.98 times the cost of the prior year in total billed cost ([CI=0.98-0.99], p<0.0001) and 0.99 times the cost of the prior year in total standard cost (CI=0.98-0.99], p=0.0007).

Table 4.9. Estimated Results for Total Cost.

Model	Total billed cost						Total standard cost					
Full Model	e^{β} total billed cost	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value	e^{β} total standard cost	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value
Age	0.99	0.002	0.98	0.99	14.19	**0.0002**	0.99	0.002	0.99	0.99	9.73	**0.002**
Gender (1=female)	1.69	0.13	1.29	2.20	15.38	**<.0001**	1.59	0.13	1.22	2.09	11.55	**0.0007**
Length of follow up	1.001	<0.001	1.001	1.002	28.10	**<.0001**	1.001	<0.001	1.001	1.002	28.47	**<.0001**
Treatment type (1=chemo+HCT)	0.12	0.32	0.06	0.22	39.79	**<.0001**	0.14	0.33	0.06	0.25	34.16	**<.0001**
Severity (4=high)												
Level 1	0.36	0.25	0.21	0.006	15.84	**<.0001**	0.35	0.26	0.21	0.59	15.87	**<.0001**
Level 2	0.39	0.18	0.27	1.08	25.72	**<.0001**	0.41	0.19	0.28	0.60	21.32	**<.0001**
Level 3	0.96	0.21	0.47	1.08	2.44	0.12	0.77	0.21	0.50	1.18	1.38	0.24
Individual county percent under poverty	0.99	0.01	0.97	1.02	0.07	0.79	0.99	0.01	0.97	1.22	0.09	0.77
Payer type (1=public)	0.77	0.13	0.59	1.01	3.56	0.06	0.79	0.13	0.59	1.04	2.72	0.10
Provider type (1=academic)	0.68	0.14	0.51	0.89	7.30	**0.007**	0.67	0.14	0.50	0.88	7.62	**0.006**
Provider zip code percent under poverty	0.99	0.01	0.98	1.02	0.21	0.65	0.99	0.01	0.97	1.16	0.47	0.49

Model	Total billed cost						Total standard cost					
Reduced model	e^{β} total billed cost	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value	e^{β} total standard cost	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value
Age	0.98	0.002	0.98	0.99	17.11	**<.0001***	0.99	0.002	0.98	0.99	11.46	**0.0007***
Gender (1=female)	1.75	0.12	1.36	2.27	19.07	**<.0001***	1.66	0.13	1.28	2.15	14.61	**0.0001***
Length of follow up	1.001	<0.001	1.001	1.002	30.85	**<.0001***	1.001	<0.001	1.001	1.002	32.08	**<.0001***
Treatment type (1=chemo+HCT)	0.13	0.32	0.06	0.23	38.63	**<.0001***	0.14	0.33	0.06	0.26	33.30	**<.0001***
Severity[2] (4=high)												
Level 1	0.44	0.22	0.28	0.70	12.94	**0.0003***	0.41	0.23	0.26	0.61	14.26	**.0002***
Level 2	0.44	0.14	0.33	0.58	32.09	**<.0001***	0.45	0.14	0.34	0.61	28.47	**<.0001***
Provider type (1=academic)	0.73	0.13	0.57	0.9	5.05	**0.02***	0.71	0.13	0.54	0.94	5.65	**0.01***

[1]Results in bold are significant in the model
[2]Severity level 3 and 4 are combined
*Significant at α=.05

4.2.2. Ancillary cost.

The estimated results for the ancillary cost are presented in Table 4.10. In the full model, there were no significant variable estimates which resulted in an increase to the cost criterion variable.

Variable estimates which significantly reduced cost included: (1) Level of severity resulted in the largest cost decrease where, severity level 1 cost was 0.23 times the cost of severity level 4 in ancillary billed cost ([CI=0.07-0.93), p=0.02), and 0.23 times the cost of severity level 4 in ancillary standard cost ([CI=.06-.97], p=0.03. Severity level 2 was 0.32 times the cost of severity level 4 in ancillary billed cost ([CI=0.16-0.60], p=0.0005), and 0.27 times the cost of severity level 4 in ancillary standard cost ([CI=0.13-0.52], p=0.0001). Severity level 3 was 0.30 times the cost of severity level 4 in ancillary billed cost ([CI=0.16-0.57], p=0.0002) and 0.25 times the cost of severity level 4 in ancillary standard cost ([CI=0.16-0.57], p=0.0002). All severity levels were significant in the model but exhibited wide confidence intervals making the estimate unreliable; (2) Provider type, where community providers ancillary billed costs were 0.50 times the cost of academic providers ancillary billed cost, ([CI=0.29-0.87], p=0.02) and 0.48 times the cost of academic providers ancillary standard cost, ([0.27-0.84], p=0.01); and (3) Age, where a per year increase in age resulted in 0.98 times ancillary billed cost, ([CI=0.97-0.99], p=0.01) and with the same result for ancillary standard cost.

Variable estimates that increased ancillary cost but were not significant in the model include: (1) Payer type, where commercial payers were estimated as 1.60 times the ancillary billed cost of public payers ([CI=.97-2.66], p=.06), and 1.21 times the

ancillary standard cost of public payers ([CI=0.73-2.10], p=0.45); and (2) Patient county % under poverty estimated 1.01 times ancillary billed cost per percentage increase in the rate under poverty ([CI=0.96-1.06], p=0.66) and was 1.007 times ancillary standard cost ([CI=0.96-1.06], p=0.77). Variable estimates that reduced cost but were not significant in the full model are: (1) Treatment type, where chemotherapy only treatment cost was 0.51 times the cost of chemotherapy and HCT in the ancillary billed cost ([CI=0.23-1.02], p=0.07), and 0.54 times the cost of chemotherapy and HCT in the ancillary standard cost ([CI=0.25-1.07], p=0.10); (2) Gender, where cost for males was 0.85 times the cost for females in ancillary billed cost, ([CI=0.50-1.44], p=0.57) and cost for males was 0.83 times the cost for females in ancillary standard cost, ([CI=0.47-1.43], p=0.52); (3) Provider % under poverty, where with a 1% increase in the % under poverty ancillary billed cost was 0.96 of the lower % under poverty, ([CI=0.92-1.01], p=0.08) and ancillary standard cost was the same; and (4) Length of follow up, where with every 1 day increase in ancillary billed cost was 0.99 times the prior day, ([0.97-0.99], p=0.58) and ancillary standard cost was 0.99 times the prior day, ([0.97-1.00], p=0.72).

Three variable estimates entered the reduced model; age, severity and provider type. Two of these variables significantly resulted in a cost reduction in the model: (1) Severity levels had the largest effect where severity level 1 was 0.29 times the ancillary billed cost of severity level 4 ([CI=0.10-1.01], p=0.05), and 0.24 times the ancillary standard cost of severity level 4 ([CI=0.07-0.95], p=0.02), severity level 2 was 0.44 times the ancillary billed cost of severity level 4 ([CI=0.24-0.81], p=0.008) and 0.34 times the ancillary standard cost of severity level 4 ([CI=0.19-0.66], p=0.001) and severity level 3 was 0.42 times the ancillary billed cost of severity level 4 ([CI=0.22-0.81], p=0.008) and

was 0.32 times the ancillary standard cost of severity level 4 (CI=0.17-0.61], p=0.0004); and (2) Commercial providers had 0.45 times the ancillary billed cost of public providers ([CI=0.26-0.75], p=0.002) and 0.46 times the ancillary standard cost of public providers ([CI=0.26-0.79], p=0.005). Age was not significant in the reduced model.

Table 4.10. Estimated Results for Ancillary Cost.

Model	Ancillary billed cost						Ancillary standard cost					
Full model[1]	e^{β} ancillary billed cost estimate	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value	e^{β} ancillary standard cost estimate	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value
Age	0.98	0.005	0.97	0.99	5.97	**0.01**	0.98	0.006	0.97	0.99	6.04	**0.01**
Gender (1=female)	0.85	0.27	0.50	1.44	0.32	0.57	0.83	0.27	0.47	1.43	0.42	0.52
Length of follow up	0.99	<0.001	0.99	1.001	0.31	0.58	0.99	<0.001	0.99	1.001	0.12	0.72
Treatment type (1=chemo+HCT)	0.51	0.36	0.23	1.02	3.23	0.07	0.54	0.36	0.25	1.07	2.75	0.10
Severity (4=high)												
Level 1	0.23	0.62	0.07	0.93	5.24	**0.02**	0.23	0.65	0.06	0.97	4.93	**0.03**
Level 2	0.32	0.32	0.16	0.60	12.29	**0.0005**	0.27	0.33	0.13	0.52	15.03	**0.0001**
Level 3	0.30	0.32	0.16	0.57	13.87	**0.0002**	0.25	0.32	0.13	0.47	18.31	**<.0001**
Individual county percent under poverty	1.01	0.02	0.96	1.06	0.19	0.66	1.007	0.02	0.96	1.06	0.09	0.77
Payer type (1=public)	1.60	0.25	0.97	2.66	3.43	0.06	1.21	0.25	0.73	2.01	0.56	0.45
Provider type (1=academic)	0.50	0.27	0.29	0.87	5.93	**0.02**	0.48	0.28	0.27	0.84	6.48	**0.01**
Provider zip code percent under poverty	0.96	0.02	0.92	1.01	3.00	0.08	0.96	0.02	0.92	1.01	2.77	0.10

Model	Ancillary billed cost						Ancillary standard cost					
Reduced model[1]	e^{β} ancillary billed cost estimate	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value	e^{β} ancillary standard cost estimate	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value
Age	0.99	0.006	0.98	1.004	2.03	0.15	0.98	0.006	0.97	1.002	2.98	0.08
Severity												
Level 1	0.29	0.60	0.10	1.01	4.00	0.06	0.24	0.61	0.07	0.95	5.36	**0.02***
Level 2	0.44	0.30	0.24	0.81	7.04	**0.008***	0.35	0.31	0.19	0.66	10.85	**0.001***
Level 3	0.42	0.32	0.22	0.81	7.09	**0.008***	0.32	0.32	0.17	0.61	12.41	**0.0004***
Provider type	0.45	0.26	0.26	0.75	9.19	**0.002***	0.46	0.27	0.26	0.79	7.95	**0.005***

[1]Results in bold are significant in the model
*Significant at α=.05

4.2.3. Inpatient cost.

The estimated result for inpatient costs are presented in Table 4.11. In the full model only gender, for billed cost only, significantly estimated an increase in the cost criterion variable with male gender 1.4 times the inpatient billed cost compared to female gender, ([CI=1.04-1.91], p=0.03.

Variable estimates that significantly reduced inpatient costs are: (1) Treatment type, where chemotherapy only treatment is 0.25 times the inpatient billed cost of treatment with both chemotherapy and HCT, ([CI=0.16-0.39], p<0.0001) and 0.28 times the cost of inpatient standard cost of treatment with chemotherapy and HCT, ([CI=0.18-0.41], p<.0001); (2) Severity level, where Level 1 severity is 0.29 times the cost of level 4 severity of inpatient billed cost ([CI=0.17-0.53], p<.0001) and 0.26 times the cost of level 4 severity of inpatient standard cost ([CI=0.18-0.53], p<.0001) and Level 2 severity is 0.54 times the cost of level 4 severity of inpatient billed cost ([CI=0.38-0.78], p=0.001) and 0.59 times the costs of level 4 severity of inpatient standard cost ([CI=0.42-0.83], p=0.002); (3) Provider type, where costs of a community provider are 0.69 times the inpatient billed costs of an academic provider, ([CI=0.5-0.94], p=0.02) and 0.71 times the inpatient standard costs of an academic provider ([CI=0.53-0.94], p=0.02); (4) Age, a per year increase in age resulted in 0.98 times the inpatient billed cost, ([CI=0.98-0.99], p<.0001) and had the same result for inpatient standard cost; and (5) Length of follow up, where the per day increase in length of follow up was 0.99 times inpatient billed cost, ([CI=0.99-0.99], p=0.03) and 0.99 times inpatient standard cost ([CI=0.99-1], p=0.02).

Variable estimates that were not significant in the model include: (1) Gender where the standard cost of males is 1.22 times the inpatient standard cost compared to female gender, ([CI=0.93-1.61], p=0.15); (2) Payer type where a commercial payer is 0.86 times inpatient billed cost of a public payer, ([CI=0.64-1.17], p=0.35) and 0.86 times inpatient standard cost of a public payer, ([CI=0.65-1.15], p=0.33) but is not significant in both models; (3) Severity level 3 is 1.06 times the cost of level 4 severity in inpatient billed cost, ([CI=0.72-1.55], p=0.75), and 1.18 times the cost of level 4 severity in inpatient standard cost, ([CI=0.84-1.66], p=0.33); (4) Patient county % under poverty where a percentile increase in the rate of county poverty is 1.01 times the inpatient billed cost, ([CI=0.98-1.05], p=0.35) and is 1.01 times the cost of the inpatient standard cost, ([CI=0.99-1.04], p=0.32); and (5) Provider % under poverty where a 1% increase in the rate of provider % under poverty is 0.99 times inpatient billed cost, ([CI=0.97-1.02], p=0.89), and the same for inpatient standard cost.

In the reduced model, billed cost gender is the only variable estimate that increased the cost criterion variables, where male gender was 1.41 times the cost of female gender of inpatient billed cost, ([CI=1.05-1.89], p=0.02).

Variable estimates that significantly reduced inpatient cost included: (1) Treatment type, where chemotherapy only treatment is 0.26 times the inpatient billed cost of chemotherapy and HCT treatment, ([CI=0.16-0.40], p<.0001), and 0.30 times the inpatient standard cost of chemotherapy and HCT treatment, ([CI=0.20-0.45], p<.0001); (2) Severity level, where level 1 severity is 0.30 times the inpatient billed cost of level 4 severity, ([CI=0.17-0.55], p<.0001) and 0.28 times the inpatient standard cost of level 4 severity, ([CI=0.17-0.49], p<.0001) and level 2 severity is 0.53 times inpatient billed cost

of level 4 severity, ([CI=0.39-0.73], p<.0001) and 0.55 times inpatient standard cost of level 4 severity, ([CI=0.41-0.74], p<.0001); (3) Provider type, where a community provider had 0.71 times the inpatient billed cost of an academic provider, ([CI=0.53-0.97], p=0.03) and 0.73 times the inpatient standard cost of an academic provider, ([CI=0.55-0.95], p=0.02); (3) Age, where a one year increase in age resulted in 0.98 times inpatient billed cost, ([CI=0.98-0.99], p<.0001), and had the same result for inpatient standard cost; and (4) Length of follow up, where a one day increase in the length of follow up resulted in 0.99 times inpatient billed cost, ([CI=0.99-1], p=0.04) and 0.99 times inpatient standard cost, ([CI=0.99-1], p=0.05), but was only just significant in both models.

Table 4.11. Estimated Results for Inpatient Cost.

