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Assessing the Risk of Developing Liver Cancer among Adults in the United States

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This is to certify that the doctoral dissertation by

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has been found to be complete and satisfactory in all respects,
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Walden University
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Abstract

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by

Magbor Oben

MSA, Trinity Washington University, 2013

BS, University of Yaoundé, 1998

Dissertation Submitted in Partial Fulfillment

Of the Requirements for the Degree of

Doctor of Philosophy

Public Health

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Abstract

The risk of developing liver cancer among adults in the United States remains a significant threat due to an increasing prevalence of the disease. Despite the identification of some biological, environmental, and socioeconomic risk factors, uncertainty exists as to the role of sociodemographic factors. In this study, participants (*N*=27,804), age 18 and over, were assessed for liver cancer outcome specific to three factors liver disease, insurance coverage, and access to healthcare. With the person-centered care model as the framework, data from the 2016 National Health and Interview Surveys were subjected to the selection criteria and quantitatively analyzed using binary logistic regression. Each predictor variable—history of liver cancer, type of health insurance coverage, and visit to general physician in the last 12 months—was analyzed separately, with liver cancer as the dichotomous outcome variable and age, gender, and race as the controls. The two younger age groups (26-40 and 41-65) were 96.9% (OR=0.031, 95% CI [.004, .234], $p < .01$) and 68.6% (OR=0.314, 95% CI [.165, .598], $p < .001$) less likely to develop cancer relative to the oldest (over 65) age group. Men had a 244.1% (OR=2.441, 95% CI [1.270, 4.691], $p < .01$) increase likelihood of liver cancer. Of the predictors tested, only a history of liver disease had a 15,506.6% (OR=155.066, 95% CI [76.123, 315.878], $p < .001$) increased odds of developing liver cancer. These findings address positive social change by identifying high-risk individuals to assign them to liver cancer prevention programs so those at risk can make more informed lifestyle and health care choices to mitigate liver cancer risk.

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Dedication

To my beloved late parents,

Chief Shadrack Bate Oben (father), cause of death, liver cancer (August 2000), and

Mama Rebecca Bate Oben (mother), post CVA complications (September 2020).

For their love and commitment to education.

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My beloved husband Christopher Abangma (Sr) for his never ended support, encouragement and patience throughout the course of my study. My children, Kerl, Chris (Jr.) and Keller for their enormous sacrifice, support and understanding. Finally,
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Table of Contents

List of Tables

List of Figures

Chapter 1: Introduction to the Study

Introduction

Cancer is a disease in which cells in the body grow out of control. When cancer starts in the liver, it is called liver cancer (Centers for Disease Control and Prevention [CDC], 2018). Liver cancer usually develops because of an existing liver disease, such as hepatitis B and C viruses, cirrhosis, nonalcoholic fatty liver disease (NAFLD), alcoholic liver disease (ALD), metabolic syndromes such as diabetes, obesity, and other cardiovascular diseases (CVD; Del Campo et al., 2018). Each year, among individuals living in the United States (US), the incidence of liver cancer is increasing, about 33,000 people get liver cancer, and about 27,000 people die from the disease (CDC, 2018). The percentage of Americans who are newly diagnosed with liver cancer is now at 7.1 cases per 100,000 person-years from several decades ago in the US (CDC, 2018). Uncertainties exist regarding the effects of risk factors for the development of liver cancer, such as liver disease (biological factor), health insurance status with focus on Medicaid (socioeconomic factor), and access to annual routine clinic visits or access to annual routine clinic visits or healthcare provider visit in the past 12 months (sociodemographic factor). An understanding of the impact of health insurance status with focus on Medicaid and access to annual routine clinic visits or healthcare provider visit in the past 12 months on the development of liver cancer have not been well explored (Suh et al., 2018).

The purpose of this study is to assess the impact of being a Medicaid health insurance recipient, with history of liver disease, and with access to annual routine clinic

visits or healthcare provider visits in the past 12 months on the risk of developing liver cancer among US adults. Assessing these risk factors improves the understanding of how they contribute to the development of liver cancer which helps inform appropriate interventions to minimize the risk of developing liver cancer thereby helping to ensure a healthy outcome due to early detection, creating evidence-based treatment strategies, and making more informed lifestyle and health care choices to effect positive social change. In this section of the dissertation, the background, problem statement, purpose of the study, research questions and hypotheses, theoretical framework, nature of the study, relevant definitions, assumptions, scope and delimitations, limitations of the study, and significance of the study is discussed.

Background

Liver cancer is identified globally as the 5th most deadly type of cancer in the world, (CDC, 2016). It is the 10th most common cancer and the 5th cause of cancer-related deaths in the US (Cancer.net, 2018). Furthermore, the incidence of liver cancer has substantially increased from 2001 to 2015 (Kanwal et al, 2016). The increase was especially dramatic among patients with cirrhosis, which was driven by Hepatitis C virus (HCV) and NAFLD (Kanwal et al., 2016). The effectiveness of liver cancer prevention in clinical and population level settings is low due to barriers linked to patient, provider, system, and societal factors; thus, liver cancer prevention processes could benefit from examination using the person-centered care model which provides a framework for evaluating efficacy and effectiveness for assessing the risk for developing liver cancer (Singal & El-Serag, 2015a). Within this framework, risk

factors such as access to or utilization of Medicaid health insurance and access to annual routine clinic visits or healthcare provider visit in the past 12 months by patients with or without liver disease should be explored in terms of available prevention and treatment options, patient involvement, and provider system supports (Singal & El-Serag, 2015a). An example of this framework for quality care is the investigation of the epidemiology of HCV infection outcomes and treatment among prisoners by Zampino et al. (2015). The authors conducted a prospective Australian study between 2005 and 2009 on 210 HCV-positive subjects with a life-time history of injection drug use observed every 6 to 12 months for up to 4 years. An incidence of HCV infection of 14.8 per 100 persons per year was observed and imprisonment was associated with high rates of HCV transmission (Zampino et al., 2015). The authors' conclusions were focused on reducing the spread of HCV infection in prisons by promoting follow-up services and treatment to prisoners with chronic HCV (Zampino et al., 2015). However, because treatment was administered less frequently to prisoners by medical staff due to inherent difficulties in management and follow-ups by both patients and providers, a new direct acting antiviral was suggested to be a better alternative for inmates because of its efficacy, short duration of treatment/follow-ups, and low incidence of adverse outcomes or side effects (Zampino et al., 2015). This study informed current study design on the importance of access to annual routine clinic visits or healthcare provider visit in the past 12 months and health insurance (Medicaid) status on early diagnosis or treatment of a liver disease or liver cancer (Zampino et al., 2015). Petrick et al. (2016) explored liver cancer incidences in the US through 2030 and

suggested that even when liver cancer incidence increases, the incidence rate of liver disease among Asian/Pacific Islanders, individuals younger than 65 years, and cohorts born after 1960 will continue to decline in future years. Preventive efforts should be focused on cohorts born in 1950 to 1959, and who are either Hispanic or Black (Petrick et al., 2016). This study informs the present study by tracking liver disease incidence rates to promote prevention and treatment strategies to decrease the burden of liver cancer in the US population (see Petrick et al., 2016). Bandeira et al., (2016) reported the association between liver cancer, hepatitis viruses (e.g. Hepatitis B or C), cirrhosis, and other diseases. Therefore, preventing or minimizing the risk of developing liver cancer could substantially reduce deaths associated with liver cancer amongst adults in the US (Bandeira et al., 2016). As research is completed about the disproportionately high incidence and prevalence of liver cancer in US population, the person-centered care approach may lead to lifestyle or behavior change to improve quality of life for those at risk for developing liver cancer (Rogers, 1979).

Though liver disease may develop into liver cancer, no link has been found between any type of liver disease, health insurance with focus on Medicaid recipient status, or access to annual routine clinic visits or health care provider visit in the past 12 months among subjects 18-85+ years old to liver cancer when compared to individuals of the same age group without liver disease, who are not Medicaid insurance recipients, and who did not schedule routine clinic visits or healthcare provider visit in the past 12months (Suh et al., 2018). Based on the gap in understanding of liver disease and its progression in young adults and adult Medicaid patients as discussed by Suh et al.,

further comparative study is warranted to explore the impact of liver disease, Medicaid health insurance, and access to annual routine clinic visits or healthcare provider visit in the past 12 months on the risk of developing liver cancer in individuals 18-85+ years old living in the US. By conducting this study, I filled the gap in knowledge and literature observed by Suh et al. (2018). In addition, assessing the risk of developing liver cancer among Medicaid health insurance recipients with liver disease and reinforcing health monitoring systems or access to annual routine clinic visits or health care provider visits for the past 12 months will further public health efforts to prevent the development of liver cancer in the US (Suh et al., 2018).

Problem Statement

Each year, about 33,000 people in the United States develop liver cancer, while roughly 26,000 people die from the disease (CDC, 2018). In 2017, the liver cancer mortality rate was 15 deaths per 100,000 men and 5 deaths per 100,000 women (Siegel, Miller & Jamal., 2017). According to the American Cancer Society in the US, about 42,200 (11,610 women and 30,610 men) new cases of liver cancer were diagnosed, while roughly 30,200 (20,540 men and 9,660 women) died from liver cancer in 2018 (Cancer. net, 2018). Overall, about 8.2% of deaths among adults in the US is associated with liver cancer (Simard, Ward, Siegel, & Jemal, 2012). According to Bandiera et al. (2016), liver cancer is associated with environmental risk factors (such as toxic carcinogens), behavioral factors (such as alcohol and smoking), and Hepatitis virus (e.g. Hepatitis B or C). Therefore, preventing or minimizing the risk of liver cancer could substantially reduce the high incidence, prevalence, and deaths associated with it. Risk factors such as

liver disease (biological), access to routine clinic visits or annual medical checkups (sociodemographic) and/or utilization of Medicaid insurance (socioeconomic), potentially influence the occurrence rate of liver cancer development among subjects 18-85+ years old living in the United States (US). However, the race or gender of a person may not directly present biological factors increasing the exposure to liver cancer (Fujiwara, Friedman, Goossens & Hoshida, 2018). For example, among men, liver cancer is the 10th most common cancer and the 5th cause of cancer-related deaths in the US, while for women, it is the 8th most common cause of cancer deaths (Fujiwara et al., 2018).

Liver cancer affects people of all ages, however there is not much information about liver cancer affecting adults less than 50 years of age (Suh et al., 2018). A retrospective cohort study by Suh et al. (2018) highlighted the issue of high burden of liver cancer. In their study, risk factors in developing liver cancer in people with and without liver disease led to liver cancer in South Korea where 66,192 patients with and without liver disease were examined using data from the National Health Insurance Service National Sample Cohort (NHIS-NSC) from 2002 to 2013 (Suh et al., 2018). An efficient neighborhood legal services program (NLCSP) of the incidences of liver cancer among patients with and without liver disease was established and within a median 8-year follow-up period, 2.68% (n = 1,772) and 0.34% (n = 210), incidences were noted, respectively (Suh et al., 2018). Cox- regression analysis for liver cancer incidence indicated cirrhosis risk hazard ratio (HR) of 18.13, 95% confidence interval [CI]: 15.24–21.58) as the highest, followed by hepatitis B (HR) of 9.32, 95% CI: 8.00–10.85. While subgroup analysis showed the presence of liver disease as an important

risk factor in younger as well as elderly people, and a higher risk of liver disease was also observed in the patients with Medicaid. Suh et al. (2018) recommended attention should be focused on the development of liver cancer in young people under 50 years old and preventive efforts was needed to decrease the incidence of liver cancer among Medicaid recipients (Suh et al., 2018).

Liver disease mortality is high in the US and globally (CDC, 2016). Researchers have identified several factors delaying progress in liver cancer health promotion measures in preventing and reducing liver cancer cases (Singal & El-Serag, 2015). Of concern is Medicaid health insurance status and liver cancer development. Forty-nine percent of people in the US are insured through their employer while 16 % of the population is insured via Medicaid. In total, 16% of the population is uninsured (see Table 1; Kaiser Family Foundation, 2012). Overall, almost 50 million Americans, including 8 million children, lack health insurance (Wilper et al., 2009). Lack of insurance can lead to deadly consequences because uninsured patients are less likely to get access to annual routine clinic visits, annual health care provider visits known as physicals, health promotion and preventive health care services, or wellness visits. Also, uninsured patients may not be able to receive quality care in case of the presence of a disease. (Wilper, et al., 2009; Halpern et al., 2008). In addition, uninsured Americans, when compared to individuals with private insurance, are less likely to receive timely cancer screenings or access to routine clinic visits or medical care (Wilper, et al., 2009; Halpern et al., 2008). As a result, this population of patients are at higher risk of being diagnosed with advanced cancer than earlier cancer diagnosis (Halpern et al., 2008). In

the US alone, 45,000 people from all health outcome, including liver cancer, die each year due to lack of health insurance (Wilper, et al., 2009).

Table 1

Insurance Status in the US

Source Health Insurance	Percentage of People Insured (%)
Employer	49
Individual	5
Medicaid	16
Medicare	12
Other Public	1
Uninsured	16

Note. From Kaiser Family Foundation. (2012). Kaiser state health facts. Retrieved from http://www.statehealthfacts.org.

According to Suh et al. (2018), liver disease is a risk factor for developing liver cancer, however, no comparative study has been done on the link between liver disease, being a Medicaid health insurance recipient, and having access to annual routine clinic visits or health care provider visits in the past 12 months among patients <50 years old (Suh et al., 2018). Based on the gap in the literature identified by Suh et al. (2018), further comparative study is warranted to explore the impact of health insurance status with focus on Medicaid and access to annual routine clinic visits or healthcare provider visits in the past 12 months on liver disease and the risk of developing liver cancer among adults 18-85years old in the US. Thus, this proposed study will address a

meaningful gap in the literature which is linking the impact of health insurance status with focus on Medicaid to liver disease, and access to annual routine clinic visits or healthcare provider visits in the last 12 months on the risk of developing liver cancer among adults 18 to 85+ years old living in the US.

Purpose of the Study

This study assessed the impact of being a Medicaid health insurance recipient, with history of liver disease, and with access to annual routine clinic visits or healthcare provider visit in the past 12 months on the risk of developing liver cancer among adults 18 to 49 years old. In this study, types of liver diseases, patient health insurance status with focus on Medicaid, and access to annual routine clinic visits or healthcare provider visits in the past 12 months were considered as barriers to facilitate liver cancer screening amongst individuals 18 to 85+ years old since liver disease has been classified as a risk factor for developing liver cancer (Suh et al., 2018).

In this study and based on the specific information contained in the 2016 National Health Interview Survey (NHIS), which only included a general question about liver cancer and liver disease, only all types of liver cancer and all types of liver conditions in this study (National Center for Health Statistics, 2017) were addressed. In the 2016 NHIS data dictionary, the liver cancer and liver disease questions were posed as follows: “Ever told by a doctor you had a liver cancer”? Similarly, they also asked, “Ever told you had any kind of chronic/long-term liver condition”? These two questions are not specific to the granular types of liver cancer or liver disease, as such, the association between any type of liver disease and any type of liver cancer were addressed because this was the

only information provided in the 2016 NHIS dataset about my study variables. In this study, liver cancer is the dependent variable for the three research questions and hypotheses under investigation. Liver disease is the independent variable for Research Question 1. Health insurance status with focus on Medicaid is the predictor variable while access to annual routine clinic visits or health care provider visits in the last 12 months is the independent variable for Research Questions 2 and 3, respectively; the covariates or confounding variables are gender and race. The study initially targeted individuals younger than 50 years old (18-49 years old). Because of smaller number of patients with the outcome variable (liver cancer), the study was revised to include individuals 18 to 85+ years after IRB approval.

Research Questions and Hypotheses

The research questions (RQs) and hypotheses addressed in this current study are:

RQ1: Is there an association between liver cancer and liver disease in individuals 18-85+ years of age, accounting for gender and race?

$H_0$1: There is no association between liver cancer and liver disease in individuals 18-85+ years of age, accounting for gender and race?

H_a1: There is an association between liver cancer and liver disease in individuals 18-85+ years of age, accounting for gender and race?

RQ2: Is there an association between liver cancer and health insurance status with focus on Medicaid in individuals 18-85+ years of age, accounting for gender and race?

H_o2: There is no association between liver cancer and health insurance status with focus on Medicaid in individuals 18-85+ years of age, accounting for gender and race?

H_a2: There is an association between liver cancer and health insurance status with focus on Medicaid in individuals 18-85+ years of age, accounting for gender and race?

RQ3: Is there an association between liver cancer and access to annual routine clinic visits or Health care provider visits in the past 12 months in individuals 18-85+ years of age, accounting for gender and race?

H_03: There is no association between liver cancer and access to annual routine clinic visits or health care provider visits in the past 12 months in individuals 18-85+ years of age, accounting for gender and race?

H_a3: There is an association between liver cancer and access to annual routine clinic visits or health care provider visits in the past 12 months in individuals 18-85+ years of age, accounting for gender and race?

Theoretical Framework

Person-centered care theory was used as the theoretical framework for this current study. Person-centered care theory is concept includes best practice codes and guidelines (Rogers, 1979). The theory focuses on tailored approaches meant to provide care to individuals to serve their unique needs and unmet needs with more emphasis on their preferences rather than the disease, expected symptoms, challenges, and the lost abilities of the person (Rogers, 1979). Public health and health care professionals used person-

centered care approach to guide and maintain the standards of their professional practices (Rogers, 1979). Researchers also used person-centered care theory to identify potential factors outside of standard clinical practices (Rogers, 1979). Donabedian model focused on structural domain related to health-care system or context in which care is delivered which influence the processes and outcomes of health-care quality improvement (Santana et al., 2018).

For example, the person-centered care theory was used as a validated, reliable, and responsive approach of the Thai palliative care outcome scale for pain and symptom management among cancer patients in a Thai public hospital (Pukrittayakamee et al., 2018). The theory was used in translating staff and patient versions of the palliative care outcome scale and to determine psychometric properties among cancer patient outcomes (Pukrittayakamee et al., 2018).

According to Jayadevappa and Chhatre (2011), person-centered care informs decision making to improve treatment choice, quality of care, outcomes and recognize the need for major changes in the process of care in health care system provided to patient or person. The authors evaluated and discussed the interplay of components of person - centered care by developing a conceptual model of person-centered care with person reported outcomes (Jayadevappa & Chhatre, 2011). However, Babilonia, (2016), integrated person-centered theory with rational emotive behavioral therapy to treat alcohol use disorder in Hispanic armed forces members (Babilonia, 2016).

While, Bayus, (2016) used the person-centered care theory for the identification of nonalcoholic fatty liver disease in patients with Hepatitis C using evidence-based

guidelines to improve diagnosis and transition of care from liver cancer specialty care provider to primary care provider (Bayus, 2016). Person-centered care theory could also be used to explain the environmental indicators, lifestyle choices, behavioral risk factors, health outcomes and exposures (Bayus, 2016).

In the current study, the associations between liver cancer and either liver disease or health insurance status, with focus on Medicaid, or access to annual routine clinic visits or healthcare provider visits in the last 12 months could be explained using the person-centered theory. As such, the predictor factors (liver disease, health insurance status with focus on Medicaid, access to annual routine clinic visits or healthcare provider visits in the past 12months) are linked to lifestyle, behavior or environmental components of the decision-making processes of the individual or individuals in need of care (Rogers, 1979). Based on the person-centered care approach, patients interact with providers from a holistic level, incorporating the emotional, mental, spiritual, social, and financial perspective which helps the at-risk individuals to make informed decisions regarding risk factors at the personal and systemic levels geared at minimizing the risk of developing the disease (Rogers, 1979). With the person-centered care theory, individuals at risk are the primary focus and are involved in the decision-making processes of care pertaining to their health care plan given their health history, lifestyle behaviors, as well as their socioeconomic status (Rogers, 1979). The person-centered approach provides an opportunity to investigate a broader scope of potential risk factors known to influence a person's health status in preventing or delaying adverse health outcomes (Rogers, 1979).

Nature of the Study

This is a quantitative study using secondary data from the 2016 NHIS, a health survey conducted by the United States (NHIS, 2016). The 2016 NHIS data were collected through survey questionnaires. It contains family-, adult-, and child-level datasets. The relevant datasets in addressing the proposed research questions are the adult and family level datasets because they contain all the variables stated in the research questions. The adult-level dataset also contains demographic, personal characteristics, and health information about the participants from over 97,169 participants in 59,230 households who were enrolled or participated in the survey (National Center for Health Statistics, 2017). Similarly, the 2016 NHIS data address the posed research questions and hypotheses and it is quantitative in nature (NHIS, 2017). The 2016 NHIS is anonymized free public data accessible in the NHIS, CDC website. Though it contains survey data for each subject, it does not contain any personal identifiers to review the subject identification (NHIS, 2017).

The research questions were addressed using a cross-sectional research design, which is useful when inquiring on the prevalence and potential risk factors or exposure to disease (liver cancer; see Creswell, 2018). A cross-sectional design aligns with 2016 NHIS data as collected (NHIS, 2016). A cross-sectional design allows for assessment of associations between variables as stated in the proposed research questions (Creswell, 2018). As previously stated, this is a quantitative study, as such, in this current study the research questions contain objective and quantifiable variables; thus, a quantitative

research method is appropriate. A comparative approach was used to address the posed research questions and hypotheses.

The dependent variable (DV) or outcome variable of interest is 'liver cancer'. The independent variable (IV) for RQ1 is liver disease or condition. The IV for RQ2 is health insurance status with focus on Medicaid. The IV for RQ3 is access to annual routine clinic visits or health care provider visits for the last 12 months. Gender and race are the two confounders or covariates for in this study.

Individuals ages 18-85+ years old living in the United States were included in this study. However, the outcome variable liver cancer had only 2 participants who responded "yes" to the liver cancer question when limited to the initial age range, making it impossible to run a valid binary logistic regression analysis. To address this data limitation, I sought IRB approval and changed the age criterion to individuals 18 to 85 years and above (see modification in chapter 4). These individuals were classified based on their health insurance coverage status (Medicaid insurance, no Medicaid insurance, or no health insurance coverage of any type and private or commercial insurance) and cancer diagnosis (liver cancer, nonliver cancer or no cancer). The descriptive analysis was conducted using appropriate tables and chart options to fit the level of measurements for the study variables. A binary logistic regression was used for the inferential statistical analysis to address the research questions. The G*Power software was used to calculate the required minimum sample size needed to achieve statistical power of 80% and a beta of 20% (Type II error). Also, a predetermined alpha (Type I error) value of 5% (0.05)

was used. Statistical Package for the Social Sciences (SPSS) software version 25 was used for the analysis.