Model	Inpatient billed cost						Inpatient standard cost					
Full model[1]	e^{β} inpatient billed cost estimate	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value	e^{β} inpatient standard cost estimate	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value
Age	0.98	0.003	0.98	0.99	22.38	**<.0001**	0.98	0.002	0.98	0.99	21.33	**<.0001**
Gender (1=female)	1.41	0.15	1.04	1.91	5.02	**0.03**	1.22	0.14	0.93	1.61	2.06	0.15
Length of follow up	0.99	<0.001	0.99	0.99	5.02	**0.03**	0.99	<0.001	0.99	1.00	5.34	**0.02**
Treatment type (1=chemo+HCT)	0.25	0.22	0.16	0.39	37.70	**<.0001**	0.28	0.20	0.18	0.41	38.30	**<.0001**
Severity (4=high)												
Level 1	0.29	0.29	0.16	0.53	16.44	**<.0001**	0.31	0.26	0.18	0.53	18.28	**<.0001**
Level 2	0.54	0.18	0.38	0.78	10.79	**0.001**	0.59	0.16	0.42	0.83	9.24	**0.002**
Level 3	1.06	0.19	0.72	1.55	0.01	0.75	1.18	0.17	0.84	1.66	0.96	0.33
Individual county percent under poverty	1.01	0.01	0.98	1.05	0.87	0.35	1.01	0.01	0.99	1.04	0.99	0.32
Payer type (1=public)	0.86	0.15	0.64	1.17	0.86	0.35	0.86	0.14	0.65	1.15	0.97	0.33
Provider type (1=academic)	0.69	0.15	0.50	0.94	5.46	**0.02**	0.71	0.14	0.53	0.94	5.52	**0.02**
Provider zip code percent under poverty	0.99	0.01	0.97	1.02	0.02	0.89	0.99	0.01	0.97	1.02	0.26	0.61

Model	Inpatient billed cost						Inpatient standard cost					
Reduced model[1]	e^{β} inpatient billed cost estimate	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value	e^{β} inpatient standard cost estimate	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value
Age	0.98	0.002	0.98	0.99	28.58	**<.0001***	0.98	0.002	0.98	0.99	22.93	**<.0001***
Gender	1.41	0.15	1.05	1.89	5.43	**0.02***	n.s.	n.s	n.s.	n.s.	n.s.	n.s.
Length of follow up	0.99	<0.001	0.99	1.00	4.04	**0.04***	0.99	<0.001	0.99	1.00	3.86	**0.05***
Treatment type (1=chemo+HCT)	0.26	0.22	0.16	0.40	36.05	**<.0001***	0.30	0.20	0.20	0.45	33.76	**<.0001***
Severity[2]												
Level 1	0.30	0.28	0.17	0.55	17.23	**<.0001***	0.28	0.26	0.17	0.49	22.76	**<.0001***
Level 2	0.53	0.15	0.39	0.73	15.88	**<.0001***	0.55	0.14	0.41	0.74	16.59	**<.0001***
Provider type (1=academic)	0.71	0.15	0.53	0.97	4.78	**0.03***	0.73	0.13	0.55	0.95	5.24	**0.02***

[1]Results in bold are significant in the model
[2]Severity level 3 and 4 are combined
*Significant at α=.05

4.2.4. Outpatient cost.

The estimated results for outpatient cost are presented in Table 4.12. In the full model variable estimates that significantly increased outpatient cost included: (1) Gender, where male gender is 1.31 times the outpatient billed cost compared to female

gender, ([CI=1.05-1.66], p=0.02) and 1.30 times the outpatient standard cost compared to female gender ([CI=1.04-1.63], p=0.02); and (2) Length of follow up, where a per day increase in length of follow up was 1.001 times the outpatient billed cost, ([CI=1.001-1.002], p=<.0001) with the same result in outpatient standard cost.

Variable estimates that significantly reduced outpatient cost included: (1) Treatment type, where chemotherapy only treatment type is 0.20 times the outpatient billed cost of chemotherapy and HCT, ([CI=0.12-0.33], p<.0001) and 0.19 times outpatient standard cost of chemotherapy and HCT, ([CI=0.11-0.32], p<.0001); (2) Severity level, where severity level 1 is 0.31 times outpatient billed cost of severity level 4, ([CI=0.19-0.50], p<.0001), and 0.32 times the outpatient standard cost of severity level 4, ([CI= 0.2-0.51], p<.0001), severity level 2 is 0.48 times outpatient billed cost of severity level 4, ([CI=0.34-0.67], p<.0001) and 0.47 times outpatient standard cost of severity level 4, ([CI=0.34-0.67], p<.0001, and severity level 3 is 0.63 times outpatient billed cost of severity level 4, ([CI=0.44-0.91], p=0.02) and 0.64 times outpatient standard cost of severity level 4 ([CI=0.44-0.92], p=0.02); (3) Provider type, where a community provider is 0.55 times the outpatient billed cost of an academic provider, ([CI=0.44-0.71], p<.0001) and 0.56 times the outpatient standard cost of an academic provider, ([CI=0.44-0.71], p<.0001); and (4) Age, where a one year increase in age is 0.99 times outpatient billed cost, ([CI=0.99-0.99], p=0.002) with the same result in outpatient standard cost and; (5) Provider % under poverty where a 1% increase in the rate of provider % under poverty is 0.97 times outpatient billed cost, ([CI=0.96-0.99], p=0.02) with the same result in outpatient standard cost.

Variable estimates that were not significant in the model include: (1) Payer type, where a commercial payer is 0.95 times the outpatient billed cost of a public payer, ([CI=0.75-1.20], p=0.70) and 0.99 times the outpatient standard cost, ([CI=0.76-1.22], p=0.76), but was not significant in both models; and (2) Patient county % under poverty where, a 1% increase in the county % under poverty is 1.007 times outpatient billed cost, ([CI=0.98-1.03], p=0.51) and but is 0.99% ,a decrease, of outpatient standard cost, ([CI=0.98-1.03], p=0.53).

In the reduced model the two variables with estimates that contributed to an increase in outpatient cost: (1) Gender, where male gender was 1.32 times the outpatient billed cost of female gender, ([CI=1.05-1.64], p=0.02) and 1.30 times the outpatient standard cost of female gender, ([CI=1.04-1.64], p=0.02); and (2) Length of follow up, where a per day increase in length of follow up was 1.001 times the outpatient billed cost, ([CI=1.001-1.002], p<.0001) with the same result for outpatient standard cost.

The variable estimates that contributed to a decrease in outpatient cost included: (1) Treatment type, where chemotherapy only treatment is 0.20 times the outpatient billed cost of chemotherapy and HCT, ([CI=0.12-0.33], p<.0001) and 0.19 times the outpatient standard cost of chemotherapy and HCT, ([CI=0.12-0.32], p<.0001); (2) Severity level, where severity level 1 is 0.31 times the outpatient billed cost of severity level 4, ([CI=0.19-0.49], p<.0001) and 0.32 times the outpatient standard cost of severity level 4, ([CI=0.20-0.51], p<.0001), severity level 2 is 0.47 times the outpatient billed cost of severity level 4, ([CI=0.34-0.66], p<.0001) with the same result in outpatient standard cost and, severity level 3 is 0.63 times the outpatient billed cost of severity level 4, ([CI=0.43-0.90], p=0.01) and 0.64 times the outpatient standard cost of severity level 4,

([CI=0.44-0.92], p=0.02); (3) Provider type, where a community provider is 0.56 times the outpatient billed cost of an academic provider, ([CI=0.44-0.71], p<.0001) and 0.56 times the outpatient standard cost of an academic provider, ([CI=0.44-0.71], p<.0001) and; (4) Provider % under poverty, where a 1% increase in the rate of % under poverty is 0.97 times the outpatient billed cost ([CI=0.96-0.99], p=0.02) with the same result in outpatient standard cost.

Table 4.12. Estimated Results for Outpatient Cost.

Model	Outpatient billed cost						Outpatient standard cost					
Full model[1]	e^{β} outpatient billed cost estimate	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value	e^{β} outpatient standard cost estimate	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value
Age	0.99	0.002	0.99	0.99	9.50	**0.002**	0.99	0.002	0.99	0.99	8.90	**0.002**
Gender (1=female)	1.31	0.11	1.05	1.66	5.61	**0.02**	1.30	0.11	1.04	1.63	5.24	**0.02**
Length of follow up	1.001	<0.001	1.001	1.002	45.39	**<.0001**	1.001	<0.001	1.001	1.002	48.12	**<.0001**
Treatment type (1=chemo+HCT)	0.20	0.25	0.12	0.33	38.86	**<.0001**	0.19	0.25	0.11	0.32	40.32	**<.0001**
Severity (4=high)												
Level 1	0.31	0.23	0.19	0.50	23.71	**<.0001**	0.32	0.23	0.20	0.51	22.82	**<.0001**
Level 2	0.48	0.16	0.34	0.67	18.72	**<.0001**	0.47	0.16	0.34	0.67	18.99	**<.0001**
Level 3	0.63	0.18	0.44	0.91	5.97	**0.02**	0.64	0.18	0.44	0.92	5.64	**0.02**
Individual county percent under poverty	1.007	0.01	0.98	1.03	0.44	0.51	0.99	0.01	0.98	1.03	0.38	0.53
Payer type (1=public)	0.95	0.11	0.75	1.20	0.15	0.70	0.96	0.11	0.76	1.22	0.09	0.76
Provider type (1=academic)	0.55	0.12	0.44	0.71	21.99	**<.0001**	0.56	0.12	0.44	0.71	22.01	**<.0001**
Provider zip code percent under poverty	0.97	0.009	0.96	0.99	5.37	**0.02**	0.97	0.009	0.96	0.99	5.77	**0.02**

Model	Outpatient billed cost						Outpatient standard cost					
Reduced model[1]	e^{β} outpatient billed cost estimate	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value	e^{β} outpatient standard cost estimate	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value
Age	0.99	0.002	0.99	0.99	10.38	**0.001***	0.99	0.002	0.99	0.99	9.69	**0.002***
Gender (1=female)	1.32	0.11	1.05	1.64	5.68	**0.02***	1.30	0.11	1.04	1.64	5.31	**0.02***
Length of follow up	1.001	<0.001	1.001	1.002	46.52	**<.0001***	1.001	<0.001	1.001	1.002	49.24	**<.0001***
Treatment type (1=chemo+HCT)	0.20	0.25	0.12	0.33	38.48	**<.0001***	0.19	0.25	0.12	0.32	40.11	**<.0001***
Severity (4=high)												
Level 1	0.31	0.23	0.19	0.49	24.23	**<.0001***	0.32	0.23	0.20	0.51	23.31	**<.0001***
Level 2	0.47	0.16	0.34	0.66	19.36	**<.0001***	0.47	0.16	0.34	0.66	19.52	**<.0001***
Level 3	0.63	0.18	0.43	0.90	6.19	**0.01***	0.64	0.18	0.44	0.92	5.82	**0.02***
Provider type (1=academic)	0.56	0.11	0.44	0.71	22.62	**<.0001***	0.56	0.11	0.44	0.71	22.84	**<.0001***
Provider zip code percent under poverty	0.97	0.009	0.96	0.99	5.14	**0.02***	0.97	0.009	0.96	0.99	5.57	**0.02***

[1]Results in bold are significant in the model
*Significant at α=.05

4.2.5. Pharmacy cost.

The estimated results for pharmacy costs are presented in Table 4.13. The pharmacy cost models had the largest differences between billed cost and standard cost results. In the full model, variable estimates that significantly increased pharmacy costs included: (1) Gender, where billed cost only, male gender is 1.47 times pharmacy cost compared to female gender, ([CI=1.03-2.09], p=0.03) and; (2) Length of follow up, where a per day increase in length of follow up is 1.001 times pharmacy billed cost ([CI=1-1.002], p=0.002) and had the same result in pharmacy standard cost.

Variable estimates that significantly reduced pharmacy costs included: (1) Severity level, where level 1 severity is 0.45 times the pharmacy billed cost of severity level 4, ([CI=0.22-0.92], p=0.03) and 0.42 times the pharmacy standard cost of severity level 4, ([CI=0.21-0.84], p=0.01), level 2 severity is 0.59 times the pharmacy billed cost of severity level 4, ([CI=0.37-0.94], p=0.03) and 0.60 times the pharmacy standard cost of severity level 4, ([CI=0.39-0.94], p=0.03) and severity level 3, standard cost only, is 0.60 times the pharmacy cost of severity level 4, ([CI=0.37-0.97], p=0.04) and; (2) Provider type, where a community provider, in standard cost only, is 0.67 times the pharmacy cost of an academic provider, ([CI=0.46-0.97], p=0.04); and (3) Provider % under poverty, standard cost only, where a one percent increase in the rate of % under poverty is 0.96 times the pharmacy standard cost, ([CI=0.93-0.99], p=0.01).

Variable estimates not significant in the full model include: (1) Gender, standard cost only, where male gender is 1.33 times pharmacy cost compared to female gender, ([CI=0.95-1.87), p=0.09); (2) Severity level 3, billed cost only, is 0.66 times the pharmacy cost of severity level 4, ([CI=0.40-1.1], p=0.11); (3) Treatment type, where

chemotherapy only treatment is 0.91 times the pharmacy billed cost of chemotherapy and HCT, ([CI=0.47-1.76], p=0.79) and 0.83 times the pharmacy standard cost, ([CI=0.44-1.55], p=0.5 6); (4) Payer type, where a commercial payer was 1.25 times the pharmacy billed cost than a public payer, ([CI=0.87-1.80], p=0.22) and 1.39 times the pharmacy standard cost, ([CI=0.99-1.07], p=0.06); (5) Patient county % under poverty, where a 1% increase in patient county % under poverty is 1.02 times pharmacy billed cost, ([CI=0.98-1.06], p=0.3) and 1.02 times pharmacy standard cost, ([CI=0.99-1.07], p=0.16); (6) Provider type, billed cost only, where a community provider is 0.73 times the pharmacy billed cost of an academic provider, ([CI=0.50-1.08], p=0.12); and (7) Provider % under poverty, billed cost only, where a one percentile increase in the rate of provider % under poverty is 0.96 times the pharmacy billed cost, ([CI=0.94-1.05], p=0.05).

In the reduced pharmacy cost model, two variable estimates significantly increased pharmacy cost: (1) Age, where a per year increase in age is 1.02 times the pharmacy billed cost, ([CI=1.01-1.03], p=<.0001) and is 1.01 times pharmacy standard cost, ([CI=1.01-1.02], p<.0001); and (2) Length of follow up, where a per day increase in length of follow up is 1.002 times the pharmacy billed cost, ([CI=1.001-1.002], p<.0001) up is <1.001 times pharmacy standard cost, ([CI=1-1.002], p=0.02).