Definitions

The terms defined in this study will give readers and scholars an understanding of the key words in this proposed study.

Cirrhosis: Replacement of the normal hepatic parenchyma with extensive thick bands of fibrous tissue and regenerative nodules, which results in clinical manifestations of portal hypertension and liver failure. Cirrhosis can be caused through various forms of liver diseases and conditions including hepatitis and chronic alcoholism (Chacko & Reinus, 2016).

Fatty liver disease: A disease resulting from prolonged acute alcohol consumption and is generally reversible with alcohol cessation. Fatty liver disease is a chronic form of liver disease and a risk factor of liver cancer which can be avoided if alcohol is consumed in moderation (Chacko & Reinus, 2016).

Hepatitis A Virus (HAV): A highly contagious liver infection caused by hepatitis A virus (HAV). HAV causes inflammation of the liver and inhibits liver ability to properly function. HAV can easily be transmitted from contaminated food or water, or infected objects (Schillie et al., 2018).

Hepatitis B Virus (HBV): A viral infection of the liver caused by hepatitis B virus (HBV). The infection can destroy the organ and may cause liver failure and cancer. It can easily be transmitted from person to person through sexual contact or any other form

of contact with infected blood, open sores, or bodily fluids. If not treated, Hepatitis B can be fatal (Schillie et al., 2018).

Hepatitis C Virus (HCV): A viral infection caused by hepatitis C virus (HCV). HCV is associated with inflammation of the liver and may cause a serious liver damage and consequently, liver cancer. HCV can spread through sexual contact or through contaminated blood or bodily fluid (Tilak et al., 2018).

Incidence: New cases of disease or event or outcome among individuals at risk within a time frame. Incidence is the ratio of total new cases within the at-risk population divided by total population at risk. For instance, reported new cases of patients with liver cancer within a given population in a year. In studying the etiology or risk of liver cancer, incidence is more important than prevalence. Incidence is expressed as cases per persons/person-years (Bray et al., 2018).

Liver Cancer: Liver cancer occurs in the liver. The liver is the largest glandular organ in the body and performs various critical functions to keep the body free of toxins and harmful substances (Li & Wang, 2016). It is in the right upper quadrant of the abdomen, right below the ribs. Liver cancer is generally classified as primary or secondary (Li & Wang, 2016). Primary liver cancer begins in the cells of the liver. Secondary liver cancer develops when cancer cells from another organ spread to the liver (Li & Wang, 2016). Types of liver cancers are hepatocellular carcinoma (HCC), a primary liver cancer constituting 80% of liver cancer, and the most common deadly liver cancer identified in the US and globally (Del Campo et al., 2018). Other types of liver

cancers are cholangiocarcinoma, liver angiosarcoma, and hepatoblastoma (Li & Wang, 2016).

Liver disease/condition: A hepatic damaging disease or disease of the liver which may contribute to the development of liver cancer and other liver related conditions (Del Campo et al., 2018).

Liver cancer therapy and management: Evidence-based processes and therapies used in controlling, treating, and preventing the development or managing of liver cancer. Liver cancer therapy and management are designed to reduce the incidence, prevalence, and mortality rates of liver cancer among general population (Kulik & El-Serag, 2019).

Health insurance coverage (Medicaid, private or commercial health insurance): Health insurance coverage is a type of insurance coverage. For example, Medicaid private or commercial insurance used in paying medical and surgical expenses incurred by the insured (Christopher et al., 2016). Medicaid health insurance is a health insurance program run by the US government to provide free or low-cost health coverage to low-income people, families, children, pregnant women, elderly, and people with disabilities in living in the US (Christopher et al., 2016). Private or commercial insurance is a group of health plans offered in connection to either employment or individually purchased to cover medical expenses or healthcare cost from illnesses or surgeries (Christopher et al., 2016).

Metabolic syndrome: A group of diseases associated with chronic liver disease (CLD), and possibly cirrhosis, of the liver. These diseases often predict the development

of liver cancer. For instance, obesity and diabetes are metabolic syndromes (Younossi & Henry, 2016).

Nonalcoholic steatohepatitis (NASH): A progressive form of NAFLD characterized by liver steatosis, inflammation, hepatocellular injury, and different degrees of fibrosis. Inflammation and liver cell damage associated with NASH can cause serious problems such as fibrosis, cirrhosis, and liver cancer. About 20% of people with NAFLD are also diagnosed with NASH (Schuster et al., 2018).

Person-centered care theory: A theoretical framework used in providing quality care to individuals to address unique health-driven needs of each patient to manage their disease outcomes, expected symptoms, and health challenges. It includes best practices and guidelines to inform standard of care and approaches (Rogers, 1979).

Risk factor of Liver cancer: Health determinants influencing the development of liver cancer. Liver cancer risk factors increase a person's chance of developing liver cancer but may not directly cause liver cancer (Hamilton & Waters, 2018).

Routine clinic visits or health care provider visits: Regular scheduled health maintenance and screening visits to the doctor to help patients manage their health status. The visits could be quarterly, twice a year, or yearly (annually). Routine clinic visits or healthcare provider visits help in detecting adverse health condition early and at an early stage (Doherty et al., 2019).

Assumptions

There is no evidence of verifiable clinical data included in this proposed cross-sectional study, because the 2016 NHIS data does not have verifiable clinical data to

confirm their exposure status. The fact that the 2016 NHIS data surveys do not suggest if the selected individuals are clinically negative from hepatitis B or C or were not exposed to these viruses besides the self-reported information has led to the assumption that the participants' self-reported information on their liver cancer, liver disease, health insurance status with focus on Medicaid and access to annual routine clinic visits status is reliable and valid.

Also, the 2016 NHIS data did not include any proof or evidence of the primary or secondary causes of liver cancer. The lack of specificity of the causes of liver cancer or disease condition was self-reported and documented in the 2016 NHIS data leading to series of unverifiable assumptions requiring additional and different set of study and design to address. This study also assumes all participants in the 2016 NHIS survey understood the need for routine clinic visits or medical care even though it is possible for participants under Medicaid health insurance to be prevented from getting access to medical care or health centers of their choice within their reach due to their social, financial, and environmental burdens or challenges.

In the 2016 NHIS questionnaire and for those participants who self-reported their liver cancer status, they were not asked whether they had liver disease or condition before developing liver cancer. This study assumes that liver disease occurred before the liver cancer because of a long latent period of cancer development. I am also assuming the patients' health insurance status with focus on Medicaid status is primarily based on their pre-existing health status (liver disease or liver cancer), rather than on health behavior status encouraged or driven by preventative care lifestyle. This is because the 2016 NHIS

questionnaire participants were not asked whether they had health insurance or Medicaid or how long they have had health insurance before developing liver cancer. Instead, for the health insurance with focus on Medicaid status question, participants were asked "What kind of health insurance or health care coverage do you have?" and different types of insurance coverage were listed for participants to select what applied to them. For the purpose of this study, three categories were identified, individuals who had Medicaid and those who do not have Medicaid including those with no insurance coverage of any type, and those with private insurance or commercial insurance.

Similarly, for access to annual routine clinic visits, it may not be possible to show if these participants are not already sick before their routine visits to health care facilities for checkup. In other words, if their primary reason for the visit is not because of the sickness or liver disease or liver cancer observed. In the 2016 NHIS questionnaire, participants were not asked whether they routinely visit their doctor or clinic for a medical checkup or how long they have been consistently adhering to their annual routine clinic visits. As a result, it is difficult to understand the attributable effects of routine care in the absence of quantifying the visits and adherence rate before observation of clinical outcome of liver cancer, assuming the participants were already sick or at risk for developing liver disease or liver cancer. Based on these assumptions observed, all assumptions are listed in Chapter 5 as part of the limitations of this study and are highly recommend for further studies to explore these gaps.

Scope and Delimitations

The study initially targeted individuals younger than 50 years old (18-49 years old). Because of smaller number of patients with the outcome variable (liver cancer), the study was revised to include individuals 18 to 85+ years after IRB approval. As such, the findings of this study applied to individuals 50 years and older in addition to the originally proposed age range. As a result, the findings of this study were not generalized outside of the scope of the subject or geographic inclusion criteria. Similarly, the findings of the study were used to infer correlational association and not a causal link.

Limitations

This study has some inherent challenges. For instance, by using a cross-sectional research design, spatiotemporal sequence between the exposure such as liver disease or insurance status or routine clinic visits and liver cancer may not be established. Based on the code book for the 2016 NHIS dataset, the survey was posed as a prevalence question. For the liver cancer, participants were asked; '*Ever told by a doctor or other health professional you had liver cancer*'. Similarly, for the liver disease question, participants were asked; '*Ever told by a doctor or other health professional you had any kind of chronic/long-term liver condition*'. Unfortunately, the way the liver disease question was posed in the 2016 NHIS data, I was not able to conclude the affirmative responses to the liver disease question which does not also include cases of liver cancer as part of liver condition or disease.

If, I was conducting this study in the form of primary data collection, meaning that I was collecting the data directly from the patients rather than the use of the 2016

NHIS data, I would have differentiated liver disease from liver cancer by asking the questions as follows; '*other than liver cancer, ever told by a doctor or other health professional you had any kind of chronic/long-term liver condition are not liver cancer'*. Unfortunately, it was not the case in this study because I used the 2016 NHIS data which lacks specificity in their questionnaire regarding liver cancer and liver disease. In addition, because the NHIS 2016 secondary data source is not necessarily focused on this proposed specific topic, I had to dig to find applicable information which may be colored by my own bias or faulty approach. Also, secondary data sources can become outdated. It was also difficult to verify the study outcome and collect additional data with secondary data.

The health insurance status with focus on Medicaid and access to annual routine clinic visits or healthcare provider visits in the past 12 months questions revealed the answer to whether the participant had Medicaid insurance or not and had access to annual routine clinic visits or health care provider visits in the past 12 months, respectively. The health insurance status with focus on Medicaid question had three categories, 'Medicaid', 'no Medicaid or coverage of any type' and third category for private or commercial insurance' response option. The access to annual routine clinic visits or health care provider visits in the past 12 months questions had a 'yes' or 'no' or 'don't know' response option. Based on this, it was difficult to establish whether the exposures under investigation preceded or proceeded the intended outcome, in this case, liver cancer and vice versa. With a cross-sectional design, it is usually challenging to establish a clear exposure/risk to outcome sequence or vice versa. In other words, it was not possible in

this study and using the 2016 NHIS data to show if liver disease occurred first before liver cancer and thus, I cannot explain the primary factors associated with liver cancer cases observed. Thus, this study was not used to infer any causal relationship because the research design was not an experimental or quasi-experimental design.

Also, no generalization was inferred because this is not a multi-site study. The correlational inference observed was limited to the participants used in this study and may not apply to individual outside of the 2016 NHIS dataset. The 2016 NHIS data collection was done via a self-reported survey method and not through a clinical diagnosis setting or provided by a medical practitioner. Therefore, possible recall bias and misclassification bias was likely to occur. Another limitation of the study was the NHIS database, which was established only for surveillance purposes, thus, did not fully match the clinical diagnosis.

Significance

This study initially targeted individuals younger than 50 years old (18-49 years old). Because of smaller number of patients with the outcome variable (liver cancer), the study was revised to include individuals 18 to 85+ years after IRB approval. In this research inquiry regarding the associations between liver cancer and liver disease, health insurance status with focus on Medicaid, and access to annual routine clinic visits or healthcare provider visits in the past 12 months, so potential preventive measures to reduce risk of liver cancer be explored, findings correlated with the proposed intent irrespective of the shift in the age criteria. Also, the literature gap stated by Suh et al (2018) was examined in detail. The information produced through this current study

could promote the continued discussion on evidence-based approaches to facilitate liver cancer screening adherence. Subsequently, it may lead to improved patient's lifestyle and health behavior and promote a comprehensive patient care process. Potential findings may also help identify information or indicators which may be implemented to improve Medicaid health insurance recipient's status, access to routine care, and subsequently reduce potential liver cancer incidence, prevalence, mortality rates and associated risk factors.

Even when I could not show the spatio-temporal sequence of insurance status and liver cancer due to the limitation of the 2016 NHIS questionnaire, the study still had substantial value to help address the research questions in terms of the overall perception of understanding the overall effects of Medicaid status on liver cancer. This piece of information was invaluable to state-wide public health care services, Medicaid services providers as well as to medical practitioners and may help them understand how to improve the Medicaid or health insurance services offered to the at-risk population. In public health programmatic and epidemiologic surveillance levels, the current study findings could be used as a reference to develop evidence-based documentations on health trends, intervention measures toward health-related goals by understanding the effects of health insurance with focus on Medicaid and access to annual routine clinic visits or healthcare provider visits in the past 12 months on chronic disease such as liver disease and liver cancer. It is possible through this current study findings, meaningful evidence-based outcome could inform the expansion of specific public health policy or inform policy makers and public health practitioners on program strategies aim at

decreasing the prevalence and incidence of liver cancer to promote a meaningful positive social change and public health goals.

Summary

In this section of the study, the incidence of liver cancer among individuals in the US was described. Also, the burden of the disease by race and socioeconomic status was discussed. The risk factors of liver cancer and its impacts were also discussed, as this current study may provide useful information which may lower the incidence, prevalence, and mortality rates associated with the development of liver cancer. Further literature review on risk factors associated with liver cancer, health insurance/Medicaid, access to annual routine clinic visits or health care provider visits in the last 12 months was explored in detail in Chapter 2 to provide detailed information on evidence-basis of this current study and its relevance to medical practice, public health services, epidemiological research and public health well-being.

Chapter 2: Literature Review

Introduction

Each year, the number of people diagnosed with liver cancer in the United States is increasing (CDC, 2018). The percentage of Americans who are newly diagnosed with liver cancer has risen to 7.1 cases per 100,000 for several decades in the US (CDC, 2018). Risk factors such as liver disease, access to annual routine clinic visits or healthcare provider visits in the past 12 months and health insurance status with focus on Medicaid, influence the trend of liver cancer development among adults 18-49 living in the US. However, the race or gender of a person may not directly present biological factors increasing the exposure to liver cancer (Fujiwara et al., 2018).

One approach suggested to address the issue of high burden of liver cancer was highlighted by Suh et al. (2018). Suh et al. (2018) explored the risk factors in developing liver cancer in people with and without liver disease and recommended further public health efforts should aim in preventing the development of liver cancer among Medicaid recipients with liver disease by reinforcing health monitoring systems or routine clinic visits (Suh et al., 2018). Similarly, Suh et al. strongly suggested preventive efforts or health promotion measures aimed at decreasing the incidence of liver cancer among health insurance (Medicaid) recipients are warranted to minimize the development of liver cancer among individuals younger than 50 years old in the US (Suh et al., 2018).

According to Bandiera et al. (2016), liver cancer is associated with hepatitis viruses (e.g. Hepatitis B or C), cirrhosis, and other diseases. Therefore, preventing or

minimizing the risk of developing liver cancer could substantially reduce deaths associated with liver cancer. As research is completed to address the disproportionately high incidence and prevalence of liver cancer in US population, the use of the person-centered care approach may lead to lifestyle or behavior change to improve quality of life for those at risk for developing liver cancer (Rogers, 1979)

The purpose of this study was to assess the impact of being a Medicaid health insurance recipient, with a history of liver disease, and with access to annual routine clinic visits or healthcare provider visit in the past 12 months on the risk of developing liver cancer among adults 18 to 85+ years old and above in the US. The study initially targeted individuals younger than 50 years old (18-49 years old), because of smaller number of patients with the outcome variable (liver cancer), the study was revised to include individuals 18 to 85+ years after IRB approval. A valid binary logistic regression of this quantitative study was successfully completed. Patient's health insurance status, with focus on Medicaid, and access to annual routine clinic visits or healthcare provider visit in the past 12-months were explored as barriers to facilitate liver cancer screening amongst individuals living the US.

Though liver disease may develop into liver cancer, no link has been found between any type of liver disease, health insurance recipient status with focus on Medicaid, or access to annual routine clinic visits or healthcare provider visits in the past 12 months among adults 18-85+ living in the US with liver disease when compared to individuals of the same age group without liver disease, who are not Medicaid health insurance recipients, and who do not schedule routine clinic visits or health care provider

visits for the previous 12 months (Suh et al., 2018). Based on the gap in understanding of liver disease and its progression in young adults and adult Medicaid patients, as discussed by Suh et al., further comparative study is warranted to explore the impact of liver disease, health insurance status with focus on Medicaid insurance, and access to annual routine clinic visits or healthcare provider visit in the last 12 months on the risk of developing liver cancer in adults 18-85+ years old living in the US (Suh et al., 2018). To more comprehensively examine the issues leading to the overrepresentation of the risk factors of developing liver cancer among adults living in the US, and what can be done to mitigate this issue, a comprehensive review of the current literature was done.

The literature review for this study provided in-depth insight on the risk factors of liver cancer among adults in the United States. In this section of the dissertation, the literature search strategy, the theoretical framework, and review of literature findings related to key variables of the study is described. The information contained within this chapter outlines the literature review, literature search strategy, and theoretical framework guides the research questions and associated hypotheses of this study.

Literature Search Strategy

The literature search was conducted using peer reviewed articles from various databases such as ProQuest Dissertations & Theses, Science Direct, Google Scholar, CINAHL Plus, Pub Med, and Thoreau multi-database. I used Walden University library to access these databases including ProQuest. Search terms or key words used included the following: *liver cancer* and *liver disease, liver cancer* and *health insurance status, Medicaid insurance, liver cancer* and *adherence to routine clinic visits or medical*

checkup, risk factors of liver cancer, liver cancer risk factors and *subjects 18-49 years old,* and *person-centered care theory* and *liver cancer*. The literature search was performed mostly for articles published between 2014 and 2019. I identified over 250 peer reviewed articles within the topic area of liver cancer and liver disease, and most of the articles were less than five years old from the search year of 2019. Of the 250 peer reviewed articles identified, 30 of the most relevant full text articles were discussed in this inquiry.

Theoretical Framework

The person-centered care (PCC) theory was used to explain the observed phenomenon and the interactions between the specified independent variables (liver disease, health insurance status with focus on Medicaid, and access to annual routine clinic visits or healthcare provider visits for the past 12 months and dependent variable (liver cancer) for this current study. PCC theoretical concepts include best practices and guidelines to inform standard of care (Rogers, 1979). The model incorporated tailored approaches to guide providers in providing quality and valued care to individuals (Rogers, 1979). This tailored patient care process is very useful in addressing the unique health-driven needs of each patient to help them manage their disease outcomes, expected symptoms, and health challenges (Rogers, 1979). Person-centered care approaches are often employed by public health practitioners and health care professionals to assess standards of care and professional practices (Rogers, 1979). This model is also applied in exploring new risk factors outside of known risks and standard clinical practices (Rogers, 1979).

According to Jayadevappa and Chatter, (2011), PCC encompasses informed decision making which may improve treatment choice, quality of care, and health outcomes and recognizes the need for major changes in the process of care that arranges health care system around the patient or person. The authors evaluated and discussed the interplay of components of PCC by developing a conceptual model of PCC with person reported outcomes (Jayadevappa & Chhatre, 2011). In addition, this conceptual model was used to aid objective and subjective evaluation of person-centered care aimed at improving the quality of care. Also, the model was useful to introduce changes in healthcare system, improvement in overall quality of care, and minimizing wasteful health resource consumption associated with rapid healthcare costs unsustainability. The authors suggested more research is needed to explore the various attributes of person-centered care, its acceptability, and comparative effectiveness in the healthcare arena (Jayadevappa & Chhatre, 2011).

Pukrittayakamee et al. (2018) used a cross-cultural, forward and backward translation expert review, and content validity index measurement to examine the outcome of person-centered care theory on cancer patients pain management symptoms in Thai hospital. The study consisted of patient and staff-rated where 379 nurses and 379 Thai cancer patients admitted to Maharaj Nakorn Chiang Mai Hospital, tested for internal consistency, known-group comparison, responsiveness, and agreement (Pukrittayakamee et al., 2018). The theory was also used in translating staff and patient versions of the palliative care outcome scale (POS) and to determine psychometric properties among cancer patient outcomes (Pukrittayakamee et al., 2018). The person-centered care theory

is regarded as a central tool to determine quality and effectiveness, making it part of universal health coverage goals enabling researchers and clinicians to apply the Palliative Outcome Scale (POS) in primary research and routine clinical practice to both determine the effectiveness of interventions and improve care designed specifically for patients and families with advanced disease such as cancer (Pukrittayakamee et al., 2018). Other indicators such as environmental factors, lifestyle choices, behavioral risk factors, outcomes, and exposures could be explained using the person-centered care model. Bayus, (2016) used the person-centered care theory for the identification of nonalcoholic fatty liver disease in patients with Hepatitis C. Evidence based guidelines were used to improve diagnosis and transition of care from liver cancer specialty care provider to primary care provider (Bayus, 2016).

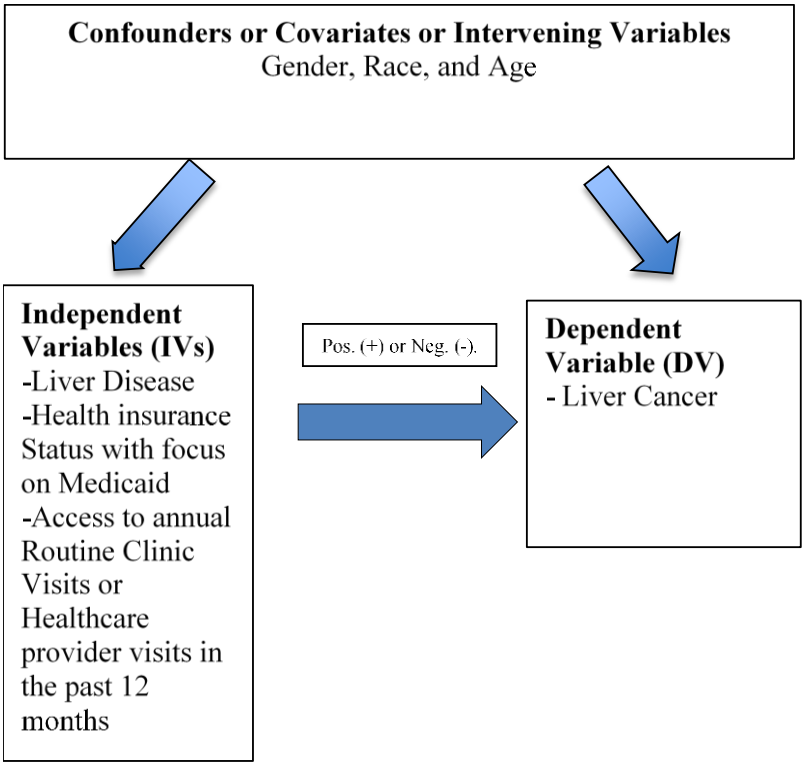
In context, the exploration of the associations between liver cancer and liver disease, Medicaid insurance status, and routine clinic visits or medical checkup was explained using this model. Liver disease, a biological factor, insurance status with focus on Medicaid, a socioeconomic factor, and access to annual routine clinic visits or healthcare provider visit in the past 12 months, a sociodemographic, are linked to determinants such as lifestyle, behavior, and environmental components of the decision-making processes of the individual and perhaps, other individual's predisposition risks (Bayus, 2016). Based on the model, constant interactions between patients and providers allow for assessment of emotional, mental, spiritual, social, and financial aspects of patient's interpersonal communication with their providers. This is crucial in helping patients make informed decisions regarding exposure to risk factors whether at the

personal or systemic levels to support meaningful efforts in minimizing the risk of diseases/health conditions (Pukrittayakamee et al., 2018). The goal in the application of the person-centered care model is to direct care resources to the persons at risk, which is the primary focus of quality care and expand every health practice to involve the patient in the decision-making processes of care while accounting for their health history, lifestyle behaviors, and socioeconomic status (Rogers, 1979). The model provides the opportunity to investigate a broader scope of potential risk factors aimed at helping patients prevent, control, delay, and manage adverse health outcomes (Rogers, 1979). Adopting the model promotes quality care for a better decision-making process and enhances plan of care and point of care practices to ultimately achieve improved patient quality of life.

In this current study, the person-centered model guides discussions relating to the assessment of the association between liver cancer, liver disease, health insurance status (Medicaid) and access to annual routine clinic visits or healthcare provider visits in the past 12 months among eligible patients (18-85+ years old) living in the US. The model is an essential tool for improving the quality of care and disease outcomes or health conditions (Rogers, 1979). The model was designed and is used to understand the need in maintaining standard care processes to improve the lives of persons at risk (Rogers, 1979). Figure 1 below represents the PCC model of liver cancer risk factors, a theoretical foundation sketch with variables as it pertains to this current study.

Figure 1

Directed Acyclic Graph of Study Variables



Note. PCC model of Liver cancer risk factors.

Figure 1 Directed Acyclic Graph (DAG) represents the current study variable interaction with some of the person-centered care constructs. The IVs described in the DAG framework are liver disease, health insurance status with focus on Medicaid, and access to annual routine clinic visits or healthcare provider visits in the last 12 months. These IVs could play a role in the onset or development of liver cancer. Each of the described IVs or factors could influence liver cancer development positively or negatively or show no effect. The DV or the health outcome variable in question is liver cancer. The specified covariates or confounder or intervening variables also known as

demographic factors (age, gender, and race) play a pivotal role in health outcome. The association of this relationship was determined in Chapter 4 analysis.

Donabedian model focused on structural domain related to health-care system or context in which care is delivered influenced the processes and outcomes of health-care quality improvement (Santana et al., 2018). Structural domains were educational programs, health promotion and prevention programs with patients. Process domains cultivates communication, engaged patients in managing their care and integrates care and finally the outcome domains provide access to care and patient-reported outcomes. This current study used PCC constructs to linked Medicaid to liver disease, and healthcare access or clinics (structure and process) to liver cancer (outcome) with gender, race, and age (covariates or demographics) as controls, while PCC attributes such as structure, process, and outcome domains of the quality model with focused on the patient established interaction of the independent, dependent variables and covariate of this current study.

Literature Review Related to Key Variables and Concepts

The literature review research section is used to deduct broad trends from existing literature. The articles reviewed were separated into concepts or themes are relevant to this current topic discussion. The areas of interest evaluated, and the search strategies employed for the literature review are as follows; study variables: *liver cancer incidence, prevalence and mortality rates, risk factors of liver cancer, liver cancer and liver diseases* (e.*g., hepatitis B and C, cirrhosis, alcoholic fatty liver, nonalcoholic fatty liver disease, and metabolic syndrome including diabetes and obesity*), *liver cancer and health*

insurance status (*Medicaid health insurance, e.g. qualification for Medicaid insurance*), *liver cancer and access to annual to routine clinic visits or health care provider visits in the past 12months, liver cancer and gender, liver cancer and race, and burden of liver cancer* (medical management and social impacts) and *Family and Societal Burden of liver cancer*. Based on the literature reviewed, each of these topics were described in detail in this section of the dissertation.

Incidence of Liver Cancer

White, Thrift, Kanwal, Davila, and El-Serag, (2017) conducted a retrospective cohort study which revealed the incidence of liver cancer is on the rise in the US. The incidence of liver cancer increased from 4.4 cases per 100,000 persons in 2000 to 6.7 cases per 100,000 persons in 2012, with an increase of 4.5% (95% confidence interval (CI) [4.3%, 4.7%]) annually, but only 0.7% annually (95% CI [–0.2%, 1.6%]) from 2010 through 2012. These data show in all 50 US states the rate of increase in liver cancer slowed from 2010 through 2012 (White et al., 2017). Based on gender, the average annual percentage change (AAPC) increases between 2000 and 2012 was higher in men (3.7%) than in women (2.7%), while the incidence of liver cancer was highest among individuals ages 55-59 years old irrespective of gender (AAPC, 8.9%; 95% CI, 7.1%–10.7%) and those ages 60-64 years old (AAPC, 6.4%; 95% CI, 4.7%–8.2%) (White et al., 2017). By 2012, the liver cancer incidence rates among Hispanics surpassed Asian population (White et al., 2017). Similarly, the incidence rate of liver cancer was slightly higher in Texas than in Hawaii (9.71 cases per 100,000 person's vs 9.68 cases per 100,000 persons) (White et al., 2017). Geographic variation within individual race and

ethnic groups was observed, but rates were highest in all major race and ethnic groups in Texas (White et al., 2017). Even though liver cancer incidence rate in all 50 US states slightly slowed from 2010 through 2012, liver cancer incidence increased in subgroups such as men ages 55-64 years old, especially those born in the peak era of Hepatitis C virus infection and among Whites/Caucasians (White et al., 2017). Also, during this period, rates in Hispanics surpassed those in Asian Americans. Thus, an influence of geographic differences was observed, with Texas having the highest age-adjusted liver cancer rates nationwide (White et al., 2017).

Prevalence of Liver Cancer

Islami et al. (2017) investigated the prevalence of liver cancer based on the national survey data from the CDC. The CDC data reported the impact of race and state-based disparities of liver cancer occurrence in the United States. Findings provided an overview of liver cancer incidence, mortality, survival rates, and trends of the disease by race, ethnicity, and state. Liver cancer was noted as a highly fatal disease with increasing death rates faster than any other cancer in the United States with substantial disparity in liver cancer death rates by race and ethnicity (from 5.5 per 100,000 in non-Hispanic whites to 11.9 per 100,000 in American Indians/Alaska Natives) (Islami et al., 2017). Similarly, disparities of the disease burden existed based on state characteristics with liver cancer prevalence in North Dakota reported at 3.8 per 100,000 persons while in District of Columbia it was 9.6 per 100,000 persons (Islami et al., 2017). It was concluded liver cancer will account for about 41,000 new cancer cases and 29,000 cancer deaths in the United States in 2017, even though, the prevalence of major risk factors of

liver cancer indicated improvement in liver cancer survival in recent decades, only one in five patients survives 5 years after the diagnosis (Islami et al., 2017).

Mortality of Liver Cancer

Liver cancer is the 3rd leading form of cancer death in the United States (Kim et al, 2014). Kim et al. (2014) characterized temporal trends in mortality from chronic liver disease and liver cancer and the associated risk factors using US population-based data. Between 1981 and 2010, 690,414 deaths (1.1%) were attributable to chronic liver disease, whereas 331,393 deaths (0.5%) were attributable to liver cancer contributing to an increased health and economic burden from liver disease in the US (Kim et al., 2014). In an observational study, Tapper and Parikh (2018) evaluated liver cancer-related mortality in the US from 1999-2016 by age, sex, race, causes of liver disease, and geographic regions. The authors used death certificate data from the US Census Bureau vital statistics and population data and a Join-point regression analysis for evaluation. A total of 460,760 deaths were attributed to liver cancer and men had a higher burden of age-adjusted mortality than women by 4:1 ratio (Tapper & Parikh, 2018). Compared with non-Hispanic Americans, individuals of Hispanic ethnicity had relatively high age adjusted mortality of 5.7 cases per 100,000 individuals compared to 3.4 cases per 100,000 persons with highest burden of age-adjusted mortality seen among Asians and Pacific Islanders (Tapper & Parikh, 2018). The south and west had the highest age adjusted mortality from liver cancer, representing 4.2 cases per 100,000 persons (Tapper & Parikh, 2018). According to the authors, the US annual deaths from liver cancer more than doubled from 5,112 in 1999 to 11,073 in 2016 (Tapper & Parikh, 2018). Also, the

age adjusted death rate due to liver cancer increased annually by 2.1% (1.9% to 2.3%, $p < .001$) (Tapper & Parikh, 2018). Only Asians and Pacific Islanders had an improvement in HCC-related mortality where death rate decreased by 2.7% (95% CI 2.2%-3.3%, $p < .001$) per year.

A similar increase was reported by Sadaf et al., (2018) in a cross-sectional study involving 30,200 deaths from liver cancer (20,540 men and 9,660 women) (Sadaf et al., 2018). According to the authors, liver cancer is the 10th-most common cancer and, the 5th cause of cancer-related deaths among men and the 8th-most common cause of liver cancer deaths among women (Sadaf et al., 2018). Tapper and Parikh (2018) observational study used Join-point regression analysis to evaluate liver cancer-related mortality in the US from 1999-2016 by age, sex, race, causes of liver disease, and geographic regions. The authors used death certificate data from the US Census Bureau vital statistics and population data (Tapper & Parikh, 2018). A total of 460,760 deaths were attributed to liver cancer and men had a higher burden of age-adjusted mortality than women by 4:1 ratio (Tapper & Parikh, 2018). Compared with non-Hispanic Americans, individuals of Hispanic ethnicity had relatively high age adjusted mortality of 5.7 cases per 100,000 individuals compared to 3.4 cases per 100,000 persons with highest burden of age-adjusted mortality seen among Asians and Pacific Islanders (Tapper & Parikh, 2018). The south and west had the highest age adjusted mortality from liver cancer, representing 4.2 cases per 100,000 persons (Tapper & Parikh, 2018). U.S. annual deaths from liver cancer more than doubled from 5,112 in 1999 to 11,073 in 2016

and the age adjusted death rate due to liver cancer increased annually by 2.1% (1.9% to 2.3%, $p < .001$) (Tapper & Parikh, 2018).

Risk Factors of Liver Cancer

According to Hamilton and Waters (2018), risk factors of liver cancer are health determinants that increase a person's odds of developing liver cancer. It is important to note some people who are exposed to several risk factors may never develop cancer, while others with minimal risks develop the disease (Hamilton & Waters, 2018). Increasing risk factor awareness, improving people's health literacy about the risk factors, and engaging in effective physician-patient communication about the risk factors may help an individual make informed lifestyle and healthcare choices (Hamilton & Waters, 2018). Though cirrhosis of the liver and non-alcoholic fatty liver disease (NAFLD) are the main risk factors of liver cancer in the US, several other factors have been reported to increase the risk of liver cancer (Hamilton & Waters, 2018). For instance, an individual with a positive result for both Hepatitis B and C has a higher risk of developing liver cancer than a person positive for only one type of the virus (Hamilton & Waters, 2018). Similarly, a person with Hepatitis C who drinks alcohol has a higher risk of developing liver cancer (Hamilton & Waters, 2018). Different factors cause different types of cancer (Hamilton & Waters, 2018). Researchers continue to investigate factors associated with liver cancer, findings could help reduce the incidence and prevalence of the disease (Hamilton & Waters, 2018). Dos Santos Marcon, Tovo, Kliemann, Fisch, and de Mattos. (2018) conducted a retrospective cohort study in Brazil to assess the incidence of liver cancer in patients co-infected with human

immunodeficiency virus (HIV), chronic hepatitis virus B or C, and patients without HIV. Patients were selected in the largest tertiary public hospital complex in southern Brazil between January 2007 and June 2014 (Dos Santos Marcon et al., 2018). Demographic and clinical data, including lifestyle habits such as illicit drug use or alcohol abuse were collected and reviewed (Dos Santos Marcon et al., 2018). In addition, the frequency and reasons for hospital admissions via medical records review were assessed for 804 patients (399 with HBV or HCV with HIV coinfection and 405 no infection with HBV or HCV; Dos Santos Marcon et al., 2018). Liver cirrhosis was observed in 31.3% of HIV-negative patients and in 16.5% of co-infected ($p < 0.001$; Dos Santos Marcon et al., 2018). Liver cancer was diagnosed in 36 patients (10 HIV co-infected and 26 non-infected) and the incidence density of liver cancer in co-infected and non-infected patients was 0.25 and 0.72 cases per 100 patient-years (95%CI: 0.12-0.46 *vs* 0.47-1.05; long-rank $p = 0.002$), respectively (Dos Santos Marcon et al., 2018). The ratio for the liver cancer incidence rate was 2.98 for HIV negative patients (Dos Santos Marcon et al., 2018). After adjusting for age or patients with cirrhosis, the absence of HIV did not produce a statistically significant effect on development of liver cancer (Dos Santos Marcon et al., 2018). The presence of HIV coinfection in chronic liver disease due to HBV or HCV showed no relation to the increase of liver cancer incidence; thus, liver cancer incidence is not different between con-infection and non-coinfection groups (Dos Santos Marcon et al., 2018). However, age and alcohol use were associated with risk of developing liver cancer (Dos Santos Marcon et al., 2018).

The incident cases of HBV and HCV declined while the prevalence of obesity nearly doubled, with over 25% of the US population categorized as obese in 2010 (White et al., 2017). A decrease in adverse drug reactions (ADRs) from all causes, all cancers, major cardiovascular disease (CVD), and diabetes over the study period were discussed, but an increase in the ADR among patients with viral hepatitis and liver cancer over same period was also observed (White et al., 2017). For each of the liver diseases examined, including viral hepatitis, cirrhosis, and liver cancer, the average annual percent change (AAPC) increased between 2006 and 2010 (White et al., 2017). They suggested fatal impact of liver cancer and other liver-related diseases will continue in the US (White et al., 2017). In a US prospective cohort study Altekruse, Henley, Cucinelli and McGlynn, (2014) linked ADR to liver cancer and other chronic liver diseases. Much attention has been given to the financial and societal impact of rising obesity rates; its impact on liver disease has been extensively investigated (Altekruse et al., 2014). It has been estimated obese and diabetic patients are at nearly twice the risk of developing liver cancer than nonobese and nondiabetic patients (Altekruse et al., 2014). Although viral hepatitis infection increases the risk of liver cancer more than any other risk factor for any given individual patient, diabetes and obesity are responsible for the greatest population-based attributable risk for liver cancer in the US (Altekruse et al., 2014).

The effects of metabolic risk factors such as obesity and Type 2 diabetes on chronic liver disease and liver cancer were explored by Sayiner et al. (2016). Obesity is a known risk factor of nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), and primary liver cancer (Sayiner et al., 2016; Sayiner, Golabi,

& Younossi, 2019). Therefore, increasing obesity rates undoubtedly contributed to the rise in the incidence of NAFLD and NASH which now affect anywhere between 12% and 46% of the US population (Sayiner et al., 2016). According to Sayiner et al. (2016), the incidence of obesity has tripled over the last three decades and three in every 10 individuals in the US in 2010 had a body mass index of 30 kg/m^2 or more (Sayiner et al., 2016). The increase in obesity potentially promoted the increase in chronic liver disease and liver cancer (Sayiner et al., 2016). Recent trends demonstrated no decrease in the rising epidemic of obesity; the subsequent impact on liver disease will likely continue to rise in the US (Sayiner et al., 2016).

The understanding of the broader scope of the risks, within the population-based perspective and treatment details are lacking in Sayiner et al. (2016) study as compared to the White and Alterkruse's studies. Another potential limitation was the lack of review of death certificate records to verify the cause of death may have been misclassified (Sayiner et al., 2016). Also, patients with multiple comorbid conditions like HBV and HCV were reported as having a single, primary cause of death on their death certificate. Information regarding the proportion of patients who might have had overlapping diseases (e.g., HCV, HBV, etc.) were unavailable (Sayiner et al., 2016). Nonetheless, compared to White and Alterkruse's studies, the use and synthesis of data from credible population-based resources were key strengths of the study (Sayiner et al., 2016).

Liver Diseases and Liver Cancer

Del Campo, Gallego, & Grande, (2018) defined liver disease as the damage to the liver by viruses, alcohol, non-alcohol factors, etc. Hepatic inflammation from the liver diseases can progress to severe fibrogenesis and subsequently liver cancer (Del Campo et al., 2018). Del Campo et al. (2018) conducted a retrospective cohort study using national census adult data for chronic liver disease to characterize the incidence and mortality of chronic liver disease in the US and assessed economic burden of liver disease. They suggested liver diseases are strongly associated with liver cancer, which increases among people older than 45 years old (Del Campo et al., 2018).

HBV, HCV, and Liver Cancer

According to Del Campo, et al, (2018) hepatitis is a virus that infects the liver. The two common types are hepatitis B and C (Del Campo, Gallego, and Grande, 2018). Viral hepatitis is the most common risk factor of liver cancer worldwide (Del Campo, et al, 2018). HCV is also the most cause of liver cancer than HBV because there is no current vaccine for HCV (Del Campo et al., 2018). Viral hepatitis can be transmitted from person to person through exposure to blood or bodily fluids (Del Campo et al., 2018). Transmission could also occur via injury, sharing needles through drug use, and sexual contacts (Del Campo et al., 2018). HBV can also be transmitted to an unborn baby or infant through their mother or surrogate. Babies or neonates can be vaccinated within 72 hours after birth to prevent the neonate from developing acute HBV infections (Del Campo et al., 2018). Nearly all individuals vaccinated for HBV are immune from the virus infection (Del Campo et al., 2018). Compared to the work of Del Campo et al.,

Goel, Ahmed, & Waked, 2019) in a retrospective cohort study revealed ADR for treatment of viral hepatitis substantially increased mortality cases to 11.6% increase from 1981 to 2000 and 11.5% from 2004 to 2007 (Goel, et al 2019). Although efforts should be directed to primary prevention, more importantly, epidemiological assessments tailored toward secondary prevention efforts to treat patients with chronic viral hepatitis infection (Goel et al., 2019).

HBV and HCV are common risk factors of liver cancer or HCC (White, Thrift, Kanwal, Davila, & El Serag. (2017) conducted a retrospective cohort study in the US to assess annual trends among sociodemographic and geographic subgroups using join point analysis. Chronic hepatic viral infections accounted for approximately 80% of all cases of liver cancer in the US (White et al., 2017). In another study, Bertuccio, et al, (2017) used an observational design to assess the prevalence of liver cancer among subjects with HCV and HBV. The incidence of HBV and HCV dropped nearly 8-fold and was estimated at 1.3 and 0.3 cases per 100,000 population, respectively (Bertuccio et al., 2017). It is likely the decline may influence a decrease in liver cancer associated with HBV and HCV (Bertuccio et al., 2017). The incidence of HBV infection has been declining since the mid-1980s post introduction and implementation of HBV vaccine (Bertuccio et al., 2017).

Cirrhosis and Liver Cancer

Cirrhosis develops when liver cells are damaged and replaced by scar tissue (Rabie, Eltoukhy, al-Shatouri, & Rashed, 2018). Rabie et al. (2018) used a cross sectional design and SEER's data to assess the risk of developing liver cancer among

cirrhotic patients. They found cirrhotic patients' highest 5-year cumulative risks occur among cirrhotic patients with HCV (17% in the West and 30% in Japan), hemochromatosis (21%), HBV (10% in the West and 15% in Asia), alcoholic cirrhosis (8%–12%), and biliary cirrhosis (Rabie et al., 2018). Also, the researchers concluded the risk of developing liver cancer in cirrhosis patients varies with underlying conditions such as alcohol abuse, NAFLD, viral hepatitis (B and C) (Rabie et al., 2018). Individuals with too much iron in the liver from hemochromatosis, and other rare types of chronic liver disease and those with prolonged history of combined alcohol abuse and hepatitis virus infection are at high risk of cirrhosis and liver cancer (Rabie et al., 2018).

In a population-based cohort study using the Ontario Cancer Registry, Anyiwe et al. (2016) linked data attributed liver cancer high incidence with cirrhosis as the most important risk factor predominantly caused by chronic viral hepatitis infection. The authors studied the impact of socioeconomic status (SES) on liver cancer incidence and stage at diagnosis among viral hepatitis cases (Anyiwe et al, 2016). Incidence rates were calculated using person-time methodology. Association between SES (income quintile) and liver cancer incidence was assessed using proportional-hazards regression. The impact of SES on liver cancer stage was investigated using logistic regression. A crude liver cancer incidence rate of 21.4 cases per 1000 person-years was observed adjusting for gender, age, urban/rural residence and year of viral hepatitis diagnosis among 11,350 individuals diagnosed with viral hepatitis between 1991 and 2010 (Anyiwe et al, 2016). A significant association was found between socioeconomic status (SES) and liver cancer incidence, with an increased risk among individuals in the lowest three income quintiles

(incidence rate ratio, IRR = 1.235; 95% CI: 1.074–1.420; IRR = 1.183; 95% CI: 1.026–1.364; IRR = 1.158; 95% CI: 1.000–1.340 respectively; Anyiwe et al, 2016). Liver cancer risk factors such as cirrhosis and HIV were associated with SES and differences in risk factors across income quintiles were noted, but no association was found between SES and liver cancer stage (Anyiwe et al, 2016). The authors recommended investigating how SES affects liver cancer incidence to facilitate an understanding of which populations are at elevated risk for developing liver cancer (Anyiwe et al, 2016).