Variable estimates that decreased pharmacy standard cost included: (1) Severity level, standard cost only, where severity level 1 is 0.34 times the pharmacy standard cost of severity level 4, ([CI=0.17-0.67], p=0.002), severity level 2 is 0.60 times the pharmacy standard cost of severity level 4, (CI=0.39-0.93], p=0.02) and, severity level 3 is 0.59 times the pharmacy standard cost of severity level 4, ([CI=0.35-0.96], p=0.03); (2) Provider type, standard cost only, where a community provider cost is 0.62 times the

pharmacy standard cost of an academic provider, ([0.44-0.89], p=0.01); and (3) Provider % under poverty, standard cost only, where a 1 % increase in the provider % under poverty rate is 0.95 times the pharmacy standard cost, ([CI=0.93-0.98], p=0.002). Gender is not significant in the reduced model.

Table 4.13. Estimated Results for Pharmacy Cost.

Model	Pharmacy billed cost						Pharmacy standard cost					
Full model[1]	e^{β} pharmacy billed cost	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value	e^{β} pharmacy standard cost	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value
Age	1.01	0.003	1.001	1.02	21.20	**<.0001**	1.01	0.003	1.007	1.02	16.34	**<.0001**
Gender (1=female)	1.47	0.18	1.03	2.09	4.63	**0.03**	1.33	0.17	0.95	1.87	2.86	0.09
Length of follow up	1.001	<0.001	1.00	1.002	4.44	**0.002**	<1.001	<0.001	1.00	1.001	5.76	**0.02**
Treatment type (1=chemo+HCT)	0.91	0.33	0.47	1.76	0.07	0.79	0.83	0.31	0.44	1.55	0.33	0.56
Severity (4=high)												
Level 1	0.45	0.35	0.22	0.92	4.71	**0.03**	0.42	0.34	0.21	0.84	6.01	**0.01**
Level 2	0.59	0.23	0.37	0.94	4.96	**0.03**	0.60	0.22	0.39	0.94	4.97	**0.03**
Level 3	0.66	0.25	0.40	1.10	2.49	0.11	0.60	0.24	0.37	0.97	4.26	**0.04**
Individual county percent under poverty	1.02	0.02	0.98	1.06	1.06	0.30	1.02	0.01	0.99	1.07	2.00	0.16
Payer type (1=public)	1.25	0.18	0.87	1.80	1.52	0.22	1.39	0.17	0.99	1.95	3.66	0.06
Provider type (1=academic)	0.73	0.19	0.50	1.08	2.43	0.12	0.67	0.18	0.46	0.97	4.40	**0.04**
Provider zip code percent under poverty	0.96	0.01	0.94	1.05	3.89	0.06	0.96	0.01	0.93	0.99	6.21	**0.01**

Model	Pharmacy billed cost						Pharmacy standard cost					
Reduced model[1]	e^{β} pharmacy billed cost	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value	e^{β} pharmacy standard cost	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value
Age	1.02	0.00	1.01	1.03	35.34	**<.0001***	1.01	0.003	1.01	1.02	16.02	**<.0001***
Gender (1=female)	1.34	0.16	0.97	1.85	3.15	0.08	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Length of follow up	1.002	<0.001	1.001	1.002	30.71	**<.0001***	<1.001	<0.001	1.00	1.002	5.55	**0.02***
Severity[3] (4=high)												
Level 1	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	0.34	0.34	0.17	0.67	9.87	**0.002***
Level 2	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	0.60	0.22	0.39	0.93	5.12	**0.02***
Level 3	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	0.59	0.24	0.35	0.96	4.48	**0.03***
Provider type (1=academic)	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	0.62	0.18	0.44	0.89	6.54	**0.01***
Provider zip code percent under poverty	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	0.95	0.01	0.93	0.98	9.36	**0.002***

[1]Results in bold are significant in the model
*Significant at α=.05

4.2.6. Professional cost.

The estimated results for the professional cost are presented in Table 4.14. In the full model only length of follow up increased professional costs where the per day increase in length of follow up is 1.001 times professional billed cost, ([CI=1.001-1.002], p<.0001), and 1.002 times professional standard cost, ([CI=1.002-1.003], p<.0001).

Variable estimates that significantly reduced professional costs included: (1) Treatment type, where chemotherapy only treatment is 0.19 times the professional billed cost of chemotherapy and HCT, ([CI=0.11-0.34], p<.0001) and 0.22 times the professional standard cost of chemotherapy and HCT, ([CI=0.12-0.37]), p<.0001); (2) Severity level, where severity level 1 is 0.44 times the professional billed cost of severity level 4, ([CI=0.28-0.69], p=0.0003) and 0.48 times the professional standard cost of severity level 4, ([CI=0.31-0.72], p=0.0006) and, severity level 2 is 0.44 times the professional billed cost of severity level 4, ([CI=0.32-0.6], p<.0001) and is 0.46 times the professional standard cost of severity level 4, ([CI=0.34-0.63], p<.0001); and (4) Age, where a per year increase in age is 0.98 times the professional billed cost, ([CI=0.98-0.99], p<.0001), with the same result for professional standard cost.

Variable estimates that were not significant in the full model included: (1) Gender, where male gender is 1.24 times the professional billed cost, ([CI=0.99-1.55]), p=0.05) and 1.21 times professional standard cost, ([CI=0.98-1.5], p=0.08); (2) Severity level 3 is 0.78 times the professional billed cost of severity level 4, ([CI=0.55-1.12], p=0.19) and 0.82 times the professional standard cost of severity level 4, ([CI=0.58-1.17], p=0.28); (3) Payer type, where a commercial payer is 0.95 times the professional billed cost of a public payer, ([CI=0.75-1.19], p=0.67) and 0.93 times the professional standard

cost of a public payer, ([CI=0.74-1.17], p=0.56); (4) Patient county % under poverty, where a 1% increase in county % under poverty is 0.99 times professional billed cost, ([CI=0.97-1.02], p=0.94), and 0.99 times professional standard cost, ([CI=0.97-1.02], p=0.66); (5) Provider type, where a community provider is 0.98 times professional billed cost, ([CI=0.97-1.003], p=0.1) and 0.99 times professional standard cost, ([CI=0.97-1.008], p=0.31); and (6) Provider % under poverty, where a 1% increase in the provider % under poverty rate is 0.98 times professional billed cost, ([CI=0.97-1.003], p=0.1) and 0.99 times professional standard cost, ([CI=0.97-1.008], p=0.31).

In the reduced model, the variable estimate that increased professional cost is length of follow up, where a per day increase in the length of follow up is 1.002 times professional billed cost, ([CI=1.002-1.003]), p<.0001) with the same result for professional standard cost.

Variable estimates that resulted in a cost reduction were: (1) Treatment type, where chemotherapy only treatment is 0.20 times the professional billed cost of chemotherapy and HCT, ([CI=0.11-0.33], p<.0001) and 0.22 times the professional standard cost of chemotherapy and HCT, ([CI=0.12-0.36], p<.0001); and (2) Severity level, where severity level 1 is 0.45 times the professional billed cost of severity level 4, ([CI=0.32-0.65], p<.0001) and 0.47 times the professional standard cost of severity level 4, ([CI=0.34-0.67], p<.0001) and severity level 2 is 0.49 times the professional billed cost of severity level 4, ([CI=0.39-0.62], p<.0001) and 0.51 times the professional standard cost of severity level 4, ([CI=0.41-0.63], p<.0001).

Table 4.14. Estimated Results for Professional Cost.

Model	Professional billed cost						Professional standard cost					
Full model[1]	e^{β} professional billed cost	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value	e^{β} professional standard cost	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value
Age	0.98	0.002	0.98	0.99	41.18	**<.0001**	0.98	0.002	0.98	0.99	47.27	**<.0001**
Gender (1=female)	1.24	0.11	0.99	1.55	3.58	0.06	1.21	0.11	0.98	1.50	3.03	0.08
Length of follow up	1.001	<0.001	1.001	1.002	59.08	**<.0001**	1.002	<0.001	1.002	1.003	77.47	**<.0001**
Treatment type (1=chemo+HCT)	0.19	0.28	0.11	0.34	33.02	**<.0001**	0.22	0.27	0.12	0.37	30.31	**<.0001**
Severity (4=high)												
Level 1	0.44	0.22	0.28	0.69	13.23	**0.0003**	0.47	0.21	0.31	0.72	11.70	**0.0006**
Level 2	0.44	0.16	0.32	0.60	25.87	**<.0001**	0.46	0.15	0.34	0.63	23.38	**<.0001**
Level 3	0.78	0.18	0.55	1.12	1.71	0.19	0.82	0.17	0.58	1.17	1.15	0.28
Individual county percent under poverty	0.99	0.01	0.97	1.02	0.01	0.94	0.99	0.01	0.97	1.02	0.19	0.66
Payer type (1=public)	0.95	0.11	0.75	1.19	0.18	0.67	0.93	0.11	0.74	1.17	0.32	0.56
Provider type (1=academic)	0.98	0.12	0.77	1.24	0.02	0.87	0.91	0.11	0.72	1.15	0.57	0.45
Provider zip code percent under poverty	0.98	0.008	0.97	1.003	2.77	0.10	0.99	0.008	0.97	1.008	1.02	0.31

Model	Professional billed cost						Professional standard cost					
Reduced model[1]	e^{β} professional billed cost	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value	e^{β} professional standard cost	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value
Age	0.98	0.002	0.98	0.99	38.15	**<.0001***	0.98	0.002	0.98	0.99	43.08	**<.0001***
Length of follow up	1.002	<0.001	1.002	1.003	111.67	**<.0001***	1.002	<0.001	1.002	1.003	136.28	**<.0001***
Treatment type (1=chemo+HCT)	0.20	0.28	0.11	0.33	32.07	**<.0001***	0.22	0.27	0.12	0.36	29.84	**<.0001***
Severity[2] (4=high)												
Level 1	0.45	0.17	0.32	0.65	20.27	**<.0001***	0.47	0.17	0.34	0.67	18.34	**<.0001***
Level 2	0.49	0.11	0.39	0.62	36.48	**<.0001***	0.51	0.11	0.41	0.63	35.04	**<.0001***

[1]Results in bold are significant in the model
[2]Severity level 3 and 4 are combined
*Significant at α=.05

4.3. Results of the Hierarchical Model.

The hierarchical model (HM) analyzes the third specific aim of the study: to investigate if patient and community enabling variables have added influence on cost over and above patient predisposing characteristics and patient need for services. The model was run using the total cost criterion data only and results are presented in Table 4.15. The hierarchical model was set up with three parts: (1) A model which included only the patient predisposing characteristics of age, gender, length of follow up and the need for services variables of treatment type and severity level and; (2) A model which included all variables included in the study: the predisposing characteristics of age, gender and length of follow up, the need for services variables of treatment type and severity level and the patient and community enabling variables of payer type, county % under poverty, provider type and provider % under poverty and; (3) A reduced model which included only those variables that were significant in the full model.

The first model of patient predisposing characteristics and need for services variables resulted in significant estimates for all variables with the exception of severity level 3 and included: (1) A per year increase in age is estimated to be 0.99 times the total billed and total standard cost outcome, ([CI=0.99-0.99]), p=0.0001) and ([CI=0.99-0.99], p=0.001) respectively; (2) Male gender is estimated at 1.78 times the cost outcome of female gender in billed cost and 1.68 times the cost outcome of female gender in standard cost, (CI=1.37-2.29], p<.0001) and (CI=1.29-2.18], p<.0001). However, while there is a significant p-value, the confidence intervals are wide and the estimate is not reliable; (3) A per day increase in length of follow up in the datamart estimated a 1.001 increase in the cost outcomes, ([CI=1-1.001], p<.0001) and ([CI=1.001-1.002]. p<.0001); (4)

Chemotherapy only treatment was estimated to be 0.12 times the billed cost outcome of chemotherapy and HCT and 0.13 times the standard cost outcome of chemotherapy and HCT, ([CI=0.05-0.21], p<.0001) and (CI=0.06-0.23], p<.0001), indicating a large difference between the treatment groups. Confidence intervals were in an acceptable range; and (5) Severity levels 1 and 2 were significant in both the billed cost and standard cost models. Level 1 estimates are 0.35 times the level 4 billed cost, ([CI=0.21-0.59], p<.0001) and 0.34 times level 4 standard cost, ([CI=0.02-0.58], p<.0001). Level 2 estimates are 0.36 times level 4 billed cost, ([CI=0.25-0.51], p<.0001), and 0.38 times standard cost, ([CI=0.26-0.54], p<.0001). Confidence intervals were in an acceptable range. Level 3 severity was not significant in the model.

The full model added the patient and community enabling resources to the analysis, patient county % under poverty, payer type, provider type and provider % under poverty. Of these additional variables, only provider type was significant where a community provider is estimated to be 0.68 times billed cost, ([CI=0.51-0.89], p=.007) and 0.67 times standard cost, ([CI=0.50-0.88], p=0.006).

The reduced model incorporated all significant variables from the full model; age, gender, length of follow up, treatment type, severity levels 1 and 2 and provider type and had the same result as the total cost predictive variables model where: (1) Gender has a large influence with male costs 1.75 times the billed cost of females ([CI=1.36-2.27], p<.0001) and 1.66 times the standard cost of females ([CI=1.28-2.15), p=0.0001), however the confidence intervals are wide and therefore the estimate may not be reliable; (2) A per year increase in age is 0.98 times billed cost, ([CI=0.98-0.99], p<.0001) and 0.99 times standard cost, ([CI=0.98-0.99], p=0.0007); (3) A per day increase in the length

of follow up increased billed cost by 1.001 times, ([CI-1.001-1.002], p<.0001) and had the same result for the standard cost outcome, (4) Chemotherapy only is 0.13 times the billed cost of chemotherapy and HCT, ([CI=0.06-0.23], p<.0001) and 0.14 times the standard cost of chemotherapy and HCT, ([CI=0.06-0.26], p<.0001); and (5) Severity levels 1 and 2 were significant in the model, however the variable continued to have a problem with wide confidence intervals. Severity level 1 is 0.44 times the billed cost of severity level 4, ([CI=0.28-0.70], p=0.0003) and 0.41 times the standard cost of severity level 4, ([CI=0.26-0.62], p=0.0002). Severity level 2 is 0.44 times the severity level 4 billed cost outcome, ([CI=0.33-0.58], p<.0001) and 0.45 times the severity level 4 standard cost outcome and; (6) Provider type is the only community enabling resource included in the reduced model. A community provider cost is 0.73 times the billed cost ([CI=0.57-0.9], p=0.02) and 0.71 times standard cost ([CI=0.54-0.95], p=0.01).

Table 4.15. Estimated Results of the Hierarchical Model.