NAFLD, NASH, ALD, CLD and Liver Cancer

NAFLD is the accumulation of fat (> 5%) in liver cells in the absence of excessive alcohol intake (Del Campo et al., 2018). NAFLD affects more than 30% of the population in the global west, especially patients suffering from metabolic syndrome, obesity (76%), and Type 2 diabetes (50%; Del Campo et al., 2018). NAFLD begins as a benign steatosis and could evolve into a NASH with scarring and tissue replacements. NASH begins with Type-I collagen, developing fibrosis, cirrhosis, and, in many cases, develops into a liver cancer (Del Campo et al., 2018). In a retrospective cohort study using the population-based SEER's datasets Younossi and Henry explored the burden of liver-related morbidity and mortality in the development of liver cancer (2016). They pinpointed NAFLD as a common cause of CLD and a risk factor of liver cancer thus the prevalence of cirrhosis among patients with liver cancer are attributed to NAFLD ranged from 36% and 90%, with most studies reporting cirrhosis rates of 70% or higher (Younossi & Henry, 2016). They concluded, NAFLD is the hepatic manifestation of metabolic syndrome, which affects about a third of the adult population in the US and it

is a common condition preceding both clinical liver and metabolic diseases, thus a risk factor of liver cancer (Younossi & Henry, 2016). Likewise, Sayiner et al. (2016) conducted a case control study on NAFLD and ALD, known risk factors of metabolic diseases, including diabetes, obesity, and cardiovascular diseases in the US. The researchers used population-based data from SEER to assess the association between ALD, NAFLD and chronic liver disease and explored the effects of cirrhosis on liver cancer and the development of liver cancer (Sayiner et al., 2016). They concluded NAFLD is associated with obesity and metabolic syndrome, whereas ALD is associated with excessive alcohol consumption (Sayiner et al., 2016). Both diseases can progress to cirrhosis, liver cancer, and liver-related deaths (Younossi & Henry, 2016). A higher proportion of patients with NAFLD die from cardiovascular disorders compared to patients with ALD, whereas a higher proportion of patients with ALD die from liver disease (Younossi & Henry, 2016). Consequently, NAFLD and ALD are associated with morbidities and impairment to health-related quality of life, but also creates health care burden (Younossi & Henry, 2016).

Beste et al. (2015a) used a population-based data from hospital records and death certificates to examine the trends of the burden of cirrhosis and HCC by assessing the liver disease cases in US veterans. Based on their findings, NAFLD is the most common cause of cirrhosis among Japanese, Latinos, and Native Hawaiians veteran's population, while ALD and HCV were the most common causes of cirrhosis among Whites and African Americans, respectively (Beste et al., 2015a). They concluded NAFLD is the most common cause of cirrhosis in veterans when stratified by race or ethnicity and

suggested NAFLD is underdiagnosed and associated with many comorbidities (Beste et al., 2015). Setiawan et al. (2016) conducted a retrospective cohort study to investigate the prevalence of CLD and cirrhosis by evaluating the underlying factors in underserved multiethnic groups in the US the influence the disease. CLD and cirrhosis are major sources of morbidity and mortality in the US, but little is known about the epidemiology in ethnic minority populations (Setiawan et al., 2016). Hence, they examined the prevalence of CLD and cirrhosis by exploring the etiologies of the disease among African Americans, Native Hawaiians, Japanese Americans, Latinos, and Whites (Setiawan et al., 2016). CLD and cirrhosis cases were identified using Medicare claims between 1999 and 2012 among the fee-for-service participants (Setiawan et al., 2016). A total of 5,783 CLD cases (3,575 without cirrhosis and 2,208 with cirrhosis) were identified (Setiawan et al., 2016). According to a retrospective cohort study by Sia et al. (2017), the prevalence of CLD ranged from 3.9% in African Americans and Native Hawaiians to 4.1% in whites, 6.7% in Latinos, and 6.9% in Japanese (Sia, et al., 2017). NAFLD was the most common cause of CLD in all ethnic groups combined (52%), followed by ALD (21%) ((Sia, et al., 2017). NAFLD was the most common cause of cirrhosis in the entire cohort (Sia, et al., 2017). By ethnicity, NAFLD was the most common cause of cirrhosis in Japanese Americans, Native Hawaiians, and Latinos, accounting for 32% of cases (Sia, et al., 2017). ALD was the most common cause of cirrhosis in whites (38.2%), while hepatitis C virus was the most common cause in African Americans (29.8%) (Sia et al., 2017). NAFLD was also the most common cause of CLD and cirrhosis in the entire cohort, and the high prevalence of NAFLD among Japanese Americans and Native

Hawaiians was new, thus, warranting further studies to understand the new findings (Sia et al., 2017). Stratified by race and ethnicity, NAFLD was the most common cause of CLD without cirrhosis in all ethnic groups and in CLD with cirrhosis among Japanese Americans, Latinos, and Native Hawaiians (Sia et al., 2017). HCV and ALD were the most common causes of cirrhosis in African Americans and whites, respectively (Sia et al., 2017). Younossi and Henry (2016) also suggested NAFLD is increasingly the most common chronic liver disease associated with obesity and include conditions such as steatosis, fibrosis, and cirrhosis all of which increases the risk of liver cancer. The incidence of liver cancer increased by 4-fold within the last four decades (1.6 per 100 000 in 1975-1977 to 4.8 per 100 000 in 2005-2007) and may continue to rise (Younossi & Henry, 2016). NAFLD accounted approximately 25% of the cases in western countries (Younossi & Henry, 2016). The prevalence of patients on the liver transplant waitlist increased dramatically within the last decade, surpassing ALD and second to chronic hepatitis C (Younossi & Henry, 2016).

Setiawan et al. (2016), in a retrospective cohort study, examined the relationship between alcohol and liver disease in the US in five racial/ethnic groups and underserved populations. They observed ALD is the most common cause of cirrhosis in Whites and who are more likely to die from alcoholic liver cirrhosis than African Americans or Blacks (Setiawan et al, 2016). In this study the use of case identification based on Medicare claim files was limiting and probably underestimated the prevalence of NAFLD because biochemical and imaging testing were not included or used to identify the observed cases (Setiawan et al., 2016). Based on the prevalence of this condition and

public health threat posed by liver disease and risk factors, further studies are needed to investigate underlying genetic, metabolic, and nutritional causes of liver related conditions (Setiawan et al., 2016).

Donati et al. (2017) used a retrospective cohort study to examine the relationship between NAFLD and liver cancer in non-cirrhotic individuals. NAFLD represented an emerging cause of liver cancer, especially in non-cirrhotic individuals, and a sequence variant associated with the development and progression of NAFLD influenced susceptibility to liver cancer (Donati et al., 2017). Variant cohort of non-cirrhotic NAFLD patients in the United Kingdom was also used to confirm the link between NAFLD and liver cancer (Donati et al., 2017). In addition, the effect of I148M variant on liver cancer risk was not independent of severe fibrosis, thus suggesting the mechanism is partly mediated by promotion of hepatic fibrogenesis and alteration of hepatic stellate cells biology (Donati et al., 2017). In conclusion, the observed differences were due to lifestyle factors and higher prevalence of clinical cofactors, as opposed to genetic risk variants (lower frequency of the I148M variant) among the United Kingdom cohort (Donati et al., 2017). As such, further studies are needed to assess whether the E167K variant is an independent risk factor for the development of liver cancer (Donati et al., 2017). In addition, they reported genetic risk variants did not significantly improve the predictive accuracy of clinical factors, so, the availability of the genetic risk profile should be assessed before evaluation of genetic risk variants can be considered or implemented in clinical practice (Donati et al., 2017).

Metabolic Syndrome (Obesity and Type 2 Diabetes) and Liver Cancer

The liver plays key roles in glucose and lipoprotein metabolism (Lallukka & Yki-Järvinen, 2016). Diabetes mellitus can also increase the risk of liver diseases (Younossi & Henry, 2016). Metabolic syndromes such as obesity and diabetes are associated with chronic liver disease and cirrhosis and are also linked to liver cancer (Younossi & Henry, 2016). Type 2 diabetes is often observed among patients who are obese (Younossi & Henry, 2016). Obesity and diabetes are a group of diseases associated with chronic liver disease and possible cirrhosis of the liver often predicts the development of liver cancer (Younossi & Henry, 2016). The increasing burden of non-communicable diseases is associated with rising rates of obesity (Samuel & Shulman, 2018). Life expectancy in the US has decreased, and the decrease is partly attributed to obesity-related metabolic syndromes, including Type 2 diabetes, kidney disease, stroke, and heart diseases (Samuel & Shulman 2018). The transition from infectious to metabolic disease is apparent in the shifting epidemiology of liver diseases (Samuel & Shulman, 2018).

Diabetes is a metabolic syndrome and patient with diabetes has a higher incidence of liver cancer (Goel et al., 2019). Using meta-analysis, Goel et al. (2019), showed independent of viral hepatitis or alcohol use, on the association between diabetes and liver cancer. They suggested cirrhosis causes glucose intolerance and Type-2 diabetes, which subsequently leads to liver cancer (Goel et al., 2019). While long-term diabetes and high HbA1c increased the risk of liver cancer, and metformin treatment decreased liver cancer risk (Goel et al., 2019). Obesity causes the deposition of fat in the liver, which subsequently leads to a condition known as NAFLD. NAFLD has been linked to

diabetes disorders and both NAFLD and diabetes has been classified as important risk factors for liver cancer in the US (Goel et al., 2019). In the meta-analysis study, Goel et al. (2019) included 26 prospective cohort studies with 25,337 primary liver cancer cases to demonstrate a BMI value of 25 kg/m^b and higher as well as a BMI value of 30 kg/m^2 and higher were associated with an increased risk of primary liver cancer (Goel et al., 2019). The relative risk for a 5-unit increment in BMI was 1.39 kg/m^2 (95% CI: 1.25–1.55) with the most pronounced increase in risk among persons with a BMI >32 kg/m^2 (Goel et al., 2019). The association between BMI and liver cancer was independent of geographic location, alcohol consumption, or history of diabetes (Goel et al., 2019). However, obese males had a higher risk of liver cancer than obese females (Goel et al., 2019). Furthermore, the association between increasing basic metabolic index (BMI) and liver cancer was much stronger in individuals with concomitant HCV infection than in persons with HBV infection (Goel et al., 2019).

Race and Gender and Liver Cancer

Liver cancer death rates in the US are increasing faster than any other cancer (Siegel, Miller & Jemal, 2019). Siegel et al. (2019) compared the disparities of liver cancer occurrence among different races in the US using the SEER and the National Center for Health Statistics (NCHS) data. They evaluated the overview of liver cancer incidence, mortality rate, and survival rate trends, by race, ethnicity, and states including the District of Columbia (Siegel et al., 2019). There is substantial disparity in liver cancer death rates by race and ethnicity (Siegel et al., 2019). For instance, there were

approximately 5.5 deaths per 100,000 non-Hispanic Whites as compared to 11.9 deaths per 100,000 American Indians/Alaska Natives in (Siegel et al., 2019)

Petrick et al. (2016) conducted a study on incidence rates of liver cancer among other racial and ethnic groups in the US. Incidence rates increased 3.5 times from 2000 and 2012 and were higher among men than women (Petrick et al., 2016). Also, liver cancer increased with each successive birth cohort through 1959 but decreased among 1960 to 1969 birth cohorts (Petrick et al., 2016). Asian-Pacific Islanders had the highest liver cancer rates in the US for many years, but the rates stabilized and began to decline in recent years (Petrick et al., 2016). Between 2013 and 2030, liver cancer incidence rates among Asian-Pacific Islanders are forecasted to decline and the decline will affect more women than men (Patrick at al., 2016). Also, by 2030, Asian-Pacific Islanders men will have the lowest liver cancer incidence rate, while Hispanic men are forecasted will have the highest rate and second highest among women (Petrick at al., 2016). Black women are forecasted to have the highest liver cancer incidence rate (Petrick at al., 2016).

Among all men, the liver cancer rates are expected to begin decreasing slightly between 2025 and 2030 (Petrick et al., 2016). Rates among Hispanics are expected to continue to increase in coming years and will stabilize between 2025 and 2030 (Petrick et al., 2016). Similarly, Ryerson et al. (2016) examined the association between liver cancer incidence and mortality decline among men and women in the US. In the study, they evaluated increasing burden of liver and intrahepatic bile duct (Ryerson et al., 2016). Based on the join point analysis for the period between 1992-2012 and mortality cases

period between 1975-2012 as well as the short-term trends between the period of 2008-2012, they concluded death rates continued to decline for all cancers combined and for most cancer sites among men and women of all racial and ethnic groups (Ryerson et al., 2016). Overall, death incidence rates decreased among men and remained stable among women from 2003 to 2012 (Ryerson et al., 2016). However, among both men and women, liver cancer incidence rates increased sharply (Ryerson et al., 2016). Men had more than twice the incidence rate of liver cancer than women (Ryerson et al., 2016).

In a retrospective cohort study done by Bertuccio et al, (2017), liver cancer incidence rates increased with age for both sexes. They revealed liver cancer incidence rates were higher for persons born after the 1938 to 1947 birth cohort (Bertuccio et al, 2017). In contrast, there was a minimal birth cohort effect for non-Hispanic Asian and Asian-Pacific Islanders (Bertuccio et al, 2017). Non-Hispanic Black men and Hispanic men had the lowest median age at death, 60 and 62 years old, respectively (Bertuccio et al, 2017). The highest average per person years of life lost per death from cancer was 21 and 20 years for Non-Hispanic Black men and Hispanic men, respectively (Bertuccio et al, 2017). HCV and liver cancer-related deaths were highest among individuals born during 1945 through 1965. However, cancer incidence was stable among women than men (Bertuccio et al, 2017).

Burden of Liver Cancer

In a prospective cohort study Younossi et al. (2017) examined the clinical and economic impact of treating Medicaid patients with HCV to assess the changes in chronic HCV disease and the economic burden associated with comprehensive treatment of

chronic HCV infection. Patients were followed for a period of 8-12 weeks (Younossi et al., 2017). A decision-analytic Markov model design was used (Younossi et al., 2017). Patients insured under Medicaid were treated under state-specific restrictions by Metavir fibrosis stage (base case) or all treated (all-patient strategy) with an approved all-oral regimen (ledipasvir/sofosbuvir [LDV/SOF]), for 8 weeks or 12 weeks depending on their cirrhosis status, viral load, and state specific LDV/SOF restrictions (Younossi et al., 2017). Treated patients were projected to have fewer cases of cirrhosis, liver transplants, liver cancer; HCV-related deaths, additional life-years per patient, and additional quality-adjusted life-years per patient (Younossi et al., 2017). Current restrictive state policies regarding HCV treatment in Medicaid populations must be reassessed because treating all Medicaid patients with chronic HCV using LDV/SOF resulted in billions of savings and decreased the proportion of total costs attributed to downstream costs of care to 18.3% for Medicaid population (Younossi et al., 2017).

Farvardin et al. (2017) also reported high levels of knowledge about liver cancer risk, surveillance logistics, and treatment among the patient population represented in a highly selected patient population (>80% Caucasian, >63% college educated, and highly insured), which may not be applicable to other populations (Farvardin et al., 2017). The survey was administered among racially diverse and socioeconomically disadvantaged cohort of patients who were followed in a large safety net health system (Farvardin et al., 2017). Patient knowledge, attitudes, and barriers observed were particularly important to understand the increased risk of liver, lower surveillance rates, and prevent worse prognosis among racial/ethnic minorities and patients of low socioeconomic status

(Farvardin et al., 2017). Despite differences in patient populations, patients demonstrated high levels of basic knowledge regarding liver cancer risk, surveillance logistics, and prognosis (Farvardin et al., 2017). Most importantly, 90% of patients understood cirrhosis is a high-risk factor for liver cancer and ultrasound-based surveillance should be performed every 6-12 months. Liver cancer surveillance rates were significantly lower among the subset of patients who did not know patients with cirrhosis were at high risk for developing liver cancer, thus highlighting the importance of increasing awareness or discussion on this issue with all patients with cirrhosis (Farvardin et al., 2017). Several knowledge deficiencies warrant targeted patient education efforts were emphasized (Farvardin et al., 2017). Nearly half of patients believed eating a healthy diet could preclude the need for liver cancer surveillance, and over one-third believed liver cancer surveillance was not necessary if they had a normal physical exam and/or were asymptomatic (Farvardin et al., 2017). Furthermore, over one-fourth of patients believed liver cancer surveillance could be stopped after two normal ultrasound exams, potentially partly explaining "surveillance fatigue" and decreasing adherence rates as patients are followed over time (Farvardin et al., 2017). Overall, patients expressed high levels of concern for developing and/or dying from liver cancer (Farvardin et al., 2017). Although they expressed reassurance in terms of liver cancer surveillance on improving early tumor detection, less than half of patients believed liver cancer surveillance reduces mortality (Farvardin et al., 2017). This uncertainty regarding liver cancer surveillance's survival benefit contributed to the health behavior where patients placed a lower priority on liver cancer surveillance, which lead to non-adherence with surveillance recommendations

(Farvardin et al., 2017). The reason for the disparity in reassurance for early tumor detection and mortality reduction is unclear but may relate to how providers communicate the benefits of liver cancer surveillance (Farvardin et al., 2017).

Beste, Harp, Blais, Evans, & Zickmund, (2015b) stated a similar pattern was noted in a survey study among primary care providers caring for patients with cirrhosis. Provider communication style and their level of enthusiasm for cancer screening benefits has been a strong predictor of adherence in colon and breast cancer screening (Beste et al., 2015b). If provider communication also impacted liver cancer surveillance adherence, this would highlight the need for higher-quality data characterizing the survival benefit of liver cancer surveillance in patients with cirrhosis (Beste et al., 2015b). This study also supported studies evaluating the impact of interventions, such as provider communication training or audit feedback, on patient attitudes and surveillance adherence (Beste et al., 2015b). Nearly half of all patients reported issues with ultrasound scheduling, costs, transportation, or uncertainty on where to get surveillance ultrasound performed (Beste et al., 2015b). Although these barriers are likely more common among socioeconomically disadvantaged patients, they highlighted the importance of interventions target at increasing liver cancer surveillance rates (Beste et al., 2015b).

Conclusively, the burden of liver cancer in the US is significant and is expected to increase in the future (Beste et al., 2015b). Moreover, despite some improvements in localized and regional disease survival rates in recent decades, the overall prognosis for liver cancer remains poor (Beste et al., 2015b). Wider disparities in liver cancer death

rates by sex, race and ethnicity, and state persist, thus, reflecting differences in the prevalence of major risk factors and, to some extent, inequalities in access to high-quality care (Beste et al., 2015b). However, most liver cancers are potentially preventable, and interventions to curb the rising burden of liver cancer and reduce racial and ethnic disparities should include the targeted application of existing knowledge in prevention, early detection, and treatment, including improvements in HBV vaccination, screening and treatment of HCV, maintaining a healthy body weight, access to high-quality diabetes care, prevention of excessive alcohol drinking, and tobacco control (Siegel et al., 2017).

Health Insurance Status and Liver Cancer

Medicaid insurance program provides free or low-cost health coverage to individuals or family with low-income, pregnant women, elderly, and people with disabilities in the US (Christopher et al., 2016). Many states expanded their Medicaid programs to cover individuals below certain income levels (Christopher et al., 2016). The monthly gross income requirements for Medicaid coverage were categorized among children, adults, pregnant women in a household While the income requirement for Medicaid for elderly people and individuals with disability was based on their needs. (Christopher et al., 2016).

Singal and El-Serag (2015) conducted a retrospective cohort study on determinants of liver cancer surveillance among 904 racially and socioeconomically homogenous diverse cohorts of cirrhotic patients. Where less than 1 in 5 patients had liver cancer, homogenous populations, of 904 cirrhotic and few used guideline-based

definitions for surveillance to characterize guideline consistent with liver cancer surveillance rates and identify determinants of liver cancer surveillance among a racially and socioeconomically diverse cohort of cirrhotic patients (Singal et al. 2015). Nine hundred and four patients were followed between July 2008 and July 2011 at an urban safety-net hospital (Singal et al., 2015). An inconsistent surveillance was defined as at least one ultrasound screening during the three-year period, while an annual surveillance was defined as ultrasounds screening every 12 months (Singal et al., 2015). A biannual surveillance was defined as ultrasounds screening every 6 months (Singal et al., 2015). Univariate and multivariate analyses were conducted to identify predictors of surveillance (Singal et al., 2015). Of 904 cirrhotic patients observed, 603 (67%) had inconsistent surveillance or ultrasound screening (Singal et al., 2015). A significant barrier to the surveillance or screening was associated to failure to identify cirrhosis ($p < .001$) (Singal et al., 2015). Insurance status was associated with inconsistent surveillance, with odd ratio of [*OR*], 1.43; 95% [CI], 1.03-1.98) (Singal et al., 2015). Surveillance among African Americans surveillance or screening *OR* value was 0.6 (95% CI, 0.42-0.99) (Singal et al., 2015). Only 98 (13.4%) of 730 patients with cirrhosis had annual surveillance or screening, while only 13 (1.7%) of 786 with cirrhosis had biannual surveillance or screening (Singal et al., 2015). There are racial and socioeconomic disparities, with lower rates of liver cancer surveillance among African Americans and underinsured patients (Singal et al., 2015). Also, Medicaid insurance qualifications were assessed, and the association between possession of Medicaid insurance or lack of Medicaid insurance and the development of liver cancer among cirrhotic patients was

evaluated (Singal et al., 2015). They concluded racial, social, clinical determinants of liver cancer surveillance, date of first medical encounter, number of primary care provider or hepatology clinic visits, and Medicaid insurance status play a role in liver cancer surveillance for both outside and inside institutions and are associated with the risk of developing liver cancer (Singal et al., 2015).

In a prospective cohort study, Farvardin et al. (2017) stated patient barriers were associated with lower liver cancer surveillance rates in patients with cirrhosis in the US and73.0% of the patients observed had Medicaid or were covered by a county medical assistance plan (Farvardin et al., 2017). They provided insights on patient-level intervention needed to increase liver cancer surveillance rates, patient knowledge, improve patient attitudes, and reduce barriers regarding liver cancer surveillance among patients with cirrhosis (Farvardin et al., 2017). Hoehn et al. (2015) conducted a retrospective cohort study on disparities in care for patients with curable liver cancer to assess the treatment of early stage of liver cancer. The study revealed reported rates of liver cancer lower than 40% due to lack of health insurance (Medicaid) during the early stage of liver cancer (Hoehn et al., 2015). In the study, underutilization of surgical approach for early stages of liver cancer was identified as the key barrier to liver cancer treatment (Hoehn et al., 2015). Surgical treatment is still underused in a potentially curable cancer cases while surgery was associated with significantly increased survival among patients with stage I/II liver cancer, yet less than 40% of patients were managed surgically (Hoehn et al., 2015). Non-medical patient factors appeared to be associated with this treatment decision (Hoehn et al., 2015). Some researchers suggested

demographic factors such as race or socioeconomic status and lack of health insurance influenced the use of surgery for liver cancer; while socioeconomic factors may influence treatment, it is unclear if they affect survival (Singal et al., 2015). According to the authors of this study, location and type of hospital are important factors affecting treatment patterns, a barrier determined by insurance status or type of insurance policy. Many of the study's data were generated in a single institution or through Medicare database and may not accurately represent national treatment patterns for all patients with liver cancer (Singal et al., 2015).

Medicaid insurance status has previously been shown to affect treatment and survival (Singal et al., 2015). Several patients with higher 30-day mortality rate and less long-term survival rate were less likely to be treated with surgical approach (Singal et al., 2015). Patients on Medicaid, or without insurance were less likely to have surgery and are among those who have worse health outcomes (Singal et al., 2015). Treatment was affected by advanced stage of liver cancer at presentation, with privately insured patients having liver cancer detected mostly at an early stage (Singal et al., 2015). Mortality and survival rates were different even among early stages liver cancer patients (Singal et al., 2015). As government insurance is being expanded nationally, it is important to have a thorough understanding of how Medicaid and Medicare outcomes compare to those of privately insured patient impact the development of liver cancer (Singal et., 2015).

Access to Healthcare and Liver Cancer

Liver cancer patients' survival rate is low, with five-year relative survival rates of only 5% from 1987 to 1989, which modestly improved to 18% from 2005 to 2011 in the

US (Wang et al., 2016). Since liver cancer is typically asymptomatic at earliest stage, effective early detection of pre-symptomatic stage is typically via routine screening and surveillance (Wang et al., 2016). Several studies have shown early detection of liver cancer and subsequent curative treatment can lead to improved clinical outcomes (Wang et al., 2016). According to Wang et al. (2016), using a meta-analysis included 47 studies with a total of 15,158 patients in the US. Liver cancer surveillance was associated with improved early-stage detection (*OR* 2.08, 95% CI [1.80, 2.37]) as well as prolonged survival (*OR* 1.90, 95% CI [1.67, 2.17]) (Wang et al., 2016). They also reported in another meta-analysis which included 28 studies and 15,244 patients, early asymptomatic liver cancer accounted approximately 30% of patients at initial liver disease manifestation stage (Wang et al., 2016). Similarly, Atiq et al. (2017) in a retrospective cohort study assessed the benefits and harms of liver cancer surveillance in patients with cirrhosis in the US. Their goal was to evaluate the impacts of surveillance benefits and harms in cirrhosis patients screened for liver cancer (Atiq et al., 2017). In the study, patients with cirrhosis were followed at a safety-net health system between July 2010 and July 2013 (Atiq et al., 2017). Surveillance-related benefits such as early tumor detection and curative treatment and surveillance-related physical harms such as computed tomography or magnetic resonance imaging scans, biopsies, other procedures for false-positive or indeterminate surveillance results were performed and sociodemographic and clinical surveillance harms were also evaluated using multivariable logistic regression (Atiq et al., 2017). They suggested factors associated with adherence to clinic and medical checkups and the development of liver cancer were examined even when

surveillance ultrasound and alpha fetoprotein (AFP) tests had minimal direct downstream harms (Atiq et al., 2017). Follow-up tests were weighed against surveillance benefits when determining the value of liver cancer screening of 680 patients with cirrhosis of whom 78 (11.5%) developed liver cancer during the three-year study period (Atiq et al., 2017). Of the 48 (61.5%) patients with liver cancers identified by surveillance, 43.8% were detected by ultrasound, 31.2% by AFP, and 25.0% by both surveillance tests, thus no significant difference was noted in tumor stage between ultrasound and AFP-detected tumors ($p = 0.53$) (Atiq et al., 2017). Over one fourth of patients with cirrhosis experienced physical harm for false-positive or indeterminate surveillance tests more often related to ultrasound than AFP, thus, interventions are needed to reduce surveillance-related harm and to increase the value of liver cancer screening programs in clinical practice (Atiq et al., 2017). Liver cancer surveillance was associated with early tumor detection and increased curative treatment receipt (Atiq et al., 2017). In fact, liver cancer surveillance was responsible for tumor detection in approximately 60% of liver cancer patients and increased early tumor detection rates from 40% to 70% (Atiq et al., 2017). Tumor detection was attributed to ultrasound alone in nearly half of cases, while AFP is attributed to one quarter of cases (Atiq et al., 2017). However, early detection and curative treatment is not different between ultrasound and AFP screening approaches, Overall, liver cancer surveillance was associated with early tumor detection and increased curative treatment received (Atiq et al., 2017).

Goldberg et al. (2017) in a retrospective cohort study identified some barriers of liver cancer surveillance among patients with cirrhosis in the US. They showed over

25,000 patients with newly diagnosed cirrhosis had low liver cancer surveillance adherence (Goldberg et al., 2017). Liver cancer surveillance barriers such as insurance access (Medicare, Medicaid, Truven Health) were identified using tracking tests including work orders, scheduling, and performance (Goldberg et al., 2017). Insights on low liver cancer surveillance rates and identified potential target interventions at the patient and physician levels were noted abdominal ultrasounds standing orders placed more than three months ahead of time were found to be less likely used due to patients' lack of medical insurance or non-adherence to routine visits (Goldberg et al., 2017). They recommended future liver cancer surveillance guidelines should address appointment lead time as a critical barrier of liver cancer surveillance compliance and future interventions should focus on reducing the lead time of tests ordered; surveillance protocols, such as patient reminder calls, could be beneficial in improving adherence (Goldberg et al., 2017). Similar studies revealed geographic isolation on liver cancer surveillance rates, where patients residing farther away from their local clinics or hospitals had lower rates of liver cancer surveillance adherence (Goldberg et al., 2017). The association between liver cancer surveillance and the number of specialty clinic visits was examined by Goldberg et al. (2017), and they showed a much stronger association between specialist visits and liver cancer surveillance and the reduction in rate of developing liver cancer, rather than seen with visits with a primary care provider alone. They suggested a patient who sees a gastroenterologist or infectious disease specialist even once in the first year after cirrhosis diagnosis doubled surveillance adherence rates, independent of primary care visits (Goldberg et al., 2017).

Tillman et al. (2018) investigated the relationship between specialist and higher test ordering. They confirmed the association between test completion rates with minimal impact of primary care visits on test ordering (Tillman et al., 2018). Diagnostic test such as ultrasounds and protocol for liver cancer screening during routine medical checkups were correlated with specialist versus primary care visits and increased surveillance were cautiously interpreted among patients with the highest number of specialist visits (Tillman et al, 2018). According to Tillman et al. the number of liver cancer ultrasounds and MRI performed was suboptimal and insufficient for obtaining appropriate liver cancer surveillance, therefore, improved access to local health care facilities for patients who are geographically isolated might improves access to liver cancer surveillance adherence (Tillman et al., 2018).

Outcome of Liver Cancer (Outcomes of Clinical or Medical Management)

Liver cancer is the fifth most common cancer and the second most frequent cause of cancer related death globally. About 90% of liver cancers are hepatocellular carcinoma (HCC), which is a major global health problem (Galle et al., 2018). Clinical or medical management of liver cancer is an important indicator because it is associated with liver cancer outcomes (Johnson et al., 2015). Johnson et al. (2015) conducted a cross-sectional study which incorporated a comprehensive approach of both primary and secondary prevention approaches to increase access to treatment and increased funding for liver-related research (Johnson et al., 2015). They indicated the need for a comprehensive approach to address high death rates associated with chronic liver disease and liver cancer in the US (Johnson et al., 2015). They concluded a comprehensive

approach involving primary and secondary prevention will increase access to treatment and utilize funding better (Johnson et al., 2015).

In a retrospective study, Hoehn et al. (2015) provided a comprehensive understanding of clinical surgical management for early-stage liver cancer by utilizing nationally validated, prospectively gathered data and a cancer database to investigate the number of patients with potentially curable diseases receiving surgical management and what variables were associated with treatment decisions and survival (Hoehn et al., 2015). Hoehn et al. (2015) reviewed the National Cancer Database (NCDB) for the assessment of all patients with curable liver cancer (Stage I/II) from 1998 to 2011. Seventy percent of all diagnosed malignancies in the US de-identified patient-level data; patient demographics, cancer staging, tumor histology, treatment types, short-term surgical outcomes, and long-term survival were standardized and coded (Hoehn et al., 2015). Two cohort groups were compared with respect to clinical stage, age, gender, race, primary insurance, income, education, Charlson–Deyo score, and facility type (Hoehn et al., 2015). However, even when the incidence-based mortality decreased due to earlier detection and improved intervention, a large population of patients with curable diseases who do not receive surgical management were identified (Hoehn et al., 2015). The rates of surgical management over time had a stronger impact on patients who were younger, less likely to be black, and more often privately insured (Hoehn et al., 2015). Income and education were directly correlated with increasing rates of surgical management of liver cancer (Hoehn et al., 2015). Also, patient and tumor characteristics were analyzed to determine predictors of having surgery (Hoehn et al., 2015). Only

39.7% of patients received surgery for early stage liver cancer (Hoehn et al., 2015). Surgical therapies included resection (34.6%), transplant (28.7%), radiofrequency ablation (27.1%) and other therapies (Hoehn et al., 2015). Surgery correlated with improved median survival (48.3 versus 8.4 months) but was only performed on 42% of stage I patients and 50% of tumors smaller than 2cm. Patients were more likely to receive surgery if they were Asian or white race, had private insurance, higher income, better education, or sought treatment at an academic center ($p < .05$). However, private insurance and treatment at an academic center were the only variables associated with improved survival ($p<.05$; Hoehn et al., 2015).

While socioeconomic factors may influence treatment, it is unclear if they affect survival (Singal et al., 2015). The location and type of hospital are important factors affecting treatment patterns, a barrier determined by insurance status or type of insurance policy (Singal et al., 2015). Yu (2016) used an observational study to examine the guidelines regarding the management of liver cancer in contrast to other cancers. The author indicated a range of liver cancer treatment options involved several multidisciplinary careers and enormous heterogeneity in management trends (Yu, 2016). Yu (2016) identified geographic differences in tumor biology (i.e., areas of increased hepatitis B prevalence) and available resources (organ availability for transplantation, medical technology, accessibility to treatment, health systems, and health resources) and suggested it made it impractical to have an internationally universal guideline for all patients with liver cancer (Yu, 2016). Since surgical resection and other therapies were considered too conservative, Asian guidelines represented consensus about surgical

resection an indication for more advanced tumor, as such tailored intervention approached are highly recommended to serve the need of the target population and geographical location (Yu, 2016).

In a prospective cohort study Sayiner et al. (2016) investigated current practice guidelines and recommendation for regular biannual liver cancer screening for cirrhotic patients with active HCV infection in the US population. However, it is still unclear whether and how post-sustained virologic response (SVR) patients should be monitored for future liver cancer development and if any of the risk-associated variables has clinical utility (Sayiner et al., 2016). They suggested molecular hallmarks of persisting liver cancer risk in post-SVR livers may serve as biomarkers to identify a subset of patients at risk, and therefore could be monitored by regular liver cancer screening (Sayiner et al., 2016). Patients who should be regularly monitored for future liver cancer (Sayiner et al., 2016). They also indicated post direct-acting antivirals (DAAs) for liver cancer development and recurrence cumulatively posed clinical experience of DAA-based treatment and Post-SVR liver cancer development and recurrence may be more frequent compared to interferon-based treatment (Sayiner et al., 2016). As such, further studies are needed to clarify whether DAAs increase liver cancer incidence and to determine the natural history and baseline post-SVR liver cancer incidence according to the type of anti-HCV therapy among specific patient population (Sayiner et al., 2016). Chronic Hepatitis B patients treated with directly acting anti-HBV drugs, entecavir, or other nucleotide analogue, showed higher liver cancer incidence compared to peg-interferon-treated patients, suggesting the difference in liver cancer-suppressive effect may be a

common phenomenon across different hepatitis viruses (Sayiner et al., 2016). Therefore, HCV-related liver cancer will remain a major health problem in the coming decades despite the clinical deployment of DAAs (Sayiner et al., 2016). Access to the new generation antiviral therapies should be substantially improved to achieve meaningful prognostic benefit at the population level (Sayiner et al., 2016). The development of a vaccine remains an important goal for global control and eradication of infection (Sayiner et al., 2016). Thus, prolonged clinical observation should be examined to determine the impact of DAA-induced SVR on HCC development and recurrence as well as on other cancer types (Sayiner et al., 2016).

In 2010, the rate of ADRs associated with chronic liver disease and liver cancer were 23.67 cases per 100,000 and 16.57 cases per 100,000 population, respectively (Altekruse et al., 2017). Also, a decrease in certain risk factors such as HBV and HCV, may not reduce the prevalence of other risk factors such as obesity (Altekruse et al., 2017). However, liver diseases cases including chronic liver disease and liver cancer strongly impacted health care due to high cased mortality (Altekruse et al., 2017).

According to Samuel & Shulman, (2018) weight loss with diet or bariatric surgery effectively treats NAFLD, but drugs specifically approved for NAFLD are not available. Some new pharmacological strategies act broadly to alter energy balance or influence NAFLD pathways while others specifically inhibit key enzymes involved in lipid synthesis (Samuel & Shulman, 2018). A novel class of liver-targeted mitochondrial uncoupling agent increases hepatocellular energy expenditure, reversing the metabolic

and hepatic complications of NAFLD which is a risk factor of Liver cancer (Samuel & Shulman, 2018).

Ioannou, Green, and Berry's (2018) examined the relationship between clinical management and liver cancer in the US population. They demonstrated the eradication of HCV infection with direct-acting antiviral (DAA) agents reducing the risk of liver cancer by 71% (Ioannou et al., 2018). Clinical data were used to assess the occurrence rate of liver cancer in patients with cirrhosis and evaluate the incident cases of liver cancer (Ioannou et al., 2018). Liver cancer occurrence was evaluated using the Kaplan-Meier curves and Cox regression analysis to assess variables associated with liver cancer development (Ioannou et al., 2018). The cox proportional hazards regression was used to determine the association between type of antiviral regimen and liver cancer risk (Ioannou et al., 2018). The incidence of liver cancer was highest in patients with cirrhosis and treatment failure, thus highlighting a decreased risk of liver cancer in multivariable models among individuals who used antiviral treatment compared to those who are under different regimen (Ioannou et al., 2018).

Cai et al. (2018) used a training cohort of 709 liver cancer patients to examine the relationship between mutual influence of liver dysfunction and malignancy, with overall survival (OS) as a composite clinical endpoint in liver cancer. The training cohort of 709 liver cancer patients validated in an international independent dataset examined the role of nomogram integrating hepatic reserve and tumor characteristics for liver cancer following curative liver resection (Cai et al., 2018). They also developed a nomogram integrating albumin–bilirubin (ALBI) grade, a new index of hepatic reserve, and tumor

characteristics of liver cancer for predicting overall survival following curative liver resection (Cai et al., 2018). As a result, an accurate prognostic nomogram for liver cancer was proposed. which provided a highly accurate estimation of OS in patients with liver cancer after curative liver resection contributing to assess patient prognosis, thus providing an easy access to reach liver cancer at risk patients (Cai et al., 2018).

Chen et al. (2019) used a sample model established by the S-index to predict the overall survival after curative resection of primary hepatocellular carcinoma (PHCC), a new way to examine prognostic prediction after curative resection of PHCC, which remains an arduous task (Cheng et al., 2019). They calculated S-index from γ-glutamyl transpeptidase, albumin, and platelets reported to predict the severity of liver fibrosis (Cheng et al., 2019). Hoehn et al. (2015) highlighted an average rate of curative surgery of 22% and ranged from 14 to 51%. The rates were higher in single-center studies, while the rate for early stage liver cancer was 59% (Hoehn et al., 2015). The rates of surgical management in in some cases range from 20 to 57% (Hoehn et al., 2015). While the phenomenon of underutilized surgical care is known, the reasons for this disparity remain unclear (Hoehn et al., 2015). Some clinical management strategies such as advances in liver transplantation and hepatic resection have improved survival for a selected population (Altekruse et al., 2017). However, the effect on the overall disease-specific mortality at the national level is limited (Altekruse et al., 2017). Furthermore, variations exist in the choice of therapy among patients with liver cancer because the type of therapy received by a patient depends on a wide variety of factors, including patient's clinical data or information (Altekruse et al., 2017). Provider and hospital-level factors

also play a crucial role in the type of therapy administered to patients because referral to a specialist varies considerably (Altekruse et al., 2017).

Family and Societal Burden of Liver Cancer

Clinical management of liver cancer has an impact on the patients, their family, and social community or environment, all of which play a crucial role on patient-centered care theoretical foundation (Johnson et al., 2015). The incidence of liver cancer impact on patients, family, and societal environment showed an increasing behavioral and outcome trend (Hoehn et al., 2015). Kendall et al. (2015) used a cross-sectional study to assess experiences and goals in several disease cases via serial interview among patients with cancer, organ failure, or frailty. They found the patients' family members and professional careers were also affected (Kendall et al., 2015). Thus, they concluded quality of care for people living with life-limiting illnesses is a global and public health priority (Kendall et al., 2015). In addition, they suggested a detailed understanding of the varied experiences of people living and dying with different health conditions, their family's experiences, and professional caregivers' perspectives should help policymakers and clinicians implement improved and effective processes to deliver person-centered care approaches (Kendall et al., 2015). Compared to the study by Kendell et al. (2015), Baumert et al. (2017) examined the role of new generation antiviral drugs on hepatitis C, which is a major cause of liver cancer as an aspect clinical management of liver using a cross-sectional study (Baumert et al., 2017). Chronic infection of HCV, estimated to affect more than 150 million individuals globally, is a major risk factor of liver cirrhosis and cancer (Baumert et al., 2017). HCC is the major liver cancer histological type, and

the second leading cause of cancer mortality worldwide (Baumert et al., 2017). Interferon-based regimens have been the mainstay of anti-HCV therapy, or SVR, in approximately 50% of patients (Baumet et al., 2017). Recently developed DAAs, which directly target the viral protease, polymerase, or non-structural proteins, have enabled interferon-free anti-HCV therapies with a revolutionary improvement of SVR rate, approaching or surpassing a 90% rate (Baumet et al., 2017). Despite the unprecedented high antiviral efficacy, access to the therapy remains limited (Baumet et al., 2017). About less than 10% of the total number of HCV-infected individuals, especially in developing countries had access to the drug due to the high drug costs (Baumet et al., 2017).

Review of Liver Cancer Risk Assessments

Zampino et al. (2015) used a prospective cohort design to investigate the epidemiology of HCV infection, outcome, and treatment among prisoners in the US. With conclusions that treatment was administered less frequently to prisoners due to inherent difficulties in management and follow-ups (Zampino et al., 2015). However, the new (DAAs) were a better alternative for inmates because of their efficacy, short duration of treatment and follow ups, and low incidence of adverse outcomes or side effects (Zampino et al., 2015). Therefore, prison authorities and medical staff should advance tailored efforts on reducing the spread of HCV infection in prisons by promoting follow-up services and treatment to prisoners with chronic hepatitis C (Zampino et al., 2015). Zampino et al. (2015) provided the basis for and informed the current study by proposing

assessment of linkages between liver disease, adherence to routine clinic visits or medical checkups, Medicaid health insurance status and liver cancer (Zampino et al., 2015).

Singal and El-Serag (2015) investigated liver cancer from the epidemiological perspective to advance preventive measures and to translate informed knowledge into practice through a quantitative study with a cross- sectional design. They emphasized the effectiveness of liver cancer prevention in clinical and population level settings are lagging due to barriers linked to patient, provider, system, and societal factors (Singal & El-Serag, 2015). They suggested liver cancer prevention processes should be examined using quality cancer care model, which provides a framework for evaluating efficacy (Singal & El-Serag, 2015). Singal and El-Serag (2015) suggested other risk factors to demonstrate prevention and treatment options and the involvement of patient, provider, system, and societal factors by proposing a person-centered approach. They utilized a mixed research method and a case control study design to inform the proposed idea of adherence to routine clinic visits or medical checkups compared to individuals without adherence to routine clinic visits or medical checkups with liver-related diseases and the development of liver cancer (Singal & El-Serag, 2015).

Summary and Conclusions

In this section of the dissertation, the body of literature relating to risk factors of liver cancer among different sets of units of analysis was summarized and synthesized. Each piece presented an in-depth understanding of risk factors associated with the development of liver cancer. Risk factors of interest were liver disease, health insurance status with focus on Medicaid, access to annual routine clinic visits or healthcare provider

visits in the last 12 months, and liver cancer (outcome variable). Sources of literature were identified as well as examples of key phrases and words used for the literature search strategies. A PCC theoretical model was discussed in detail. In this chapter, arguments that liver cancer is a social problem as much as biological issue with multifactorial determinants were presented. The literature review process and synthesis performed in Chapter 2 provided the basis on how to describe and operationalize the methodology section of this dissertation, which is discussed in Chapter 3.

Chapter 3: Methods

Introduction

Each year, the number of individuals living in the US, people with liver cancer are increasing (CDC, 2018). This proposed study links the impact of health insurance status with focus on Medicaid to liver disease, and access to annual healthcare provider visits on the risk of developing liver cancer. The original purpose specifically emphasized a focus on ages 18 to 49 years, however, due to the limitation on the outcome variable in the 2016 NHIS data set participants, the age criterion was modified to include participants 18-85+ after IRB approval which enabled a successful binary logistic regression analysis. In this chapter, the research design and rationale, methodology, sample and sampling procedures, data analysis plan, threats to validity, and ethical considerations are discussed.

Research Design and Rationale

The dependent variable (DV) for this current study is liver cancer. The 2016 NHIS data define all types of liver cancer as liver cancer (NHIS, 2017). In the 2016 NHIS questionnaire, the participants were asked the following question: "*Ever told by a doctor you had cancer*", which is operationalized to a 'yes' or 'no" response (NHIS, 2017). Following "*Ever told by a doctor you had cancer*", participants were asked; "*What kind of cancer*" (NHIS, 2017). For '*what kind of cancer*' question, the different types of cancer options were provided including '*liver cancer*' (NHIS, 2017). Based on the information presented in the 2016 NHIS data dictionary regarding the DV (liver cancer) question, all the variables in the three research questions in this current study are

nominal variables, which includes population of participants with liver cancer, and those without liver cancer.