Model	Total billed cost						Total standard cost					
Predisposing characteristics and need model	e^{β} total billed cost	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value	e^{β} total standard cost	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value
Age	0.99	0.002	0.99	0.99	15.12	**0.0001**	0.99	0.002	0.99	0.99	10.17	**0.001**
Gender (1=female)	1.78	0.12	1.37	2.29	19.93	**<.0001**	1.68	0.13	1.29	2.18	15.14	**<.0001**
Length of follow up	1.001	<0.001	1.00	1.001	36.79	**<.0001**	1.001	<0.001	1.001	1.002	36.06	**<.0001**
Treatment type (1=chemo+HCT)	0.12	0.32	0.05	0.21	42.53	**<.0001**	0.13	0.33	0.06	0.23	37.46	**<.0001**
Severity (4=high)												
Level 1	0.35	0.25	0.21	0.59	16.59	**<.0001**	0.34	0.25	0.20	0.58	17.11	**<.0001**
Level 2	0.36	0.18	0.25	0.51	30.78	**<.0001**	0.38	0.18	0.26	0.54	26.78	**<.0001**
Level 3	0.71	0.21	0.46	1.07	2.61	0.11	0.76	0.21	0.50	1.17	1.52	0.22

Model	Total billed cost						Total standard cost					
Full Model	e^{β} total billed cost	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value	e^{β} total standard cost	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value
Age	0.99	0.002	0.98	0.99	14.19	**0.0002**	0.99	0.002	0.99	0.99	9.73	**0.002**
Gender (1=female)	1.69	0.13	1.29	2.20	15.38	**<.0001**	1.59	0.13	1.22	2.09	11.55	**0.0007**
Length of follow up	1.001	<0.001	1.001	1.002	28.10	**<.0001**	1.001	<0.001	1.001	1.002	28.47	**<.0001**
Treatment type (1=chemo+HCT)	0.12	0.32	0.06	0.22	39.79	**<.0001**	0.14	0.33	0.06	0.25	34.16	**<.0001**
Severity (4=high)												
Level 1	0.36	0.25	0.21	0.006	15.84	**<.0001**	0.35	0.26	0.21	0.59	15.87	**<.0001**
Level 2	0.39	0.18	0.27	1.08	25.72	**<.0001**	0.41	0.19	0.28	0.60	21.32	**<.0001**
Level 3	0.96	0.21	0.47	1.08	2.44	0.12	0.77	0.21	0.50	1.18	1.38	0.24
Individual county percent under poverty	0.99	0.01	0.97	1.02	0.07	0.79	0.99	0.01	0.97	1.22	0.09	0.77
Payer type (1=public)	0.77	0.13	0.59	1.01	3.56	0.06	0.79	0.13	0.59	1.04	2.72	0.10
Provider type (1=academic)	0.68	0.14	0.51	0.89	7.30	**0.007**	0.67	0.14	0.50	0.88	7.62	**0.006**
Provider zip code percent under poverty	0.99	0.01	0.98	1.02	0.21	0.65	0.99	0.01	0.97	1.16	0.47	0.49

Model	Total billed cost						Total standard cost					
Reduced model	e^{β} total billed cost	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value	e^{β} total standard cost	SE	e^{β} 95% CI low	e^{β} 95% CI high	χ^2	p-value
Age	0.98	0.002	0.98	0.99	17.11	**<.0001***	0.99	0.002	0.98	0.99	11.46	**0.0007***
Gender (1=female)	1.75	0.12	1.36	2.27	19.07	**<.0001***	1.66	0.13	1.28	2.15	14.61	**0.0001***
Length of follow up	1.001	<0.001	1.001	1.002	30.85	**<.0001***	1.001	<0.001	1.001	1.002	32.08	**<.0001***
Treatment type (1=chemo+HCT)	0.13	0.32	0.06	0.23	38.63	**<.0001***	0.14	0.33	0.06	0.26	33.30	**<.0001***
Severity[2] (4=high)												
Level 1	0.44	0.22	0.28	0.70	12.94	**0.0003***	0.41	0.23	0.26	0.61	14.26	**.0002***
Level 2	0.44	0.14	0.33	0.58	32.09	**<.0001***	0.45	0.14	0.34	0.61	28.47	**<.0001***
Provider type (1=academic)	0.73	0.13	0.57	0.9	5.05	**0.02***	0.71	0.13	0.54	0.94	5.65	**0.01***

[1]Results in bold are significant in the model [2]Severity level 3 and 4 are combined *Significant at α=.05

4.4. Summary of Study Results.

A summary of the study results are provided for predictor variable characteristics, criterion variable mean, the reduced models predictions and the hierarchical model predictions.

4.4.1. Summary of predictor variable characteristics.

A summary of predictor variable characteristics for each cost criterion is presented in Table 4.16.

Acute leukemia patient characteristics of the study sample are consistent with what is reported nationally (http://seer.cancer.gov). Patient demographics were similar for each criterion with a mean age of either 27 or 28 and a higher percentage of males, ranging from 56%-66%, as expected from the higher rate of leukemia diagnoses in males. This is similar to Surveillance Epidemiology and End Results (SEER) statistics showing a higher percentage of men with acute leukemia diagnoses and a combination of a younger ALL population and an older AML population.

The length of follow (LOF) up variable methodologically controls for systematic differences in dates of service available in the data as recommended by Diehr (Diehr, et.al, 1999). In this sample, mean LOF ranged from 330-445 days and had a range of 0-729. Much of the date of service data indicated same day service, or a zero LOF. Total and professional costs were larger samples and contain more of the zero LOF data resulting in lower means, 330 days and 354 days respectively. Ongoing treatment is more likely to be seen in ancillary cost, mean 439 day, inpatient cost, mean 420 days, and outpatient cost, mean 388 days and would be expected to have a longer and more

consistent LOF. The highest mean LOF present in pharmacy cost, mean 445 days, reflects a higher level of ongoing pharmaceutical use.

Most of the patients were treated with chemotherapy only. Treatment type is dominated by chemotherapy only, ranging from 94% - 97% in the total cost, outpatient cost, pharmacy cost and professional cost. Ancillary cost and inpatient cost with slightly lower percentiles of 88% and 89% respectively, reflect the higher use of services by the HCT treated patients with males representing 63% of the HCT treatment type.

Level of severity is not similar between costs. Severity is measured by 4 levels with1 as the lowest and 4 as the highest. Higher levels of severity of illness and related hospitalization are reflected in the higher levels of severity in the hospital-based ancillary cost and inpatient cost which show a higher percentage of high/medium to high levels of severity, 38% and 51%. Total cost, outpatient cost, pharmacy cost and professional cost show more low to low medium levels of severity, 57% to 65%.

Patient % under poverty had little variation between the mean percentages with a limited range of 11.98% - 12.41%. The % under poverty rate was collected from U.S. census data using the county zip code data from the WHIO datamart. Patient zip code was available in the WHIO datamart at the county level only as part of data de-identification. Unfortunately, county level zip code data is very broad; limiting the strength of the patient poverty measure.

There is a higher percentage of use of public payers in the acute leukemia population. Payer type was similar in all costs and showed a higher percentile of public payers compared to commercial payers, 52% to 56%; a result different from the U.S.

census reported percentage of 31% of all Americans covered by public insurance in 2011 (www.census.gov/hhes).

The majority of acute leukemia patients receive care from a community provider only. Provider type was similar in all costs with the majority of patients treated at a community provider only, 45% - 52%. However of the 839 provider available, only 792 were identifiable, resulting in percentages of missing data ranging from 13% in inpatient cost to 24% in total cost. Patient records with missing provider data were not used in analysis. In addition, overall use of community providers is under represented due to coding all claims for a patient who used an academic center as 'academic'.

Providers that treat acute leukemia are located in areas with relatively low levels of poverty. The provider % under poverty variable represents the U.S. census poverty rate of the zip code of the provider and had a mean range of 5.97%-6.70%. Provider zip code was obtained through the contact information listed in the WHIO datamart.

Table 4.16. Summary of Predictor Variable Characteristics.

Variables	Total cost	Ancillary cost	Inpatient cost	Outpatient cost	Pharmacy cost	Professional cost
Predisposing characteristics						
Age, *n*	837	164	232	639	390	748
Mean	27	28	27	27	27	27
Gender, *n (%)*	837	164	232	639	390	748
Male	470 (56)	102 (62)	153 (66)	365 (57)	232 (59)	419 (56)
Length of follow up, *n*	837	164	232	639	390	748
Mean	330	439	420	388	445	354
Need						
Treatment type, *n (%)*	837	164	232	639	390	748
Chemotherapy only	810 (97)	145 (88)	206 (89)	612 (96)	365 (94)	722 (97)
Chemotherapy and HCT	27 (3)	19 (12)	26 (11)	27 (4)	25 (6)	26 (3)
Severity, *n (%)*	837	164	232	639	390	748
Low	95 (11)	10 (6)	19 (12)	71 (11)	38 (10)	84 (11)
Low/medium	445 (53)	53 (33)	92 (39)	338 (53)	185 (47)	405 (54)
High/medium	152 (18)	40 (24)	60 (24)	131 (21)	84 (22)	138 (18)
High	145 (17)	61 (37)	61 (25)	99 (15)	83 (21)	121 (16)
Enabling resources						
Patient % under poverty, *n*	837	164	232	639	390	747
Mean	12.36	12.43	11.98	12.23	12.40	12.41
Payer type, *n (%)*	837	164	232	639	390	748
Commercial	400 (48)	72 (44)	102 (44)	309 (48)	173 (44)	352 (47)
Public	437 (52)	92 (56)	130 (56)	330 (52)	217 (56)	396 (53)
Provider type, *n (%)*	837	164	232	639	390	618
Community	410 (49)	74 (45)	111 (48)	303 (47)	185 (47)	390 (52)
Academic medical center	228 (27)	64 (39)	90 (39)	194 (30)	140 (36)	228 (31)
Not determined	199 (24)	26 (16)	31 (13)	142 (23)	65 (17)	130 (17)
Provider % under poverty, *n*	638	138	201	497	325	618
Mean	6.35	5.97	6.10	6.41	6.70	6.44

4.4.2. Summary of criterion variable means.

A summary of the mean of each criterion variable by cost type is presented in Table 4.17. Both types of cost, billed and standard, are analyzed to determine if their model results are consistent.

Billed costs to patients do not reflect actual costs of service and are, with the exception of ancillary cost, highly inflated. Average standard total cost is 50% less than billed total cost with a mean of $43,379 versus $86,309, and represents a reduction between the charges to the patient versus a valuation of actual cost of services. The differences support concerns regarding the lack of financial transparency within the health care sector.

Mean standard ancillary cost is equivalent to mean billed ancillary cost; $4,123 versus $4,101. Standard ancillary cost is based on relative value units, RVU's, from the Medicare fee schedule and in this sample the hospital facility charges are not higher than the standard RVU rate.

Mean standard inpatient cost is 48% lower than mean billed inpatient cost; $80,787 versus $155,435. Inpatient cost is standardized using a per diem cost, calculated with the diagnosis-related group (DRG) and the length of stay, taking into account the facility type and whether major surgery occurred. The differences between the mean billed cost and mean standard cost identify differences in what is charged to the patient versus an estimate of the actual cost of inpatient services.

Mean standard outpatient cost is 61% lower than mean billed outpatient cost; $8,410 versus $21, 424. Outpatient standard cost uses a percentage of the billed amount and is adjusted by a WHIO-specific conversion factor to approximate an allowed amount.

Mean standard pharmacy costs are 29% lower than mean billed cost, $17,078 versus $24,108. Pharmacy costs are standardized using the average wholesale price (AWP) for the National Drug Code (NDC), adjusted by the therapeutic category and generic status.

Mean standard professional costs are 60% lower than mean billed costs; $6,491 versus $16,077. Professional cost also uses RVU's to standardize cost and the variation represents differences between what is charged to the patient and the RVU rate from the Medicare fee schedule.

Table 4.17. Summary of Criterion Variable Means.

Criterion variable ($)	Mean billed cost	Mean standard cost
Total cost	86,309	43,379
Ancillary cost	4,101	4,123
Inpatient cost	155,435	80,787
Outpatient cost	21,424	8,410
Pharmacy cost	25,108	17,078
Professional cost	16,077	6,491

4.4.3. Summary of reduced model predictions.

A summary of the reduced model predictions for billed cost, Table 4.18, and standard cost, Table 4.19, of each criterion variable is presented.

4.4.3.1. Billed cost.

Younger age is predictive of higher cost in the acute leukemia population; with the exception of pharmacy cost and is the only variable included in every billed cost reduced model. A per year increase in age generally resulted in a cost reduction by an estimated 0.98-0.99 times the cost criterion, however pharmacy cost had an estimated increase in cost of 1.02 times. In each of the reduced models, the confidence intervals are small and, except for ancillary cost, p-values were significant. The result is opposite the

documented increase in healthcare cost with increasing age as described in Seshamani and Grey, and, Garrett and Martini reflecting the higher use and more aggressive treatment of younger patients within the acute leukemia population. Pharmacy cost follows the trend of higher cost associated with increasing age (Seshamani & Grey, 2004; Garret & Martini, 2007). .

Male gender is significantly predictive of higher cost in total cost, inpatient cost, and outpatient cost. Gender was not included in the ancillary cost and professional cost reduced models and was not significant in the pharmacy cost reduced model. The gender estimates in total cost, inpatient and outpatient cost models indicated a significantly strong increase in cost for males ranging from 1.32 to 1.75 times female cost. While the p-values were significant, the confidence intervals were wide for this variable making the specific estimate not reliable. The result in this sample is opposite what is generally reported in healthcare utilization where females have been shown to have a higher utilization rate, and would be expected to have higher costs (Bertakis, et.al, 2000).

Length of follow up has a small but significant impact on the cost criterion. With the exception of ancillary cost, length of follow up significantly entered every reduced model and was significant in each of the models. In total, outpatient, pharmacy and professional cost, length of follow up estimated a small per day increase in the costs with estimates ranging from 1, no change, to <1.001. Inpatient cost showed a slight decline as follow up increased with an estimate of 0.99 times a per day increase. Because this variable controls for systematic differences in length of follow up in the sample, the relative small effect indicates that these differences may not have a large influence on the overall cost criterion but should not be ignored.

Lower levels of severity show a large reduction in most costs. Severity level entered every reduced model but pharmacy cost and is significant in every model except for ancillary cost severity level 1. Lower levels of severity had a range of 0.3-0.53 times the cost of severity level 4 and with p-values that are strong and similar between the models. The confidence intervals for this variable are wide making the estimates unreliable. However, while a specific rate may not be easily identified, it can be concluded that lower levels of severity are significantly less costly than higher levels of severity with between a 47% to 70% reduction in cost.

Patients treated with HCT experience significantly higher costs, up to 87% more than patients treated with chemotherapy only. Treatment type estimates were significant and included in each cost with the exception of ancillary cost and pharmacy cost. The significant estimates predicted the chemotherapy only cost ranging from 0.13 times to 0.26 times the billed cost of patients treated with HCT. The variable estimate is strongly significant in each model and had acceptable confidence intervals.

Community provider costs can be up to 55% lower than academic medical centers; however the degree of reduction is dependent on the cost criterion. Except for professional cost, provider type was included in all reduced models and was significant in each. The estimated influence was mixed; it was strong in ancillary cost where a community provider cost is 0.45 times that of an academic provider. However, its confidence interval is wide and the specific estimate is not reliable. Total and outpatient estimates of 0.73 and 0.71 respectively indicated a moderate influence; the confidence intervals were better but still wide. The outpatient estimate of 0.97 was small, but the confidence intervals were also small resulting in a more reliable estimate.

Table 4.18. Summary of Estimated Reduced Model Results for Billed Cost.

		Billed Cost				
	Total	Ancillary	Inpatient	Outpatient	Pharmacy	Professional
Predisposing characteristics						
Age						
e^{β}	0.98	0.99	0.98	0.99	1.02	0.98
95% CI	0.98-0.99	9.98-1.004	0.98-0.99	0.99-0.99	1.01-1.03	0.98-0.99
p-value	<.0001	0.15	<.0001	0.001	<.0001	<.0001
Gender						
e^{β}	1.75		1.41	1.32	1.34	
95% CI	1.36-2.27		1.05-1.89	1.05-1.64	0.97-`.85	
p-value	<.0001		0.02	0.02	0.08	
Length of follow up						
e^{β}	1		0.99	1.001	<1.001	1.002
95% CI	0-1		0.99-1	1.001-1.002	1.001-1.002	1.002-1.003
p-value	<.0001		0.04	<.0001	<.0001	<.0001
Need characteristics						
Treatment type						
e^{β}	0.13		0.26	0.2		0.2
95%CI	0.06-0.23		0.16-0.4	0.12-0.33		0.11-0.33
p-value	<.0001		<.0001	<.0001		<.0001
Severity level 1						
e^{β}	0.44	0.29	0.3	0.31		0.45
95% CI	0.28-0.7	0.10-1.01	0.17-0.55	0.19-0.49		0.32-0.65
p-value	0.0003	0.06	<.0001	<.0001		<.0001
Severity level 2						
e^{β}	0.44	0.44	0.53	0.47		0.49
95% CI	0.33-0.58	0.24-0.81	0.39-0.73	0.19-0.49		0.39-0.62
p-value	<.0001	0.008	<.0001	<.0001		<.0001
Severity level 3						
e^{β}		0.42		0.63		
95% CI		0.22-0.81		0.43-0.90		
p-value		0.008		0.01		
Enabling resources						
Provider type						
e^{β}	0.73	0.45	0.71	0.97		
95% CI	0.57-0.96	0.26-0.75	0.53-0.97	0.96-0.99		
p-value	0.02	0.002	0.03	0.02		

4.4.3.2. Standard cost.

Younger age is predictive of higher cost in the acute leukemia population; with the exception of pharmacy cost. This result in the standard cost type is the same as the

result in the billed cost type. Age is the only predictor variable that is present in each of the standard cost reduced models. In general, age estimated a reduction in standard cost of 0.98-0.99 times per year increase in age, with the exception of pharmacy cost which increased with age at an estimated 1.01 times per year. Age was not significant in the final ancillary cost model. The confidence intervals in each of the significant models were small and the p-values were strong.

Male gender is significantly predictive of higher cost in total cost, outpatient cost and pharmacy cost. This result is different from the billed cost model in a few ways; the variable did not enter the inpatient cost model as it did for billed cost, its estimates were smaller for the models it did enter, and it was significant in pharmacy standard cost. The significant estimates followed a similar trend as in billed cost with total costs resulting in the highest estimate of a male gender cost being 1.66 times female cost, followed by outpatient cost of 1.30 times and finally pharmacy cost of 1.002. However, only the pharmacy cost had confidence intervals small enough to consider the result reliable.

Length of follow up has a small but significant impact on all cost criterions. This result is similar to that of billed cost; length of follow up is present in all reduced models with the exception of ancillary cost and was not significant in the inpatient cost reduced model. In the standard total cost, outpatient cost, pharmacy cost and professional cost reduced models LOF estimated a small per day increase in cost outcome ranging from <1.001 – 1.002. The confidence intervals were small for this variable.

Lower levels of severity are predictive of lower cost. Severity level 1 and level 2 were significant in each of the models where both estimates resulted in a large reduction in the standard cost when compared to the severity level 4 cost and ranged from 0.24

times the level 4 cost in level 1 ancillary cost to 0.6 times the level 4 cost in level 2 pharmacy cost. While the p-values are strong, the confidence intervals are wide and the specific estimates are not strongly reliable. Severity level 3 also estimated a reduction from severity level 4 costs in the ancillary cost, outpatient cost and pharmacy cost models and while p-values were significant, confidence intervals were, again, wide and the estimates are unreliable. Overall the results are similar to those found in billed costs except for a notable difference in pharmacy cost. In pharmacy billed cost, severity level did not enter the reduced model; however, in pharmacy standard cost all levels of severity entered the reduced model and all levels identified significantly lower costs compared to level 4. It is important to clarify that pharmacy cost data does not include retail pharmacy costs, only costs associated with a clinical or hospital provider. Differences between billed costs and standard costs may be attributed to patient pharmacy charges not reflecting hospital and clinic pharmacy cost efficiencies obtained through the use of lower cost generics, bulk purchasing, other contractual reductions in price or eligibility for the government's 340B program, a program which reduces pharmacy cost to providers who serve disadvantaged populations (www.nachc.org).

Patients treated with hematopoietic stem cell transplant (HCT) experience significantly higher costs, up to 86% more, than patients treated with chemotherapy only. Treatment type entered each of the reduced models with the exception of ancillary cost and pharmacy cost. It estimated a large decrease in cost of treatment with chemotherapy only with estimates ranging from 0.14 times in the total cost to 0.30 times in the inpatient cost. Similar to billed cost, all reduced models were strongly significant for this variable and confidence intervals are acceptable.

Community provider costs can be up to 54% less than academic medical centers, however the degree of reduction is dependent on the cost criterion. Provider type significantly entered the models of total cost, ancillary cost, outpatient cost and pharmacy cost with estimates reducing the cost criterion by 0.71 times, 0.46 times, 0.97 times and 0.62 times. The confidence interval for outpatient cost was small; however, confidence intervals for the other estimates were wider making them less reliable. Still it may be interpreted that in these costs, a community providers cost is significantly lower than an academic medical center provider. This result is consistent with other studies that have reported higher cost of academic medical centers, (Hays, 2003; Yuan, et.al, 2000). Provider type results were different between standard cost and billed cost in two instances: (1) A significant impact in inpatient billed cost but not in inpatient standard cost; and (2) A significant impact in pharmacy standard cost but not in the pharmacy billed cost. A possible explanation for the difference between inpatient cost types may be that while the same services have the same actual cost in both types of providers there is a significant difference between how the two provider types bill for those services. Differences between pharmacy costs may be explained by academic medical centers using newer, higher cost, non-generic drugs versus community providers or they may reflect more community provider participation in the reduced cost 340B program (Hay, 2003; www.nachc.com). Interestingly, pharmacy billed charges to the patient were not significantly different by provider type and may be attributed to providers who experience cost efficiencies not passing on those reductions to the patient charges.

Providers located in areas with higher poverty rates have significantly lower inpatient and pharmacy costs. Provider % under poverty significantly entered the reduced

models with an inpatient estimate of 0.73 and a pharmacy estimate of 0.95. Both estimates are significant, but the inpatient cost confidence interval is moderately wide and makes the specific estimate less reliable. Inpatient standard cost is calculated using a per diem cost, length of stay and the presence of surgery. This finding may reflect disparities in clinical practice in areas of higher % under poverty levels and may be associated with differences in diagnosis, treatment, effective use of evidence based medicine and, ultimately, quality of care. The acute leukemia patient population is regularly treated with chemotherapy and other high end pharmaceuticals. The estimated lower pharmacy cost in higher poverty locations may be related to the higher use of generics or lower cost pharmaceuticals in these locations as well as a higher rate of participation in the 340B program which reduces pharmaceutical costs to providers serving disadvantaged populations (www.nachc.com). From a different perspective, it may relate to a higher use of more expensive, higher cost pharmaceuticals in wealthier communities.

Table 4.19. Summary of Estimated Reduced Model Results for Standard Cost.

		Standard Cost				
	Total	Ancillary	Inpatient	Outpatient	Pharmacy	Professional
Predisposing characteristics						
Age						
e^{β}	0.98	0.98	0.98	0.99	1.01	0.98
95% CI	0.98-0.99	0.97-1.002	0.98-0.99	0.99-0.99	1.01-1.02	0.98-0.99
p-value	0.0007	0.08	<.0001	0.002	<.0001	<.0001
Gender						
e^{β}	1.66			1.3	1.002	
95% CI	1.28-2.15			1.04-1.64	1.001-1.002	
p-value	0.0001			0.02	<.0001	
Length of follow up						
e^{β}	1.001		0.99	1.001	<1.001	1.002
95% CI	1-1.002		0.99-1	1.001-1.002	1-1.002	1.002-1.003
p-value	<.0001		0.05	<.0001	0.02	<.0001
Need characteristics						
Treatment type						
e^{β}	0.14		0.3	0.19		0.22
95% CI	0.06-0.26		0.2-0.45	0.12-0.32		0.12-0.36
p-value	<.0001		<.0001	<.0001		<.0001
Severity level 1						
e^{β}	0.41	0.24	0.28	0.32	0.34	0.47
95% CI	0.26-0.61	0.07-0.95	0.17-0.49	0.20-0.51	0.17-0.67	0.34-0.67
p-value	0.0002	0.02	<.0001	<.0001	0.002	<.0001
Severity level 2						
e^{β}	0.45	0.35	0.55	0.47	0.6	0.51
95% CI	0.34-0.61	0.19-0.66	0.41-0.74	0.34-0.66	0.39-0.93	0.41-0.63
p-value	<.0001	0.001	<.0001	<.0001	0.02	<.0001
Severity level 3						
e^{β}		0.32		0.64	0.59	
95% CI		0.17-0.61		0.44-0.92	0.35-0.96	
p-value		0.0004		0.02	0.03	
Enabling resources						
Provider type						
e^{β}	0.71	0.46		0.97	0.62	
95% CI	0.54-0.94	0.26-0.79		0.96-0.99	0.44-0.89	
p-value	0.018	0.005		<.0001	0.01	
Provider % under poverty						
e^{β}			0.73		0.95	
95% CI			0.55-0.95		0.93-0.98	
p-value			0.02		0.002	

4.4.4. Summary of the hierarchical model results.

Results of the hierarchical model (HM) are presented in Section 4.3 and Table 4.15.

Patient predisposing characteristics and need for services have a significant influence on the cost of care. In this acute leukemia sample, increasing age is associated with decreasing cost, a finding different from what is generally observed, and men have higher costs when compared to women, also a result different from the population norm (Seshamani & Grey, 2004; Garret & Martini, 2007; Bertakis, et.al., 2007). The length of follow up within the data set does have a slight influence on the cost outcome, and should be kept in the model to control for differences. Type of treatment highly influences cost, with patients who receive HCT having significantly higher costs compared to patients receiving chemotherapy only. Lower severity of the disease episode reduces the cost outcome when compared to higher levels of severity.

Only type of provider was significant when patient and community enabling resources variables were added to the model. A community provider costs were less than the costs of an academic medical center. Results are similar between billed cost and standard cost. All other enabling resource variables did not enter the total cost reduced model and did not significantly influence the cost outcome.

The reduced model of total cost resulted in the same set of variables of age, gender, length of follow up, treatment type, severity level 1 and 2 and provider type and all were significant in the final model. HM was performed for total cost only because of this redundancy in the reduced model results. However, HM does identify the strong

influence of patient predisposing characteristics and need for services variables on the cost criterions.

CHAPTER 5: Discussion

This study is a cross-sectional secondary analysis of WHIO insurance claims data for patients diagnosed with acute leukemia. The primary objective was to investigate how patient and community factors influence health care claims cost from the State of Wisconsin. A secondary objective was to evaluate whether patient and community enabling factors have added influence on cost over and above patient characteristics and need factors. An underlying objective of the study was to assess the type of data available in the WHIO datamart and its usefulness for cost research. This chapter will provide: (1) An overview of the study findings; (2) Study limitations; and (3) Recommendations for future research.

5.1. Discussion of Study Findings.

Anderson's basic model of health care utilization suggests that certain patient and community characteristics are considered to be predictive of a higher use of health care services (Andersen, 1968). The model guides how to investigate the influence of a limited set of administrative variables on cost. Because acute leukemia is a relatively uncommon disease holds promise to have high treatment costs the use of an administrative database is of interest because it is expected to contain a large enough sample of patients for the analysis of costs. From the study results it can be concluded: (1) Predisposing characteristics of acute leukemia patients may not follow the commonly reported direction of cost where higher cost is associated with older age and female gender. Instead their costs are expected to be higher in younger, male patients; (2) As expected, the need for service variables of treatment type and severity level influence cost and are significant cost drivers; (3) Community enabling resources of provider type and

provider location influence cost where academic medical centers are associated with higher cost and providers located in areas with higher poverty are associated with lower costs; both raise questions of equity in treatment offered to patients dependent on where they receive treatment; and (4) Costs related to different service types cannot be assumed to follow similar predictive patterns and will subsequently have differences in interpretation. Research involving cost estimation and cost effectiveness should clearly identify the type of service costs being analyzed.

5.1.1. Influence of patient predisposing characteristics.

As expected, this study has confirmed that certain patient characteristics are predictive of cost. However, their influence on cost in an acute leukemia population was not always similar to what is more generally found. Prior research has shown that as the age of the U.S. population increases, the utilization rate and cost of health care also increases (Seshamani & Grey, 2004; Garret & Martini, 2007). As age increased in the acute leukemia sample the cost criterion decreased in all but pharmacy cost. This may be attributed to a number of factors including more aggressive and costly treatment of younger patients as well as less treatment options and therefore lower cost for older patients. Hematopoietic stem cell transplant (HCT) is not common in patients over 70 years of age and both HCT and chemotherapy treatment becomes increasingly less aggressive in patients over the age of 60. Interestingly, Zweifel and colleagues argue that age as a driver of higher cost becomes insignificant when proximity to death, and the resulting costs, is controlled for. This study supports cost of treatment being the important cost driver rather than age (Zweifel, Felder, Werblow, 2004).

Bertakis identified a gender difference in the use of healthcare services with women having a higher rate of use (Bertakis, et.al, 2000). However, in this study men had higher costs; over 50% more in some instances. The percentage of males in the study sample was comparable to the Surveillance Epidemiology and End Results (SEER) reported diagnosis population for the acute leukemia's; 56% in the study sample versus SEER reported 58% in ALL and 53% in AML.