The IV for RQ1 is liver disease; the 2016 NHIS survey did not differentiate specific types of liver disease, it asked participants "*Has a doctor or other health professional ever told you that you had any kind of chronic, or long-term liver condition"*? (NHIS, 2017). The response was a nominal variable with 'yes' (had any kind of chronic or long-term liver disease) or 'no' (no kind of chronic or long-term liver disease) answer (NHIS, 2017).

The IV for RQ2 is "Health insurance status with focus on Medicaid; Participants were asked "*What kind of health insurance or health care coverage do you have?*" Various types of insurance coverage were listed, and the participants were asked to select all applicable insurance categories. For the purpose of this study, participants responses are placed in one of three categories to account for other than Medicaid and no coverage, grouping the variable health insurance status with focus on Medicaid into three categories: Individuals who have Medicaid, individuals who do not have Medicaid or have no coverage of any type, and individuals who have private or commercial health insurance. As such and for the purpose of this current study, health insurance status with focus on Medicaid is mutually exclusive and a nominal variable (NHIS, 2017).

The IV for RQ3 is the 'Access to annual routine clinic visits or healthcare provider visits in the past 12 months status'. Unlike the health insurance status with focus on Medicaid question grouped in three categories, access to annual routine clinic visits or healthcare provider visit in the past 12 months status was grouped into two

categories, those who had access to annual to routine clinic visits or healthcare provider visit in the past 12 months and those who did not have annual routine clinic visits or healthcare provider visit in the past 12 months. As such, the access to annual routine clinic visits or healthcare provider visit in the past 12 months category is a nominal variable. Based on the codebook, the 2016 NHIS dataset contains information on access to annual routine clinic visits or healthcare provider visit in the past 12 months in which the participants were asked "*during the past 12 months, have you seen or talked to any of the following health care providers about your own health? (a general doctor who treats a variety of illnesses e.g., a doctor in general practice, family medicine, or internal medicine)* and the response options included in this study for this survey question are 'yes' and 'no' (NHIS, 2017). By the nature of the response option provided, access to annual routine clinic visits or healthcare provider visits in the past 12 months for this current study is a nominal variable.

The three research questions and hypotheses were addressed using a cross-sectional, design and quantitative approach which is useful when evaluating an association between the risk factor or exposure status and prevalence of an outcome (Creswell, 2018). A cross-sectional design was used for this study as it aligns with 2016 NHIS survey data collection and is used as default to maintain consistency (NHIS, 2017). Also, a cross-sectional design in many cases is cost-effective, reliable and useful in estimating the snapshot of risk and prevalence (Creswell, 2018). However, a cross-sectional design is prone to selection, participation, recall, misclassification, and participation biases (Creswell, 2018). In addition, a cross-sectional design on its own

without the support of a quasi-experiment or an experimental design cannot be used to draw a causal association (Creswell, 2018). A cross-sectional design can only be used to infer and establish correlational relationship between a predictor and outcome variable (Creswell, 2018). In this current study, therefore, the statistical analysis performed with the 2016 NHIS dataset will only provide information that will allow for a correlational inference. The research method used is quantitative because the 2016 NHIS data and current research questions contains quantitative parameters and metrics (NHIS, 2017).

Data Source

The secondary data used for this study are from the National Health Interview Survey (NHIS) conducted in 2016 (NHIS, 2017). The 2016 NHIS includes a representative sample for the US population, with a survey, questionnaire approach conducted using a two-stage cluster sampling design (NHIS, 2017). The NHIS, 2016 contains core family, sample adult, and child level questionnaires (NHIS, 2017). The data of interest to this study were obtained from sample adult and family level questionnaires (NHIS, 2017). The two questionnaires were merged using the unique identification number provided in the data set to link participants with their responses in these separated questionnaires. The sample adult level questionnaire in addition to health outcome and health information questions, also contained demographic and personal characteristics about the participants. The family level question contained basic information about the family unit and household including insurance status, medical visits, and family-oriented demographic questions (NHIS, 2017). Shown in Table 2 are

the research questions DVs and IV, the comparison criteria, and unit of analysis for the current study.

Table 2

Study Variables Defined

RQs	Independent Variable	Dependent Variable	Confounders/ Covariates	Key Research Comparison Criteria	Key Unit of Analysis Inclusion Criteria
RQ1	Liver Disease (Yes vs. No)	Liver Cancer (Yes vs. No)	Gender (Male vs Female) & Race/ethnicity (White, Asian, Black/African Americans, Hispanics, Native American/Alaska Natives)	Liver Disease Status	Individuals ages 18-85+ years old
RQ2	Health insurance status with focus on Medicaid (Medicaid, other private insurance, No Medicaid or insurance coverage of any type)	Liver Cancer (Yes vs. No)	Gender (Male vs. female) & Race/ethnicity (white, black, White, Asian, Black/African Americans, Hispanics, non-Hispanics, Native American/Alaska Natives)	Health insurance status with focus on Medicaid (Medicaid, other private or commercial insurance, No insurance coverage of any type)	Individuals ages 18-85+ years old
RQ3	Access to annual routine clinic visits or healthcare provider visit in the past 12 months. (Yes vs. No)	Liver Cancer (Yes vs. No)	Gender (male female) & Race/ethnicity (White, Asian, Black/African Americans, Hispanics, Native American/Alaska Natives)	Access to annual routine clinic visits or healthcare provider visits in the past 12 months. Status	Individuals ages 18-85+ years old

Liver cancer was grouped into two categories, liver cancer (yes) and no liver cancer (no), and liver disease was grouped into two categories, the liver disease group

(yes) and no liver disease (no), making them both nominal variables. Similarly, health insurance status with focus on Medicaid is a nominal variable and was grouped into three categories to represent individuals who have Medicaid or those did not have Medicaid or no coverage of any type, and those with private or commercial insurance. Access to annual routine clinic visits or healthcare provider visits in the past 12 months in this current study is a nominal variable and was grouped into two categories, those reported had their annual routine clinic visit or healthcare provider visits in the past 12 months (yes) and those who did not have their annual routine clinic visit or healthcare provider visit in the past 12 months (no). For the covariates, sex was nominal (male or female), while race/ethnicity was categorical with five categories, (White, Asian, Black/African American, Hispanic, Native American/Alaska Native; see Table 3).

Table 3

Study Variable Level of Measurement Categories

Variables	Nominal	Categorical
Liver Cancer	Yes or No	-
Liver Disease	Yes or No	-
Health Insurance with focus on Medicaid	Yes or No or other private or Commercial insurance	-
Visit to provider in the past 12 months	Yes or No	-
Gender	Male or Female	
Race/Ethnicity		White, Asian, Black/African American, Hispanic, non-Hispanic, Native American/Alaska Native

Based on the information presented in Tables 2 and 3 the use of a quantitative research method for addressing the three research questions is appropriate. For instance,

liver cancer, liver disease, health insurance with focus on Medicaid, and access to annual routine clinic visits or healthcare provider visit in the past 12 months, deals with cases of counts, which is a quantifiable unit. Quantifiable units can be evaluated using a quantitative research method. Time and constraints are inherent with the use of a cross-sectional design because the 2016 NHIS data were collected at a specific point in time as a surveillance tool to track risk factors and health outcomes within a given time period. Despite this, the use of these data is appropriate because it provides a snapshot of the population at a specific point in time (Creswell, 2018; NHIS, 2017).

The research questions and hypotheses address the gap in the research proposed by Suh et al. (2018) in which they suggested further comparative study is warranted to explore the impact of Medicaid, liver disease, and adherence to routine clinic visits or medical checkups on the risk of developing liver cancer among subjects <50years (18-49) years old living in the US.

Methodology

Population

The study population are participants of the 2016 NHIS survey who met all inclusion/exclusion criteria

Inclusion criteria

- Male and female of any race who were 18-85+ years old.
- Participants who had valid answers to health insurance coverage question as Yes for Medicaid, no Medicaid, or any coverage whatsoever, and have private or commercial insurance coverage.

- Participants who had valid answers to liver disease question as Yes or No.
- Participants who had liver cancer, no liver cancer, or any other type of cancer Participants with liver disease and those with no liver disease.
- Participants with valid answers (i.e., yes, and no) to question about access to annual routine clinic visits or healthcare provider visits in the past 12 months. And participants who do not have access to annual routine clinic visits or healthcare provider visit in the past 12 months.

***Exclusion criteria*:**

- Participants who refused to answer or do not know about their health insurance coverage (i.e. Medicaid, Private health insurance, no coverage of any type).
- Participants who refused to answer or do not know about their liver cancer status.
- Participants who refused to answer or do not know the type of cancer they have.
- Participants who had other types of liver disease such as fatty liver disease and participants who had hepatitis vaccine.
- Persons with non-liver cancer.
- Persons with family history of liver disease.
- Persons with family history of liver cancer was excluded as well because their liver disease or liver cancer onset could be mainly attributed to the familial history, gender, race, smoking status, alcohol consumption status rather than the Medicaid health insurance status or their routine clinic visits or medical checkup status.

Sampling and Sampling Procedures

The sample population for this study were adults 18-85+ years of age who met inclusion criteria. The 2016 NHIS sample includes a representative sample for the US population. For the estimation of the sample size, the G*Power 3.1.9.4 software version was used to calculate the required minimum sample size for a logistic regression analysis (Buchner, Erdfelder, Faul, & Lang, 2017). The G power calculated total sample size is 8771. Two tails instead of one tail was used to account for the possibility of both positive and negative effect of the predictors, also, the R2 other X was changed to 0.5 to account for a possible moderate type interaction between the independent variables. 'Binomial' for X distribution instead of "Normal" is suitable and applicable to all three research questions and predictors in question, e.g. RQ2 with 3 categories. For the sample size estimation, a predetermined odds ratio of 1.3 was used as effect size value to calculate the minimum sample size required for this current study. This effect size was based on the upper limit of other effect sizes in similar liver cancer studies (Bai, Cai, Jiang, & Lv, 2016; Chuang et al., 2015; Murff et al., 2018). To minimize the likelihood of a Type II error, the beta value was set at 20% (0.20) while the corresponding statistical power value was set at 80% (0.80). For type I error, the predetermined alpha (Type I error) value was set at 5% (0.05) and corresponding level of confidence was set at 95% (0.95) for a priori power calculation for logistic regression analysis (Buchner, et al, 2017). Under these assumptions, a minimum of 8,771 participants (male and female) were needed in this study to achieve a statistical power of 80% in order to observe at least an effect size of 1.3. For statistical analysis, SPSS version 25 was used for descriptive an inferential

analysis (IBM Corp., 2017). In total, there were 97,169 participants including participants of all ages in the NHIS data set. Participants were selected for this study based on inclusion criteria, the 2016 NHIS was stratified by age to select individuals between 18- 49 years old for the data analysis, but just 2 participants with liver cancer noted, not permitting a valid logistic regression analysis. After consulted with the Walden IRB, and approved, Participants 18-85+ were included. Data variables in SPSS were recorded to exclude all participants younger than 18 years old. For the 18-85+ years old age criterion, there were ~33,000 participants. However, this exceeded the minimum sample size of 8,771 required to generate a statistical power of 80%, so, all the eligible participants ages 18-85+ years old reported in the 2016 NHIS data were used for the analysis.

Data Collection

Secondary Data Source

The sample data for this study came from the 2016 NHIS data set. A case prioritization experiment was conducted by NCHS, the U.S. Census Bureau, and the NHIS during the third calendar quarter of 2016. It was conducted with the intent to improve sample representativeness, to minimize nonresponse bias, and maintain current or high response rates given the existing budgetary constraints that year project (NHIS, 2017). Two response propensity models were used to determine case priorities (high, medium, low) and prioritizing covariates associated with key health outcomes (NHIS, 2017). Preliminary analysis suggests the case prioritization experiment was largely cost neutral and had minimal effects on response rates and unfortunately it did point to in a

greater sample representativeness in the control group than in the treatment group (NHIS, 2017).

Despite the case prioritization experiment, the 2016 NHIS included 35,000 households, consisting of 87,500 individuals the overall household response rate was 67.9% (NHIS, 2017). For interviews the response rate varied slightly for each survey component. For the family component, the conditional response was 98.9% and the unconditional or final response rate was 67.1% (calculated by multiplying the conditional response rate of 98.9% by the household response rate of 67.9%, NHIS, 2017). For the sample adult component, the conditional response rate was 80.9% and the unconditional or final response rate of 54.3% (multiplied to the conditional rate of 80.9% by the final family response rate 67.1% (NHIS, 2017).

Data Analysis Plan

For all the research questions and hypotheses, the outcome variable under investigation is 'liver cancer'. As described in Table 2 and 3 above, liver cancer is a nominal variable. The IVs for RQ1, RQ2, and RQ3 (liver disease, health insurance status with focus on Medicaid, and access to annual routine clinic visits or healthcare provider visit in the last 12 months status, respectively) are nominal variables as well. Gender and race confounders or covariates were included in the inferential analysis. During the inferential analysis stage, gender and race variables were analyzed as categorical covariates in SPSS. For the covariates gender and race baseline variables, male was the baseline for the gender category and whites was the baseline category for race. Identifying these baselines facilitated the interpretation of results of this proposed study.

SPSS version 25 was used for the descriptive and inferential analysis of the study variables (IBM Corp. (2017). The secondary data was recoded to align with the level of measurements of the variables stated in the research questions and described in Table 2 and 3 above. All the variables groups representing a 'yes' response to each of the questions asked in the survey were coded as 1, and those representing a no response were coded 2 in the SPSS. Males were coded as 1, while females as 2. Only variables pertaining to my research questions were analyzed. The study initially targeted individuals younger than 50 years old (18-49 years old). Because of smaller number of patients with the outcome variable (liver cancer), the study was revised to include individuals 18 to 85+ years after IRB approval. Findings correlated with the initial intent irrespective of the shift in the age criteria.

Research Questions and Hypotheses

RQ1: Is there an association between liver cancer and liver disease in individuals 18-85+ years of age, accounting for gender and race?

$H_0$1: There is no association between liver cancer and liver disease in individuals 18-85+ years of age, accounting for gender and race?

H_a1: There is an association between liver cancer and liver disease in individuals 18-85+ years of age, accounting for gender and race?

RQ2: Is there an association between liver cancer and Health insurance status with focus on Medicaid in individuals 18-85+ years of age, accounting for gender and race?

H_o2: There is no association between liver cancer and Health insurance status with focus on Medicaid in individuals 18-85+ years of age, accounting for gender and race?

H_a2: There is an association between liver cancer and Health insurance status with focus on Medicaid in individuals 18-85+ years of age, accounting for gender and race?

RQ3: Is there an association between liver cancer and access to annual routine clinic visits or Health care provider visits in the past 12 months in individuals 18- 85+ years of age, accounting for gender and race?

$H_0 3$: There is no association between liver cancer and access to annual routine clinic visits or Health care provider visits in the past 12 months in individuals 18-85+ years of age, accounting for gender and race?

$H_a 3$: There is an no association between liver cancer and access to annual routine clinic visits or Health care provider visits in the past 12 months in individuals 18-85+ years of age, accounting for gender and race?

Two types of analysis were performed in this study. The first was descriptive and the second was inferential analyses. Descriptive analysis was used to describe the test variables including confounders and all demographic variables. All the nominal and categorical variables was described with a frequency or count table. Frequency tables are appropriate to describe a nominal or categorical variable. The ratio variable such as age in years was described with a mean, median, standard deviation, and range, as well as histogram to represent the distribution of the participants.

Based on the level of measurement described in Table 3 for the key test variables implicated in this study which are all nominal variables, a binary logistic regression was used for the inferential analysis because a nominal DV and a nominal or categorical IV met the assumption of binary regression (Statistics Solutions, 2016). Therefore, a binary logistic regression was used for the inferential analysis to address the research questions and hypothesis. In other words, the significance of the inferential analysis was evaluated using p-value estimate for each of the three research questions. For the inferential analysis, the significance reference was the predetermined alpha value of 0.05 (5%). For example, if the inferential analysis produced a p-value less than the alpha value of 0.05 (5%) [$p < .05$], the finding is statistically significant, therefore, the null hypothesis was rejected. Rejection of the null hypothesis in this study for either RQ1 or RQ2 or RQ3 imply there is an association between liver disease and liver cancer or Medicaid and liver cancer or routine medical visits and liver cancer, respectively.

In contrast, if the inferential analysis produced a p-value greater than the predetermined alpha value of 0.05 (5%) [$p > .05$], the analysis is not statistically significant, as such, I will fail to reject the null hypothesis. The failure to reject the null hypothesis for either RQ1 or RQ2 or RQ3 imply there is no association between liver disease and liver cancer or Medicaid and liver cancer or access to annual routine clinic visits or health care provider visits in the past 12 months and liver cancer, respectively. In other words, suggesting the DV under investigation did not significantly predict liver cancer outcome. Since the predetermined alpha value was set at 5%, the corresponding level of confidence for all the estimated p-values was 95%. Thus, all p-values or test

statistic values generated were interpreted with a 95% level of confidence, so findings were not by chance or random event.

Odds ratio (*OR*) was used also a statistical measure used to assess the magnitude the effect or public health significance of the inferential findings. The *OR* value was estimated using the binary logistic regression. (odds = 1/1-P = Probability of presence/probability of absence). The *OR* calculation was based on the function of the ratio estimation of the odds of the exposed group and odds of the non-exposed groups. For instance, an *OR* value of 1.00 suggest there is no difference in the risk of an event or outcome for persons exposed compared to individuals who are not exposed to the risk. An *OR* value greater than 1.00, suggest the risk of the exposed group is greater than unexposed group. On the other hand, an *OR* value less than 1.00, suggest the exposed group has lower risk than unexposed group.

Threats to Validity

Internal and external validity of the study design, method, statistical approach, sample selection, and content was discussed. Parameters used in assessing consistency and accuracy of study procedures vary depending on the focus of the study (Creswell, 2018; Forthofer et al., 2007). For instance, subject selection could influence internal and external validity (Creswell, 2018; Forthofer et al., 2007). All relevant determinants of internal and external validity were discussed in this section.

External Validity

External validity dealt with the extent to which findings can be generalized beyond the original target population from which the observation was made (Creswell,

2018; Forthofer et al., 2007). One of the data collection validations used by NHIS staff to address external validity of 2016 NHIS data was the random sampling selection of the 2016 population across several states in the US (NCHS, 2017). However, because the survey is a cross-sectional design only correlational inference can be made (Creswell, 2018; Forthofer et al., 2007). In addition, a cross-sectional design lacks the ability to detect predictor-outcomes' spatiotemporal sequence (Creswell, 2018; Forthofer et al., 2007). Therefore, the findings from this current study will only be restricted to the target population used and will not be generalized (Creswell, 2018; Forthofer et al., 2007).

Internal Validity

Internal validity deals with intrinsic factors such as random sample selection other than the primary predictor variables such as Medicaid or routine visit influence the consistency of the study findings (Creswell, 2018; Forthofer et al., 2007). The NHIS is secondary data has been collected overtime in the US, with much revision to improve the process (NHIS, 2017). Therefore, threats to internal validity regarding data collection process and consistency may have been substantially minimized overtime. However, NHIS is a self-reported survey with no clinical or social data to verify the self-reported responses provided by the respondents. Therefore, there is still some level of threats for accuracy regarding respondents' self-reported information. Incurring recall bias is a possible threat to internal and external validity for two reasons. If the respondents provided incorrect information, the participants were misclassified and placed in the wrong category. In addition, if there is a high volume of misclassification bias occurrence, the findings could be distorted towards either a Type I (false positive) or

Type II (false negative) error. Another threat to validity is the NHIS database was designed for surveillance purposes, thus, may not fully match the clinical diagnosis documented in the medical records for the participants.

Interviewers and participants demographic variability is important, but it is also a common threat to internal and external validity in terms of maintaining the interview consistency or reliability and accuracy of interview processes and contents as intended (Creswell, 2018; Forthofer et al., 2007). Individual interviewers have unique personality could affect people behavior and perhaps the way they answer the questions in the presence of another person deemed and a stranger and perhaps a threat. As such NHIS provided procedural or guidance training to the interviewers prior to actual survey kickoff (NCHS, 2017). Also, unreliable interviewer or interview approach will adversely influence responses and will induce distortion towards a Type I or Type II error (Creswell, 2018; Forthofer et al., 2007). NHIS provided training to avert these types of error, and content or procedural errors were addressed during the training sessions (NCHS, 2018). Also, raining enhancements were provided to interviewers to influence adherence to interview guidelines (NHIS, 2018).

Ethical Procedures

Walden's Institutional Review Board (IRB) approval was requested and obtained prior to performing the analysis on this secondary data set (IRB approval number, 06-12-20-0616363). Once approved, the zipped files for 2016 NHIS data sets were downloaded from the CDC's website, then unzipped, saved and password protected. The comma-separated values files (adult and household data sets) were imported into the SPSS

application and transformed for data analysis. The transformation involved checking for missing data and outliers as well as for any other source of inaccuracies in the data set. Following the application of the selection criteria to the variables in question, the descriptive and inferential data analyses were performed and reported. All results reported in this study are from the analysis of the publicly available, de-identified (anonymous) 2016 NHIS data (NCHS, 2018; NHIS, 2017).

Summary

In this Chapter, I described the research design and rational, methodology, target population, sampling procedures, data analysis plan, internal and external validity and the ethical procedures proposed in this study. The information described in Chapter 3 provided the basis for data analysis and result and perhaps, the interpretation sections of the dissertation was described in Chapter 4 and 5, respectively. Detailed information on data analysis and result and interpretation of the research findings was described in Chapter 4 and 5.

Chapter 4: Results

Introduction

This study assessed a history of liver disease with an impact of being a Medicaid health insurance recipient and with access to annual routine clinic visits or healthcare provider visit in the past 12 months involved in the risk of developing liver cancer among adults18-85+ in the United States. The study initially targeted individuals younger than 50 years old (18-49 years old). Because of smaller number of patients with the outcome variable (liver cancer), the study was revised to include individuals 18 to 85+ years after IRB approval.

Data Collection

Discrepancies in Data Collection from Proposal

The 2016 NHIS data set was obtained from the CDC's website after IRB approval and selected based on the criteria as described in Chapter 3. A total of 14,617 participants 18-49 years of age met all inclusion criteria but only two of them reported having liver cancer (see Table 4), resulting in a number too low (2 of 14617 or 0.014%) to allow for reliable statistical analysis. After consulting with the Walden University IRB, the age restriction was revised, to include adults 18 to 85+ and 28,704 participants were eligible for the study as shown in Figure 2 and 40 participants reported having liver cancer (Table 5). This resulted in modifications to research questions and hypotheses.