5.1.2. Influence of patient need for services.

The results of this study confirm the expected higher health care costs for acute leukemia patients associated with their high need for health care services. A higher level of severity, related to more comorbidity, would be expected to increase the cost of care and this variable was significant in each cost service type. Treatment type was significant in all models with the exception of ancillary cost and pharmacy cost and represents a major driver of cost. Treatment with hematopoietic stem cell transplant (HCT) significantly increases the cost of care in all other service types; total, inpatient, outpatient and professional. It is not unexpected that HCT influences cost, however, the strength of its influence, with costs up to 86% higher than chemotherapy only treatment was more than expected. The result is consistent with HCT's identification as the procedure with the most rapidly increasing cost between 2004 and 2007 and it is assumed that the cost will continue to increase over time (Stranges, et.al, 2009). HCT cost has been reported in numerous articles with subjects ranging from cost effectiveness of different treatment options to its overall cost of treatment (Majhail, et.al, 2009; Westerman, et.al., 1996; Waters, et.al., 1998; Cordonnier, et.al., 2005; Lee et.al., 2000; Lin et.al., 2010). Khera and colleagues provide a comparison of HCT economic studies

and identify the need for high quality measures of cost and value-based assessments (Khear, Zeliadt, & Lee, 2012). This study provides a quality measure of cost; the challenge will be to link the cost to clinical outcome and to create a value measurement. Given that HCT is intended to be a life-saving treatment, usually of last resort, a quality adjusted life years (QALY) study could be designed to investigate the cost per year of life saved. Advances in scientific knowledge have expanded its use to a variety of hematologic diseases, disorders as well as patients. However, it's extremely high cost makes it vulnerable to cost containment processes. In order to insure that this type of treatment is equitably offered based on clinical outcome rather than the ability to pay, valued-based research (i.e. value=cost+outcome) needs to be used to support well-informed policy decision making.

5.1.3. Influence of community enabling resources.

An important finding of this study is that the community enabling variables provider type and provider location influence some costs. In Anderson's model, socioeconomics is considered a factor that may impact how patients use heath care services where higher socioeconomic status is related to factors that support higher utilization, (i.e. if a healthcare provider is located in the community, all services are easily accessible, if there are preventive services, etc.). In this study, the rate of poverty around the location of the provider is a socioeconomic measure of differences between providers located in areas with higher poverty versus providers located in wealthier areas. The provider % under poverty variable estimate was significant in both inpatient standard cost and pharmacy standard cost and resulted in a cost reduction where lower costs were associated with providers located in areas of higher levels of poverty.

Inpatient costs are standardized using a per diem cost calculated with the factors of; diagnosis related group (DRG), length of stay, facility type and presence of major surgery. Provider percent under poverty uses the U.S. census defined % under poverty rate identified through the zip code of the provider. Reduced costs in areas of higher poverty would reflect a reduction in any one of the defined factors of; lower cost DRG's, shorter length of stays, lower cost facility types and less major surgery or some combination. A study by Billings and colleagues identified higher hospitalization rates in low-income areas due to less timely and effective outpatient care; however, this study found the opposite result for inpatient cost (Billings, Zeitel, Lukomnik, Carey, Blank, & Newman, 1993). Whereas it is not in the scope of this study to assess the type of health care services provided at different provider locations, future work could investigate possible differences in the types of services provided, the provider's availability to offer certain services, and whether access to needed health care services is compromised in low income areas.

In the pharmacy cost sample lower standard cost is also associated with higher levels of poverty of the provider's location. Pharmacy costs are standardized using the average wholesale price from the National Drug Code (NDC), adjusted by therapeutic category and generic status. Pharmacy costs in this study did not include retail pharmacy costs. Using the standardization definition, a reduction in pharmacy cost would be associated with either different therapeutic categories, use of more generic statuses or participation in the 340B Drug Pricing Program where drug manufacturers provide a reduced 340B price for covered outpatient drugs to certain safety net providers who participate in the program. Safety net providers include health centers receiving grant

funding under Section 330 of the Public Health Service Act and similar centers. Most providers in lower socioeconomic locations would be eligible for participation in this program and the National Association of Community Health Centers (NACHC) report that the program can help them save between 15%-60% on their prescription drug costs. (www.nachc.com/client/documents). In this study, the lower pharmacy cost for providers in poorer locations may be a reflection of participation in this program. Another interpretation of the finding is that providers in poorer locations offer fewer therapeutics, more generic drugs or some combination. A potential use of WHIO data could be an assessment of differences in the type of services offered by provider location; the data may support research related to the socioeconomic influence on availability of care and access to care. Finally, it is concerning that the cost difference found in the pharmacy standard cost model is not present in the billed cost model and it appears that lower costs attained by the provider are not passed on to the consumer.

5.1.4. Variation in type of service cost estimators.

The study findings highlight the variation in predicted cost estimators between type of service, (i.e., total, ancillary, inpatient, outpatient, pharmacy and professional), resulting in sometimes significantly different interpretations. Overall, results vary in both direction and degree of influence and are dependent on the type of services which creates the cost. Only total cost and outpatient cost contained the same variables in the reduced standard cost model with estimators that followed the same direction and with similar influence. Significant variables in the total and outpatient cost samples relate to many components of Anderson's model with; the patient predisposing characteristic variables age and gender, the patient need for services variables treatment type and severity level,

and the community enabling resources variable provider type. All other costs identified a mixed group of variables which significantly influenced the cost criterion. The ancillary standard cost and professional standard cost reduced models resulted in the fewest number of significant variables, but did not include the same significant variables in the final models, creating differences in model interpretation. For example, treatment type is significant in the professional cost sample, but not in the ancillary cost sample, and may be related to a larger number of health care professionals involved in HCT treatment, a higher cost of at least some of those professionals, as well as the longer treatment time. Whereas provider type was significant in the ancillary cost sample, but not in the professional cost sample, and estimated lower costs in community providers versus academic providers. This finding is possibly related to differences in the facilities cost and staff labor cost, an interpretation supported by Hay's article of hospital cost drivers (Hay, 2003). Pharmacy cost contained the largest number of significant variables in the reduced model and resulted in variable estimates that did not always follow the same direction of the other costs.

Overall, it can be concluded that there is inherent complexity in assessing cost drivers that cannot be addressed through investigating total costs alone. All cost research, whether it relates to cost effectiveness, estimation or value, should thoughtfully determine what cost type is best for its design and then clearly define all costs that are included.

A separate interest of this study was to investigate whether different cost types, billed and standard, would have similar patterns in their results. This question is considered important because of the difference in the cost perspective of the two; billed

cost represents what is charged to the patient or consumer perceived cost and standard cost is the expected actual cost of service or the hospital perceived cost. Whereas billed cost and standard cost were similar in some service types there were large differences present for both inpatient cost and pharmacy cost.

Because standard cost reduces variation caused by factors such as insurance contractual differences and regional billing practices it makes it easier to interpret the actual value of the cost result. This study's findings defend standard cost as a more meaningful research variable. Use of standard cost in research is discussed in the literature which consistently identifies it as providing a valuation of actual cost and more meaningful interpretation of findings (Finkler, et.al., 1982). However, differences between billed and standard cost raise serious questions regarding the lack of transparency in healthcare costs to the consumer. For example, lack of cost transparency may result in an inflated patient perception of cost and interesting questions may relate to; how the patient perceives cost and those perceptions behavioral impact on how they obtain healthcare services, how patients perceive the accessibility of higher cost providers, and ultimately the clinical outcomes of care they receive. Questions like these have national healthcare political and policy implications. Finally, paid cost, a variable not available for use in this study but is present in the WHIO database, could provide a payer perspective of health care cost as well as relevant information regarding if and when patients change payer type. This variable would define the amount actually paid by insurance for services, and along with the billed and standard cost, would provide a more complete picture of how costs operate within the healthcare sector.

5.2. Study Limitations.

Limitations of this study include issues such as meaningfulness of data available in administrative databases, disease sample size limitations, and generalizability of results outside the State of Wisconsin. Research using the WHIO all payer claims data should be designed to accommodate these inherent limitations. Administrative data will generally restrict both the type and scope of research questions that can be addressed. Healthcare claims data has limitations due to data censoring related to the both the amount of available follow up and death, where time of death is unknown. Finally, data collection issues outside of the researcher's control, such as coding errors and diagnosis errors, may impact the data. Limitations to the data include:

All payer claims databases are constructed for operational administration and reimbursement of health care charges rather than research projects. The WHIO data does not provide critical clinical outcomes which would allow the investigation of important questions related to healthcare value and quality of life. Comorbidity data relates only to that reported through insurance claims and may not be fully inclusive of other factors impacting health.

About 6% of provider demographic information was not available in the datamart. This represented either State of Wisconsin providers that were unidentifiable or out of state providers. Lack of provider information reduced the size of the analysis sample in all costs.

Patient zip code data were only available on the county level, reducing its specificity. The variable was not significant in any of the models, but may have been too broad of a measure to identify differences.

Because the dataset contains only two years of insurance claims data it is not possible to assess longitudinal cost results for this sample. Costs of care for these diseases are expected to be high and a longer time frame would be of interest to assess longer term trends in cost.

Given the limited patient demographic and clinical outcome information, there is an increased risk of sample size bias due to factors that were unavailable, (i.e. patient race). This may be particularly obvious for variables such as % under poverty, because of its broad measure and provider type, which contained missing data.

Healthcare claims will contain censored data due to inherent differences in patient follow up or death. While this study adjusted for censoring within the regression equations, more robust statistical methods should be explored to better handle differences in follow up. In addition, a future model may choose to define length of follow up as a confounding variable rather than using the predisposing characteristic definition used in this study. Finally, acquisition of survival data would need to be explored prior to an expansion of the statistical method to better handle censoring due to death.

Study results do not reflect uninsured costs of treatment and are limited in regional scope. This State of Wisconsin all payer claims dataset does not contain information from insurance claims from outside the state nor does it provide uninsured costs of treatment. In September, 2011, the U.S. census bureau estimated that 16.3% of

the U.S. population was uninsured in 2010 and Stranges and colleagues report approximately 25% of hospital stays from 2004-2007 for HCT treatment were uninsured, raising a question of whether the overall uninsured percentage in patients with an acute leukemia diagnosis may be higher than that found in the general population (Stranges, et.al, 2009). Finally, because this is a single State dataset, it may have limited generalizability to populations outside of the State of Wisconsin given regional variations in health care cost.

5.3. Recommendations for Future Research.

A number of future research opportunities result from this study and include proposals to expand the current study dataset with increased years of data as well as additional types of claims along with proposals for investigating the potential to link the cost data to outcomes data. A discussion of each is provided.

In order to address questions of value in health care it is necessary that a study include both cost and outcome. Linking cost data to outcomes data such as mortality, comorbidity and quality of life would provide the necessary two components of the value equation; cost and outcome. While the WHIO data provides a large amount of cost data, it can only construct outcomes data as it relates to insurance claims; for example comorbidities are used to determine severity level. However, because the calculated severity level is restricted to insurance claims it does not capture all pertinent clinical features of the patient. It will be important to explore avenues to obtain outcomes data either through potential direct linkages to clinical datasets, such as State level mortality data, or through possible statistical methods available to relate group cost outcomes to

group clinical outcomes. An example would be to investigate a relationship between the male gender cost outcomes to a male gender HCT survival outcome.

This study's data is restricted to costs associated with an acute leukemia diagnosis due to both data availability and dataset size. Expanding this diagnosis based dataset to a dataset of all insurance claims for these patients would create a more complete record of health care use. The acute leukemia population is expected to utilize health care resources at a higher rate, costs associated with all claims would provide important information about both the use of and cost of services not directly tied to the leukemia diagnosis. It is important to note that the total amount of claims data for this group would be large and would require a high level of technical resources to manage the dataset.

WHIO refreshes the datamart every six month and new patient records are added or current patient records are extended. Adding future WHIO data to the study dataset as it become available would enhance the current data and create the ability to design longitudinal cost studies and creating a larger sample of HCT data. Because cost studies of HCT are difficult due to small sample sizes, creating a dataset of HCT treatment cost would allow investigations of not only longitudinal cost outcomes and cost effectiveness analyses but would also provide support for cost comparison studies of HCT treatment versus non-HCT treatment. As supported by this study, HCT costs are very high, having the ability to study them in more depth impacts questions related to value of care and ultimately healthcare decisions and policy. In addition, because the cost of HCT is high and treatment type had a strong influence on cost, it will be important to assess cost predictors when HCT is not present. Creating a dataset of chemotherapy only treatment

cost would allow the opportunity to investigate health care costs of an acute leukemia population without the dominance of HCT costs.

Further exploration of cost disparities findings related to academic medical center and community providers, the location of the provider and the potential of differences in use of evidence based medicine practices and quality of care.

Sub-analyses of interactions between variables were not within the scope of this study; however, conceptually they may be important. Because of the number of variables there are a large number of potentially important interactions. For example, given the significant differences in provider type cost and the significance of treatment type, it would be of interest to investigate if there is a significant interaction between the two and to determine if treatment type is influencing the differences in provider type. In fact, because of the strong treatment type cost finding, it would be of interest to explore its influence on many of the significant variables. Rather than analyzing each interaction separately, a study design incorporating the use of structural equation modeling (SEM) should be explored. SEM would allow a simultaneous investigation of the relationships between the variables and could be used to direct research toward analyses of the resulting significant relationships.

REFERENCES

Aday, L. (2001). Establishment of a conceptual base for health services research. *Journal of Health Services Research Policy,* vol. 6 (3), 183-185.

American Cancer Society. (2012). *Cancer Facts & Figures 2012*. Atlanta: American Cancer Society. Retrieved from http://www.cancer/org/acs/groups/content/@epidemiologysurveilance/documents.

American College of Physicians. (2011). How Can Our Nation Conserve and Distribute Health Care Resources Effectively and Efficiently*? College of Physicians Policy Paper,* Philadelphia: American. Retrieved from http://www.acponline.org/advocacy/where_we_stand/policy/health_care_resources.pdf.

Andersen, R.M. (1968). Behavioral Model of Families' Use of Health Services. *Research Series No. 25,* Center for Health Administration Studies, University of Chicago.

Andersen, R.M. (1995). Revisiting the Behavioral Model and Access to Medical Care: Does It Matter? *Journal of Health and Social Behavior,* vol. 36 (1), 1-10.

Ashfaq, K., Yahaya, I., Hyde, C., Andronis, L., Barton, P., Bayliss, S., & Chen, Y.F. (2010). Clinical effectiveness and cost-effectiveness of stem cell transplantation in the management of acute leukemia: a systematic review. *Health Technology Assessment,* vol. 14 (54); DOI: 10.3310/htal4540.

Baker, K .S., Davies, S. M., Majhail, N.S., Hassebroek, A., Klein, J.P., Ballen, K.K., Bigelow, C.L., Frangoul, H.A., Hardy, C.L., Bredeson, C., Dehn, J., Friedman, D., Hahn, T., Hale, G., Lazarus, H. M., LeMaistre, C.F., Lobreiza, F., Maharaj, D., McCarthy, P., Setterholm, M., Spellman, S., Trigg, M., Maziariz, R.T., Switzer, G., Lee, S.J., Rizzo, J.D. (2009). Race and Socioeconomic Status Influence Outcomes of Unrelated Donor Hematopoietic Cell Transplantation. *Blood,* 15, 1543-1554.