Research Questions and Hypotheses

RQ1: Is there an association between liver cancer and liver disease in adults in the US accounting for gender and race?

$H_0$1**:** There is no association between liver cancer and liver disease in adults in the US accounting for gender and race.

H_a1: There is an association between liver cancer and liver disease in adults in the US accounting for gender and race.

RQ2: Is there an association between liver cancer and health insurance status with focus on Medicaid in adults in the US accounting for gender and race?

H_O2: There is no association between liver cancer and health insurance status with focus on Medicaid in adults in the US accounting for gender and race.

H_a2: There is an association between liver cancer and health insurance status with focus on Medicaid in adults in the US accounting for gender and race.

RQ3: Is there an association between liver cancer and access to annual routine clinic visits or health care provider visits in the past 12 months in adults in the US accounting for gender and race?

$H_0$3: There is no association between liver cancer and access to annual routine clinic visits or health care provider visits in the past 12 months in adults in the US accounting for gender and race.

H_a3: There is an association between liver cancer and access to annual routine clinic visits or health care provider visits in the past 12 months in adults in the US accounting for gender and race.

To address each question, this chapter detailed the descriptive, bivariate, and inferential statistics conducted and the results obtained.

Figure 2

Flowchart of Exclusion/Inclusion Criteria for Ages 18-85+

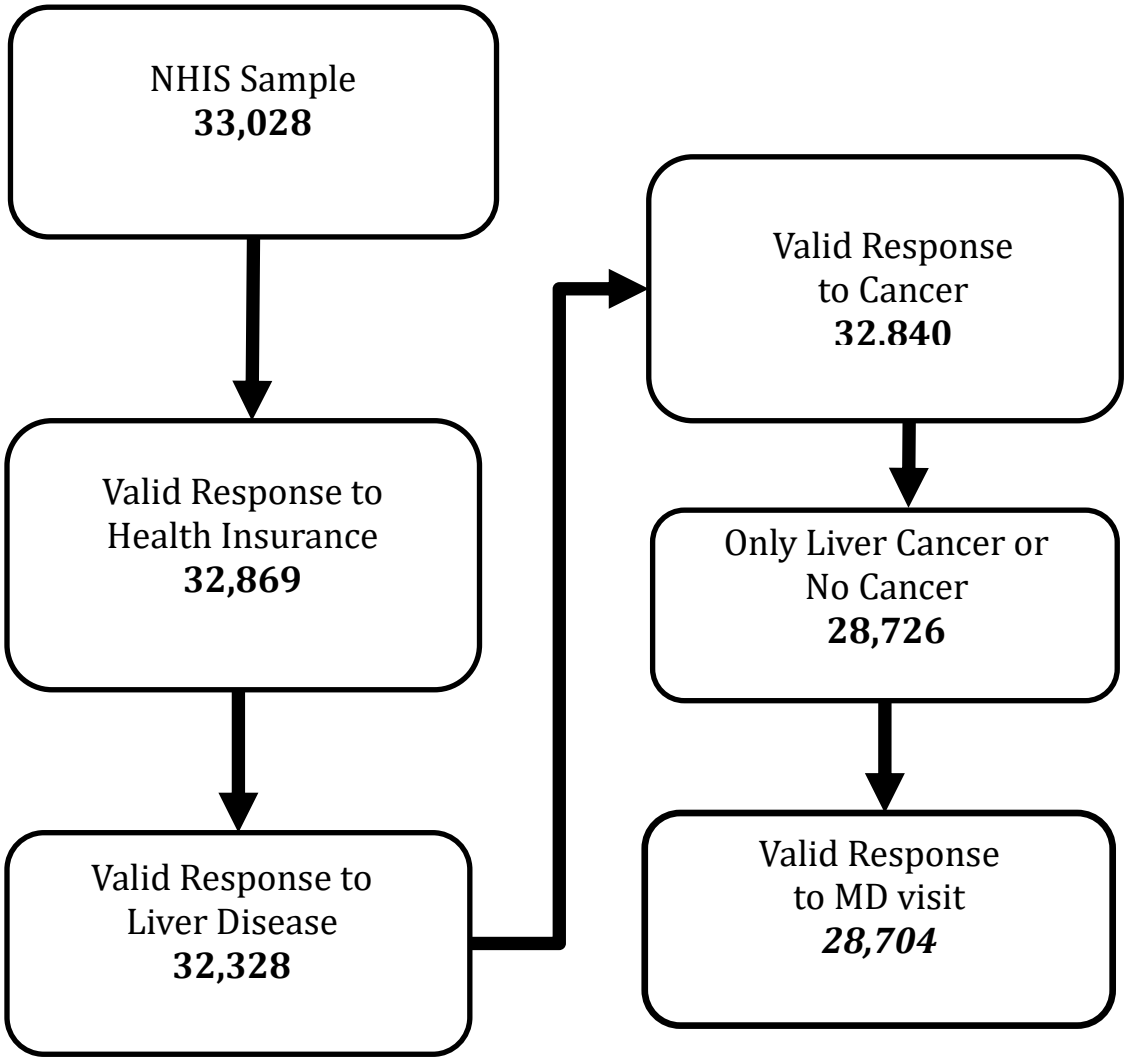


Table 4

Frequency Table for Ages 18-49 Years

	Frequency	Percent
Liver Cancer	2	.014
No Liver Cancer	14,615	99.986
Total	14,617	100.000

Table 5

Frequency Table for Adults, 18-85+Years of Age

	Frequency	Percent
Liver Cancer	40	0.139
No Liver Cancer	28,664	99.861
Total	28,704	100.000

Results of Descriptive Statistics

Descriptive Statistics

Frequency Distribution of Demographic Variables

Table 6 presents the demographics characteristics of the participants for the study population. Among a total of 28,704 participants, 54.3% were women and 45.7% were men. The majority were White, 79.3%; Black, 11.7%; Native American, 1.2%; Asian 5.4%; and 'Other,' 2.5%; only 12.4% of participants identified as Hispanic (see Table 6). These racial and ethnic percentages were different from the distribution reported in the original (33,028) sample and from the larger U. S. population from which data were collected (NHIS, 2016)

Participant age ranged from 18 to 85+ with four age groups identified. The age distribution was approximately normal with a mean of 48.88 years, a standard deviation of 18.226 (See Figure 3). There was some left skewness, mainly caused by mode (85) that was higher than the mean (see Table 7). As Table 6 shows, almost two-thirds (63.0%) of the participants were over 45, with the largest group (41.9%) between the ages of 45 and 65.

Table 6

Demographic Statistics of Study Participants

Variable	*N*	Percent
Gender		
Male	13126	45.7
Female	15578	54.3
Race		
White	22748	79.3
Black	3359	11.7
Native Amer	334	1.2
Asian	1554	5.4
Other	709	2.5
Ethnicity		
Hispanic	3558	12.4
Non-Hispanic	25146	87.6
Age Groups		
18-25	3385	11.8
26-45	7244	25.2
45-65	12025	41.9
*65-85+	6050	21.1
Total	**28,704**	--

Note. *85+ *as reported in the NHIS file.*

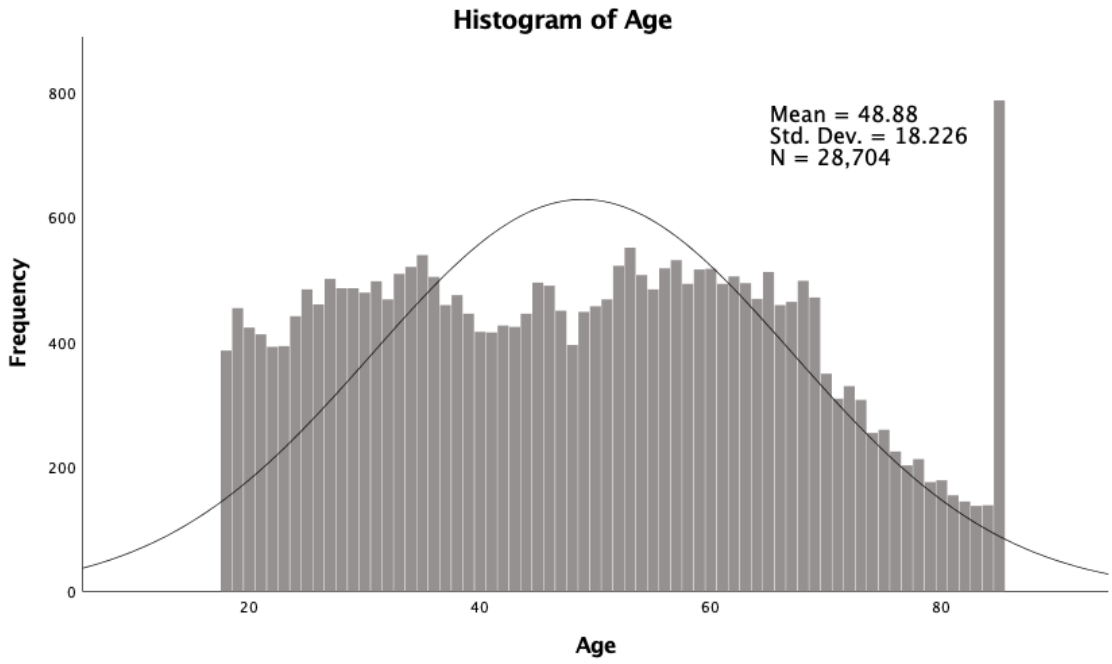
Table 7

Table of Descriptive Statistics of the Age variable.

AGE			
N Valid	28704	*N* Missing	0
Mean	48.88	Std. Error of Skewness	.014
Median	49.00	Skewness	.127
Mode	85	Std. Error of Kurtosis	.029
Std. Deviation	18.226	Kurtosis	-.996

Figure 3

Histogram of Age Distribution



Frequency of Liver Cancer and Predictor Variables

The three risk factors evaluated as variables in this study were: (a) liver disease history, (b) Medicaid coverage, and (c) access to a healthcare professional. For history of liver disease there was a direct specific question, and the information is represented in Table 9. For Medicaid coverage, the information from several questions were combined and the information is presented in Table 10. For access to healthcare, the information was obtained from the question of 'visit to an MD in the last 12 months' and the information is presented in Table 11. The descriptive statistics performed on these variables, as well as the dependent variable (Table 12), presented below, give a picture of the distribution of all the critical variables in the data set.

The first set of descriptive statistics addressed the prevalence of the measure used as the outcome or dependent variable in this study. The operating frequency of liver cancer in this study population was 0.139%, representing those who indicated having been diagnosed with the disease at the time of the data collection (see Table 8). There were 3,687 (11.4%) who responded 'yes' to the question of any type of cancer diagnosis (see Table 8). The other responses included 'No,' 'Refused,' 'Not ascertained,' and 'Don't know.' Of those with cancer (3,687), only 40 (1.1% of all cancers) indicated that they had liver cancer. Those with cancer other than liver cancer (3,647) were eliminated from the data set, leaving a working data set made up of only 28,664 cancer free subjects and 40 subjects with liver cancer (0.1%) for a total of 28,704 in the study population (Table 8).

Table 8

Cancer Incidence

Cancer Diagnosis	Frequency	Percent	
All Cancers	*3,687*		*(11.383)*
Liver Cancer	40	*(0.124)*	0.139
No Cancer	28,664		99.861
***Total (only Liver CA)**	***28,704**		**100.000**
Total (all CAs included)	***32,391***		*(100.000)*

Note: *=Study population.

The distribution of the first independent or predictor variable being assessed, a history of liver disease, is presented in Table 9. The information in this frequency table was ascertained with the question "any kind of chronic/long-term liver condition?" The incidence of a history of liver disease in this study population was approximately 10 times that for liver cancer, with 1.4% responding yes, 98.6% responding no to the question of any history of liver disease (see Table 9). There were respondents who expressed uncertainty about their history of liver disease, but these were excluded from the study population, along with those who did not know and those who refused to answer.

Table 9

Liver Disease Incidence

Liver Disease History	Frequency	Percent
Liver Disease	398	1.387
No Liver Disease	28,306	98.613
Total	**28,704**	**100.000**

The second predictor variable examined was that of health insurance coverage, with a focus on Medicaid. Of all those with insurance coverage, 10.8% were covered by Medicaid, with (7.9%) having Medicaid as their only insurance (see Table 10). There were 23.6% with Medicare coverage and 5,134 (17.9%) Medicare only, while 38.5% were covered by Private insurance and 10,197 (35.5%) having only Private insurance. There were 1,658 (8.8%) subjects who had multiple insurance types, with 5 of those having all three (Medicaid, Medicare, and Private insurance coverage). Approximately one quarter (6,948 or 24.2%) of the study population had insurance coverage other than the three main types (Medicaid, Medicare or Private) and 2,500 (8.7%) were without any type of insurance coverage at all.

Table 10

Health Insurance Coverage

Health Insurance	Frequency	Percent	Cumulative Percent
Medicaid	2,267	7.898	7.898
Medicare	5,134	17.886	25.784
Private	10,197	35.525	61.309
Medicaid & Medicare	795	2.77	64.079
Medicaid & Private	38	0.132	64.211
Medicare & Private	820	2.857	67.068
Mcare, Mcaid, & Private	5	0.017	67.085
Other	6,948	24.206	91.291
No Insurance	2,500	8.71	100.001
Total	**28,704**	**100.000**	

The third and final risk factor involved assessing the impact of access to a healthcare provider or clinic in the last 12 months and its frequency distribution is reported in Table 11. This variable was based on the information obtained from the question of "…seen/talk to a general doctor in the last 12 months?" For this study, 8,466 (29.5%) reported they communicated with a general physician in the last 12 months (see Table 11). The other 20,704 (70.5%) had not been in contact with a general physician in the last 12 months. Contact with other healthcare professionals was not evaluated.

Table 11

Healthcare Provider visits in Last 12 Months

Healthcare Visit	Frequency	Percent
Visited MD	8,466	29.494
No Visit to MD	20,238	70.506
Total	**28,704**	100.000

Bivariate Analysis

Association Between Demographic Variables with Outcome Variable

Before performing the analyses for the inferential statistics to answer the research questions, a series of bivariate analyses were conducted. The first set of bivariate analyses was used to measure the association between each of the demographic variable (age, gender, race, and ethnicity) and the dependent variable (liver cancer outcome). The Chi-square value for each cross-tabulation indicated the strength of the association between the two categorical variables. However, it was the corresponding *p*-value that was used to determine the likelihood of the distribution relative to a chance distribution and the statistical significance of the association between each variable pair. Pearson's chi-square test of independence analysis is a statistical test commonly used to describe the empirical relationship between two variables (Vaske, 2019).

Of the four demographic characteristics, two (gender and age) had differences in the distribution, of the liver cancer outcome, and were statistically significant. The strongest relationship (Table 12), relative to the others, was that between age groups and the liver cancer outcome, with the largest chi-square (χ^2= 38.175) and the smallest *p* values ($p < .001$). According to this cross-tabulation results, the percentage of liver

cancer positive patients is zero for the youngest age group (18-25), and only one in the next youngest (26-40). For the two older age groups, frequency increases almost 10-fold and 30-fold in liver cancer, with 0.1% (16) for the 41-65-year-olds and 0.4% (23) for those older than 65 years.

The other variable with a difference in the distribution with liver cancer and was statistically significant was gender, with χ^2=5.994 and p = 0.014. The prevalence of liver cancer in men was 0.2%, which is approximately twice that of the 0.1% for women (Table 12). The liver cancer distribution among the categories for each of the other two demographic variables (ethnicity and race) had p-values > 0.05 and were therefore not statistically significant. It should be noted that these numbers apply to this specifically stratified study population data set and given the lower than typical prevalence of liver cancer, the percentage representing any of these distributions may not be otherwise pertinent.

Table 12

Association Between Liver Cancer and the Demographic Covariates

Variable	No Liv CA *N*	Liv CA *N*	% (Total)	Chi-Square	*p*-value
Gender					
Male	13,100	26	0.198 (13,126)	5.994	0.014
Female	15,564	14	0.090 (15,578)		
Race					
White	22,716	32	0.141 (22,748)	0.730	0.948
Black	3,355	4	0.119 (3,359)		
Nat. Amer.	333	1	0.299 (334)		
Asian	1,552	2	0.129 (1,554)		
Other	708	1	0.141 (709)		
Ethnicity					
Hispanic	3,552	6	0.169 (3, 558)	0.074	.786
Non-Hispanic	25,112	34	0.135 (25,146)		
Age Groups					
18 - 25	3,385	0	0.000 (3,385)	38.175	.000
26 - 40	7,243	1	0.014 (7,244)		
41 - 65	12,009	16	0.133 (12,025)		
65 - 85+	6,027	23	0.380 (6,050)		
Total	**28,704**	**40**			

Note. *85+ *as reported in the NHIS file.*

Association Between Demographic Variables and Independent Variables

Testing the relationship between the explanatory variables and the predictor variables, provides an assessment of the strength of the association without any assumption of causation or of interference from other variables (Field, 2013). Bivariate analysis can be used to probe any latent interaction between the control variables and the predictor variables, in their potential predictive relationship with the dependent variable (Bertani, Di Paola, Russo, & Tuzzolino, 2018). The three explanatory variables (liver

disease, health insurance coverage, and access to healthcare) were tested against the four main demographics (gender, age, race, and ethnicity). Chi-square analysis was again used to assess the statistical significance and the relative strengths of these relationships.

Liver disease. Chi-square analysis resulted in a statistically significant association between liver disease and two of the demographic variables, age and gender. For gender, males had a higher percentage of liver disease (1.6%) than did females (1.3%), and this difference, though marginal, was statistically significant as confirmed by the X^2=4.527 and p = 0.033 values (see Table 13). The other statistically significant relationship with liver disease outcome was that with age, X^2=82.423, p < .001. The older age groups had much higher incidences of liver cancer, and as the age groups advanced so did the percentage of those participants with liver disease, going from 0.2% for the 18–25-year-olds, to 0.8%, 1.9%, 1.9% for the 26-40, 41-65, 66+ year-olds, respectively (Table 13). There was no statistically significant relationship with the other two (race or ethnicity) for a liver disease outcome.

Table 13

Association Between Liver Disease and Demographic Variables

Variable	No Liv Dis	Liv Dis	% w/ Liv Dis	Chi-Square	*p*-value
Gender				4.527	.033
Male	12923	203	1.547		
Female	15383	195	1.252		
Race				5.139	.273
White	22418	330	1.451		
Black	3323	36	1.072		
Nat. Amer.	330	4	1.198		
Asian	1538	16	1.030		
Other	697	12	1.693		
Ethnicity				.065	.799
Non-Hispanic	3507	51	1.433		
Hispanic	24799	347	1.380		
Age Groups				82.423	.000
18 - 25	3377	8	0.236		
26 - 40	7189	55	0.759		
41 - 65	11803	222	1.846		
65 - 85+	5937	113	1.868		
Total	**28,306**	**398**	**1.387**		

Note. *85+ *as reported in the NHIS file.*

Health insurance. For health insurance coverage (see Table 14), all four demographic variables had a statistically significant relationship, with $p < .001$ for each. Based on the chi-square values, the relationship between insurance coverage and age was the strongest (χ^2=18935.770) relative to the others. The cross-tabulation revealed that in the youngest groups (18-25) the highest frequency (41.4%) was for those with insurance other than Medicaid, Medicare or Private. For the oldest age group, almost two-thirds

were Medicare recipients (69.7% alone; 90.0% Medicare/Medicare plus other), and for the other two age groups (26-40 and 41-65), almost half were covered by Private insurance (46.5% and 45.4%, respectively). There was also notable contrast in the distribution for no insurance coverage, with the three younger age groups averaging 11.06% (10.6%, 13.4%, and 9.2%, respectively), compared with only 1.0% for those over 65. A similar relationship was reflected in those with 'other' insurance, 36.9% on average for the three youngest age groups compared to only 5.2% for those over 65. Finally, the converse relationship is reflected in the frequencies for Medicare, 69.7% for those over 65 compared with an average of 2.8% for the three younger age groups.

Table 14

Association Between Health Insurance and Demographic Variables

Variable	No Insurance *N* (%)	Medicaid *N* (%)	Medicare *N* (%)	Private *N* (%)	Multiple *N* (%)	Other *N* (%)	Chi-Square (*p*)
Gender							
Male	1345 (10.2)	773 (5.9)	2076 (15.8)	5023 (38.3)	668 (5.1)	3241 (24.7)	320.485 (.000)
Female	1155 (7.4)	1494 (9.6)	3058 (19.6)	5174 (33.2)	990 (6.4)	3707 (23.8)	
Age							
18 - 25	359 (10.6)	440 (13.0)	11 (0.3)	1156 (34.2)	19 (0.6)	1400 (41.4)	18935.770 (.000)
26 - 40	973 (13.4)	797 11.0)	69 (1.0)	3369 (46.5)	69 (1.0)	1967 (27.2)	
41 - 65	1105 (9.2)	948 (7.9)	838 (7.0)	5462 (45.4)	407 (3.4)	3265 (27.2)	
65+	63 (1.0)	82 (1.4)	4216 (69.7)	210 (3.5)	1163 (19.2)	316 (5.2)	
Race							
White	1906 (8.4)	1475 (6.5)	4310 (18.9)	8354 (36.7)	1265 (5.6)	5438 (23.9)	740.774 (.000)
Black	399 (11.9)	538 (16.0)	513 (15.3)	885 (26.3)	263 (7.8)	761 (22.7)	
Native	33 (9.9)	66 (19.8)	33 (9.9)	59 (17.7)	18 (5.4)	125 (37.4)	
Asian	97 (6.2)	112 (7.2)	190 (12.2)	645 (41.5)	74 (4.8)	436 (28.1)	
Other	65 (9.2)	76 (10.7)	88 (12.4)	254 (35.8)	38 (5.4)	188 (26.5)	
Ethnicity							
Hispanic	712 (20.0)	474 (13.3)	338 (9.5)	990 (27.8)	164 (4.6)	880 (24.7)	984.444 (.000)
Non-Hispanic	1788 (7.1)	1793 (7.1)	4796 (19.1)	9207 (36.6)	1494 (5.9)	6068 (24.1)	
Total	2500 (8.7)	2267 (7.9)	5134 17.9)	1019 (35.5) 7	1658 (5.8)	6948 (24.2)	

Access to healthcare. As with health insurance distributions, access to healthcare, assessed from the visit to general physician in the last 12 months, had a statistically significant ($p < .001$) association with all four of the demographic variables, and the strongest relationship was with age (X^2=1400.252, $p < .001$) (Table 15). A visit to a general physician was more common among the younger participants, with 40.4% and 41.5% for those ages 18-35 and 26-40, respectively. The frequency was lower for the next oldest age group (26.8% for those 41-65, and even lower for the oldest age group, 14.4% for those over 65. The association with gender (X^2=219.015, $p < .001$) and ethnicity (X^2=147.878, $p < .001$), with men (33.8%) were more likely to visit a general physician than women (25.8%), and non-Hispanic (38.2%) more than those recorded as Hispanic (28.3%). The frequency among the different race group was not as large, but still statistically significant (X^2=18.144, $p < .001$), with the Native Americans having the highest (37.1%) and all others being approximately similar (29.2%, 29.1%, 31.8, 32.7%, for Caucasians (whites), African Americans, Asian Americans, and Other, respectively.