Basu, A. (2005). Extended generalized linear models: Simultaneous estimation of flexible link and variance functions. *The Stata Journal,* 5 (4), 501-516.

Basu, A., & Manning, W.G. (2009). Issues for the Next Generation of Health Care Cost Analyses. *Medical Care,* vol. 47 (7, suppl 1), S109-S114.

Basu, A., Manning, W.G., Mullahy, J. (2004). Comparing alternative models: log vs. Cox proportional hazard? *Health Economics,* 13, 749-765.

Bennett, C.L., Waters, T.M., Stinson, T.J., Almagor, O., Pavletic, Z., Taratolo, S., & Bishop, M. (1999).Valuing clinical strategies early in development: a cost analysis of allogeneic peripheral blood stem cell transplantation. *Bone Marrow Transplantation,* vol. 24, 555-560.

Barber, J., & Thompson, S. (2004). Multiple regression of cost data: use of generalized linear models. *Journal of Health Services Research & Policy,* vol. 9 (4), 197-204.

Bertakis, K.D., Azari, R., Helms, L.J., Callahan, E. J., & Robbins, J.A. (2000). Gender Differences in the Utilization of Health Care Services. *The Journal of Family Practice,* vol. 49 (2), 147-152.

Billings, J., Zeitel, L., Lukomnik, J., Carey, T.S., Blank, A.E., & Newman, L. (1993). Impact of Socioeconomic Status on Hospital Use in New York City. *Health Affairs,* 12 (1), 162-173.

Centers for Medicare & Medicaid Services. (2012). NHE *Fact Sheet.* Retrieved from https://www.cms.gov/NationalHealthExpendData.

Chang, S., Long, S.R., Kutikova, L., Bowman, L., Finley, D., Crown, W.H. & Bennett, C.L. (2004). Estimating the Cost of Cancer: Results on the Basis of Claims Data Analyses for Cancer Patients Diagnosed with Seven Types of Cancer During 1999-2000. *Journal of Clinical Oncology,* vol. 22 (17), 3524-3530.

Clegg, L.X., Reichman, M.E., Miller, B.A., Hankey, B.F., Singh, G.K., Lin, Y.D., Goodman, M.T…. & Edwards, B.K. (2009). Impact of socioeconomic status on cancer incidence and stage at diagnosis: selected findings from the surveillance, epidemiology, and end results: National Longitudinal Mortality Study. *Cancer Causes Control,* vol. 20, 417-435.

Cohen, J., Cohen, P., West, S., & Aiken, L. (2003). *Applied Multiple Regression/Correlation Analysis for the Behavioral Sciences, 3rd edition.* Mahwah, New Jersey: Lawernce Earlbaum Associates, Inc.

Cordonnier, C., Maury, S., Esperou, H., Pautas, C., Beaune, J., Rodet, M., Lagrange, J.L…. & Durand-Zaleski, I. (2005). Do minitransplants have minicosts? A cost comparison between myeloablative and nonmyeloablative allogeneic stem cell transplant in patients with acute myeloid leukemia. *Bone Marrow Transplantation*, 36, 649-654.

Costa, V., McGregor, M., Laneuville, P., & Brophy, J.M. (2007). The Cost-Effectiveness of Stem Cell Transplantations from Unrelated Donors in Adult Patients with Acute Leukemia. *Value in Health,* vol. 10 (4), 247-255.

Deschler, B., & Lubbert, M. (2006). Acute Myeloid Leukemia: Epidemiology and Etiology. *Cancer,* 107 (9), 2099-2107.

Diehr, P., Yanez, D., Ash, A., Hornbrook, M., & Lin, D.Y. (1999). Methods for Analyzing Health Care Utilization Costs. *Annual Review Public Health*, 20, 125-44.

Dodd, S., Bassi, A., Bodger, K., & Williamson, P. (2006). A comparison of Multivariable Regression models to analyze cost data. *Journal of Evaluation in Clinical Practice*, 12(1), 76-86.

Fielding, A.K., Richards S.M., & Chopra, R. (2007). Outcome of 609 adults after Relapse of acute lymphoblastic leukemia (ALL); an MRC $UKALL_{12}$/$ECOG_{2993}$ study. *Blood,* 109, 944-950.

Finkler, S. (1982). The Distinction between Cost and Charges. *Annals of Internal Medicine,* 96,102-109.

Gajewski, J.L., Foote, M., Tietjen, J., Tietjen, J., Melson, B., Simmons, A., & Champlin R. (2004). Blood and Marrow Transplantation Compensation: Perspective in Payer and Provider Relations. *Biology of Blood and Marrow Transplantation,* 10, 427-432.

Garrett, N., & Martini, E.M. (2007). The Boomers Are Coming: A Total Cost of Care Model of the Impact of Population Aging on the Cost of Chronic Conditions in the United States. *Disease Management,* 10 (2), 51-60.

Geronimus, A., & Bound, J. (1998). Use of Census-based Aggregate Variables to Proxy for Socioeconomic Group: Evidence from National Samples. *American Journal of Epidemiology,* vol. 14 (5), 475-486.

Hann, I.M., Stevens, R.F., Goldstone, A.H., Rees, J.K.H., Wheatley, K., Gray, R.G., & Burnett, A.K. (1997). Randomized comparison of DAT versus ADE as induction chemotherapy in children and younger adults with acute myeloid leukemia. Results of the Medical Research Council's 10th AML Trial (MRC AML10). *Blood,* 89 (7), 2311-2318.

Hay, J. (2003). Hospital Cost Drivers: An Evaluation of 1998-2001 State-Level Data. *The American Journal of Managed Care,* 9:SP13-SP24.

Healthcare.gov, *Report to Congress: National Strategy for Quality Improvement in Health Care: March 2011.* Retrieved from htttp://www.healthcare.gov/law/resources/reports.

Jacobs, P., Hailey, D., Turner, R., & MacLean, N. (2000). Allogeneic Stem Cell Transplantation An Economic Comparison of Bone Marrow, Peripheral Blood, and Cord Blood. *International Journal of Technology Assessment in Health Care,* 16 (3), 874-884.

Kaiser Family Foundation. (2011) *Health Care Spending in the United States and Selected OECD Countries.* Retrieved from http://www.kff.org/insurance/snapshot/OECD042111.cfm.

Kaiser Family Foundation. (2011). Summary *of New Health Reform Law.* Retrieved from http://www.kff.org/healthreform/upload/8061.pdf.

Kantarjian, H.M., & O'Brien, S. (2009). Insurance Policies in the United States may explain part of the outcome differences of adolescents and young adults with acute lymphoblastic leukemia treated on adult versus pediatric regimens. *Blood,* 113, 1861.

Kattan, M.W., Inoue, Y., Giles, F.G., Talpaz, M., Ozer, H., Guilhot, F., Zuffa, E., Huber, S.L., & Beck, J.R. (1996). Cost-Effectiveness of Interferon-α and Conventional Chemotherapy in Chronic Myelogenous Leukemia. *Annals of Internal Medicine,* 125 (7), 541-548.

Khera, N., Zeliadt, S.B., & Lee, S.J. (2012). Economics of hematopoietic cell transplantation. *Blood,* vol. 120 (8), 1545-1551.

Kohler, B.A., Ward, E., McCarthy, B., Schymura, M.J., Ries, L.A., Eheman, C., Jemal, A…. & Edwards, B.K. (2011). Annual Report to the Nation on the Status of Cancer, 1975-2007, Featuring Tumors of the Brain and Other Nervous System. *Journal of the National Cancer Institute,* 103 (9),1-23.

Krieger, N., Chen, J.T., Waterman, P.D., Soobader, M.J., Subramanian, S.V., & Carson, R. (2002). Geocoding and Monitoring of US Socioeconomic Inequalities in Mortality and Cancer Incidence: Does the Choice of Area-based Measure and Geographic Level Matter? *American Journal of Epidemiology*, vol. 156 (5), 471-482.

Krieger, N., Waterman, P.D., Chen, J.T., Soobader, M.J., Subramanian, S. V., & Carson, R. (2002). Zip code Caveat: Bias due to Saptiotemporal Mismatches between Zip Codes and US Census-Defined Geographic Areas-The Public Health Disparities Geocoding Project. *American Journal of Public Health*, vol. 92 (7), 1100-1102.

Lee, S., Klar, N., Weeks, J.C., & Antin, J.H. (2000). Predicting Costs of Stem-Cell Transplantation. *Journal of Clinical Oncology,* vol.18 (1), 64-71.

Leukemia and Lymphoma Society. *Facts 2012.* Retrieved from www.lls.org/content/nationalcontent/resourcecenter/pdf/facts.pdf.

Lin, D.Y. (2000). Linear regression analysis of censored medical costs. *Biostatistics,* 1 (1), 35-47.

Lin, Y., Lairson, D., Chan, W., Du, S.L., Leung, K.S., Kennedy-Nassar, A.A., Martinez, C.A.… & Krance, R.A. (2010). The Costs and Cost-Effectiveness of Allogeneic Peripheral Blood Transplantation versus Bone Marrow Transplantation in Pediatric Patients with Acute Leukemia. *Biology of Blood and Marrow Transplantation,* 16, 1272-1281.

Majhail, N.S., Mothukuri, J.M, MacMillan, M.L, Vemeris, M.R., Orchard, P.J., & Weisdorf, D.J. (2010). Costs of Pediatric Allogeneic Hematopoietic-Cell Transplantation. *Pediatric Blood Cancer,* 54, 138-143.

Majhail, N.S., Mothukuri, J., Brunstein, C., & Weisdorf, D. (2009). Costs of Hematopoietic Cell Transplantation: Comparison of Umbilical Cord Blood and Matched Related Donor Transplantation and the Impact of Posttransplant Complications. *Biology of Blood and Marrow Transplant,* 15, 564-573.

Manning, W. & Mullahy, J. (2001). Estimating log models: To transform or not to transform? *Journal of Health Economics,* 20, 461-494.

Meropol, N.J., Schrag, D., Smith, T.J., Mulvey, T.M., Langdon, R.M. Jr., Blum, D., Ubel, P.A., & Schnipper, L.E. (2009). American Society of Clinical Oncology Guidance Statement; The Cost of Cancer Care. *Journal of Clinical Oncology,* 27 (23), 3868-3874.

Motheral, B., Brooks, J., Clark, M.A., Crown, W.H., Davey, P., Hutchins, D., & Martin, B.C. (2003). A Checklist for Retrospective Database Studies-Report of the ISPOR Task Force on Retrospective Databases. *Value in Health,* 6 (2), 90-97.

Narayanan, S., & Shami, P.J. (2011). Treatment of acute lymphoblastic leukemia in adults. *Critical Reviews in Oncology Hematology,* doi:10.1016/j.critrevonc.2011.01.014.

National Association of Community Health Centers. (2011). *Understanding the 340B Program: A Primer for Health Centers.* Retrieved from http://www.nachc.com/.

National Cancer Institute, *Cancer Stat Fact Sheets*. Retrieved from http://seer.cancer.gov/statistics/.

National Cancer Institute, *Cancer Statistics Review 1975-2008.* Retrieved from http://srab.cancer.gov/prevalence/canques.html.

National Cancer Institute, *Cancer Trends Progress Report 2009/2010.* Retrieved from http//progressreport.cancer.gov/doc_detail.asp?pid

National Cancer Institute. *The Cost of Cancer, 2010.* Retrieved from http://cancer.gov/aboutnci/servingpeople/cancer-statistics/costofcancer.

National Marrow Donor Program, *Understanding Your Treatment Options.* Retrieved from http://marrow.org/Patient/ Disease_and_Treatment/Treatment_Options.

Neal, D.J. & Simons, J.S. (2007). Inference in Regression Models of Heavily Skewed Alcohol Use Data: A Comparison of Ordinary Least Squares, Generalized Linear Models, and Bootstrap Resampling. *Psychology of Addictive Behaviors,* vol. 21 (4), 441-442.

Orsi, C., Bartolozzi, B., Messori, A., & Bosi, A. (2007). Event-free survival and cost-effectiveness in adult acute lymphoblastic leukaemia in first remission treated with allogeneic transplantation. *Bone Marrow Transplantation,* 40, 643-649.

Pasquini, M.C., & Wang, J. (2011). Use and outcome of hematopoietic stem cell transplantation; *CIBMTR Summary Slides*. Retrieved from http://www.cibmtr.org.

Paulson, K., Szwajcer, D., & Steftel, M.D. (2011). The role of allogeneic stem cell transplantation for adult acute lymphoblastic leukemia. *Transfusion and Apheresis Science,* 44, 197-203.

Pickard, S., Topfer, L., & Feeny, D. (2004). A Structured Review of Studies on Health-Related Quality of Life and Economic Evaluation in Pediatric Acute Lymphoblastic Leukemia. *Journal of the National Cancer Institute Monographs,* No. 33, 102-125.

Pui, C.H. & Evans, W.E. (2006). Treatment of Acute Lymphoblastic Leukemia. *The New England Journal of Medicine,* 354, 166-78.

Ramsey, S. & Schickedanz, A. (2010). How Should We Define Value in Cancer Care? *TheOncologist,*15 (suppl 1), 1-4. Retrieved from www.TheOncologist.com.

Redaelli, A., Botteman, M.F., Stephens, J.M., Brandt & S., Pashos, C.L. (2004). Economic burden of acute myeloid leukemia: a literature review. *Cancer Treatment Reviews,* 30, 237-247.

Saito, A.M, Cutler, C., Zahrieh, D., Soiffer, R.J., Ho, V.T., Alyea, E.P., Koreth, J.… & Lee, S.J. (2008). Costs of Allogeneic Hematopoietic Cell Transplantation with High-Dose Regimens. *Biology of Blood and Marrow Transplantation,* 14, 197-207.

Saito, A.M, Zahrieh, D., Cutler, C., Ho, V.T., Antin, J.H, Soiffer, R.J., Alyea, E.P., & Lee,S.J. (2007). Lower costs associated with hematopoietic cell transplantation using reduced intensity vs. high-dose regimens for hematological malignancy. *Bone Marrow Transplantation* 40 (20),9-217.

Statistics Calculators, *Sample size.* Retrieved from http://daneilsoper.com/statcalc3/.

Schafer, E.S. & Hunger, S. (2011). Optimal therapy for acute lymphoblastic leukemia in adolescents and young adults. *Nature Reviews/Clinical Oncology*, 8, 417-424.

Sclar, D., Robison, L.M., Vavrun, C., Slaer. T. L. (2008). Hospital length of stay for children and adolescents diagnosed with depression: is primary payer an influencing factor?, *General Hospital Psychiatry,*30, 73-76.

Schneeweiss, S,. & Avorn, J. (2005). A review of uses of health care utilization Databases for epidemiologic research on therapeutics. *Journal of Clinical Epidemiology,* 58, 323-337.

Seshamani, M., & Gray, A. (2004). Ageing and health-care expenditure: the red herring argument revisited, *Health Economics,* 13(4), 303-314.

Shi, Leiyui, (2008). *Health Services Research Methods, 2nd edition.* Clifton Park, New York: Delmar, Cengage Learning.

Stanton, M. *Reducing Costs in the Health Care System; Learning From What Has Been Done.* U.S. Department of Health & Human Services, Agency for Healthcare Research and Quality. Retrieved http://www.ahrq.gov/research/costsria/.

Stephens, J.M., Gramegna, P., Laskin, B., Botteman, M., & Pashos, C. (2005). Chronic Lymphocytic Leukemia: Economic Burden and Quality of Life. *American Journal of Therapeutics,* 12, 460-466.

Stock, W., La, M., Sanford, B., Bloodfield, C.D., Vardiman, J.W., Gaynon, P., Larson, R.A., & Nachman, J. (2008). What determines the outcomes for adolescents and young adults with acute lymphoblastic leukemia treated on cooperative group protocols? A comparison of Children's Cancer Group and Cancer and Leukemia Group B Studies. *Blood,* 112, 1646-1654.

Stranges, E., Russo, A., & Friedman, B. (2009). *Procedures with the Most Rapidly Increasing Hospital Costs, 2004-2007.* HCUP Statistical Brief #82. December, 2009. Agency for Healthcare Research and Quality, Rockville, MD. Retrieved from http://www.hcup-us.ahrq.gov/reports/statbriefs/sb82.pdf.

Tabachnick, B., & Fidell, L. (2001). *Using Multivariate Statistics, 4th edition.* NeedhamHeights, Massachusetts: Allyn & Bacon.

U.S. Census Bureau. (2010). *Income, Poverty and Health Insurance Coverage in the United States: 2010.* Retrieved from http://www.census.gov/newsroom/releases/archives/income_wealth.

U.S. Department of Labor, Bureau of Labor Statistics. (2010). *Economic News Release: Consumer Expenditures-2010.* Retrieved from http://www.bls.gov/news.release/cesan.nr0.htm.

Van Litsenburg, R.R.L., Uyl-de Groot, C.A., Raat, H., Kaspers, G.J., & Gemke, R.J. (2011). Cost-Effectiveness of Treatment of Childhood Acute Lymphoblastic Leukemia with Chemotherapy Only: The Influence of New Medication and Diagnostic Technology. *Pediatric Blood Cancer,* DOI 10.1002/pbc.23197. Retrieved from www.wileyonlinelibrary.com.

Vila, P.M., Swain, G.R., Baumgardner, D.J., Halsmer, S.E., Remington, P.L., & Cisler, R. A. (2007). Health Disparities in Milwaukee by Socioeconomic Status. *Wisconsin Medical Journal,* 106 (7), 366-372.

Waters, T., Bennett, C., & Pajeau, T. (1998). Perspective: Economic analyses of bone marrow and blood stem cell transplantation for leukemia's and lymphoma: what do we know? *Bone Marrow Transplantation,* 21, 641-650.

Westerman, I. & Bennett, C. (1996). A review of the Costs, Cost-Effectiveness and Third-Party Charges of Bone Marrow Transplantation. *Stem Cells,* 14, 312-319.

Wisconsin Department of Health Services, Division of Public Health, Office of Health Informatics, *Wisconsin Cancer Incidence and Mortality; 2002-2006.* Retrieved from http://www.dhs.wisconsin.gov/wcrs/pdf/cancerwi0206.

Wisconsin Health Information Organization, *Our Members.* Retrieved from http://www.wisconsinhealthinfo.org/.

Wisconsin Health Information Organization, *WHIO DMV6 training notes, 1-6-2012.*

Yu, Y.B., Gau, J.P., You, J.Y., Chern, H.H., Chau, W.K., Tzeng, C.H., Ho, C.H., & Hsu, H. C. (2007). Cost-effectiveness of post-remission intensive therapy in patients with acute leukemia. *Annals of Oncology,* 18, 529-534.

Yuan, Z., Cooper, G., Einstadter, D., Cebul, R.D., & Rimm, A.A. (2000). The Association between Hospital Type and Mortality and Length of Stay: A Study of 16.9 Million Hospitalized Medicare Beneficiaries. *Medical Care,* 38 (2), 231-24.

Zweifel, P., Felder, S., & Werblow, A. (2004). Population Ageing and Health Care Expenditure: New Evidence on the "Red Herring". *The Geneva Papers on Risk and Insurance,* vol. 29 (4), 652-666.

APPENDICIES

Appendix A. WHIO DMV6 Characteristics.

Table A. Characteristics of WHIO DMV6 data mart, WHIO lymphoma and leukemia, and WHIO acute leukemia population.

Source: WHIO DMV6 training notes 1-6-2012

Variable	WHIO	WHIO Lymphoma/ Leukemia	WHIO Acute Leukemia
Population	3,863,345	12,504	837
% WI Population	64.9%	.3%	.02%
Age			
<18	29%	14%	50%
18-64	58%	34%	39%
65+	13%	52%	12%
Claim service records	247,620,120		271,121
Medical	183,554,190	1,048,576	234,450
Pharmacy	64,065,930	Not available	36,671
Claim service record by payer type			
Private/commercially insured	42%	32%	47%
Public insured	58.1%	68%	53%
Federal Employee Program	0.1%		
Medicare	13%		
Medicaid	45%		
Unknown	1%		
Episodes of care	23.1M	18,324	8133
Claims $ included (Billed cost/Std. cost)	$64B/$34.4B	$360M (billed)	$46M/$23M

Table B. Characteristics of acute leukemia analysis samples.

Variable	Total	Ancillary	Inpatient	Outpatient	Pharmacy	Professional
Sample, n	638	138	201	497	325	618
% WI Population	.01%	.002%	.003%	.008%	.005%	.01%
Age						
<18	49%	51%	52%	52%	54%	50%
18-64	39%	40%	36%	36%	34%	39%
65+	12%	9%	12%	12%	12%	11%
Male gender	56%	64%	66%	59%	62%	57%
Claim service records	262,524	3,869	19,683	111,488	36,671	99,410
Claim service record by payer type						
Commercial	48%	46%	43%	48%	43%	47%
Public insured	52%	54%	57%	52%	57%	53%
Claims $ included (Billed/Std. cost)	$44M/ $21M	$672,577/ $676,253	$15M/ $7.9M	$6.9M/ $2.7M	$7.4M/ $5M	$11M/ $4.4M

Appendix B. WHIO Definitions.

Source: Ingenix Reporting System User Guide; WHIO training materials; Vila, et.al, Health Disparities in Milwaukee by Socioeconomic Status, 2007.

WHIO Episode Treatment Groups (ETGs): ETGs are an illness classification method that combines medical and pharmacy services into mutually exclusive and exhaustive categories; providing a meaningful statistical unit representing an episode of care.

WHIO severity level: Severity is modeled per episode and uses the episode's associated complications and comorbidities in addition to patient age and gender.

Severity model markers, each is assigned a weight:

- Age and gender
- Co-morbidities and condition status
- Treatments not used in severity model

Severity score:

- The sum of the weights for all markers
- Relative to costs for the episode

Severity level:

- 1-4; using score and preset ranges

WHIO standard cost: Standard cost is calculated with billed amount as input. For inpatient services, the standard cost is based on a per diem cost calculated, primarily, with the DRG and length of stay in addition to facility type and presence of major surgery. Professional and ancillary services standard cost is based on Relative Value Unit's (RVU) from the Medicare Fee Schedule and pharmacy services standard cost uses the average wholesale price (AWP) for the National Drug Code (NDC), adjusted by therapeutic category and generic status. Facility and outpatient claims are based on a

percentage of the billed amount and, in some cases, are adjusted by a WHIO-specific conversion factor to approximate a allowed amount.

WHIO type of service: Claims are categorized based on the major type of services and the procedure codes used in describing the service. There are four major types of service used after assigning a service to these categories; CPT, HCPCs and Revenue codes are used to further differentiate services at each level.

1. Ancillary
2. Facility Inpatient
3. Facility Outpatient
4. Professional

Pharmacy is the fifth service type used in the study: all claims assigned to a pharmacy service code at any of the levels of type of service are specific to a drug cost and does not include procedures or administration of the drug.

WHIO ZIP code: The largest 5-digit ZIP code within a region that represents a population of >20K with the selection criteria of:

- True county,
- 3-ZIP area excluding counties > 20K,
- Full 3-ZIP area,
- State

All patients within the same region of the State are assigned the same ZIP-code for de-identification purposes and the lowest level of patient geographic region identification is the county level. A small number of patients from counties <20K are assigned to

neighboring counties, i.e. the largest 5-digit ZIP code in a 3-ZIP area that represents a population of >20K.

Appendix C. WHIO DMV6 Data Information.
Source: WHIO DMV6 Impact Intelligence Training Notes, 1/6/2012

Types of Data

Data includes combined Eligibility, Medical and Pharmacy Claims and Provider information from 15 health plans or other payers active in Wisconsin: Anthem, Dean, Group Health Cooperative of South Central Wisconsin, Gundersen Lutheran, Health Tradition Health Plan, Humana, MercyCare, Network Health Plan, Physicians Plus Insurance Corporation, Security, State of Wisconsin Medicaid (FFS and HMO), United HealthCare, Unity Health, Wisconsin Education Association Trust and Wisconsin Physicians Service. The aggregated data does not contain any proprietary payer information. Data does not include lab results or patient satisfaction information.

Raw data includes all activity provided to Wisconsin members, regardless of whether the service was incurred by a Wisconsin provider, as well as all activity performed by Wisconsin providers, regardless of whether the member resides in Wisconsin.

Eligibility and claims information provided by data contributors is included in the WHIO datamart; exceptions are provided below.

There are a small percentage of non-Wisconsin members that are included in the WHIO data mart (e.g., from Border States, students, snowbirds) because they were identified as having a complete claims experience. Claims serviced by non-Wisconsin providers for some members of this group may be included.

All Wisconsin-related data is requested from data contributors including members with Commercial, fully insured and full medical coverage; Commercial ASO members; Medicare members administered by the data contributors; Medicare Supplemental

members; other non-Commercial full-coverage members; other Commercial or non-Commercial partial-coverage members; and uncommon situations or other members. The ability of data contributors to send data beyond their core Commercial business is challenging and has varied by payer.

All Medicaid data is supplied by the State of Wisconsin only and include FFS and HMO members with full medical coverage, Medicare dual members with supplemental medical coverage through Medicaid, and a few members with Rx-only coverage.

Medicare supplemental or Medicare/Medicaid dual members are represented by only their non-Medicare data in the data mart unless their Medicare coverage is administered by a private carrier (i.e., Medicare Advantage members) and the private carrier is a WHIO data contributor. When Medicare data is included for these members, the member's eligibility for the overlapping eligibility period will reflect their full medical coverage through Medicare and any supplemental claim lines is categorized as pseudo claims.

Employee Trust Fund (ETF) members and claims are included. They are identified in the raw data but not in the final WHIO data mart to mask any member- or payer-specific information.

Appendix D. WHIO Provider Data.

1. Provider records.

Provider information	Number of provider records
Total provider records	837
Identified Wisconsin provider records	638
Unidentified Wisconsin provider records	121
Out of state provider records	53
Unspecified provider records	25

2. U.S. State where care was provided.

U.S. States with provider records
ARIZONA
CALIFORNIA
GEORGIA
ILLINOIS
INDIANA
IOWA
KENTUCKY
MASSACHUSETTS
MICHIGAN
MINNESOTA
MISSOURI
OHIO
PENNSYLVANIA
SOUTH DAKOTA
TENNESSEE
TEXAS
WISCONSIN

Appendix E. Dataset Coding.

1. Disease type (AML_ALL) code: patients with a diagnosis of AML or ALL present in the database are coded as AML_ALL and included in the study population.

Disease type	Disease type code
AML_ALL	1
Other	0

2. Episode severity code:

Episode severity	Episode severity code
Low	1
Medium low	2
Medium high	3
High	4

3. Episode Treatment Group-ID:

ETG type	ETG-ID
Leukemia without surgery	85
Leukemia with surgery	86
Leukemia with active management without surgery	87
Leukemia with active management with surgery	88

3. Payer type code:

Payer type	Payer type code
Commercial	0
Public	1

4. Provider type code:

Provider type	Provider type code
Community	0
Academic medical center	1

5. Service type code:

Service type	Service code
Ancillary	1
Inpatient	2
Outpatient	3
Professional	4
Pharmacy	7

6. Treatment type code:

Treatment type	Treatment type code
Chemotherapy only	0
Chemotherapy and HCT	1

Appendix F. Institutional Review Board Approval Letter.

UNIVERSITY of WISCONSIN
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Department of University Safety & Assurances

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New Study - Notice of IRB Exempt Status

Date: April 13, 2012

To: Ron Cisler, PhD
Dept: Health Sciences

Cc: Patricia Steinert

IRB#: 12.334
Title: Predictors of Healthcare Cost in a Wisconsin Acute Leukemia Population: Utillization of a State-level All Payer Claims Database

After review of your research protocol by the University of Wisconsin – Milwaukee Institutional Review Board, your protocol has been granted Exempt Status under Category 4 as governed by 45 CFR 46.101(b).

Unless specifically where the change is necessary to eliminate apparent immediate hazards to the subjects, any proposed changes to the protocol must be reviewed by the IRB before implementation. It is the principal investigator's responsibility to adhere to the policies and guidelines set forth by the UWM IRB and maintain proper documentation of its records and promptly report to the IRB any adverse events which require reporting.

It is the principal investigator's responsibility to adhere to UWM and UW System Policies, and any applicable state and federal laws governing activities the principal investigator may seek to employ (e.g., FERPA, Radiation Safety, UWM Data Security, UW System policy on Prizes, Awards and Gifts, state gambling laws, etc.) which are independent of IRB review/approval.

Contact the IRB office if you have any further questions. Thank you for your cooperation and best wishes for a successful project

Respectfully,
Melissa C Spadanuda
Melissa C. Spadanuda
IRB Administrator

CURRICULUM VITAE

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Teaching
University of Wisconsin-Milwaukee, Teaching Assistant: *Population Health Outcomes*, Fall, 2010

Presentations
- Predictors of Healthcare Cost in a Wisconsin Acute Leukemia Population: Utilization of a State-Level All Payer Claims Database, WHIO Symposium, poster presentation, November, 2012
- Predictors of Healthcare Cost in a Wisconsin Acute Leukemia Population: Utilization of a State-Level All Payer Claims Database, UWM College of Health Sciences Fall Research Symposium, poster presentation, December, 2012
- Kepivance Long Term Follow Up study presentation, NMDP Council Meeting, 2008 and 2010
- Kepivance Long Term Follow Up study roundtable, NMDP Council Meeting, 2008 and 2010
- Kepivance Long Term Follow Up study roundtable, CIBMTR/ASBMT Tandem Meeting, 2009 and 2011
- Assessing the Quality of Hip Fracture Treatment in Louisiana Hospitals, Louisiana Health Care Review, 1996