Table 15

Association Between Doctor Visits and Demographic Covariates

Variable	GP Visits	No GP Visits	% w/ GP Visits	Chi-Square	*p*-value
Gender				219.015	.000
Male	4441	8685	33.8		
Female	4025	11553	25.8		
Race				18.144	.001
White	6637	16111	29.2		
Black	979	2380	29.1		
Nat. Amer.	124	210	37.1		
Asian	494	1060	31.8		
Other	232	477	32.7		
Ethnicity				147.878	.000
Non-Hispanic	1359	2199	38.2		
Hispanic	7107	18039	28.3		
Age Groups				1400.252	.000
18 - 25	1366	2019	40.4		
26 - 40	3007	4237	41.5		
41 - 65	3222	8803	26.8		
65 - 85+	871	5179	14.4		

Note. *85+ *as reported in the NHIS file.*

Results of Inferential Statistics: Binary Logistic Regression

Evaluating the Covariate Variables

Using the binary measure of liver cancer diagnosis as the dependent variable (liver cancer =1, no liver cancer = 0), a logistic regression analysis was conducted to answer the three research questions. However, prior to testing each model, binary logistic regression (BLR) was used to assess relationships and obtain the baseline measure of their odds ratio for each explanatory variable that should be included in the regression formula. According to the research questions, sex (gender) and race were

intended to be used as confounding or covariate variables. Race was included as two separate variables, since the information was collected as two separate variables and allowance was made for overlap (multiple racial identities), there was no way to combine them into one. The age demographic was also included as a control, given that the original age criteria was not applied and that the descriptive statistics showed its strong association with the predictor variables as well as the outcome.

The four demographics (gender, age, race, and ethnicity) were evaluated to decide which were statistically significant and therefore should be included in the prediction model of the logistic regression formula. The outcome variable for all the logistic regression is the binary distinction of reported liver cancer versus no reported liver cancer. The logistic regression provided direct evaluation of the effect size and the statistical significance of each demographic variable, while controlling for the other demographic variables. All the variables were included as categorical variables, with female (gender), over 65 (age group), and Whites and non-Hispanic used as the control categories for the race and ethnicity variables, respectively.

From the preliminary BLR, only age and gender were statistically significant predictors for liver disease outcome. This base-line model predicted 8.3% (Nagelkerke's $R^2 = .0833$) of the variability in the data set and the classification was 99.9% accurate. In this model gender, with women as the reference, men had a 244.1% (OR=2.441, 95% CI [1.270, 4.691], $p = .007$), increased odds of developing liver cancer than women (Table 16). For age, with the oldest group as the reference, the two younger age groups (26-40 and 41-65), were 96.9% (OR=0.031, 95% CI [.004, .234], $p = .001$) and 68.6%

(OR=0.314, 95% CI [.165, .598], $p < .001$) reduced odds for liver cancer, respectively. The youngest group (18-25) was not significant, as there were zero liver cancer subjects. Consequently, age was added to race and gender for the controlling variables in the subsequent logistic regression analyses.

Eliminating statistically insignificant variables, even though there were part of the original research questions, is the parsimonious approach recommend for model building using logistic regression (Field, 2017; Karim, Reid, Tran, Cochrane, & Billah, 2017; Sperandei, 2014). Keeping the number variables in the equation was important given the low number of outcomes (only 40) in this study data set. Also, including age as a control became necessary since the age criterion was no longer applied and because its strong predictive factor, failing to-include it as a control variable would comprise the accuracy of the results for the main variables being investigated (Stoltzfus, 2011; Zhang, 2016). Adding the right covariates elucidates the precise contribution of independent variable and the development of a well-constructed logistic regression analysis for effective risk prediction model (Shipe, Deppen, Farjah, & Grogan, 2019; Zhang, 2016). The assumptions for logistic regression analysis are all met with these models. The assumptions include- binary dependent variable and the outcome of interest coded as 1 (liver cancer =1, no liver cancer = 0); inclusion of all meaningful variables (three covariates and independent variables); independence of observations (all observations from different subjects); and large sample size are all met (28,704 study sample size). The assumption of linearity does not apply as all the variables, including age, are included as categorical variables (Field, 2017).

Table 16

Odds Ratio of Demographic Variables for Liver Cancer Outcome

Variable	B	S.E.	Wald	df	Sig.	OR	95% C.I.
Gender (female)	.892	.333	7.162	1	.007	2.441	1.270 - 4.691
Age (65+ ref)			20.974	3	.000		
18 - 25	-15.781	678.541	.001	1	.981	0.000	.
26 - 40	-3.461	1.024	11.415	1	.001	0.031	.004 - .234
41 - 65	-1.159	.329	12.438	1	.000	0.314	.165 - .598
Race Group (ref: White)		1.012	2.365	4	.669		
Afr. American	.059	.534	.012	1	.912	1.061	.372 - 3.024
Nat. American	.799	1.021	.613	1	.434	2.224	.301 - 16.443
Asian American	.118	.731	.026	1	.871	1.126	.268 - 4.721
Other	1.375	1.022	1.807	1	.179	3.953	.533 - 29.329
Hispanic Ethnicity	.602	.449	1.794	1	.180	0.548	.757 - 4.403
Constant	-4.919	.888	30.702	1	.000	0.007	

Research Question 1: History of Liver Disease

Research Question 1**: Is** there an association between liver cancer and liver disease in adults in the US accounting for gender and race?

$H_0$1: There is no association between liver cancer and liver disease in adults in the US accounting for gender and race.

H_a1: There is an association between liver cancer and liver disease in adults in the US accounting for gender and race.

To answer this question, binary logistic regression analysis was used with gender, race, and age as the covariates, liver disease as the predictor variable, and liver cancer as

the outcome (1= liver cancer, 0= no liver cancer). The results of the bivariate analysis indicate that not only is liver disease strongly associated with liver cancer (X^2=1,481.468, $p < .001$), but also with health insurance (X^2=126.218, $p < .001$) and access to health (X^2=53.999, $p < .001$), as well as to the age (X^2=4.527, p<.033) and the gender (X^2=82.423, $p < .01$) demographics (see Tables 17).

Table 17

Association Between Predictor and Outcome Variables and Liver Disease

Variable	No Liver Disease *N*	Liver Disease *N*	No Liver Disease %	Chi-Square	*p*-value
Insurance				126.218	.000
No Insurance	2471	29	1.16		
Medicaid	2214	53	2.34		
Medicare	5016	118	2.30		
Private	10123	74	0.73		
Multiple	1605	53	3.20		
Other	6877	71	1.02		
Visit to GP				53.999	.000
No Visit	19891	347	1.71		
MD Visit	8415	51	0.60		
Liver Cancer				1,481.468	.000
Liver Cancer	11	29	72.50		
No Liver Cancer	28295	369	1.29		
Total	28306	398	1.39		

Liver disease is a major predictor of liver cancer as those with a history of liver disease having a 15,506.6% (OR=155.066, 95% CI [76.123, 315.878], p < .001) increased odds of developing liver cancer relative to those with a history of liver disease, when controlling for race, age and gender (see Table 18).

In this liver disease model, gender and age remained predictive, with minor changes in the odds ratio and probability of each. Here, men had 205.3% (OR=2.053, 95% CI [1.036, 4.068], $p = .039$) increased odds of liver cancer and the younger age groups (26-40 and 41-65) maintained similar reduced odds 94.3% (OR=0.057, 95% CI [.008, .430], $p = .005$) and 68.4% (OR=0.316, 95% CI [.162, .617], $p = .001$) for a liver cancer outcome (Table 18). This liver disease model predicted 39.1% (Nagelkerke's $R^2 = .391$, data not shown) of the variability in the data set and the classification was 99.9% accurate. Based on these results, the null hypothesis is rejected in favor of the alternative hypothesis, as a history of liver disease increases the likelihood of liver cancer by 39.1%, when controlling for gender, race, and age.

Table 18

Odds Ratio of History of Liver Disease for Liver Cancer Outcome

Variable	B	S.E.	Wald	df	Sig.	OR	95% C.I.
Gender (ref: female)	.719	.349	4.251	1	.039	2.053	1.036 - 4.068
Age (ref: 65+)			16.786	3	.001		
18 - 25	-14.638	664.217	.000	1	.982	0.000	
26 - 40	-2.861	1.030	7.722	1	.005	0.057	0.008 - 0.430
41 - 65	-1.151	.341	11.390	1	.001	0.316	.0162 - 0.617
Race (ref: White)			2.975	4	.562		
Afr. American	.095	.555	.029	1	.864	1.100	0.370 - 3.268
Nat. American	.758	1.111	.466	1	.495	2.135	0.242 - 18.834
Asian American	-.067	.774	.007	1	.931	0.936	0.205 - 0.262
Other	1.805	1.137	2.519	1	.112	6.079	0.654 - 56.471
Liver Dis (ref: no LD)	5.044	.363	193.049	1	.000	155.066	76.123 - 315.878
Constant	2.840	.579	24.053	1	.000	17.119	

Research Question 2: Medicaid Insurance Coverage

Research Question 2**:** Is there an association between liver cancer and Health insurance status with focus on Medicaid in adults in the US accounting for gender and race?

$H_0$2: There is no association between liver cancer and Health insurance status with focus on Medicaid in adults in the US accounting for gender and race.

H_a2: There is an association between liver cancer and Health insurance status with focus on Medicaid in adults in the US accounting for gender and race.

The second research question assessed the role of the different types of health insurance coverages play in the risk of developing liver cancer. The insurance variable is made up of a combination of several different variables because the insurance information was collected from a series of questions. Here the controls were also gender, race, and age, with the insurance variable as the tested predictor, and liver cancer as the outcome (1=liver cancer, 0=no liver cancer). The chi-square bivariate analysis indicated that health insurance was significantly associated with liver cancer (X^2=45.378, $p <$ *.001*). According to the cross-tabulation, the Medicare group had 0.4% association with the disease compared with 0.30%, 0.1%, 0.07%, 0.04% and 0.04%, for Multiple, Medicaid, Other, No Insurance, and Private categories, respectively (see Table 19).

Table 19

Association Between Insurance Type and Liver Cancer

Variable	No Liver Cancer *N*	Liver Cancer *N*	Liver Cancer % (Total)	Chi-Square	*p*-value
Insurance				45.378	.000
No Insurance	2499	1	0.04 (2,500)		
Medicaid	2264	3	0.13 (2,267)		
Medicare	5112	22	0.43 (5,134)		
Private	10193	4	0.04 (10,197)		
Multiple	1653	5	0.30 (1,658)		
Other	6943	5	0.07 (6,948)		
Total	**28664**	**40**	**1.39 (28,704)**		

In the BLR, the 'no insurance' category was used as the reference and there was no statistically significant difference ($p > .05$) for any of the types of insurance coverage as a predictor of liver cancer disease (see Table 20) for this study population. In this formula, gender remained a significant predictor (OR=2.532, 95% CI [1.317, 4.870], p = .005), and age was no longer a significantly associated (Table 20). This health insurance model predicted 10.0% (Nagelkerke's R^2 = .100) of the variability in the data set and the classification was 99.9% accurate. Based on these results, for the analysis of this data set, the null hypothesis cannot be rejected as there was no association between liver cancer and health insurance status, accounting for gender, race, and age.

Table 20

Odds Ratio of Health Insurance Coverage for Liver Cancer Outcome

Variable	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.
Gender (ref: female)	.929	.334	7.754	1	.005	2.532	1.317 - 4.870
Age (ref: 65+)			4.042	3	.257		
18 - 25	-14.542	672.436	.000	1	.983	.000	.
26 - 40	-2.155	1.113	3.750	1	.053	.116	0.013 - 1.026
41 - 65	-.091	.458	.039	1	.843	.913	0.372 - 2.243
Race (ref: White)			2.447	4	.654		
Afr. American	-.064	.536	.014	1	.905	.938	0.328 - 2.682
Nat. American	.683	1.026	.444	1	.505	1.981	0.265 - 14.796
Asian American	.162	.732	.049	1	.825	1.175	0.280 - 4.932
Other	1.440	1.024	1.977	1	.160	4.221	0.567 - 31.418
Health Insurance (Ref: No Ins.)			10.458	5	.063		
Medicaid	1.326	1.158	1.312	1	.252	3.767	0.390 - 36.436
Medicare	1.777	1.087	2.673	1	.102	5.910	0.703 - 49.716
Private	-.135	1.120	.015	1	.904	.874	0.097 - 7.843
Multiple	1.458	1.144	1.624	1	.202	4.296	0.457 - 40.409
Other	.563	1.097	.263	1	.608	1.755	0.204 - 15.068
Constant	-7.704	1.120	47.290	1	.000	.000	

**Multiple = Medicaid, Medicare, and Private Insurance*

Research Question 3: Access to Healthcare Provider

Research Question 3**:** Is there an association between liver cancer and access to annual routine clinic visits or Health care provider visits in the past 12 months in adults in the US accounting for gender and race?

$H_0$3: There is no association between liver cancer and access to annual routine clinic visits or Health care provider visits in the past 12 months in adults in the US accounting for gender and race.

H_a3: There is an association between liver cancer and access to annual routine clinic visits or Health care provider visits in the past 12 months in adults in the US accounting for gender and race.

The third research question addressed access to healthcare using the information collected from the 'visit to a general physician in the last 12 months?' This was a binomial variable and was entered as such in the BLR, along with race, gender, and age the controls. The bivariate analysis indicated that visit to general physician (GP) was statistically associated with insurance (X^2=2040.204, $p < .001$), and liver cancer (X^2=7.320, $p < .01$), as well as to all the demographics, age, gender, race, ethnicity (p <.001, see Table 21).

Table 21

Association Between Independent and Outcome Variable with GP Visit

Variable	No GP Visit *N*	GP Visit *N*	GP Visit % (Total)	Chi-Square	*p*-value
Insurance				2,040.204	.000
No Insurance	950	1550	62.00 (2,500)		
Medicaid	1582	685	30.22 (2,267)		
Medicare	4359	775	15.10 (5,134)		
Private	7265	2932	28.75 (10,197)		
Multiple	1438	220	13.27 (1,658)		
Other	4644	2304	33.16 (6,948)		
Liver Cancer				7.320	.007
Liver Cancer	36	4	10.00 (40)		
No Liver Cancer	20202	8462	29.52 (28,664)		
Total	**20,238**	**8466**	**29.49 (28,704)**		

However, the binary logistic regression results indicate that, for this study population, a visit to a general physician was not a predictive factor for the liver cancer outcome, when controlling for race, gender, and age. In this model, gender remained predictive, with OR=2.476, 95% CI [1.288, 4.758], p =.006, for men, as did age, with the two middle age groups, (ages 26-40: OR=.042, 95% CI [.006, .311], p =.002 and ages 41-65: OR=0.354, 95% CI [.185, .675], p = .002), having reduced risk relative to the oldest. This visit to general practitioner model predicted 8.8% (Nagelkerke's R^2 = .088) of the variability in the data set and the classification was 99.9% accurate. According to this result, the null hypothesis is not rejected as there is no statistically significant association between access to healthcare provider (as measured by visit to general physician in the last 12 months), when controlling for race, gender, and age.

Table 22

Odds of Visit to General Practitioner for Liver Cancer Outcome

Variable	B	S.E.	Wald	df	Sig.	Exp(B)	95% C. I.
Gender (ref: female)	.906	.333	7.393	1	.007	2.476	1.288 - 4.758
Age (ref: 65+)			17.122	3	.001		
18 - 25	-15.500	675.656	.001	1	.982	.000	
26 - 40	-3.179	1.027	9.591	1	.002	.042	0.006 - 0.311
41 – 65	-1.040	.329	9.954	1	.002	.354	0.185 - 0.675
Race (ref: White)			2.522	4	.641		
Afr. American	.004	.532	.000	1	.994	1.004	0.354 - 2.851
Nat. American	.878	1.020	.741	1	.389	2.406	0.326 - 17.773
Asian American	.066	.730	.008	1	.928	1.068	0.255 - 4.469
Other	1.386	1.023	1.836	1	.175	3.997	0.539 - 29.656
MD Visit (ref: no visit)	.891	.533	2.796	1	.095	.410	0.144 - 1.166
Constant	-6.869	.589	136.009	1	.000	.001	

Summary

The study population that made up the sample data for the statistical analysis was created after the application of the various inclusion and exclusion criteria specified in the proposal. This study sample data set had a minimal excess of women than men, who were predominantly Caucasian, and almost two-thirds were older than 45 years. The study sample data was analyzed using binary logistic regression to examine the likelihood of a liver disease outcome, included dichotomously (liver disease =1, no liver disease =0). The three independent variables investigated were history of liver disease; visit to a general practitioner in the last 12-months; and health insurance coverage. Bivariate

analysis indicated that gender, race, and age were all associated with liver disease and were therefore included as the control variables.

The results of the BLR indicated that several variables were predictive of a liver cancer outcome. The preliminarily BLR showed both gender and age to be strong predictors of a liver disease outcome, with men being twice as likely to develop the disease relative to women and increase age equated to an increased probability of being liver cancer diagnosis. The subsequent BLRs indicated that only liver disease was a statistically significant predictor of liver cancer and consequently a major risk factor for the disease. Participants with a history of liver disease had an almost 15-times increased odds of developing liver cancer, even while controlling for age, race, and gender.

Chapter 5: Discussion, Recommendation, and Conclusion

Introduction

Purpose of the Study

Liver cancer is the 3rd leading cause of cancer death in the United States (Endeshaw, 2019), and approximately only 1 in every 5 patients diagnosed with this disease survives 5 years after the diagnosis (Islami et al., 2017). Research on the biological factors have shown that in many cases, liver cancer patients also had one of the following: a history of liver disease, Hepatitis B or C, cirrhosis of the liver, NAFLD, or alcoholic liver disease (Sayiner et al., 2016; Rabie et al., 2018). Other researchers indicated that in the case of liver cancer patients with no history of liver disease, there was usually a diagnosis of other chronic conditions such as diabetes, obesity, or cardiovascular diseases (Del Campo et al., 2018; Younossi & Henry, 2016). Despite these findings, liver cancer prevention programs tend to have low success rates and the incidences of liver cancer continue to rise, contributing to continuing uncertainty about the risk factors involved in developing this disease.

The gap in the understanding of the development and the etiology of liver cancer continues to drive many related studies. Successful efforts in minimizing the risk or halting the development of liver cancer could significantly reduce the mortality of this disease. There are several avenues being pursued, including assessing potential environmental, behavioral, and/or biological factors as well as other indirect related risk factors and comorbidities. This current study assessed the role of a biological factor (liver disease) and that of two demographic factors (health insurance and healthcare

access) in addressing the information gap, on what puts patients at risk of developing liver cancer. The specifics involved in this study—impact of any history of liver disease, type of health insurance coverage with focus on Medicaid, and access to healthcare as represented by at least one visit to a healthcare provider in the last 12 months—on the risk of developing liver cancer among adults living in the US. The findings indicated that liver disease was the only predictive factor and that a history of liver disease is associated with a high risk of developing liver cancer.

Interpretation of the Findings

History of Liver Disease and Liver Cancer

The first research question assessed and established a significant predictive relationship between liver disease and liver cancer. The results indicated that a history of liver disease is a strong predictor of liver cancer, as those with liver disease had a 15,506.6% (OR=155.066, $p < .001$) increased odds of developing liver cancer relative to those without a history of liver disease. This excessively large OR (and large CI= 76.12-315.89) is expected from a data set where the outcome is very rare (sparse data set) that precise parameter estimation is challenged by the variability in regression coefficients and even greater standard errors (Siddarth, 2018; Norton, Dowd, & Maciejewski, 2018). Additionally, some participants affirmative response to history of liver disease question may have included their liver cancer diagnosis, thereby duplicating information, and exaggerating the association. An independent variable that measures the same factor as the dependent variable results in extremely large regression coefficients (Norton, Dowd, & Maciejewski, 2018).

Based on the generalized nature of the research questions and the assumptions on which the data used is based, the strength of the association or predictive power (as indicated in binary logistic regression results) must be tempered and not assumed to indicate that a history of liver disease conclusively leads to liver cancer. Future research should entail distinguishing liver disease from liver cancer, then distinguishing lifestyle liver disease from inherited liver disease, and differentiating among all the different forms of liver conditions. As previous epidemiological findings indicate, most liver cancers are not primary (originating in the liver) liver cancer but secondary or metastatic (originating elsewhere in the body) liver cancers (Cross, & Palmer, 2019; Loftfield, 2020), making identification of the nature of the liver disease crucial to understanding what type of liver disease, and how it is linked to liver cancer (Mansournia, et al., 2018).

Health Insurance Coverage and Liver Cancer

In this study, the logistic regression analysis indicated that type of insurance was not a statistically significant predictor of a liver cancer outcome. The three types of insurance coverage, Medicaid, Medicare and Private, were assessed relative to no insurance coverage. A previous study by Suh et al. (2018) found that persons with Medicaid insurance coverage had a higher incidence of liver cancer than those with other insurance type, but that significance occurred when the data was stratified by age. Another study found a higher risk of liver cancer among Medicaid insured residents of NYC, but there was also a higher incidence of hepatitis among those residents (Kamath et al. 2018).

The nature of the NHIS data collection process, where the information for insurance coverage information was gained using several different questions for each, allowed for overlapping categories and reduced the strength of the relationship being assessed. The NHIS data used for this analysis was self-reported and responses to the health insurance questions are among those that were subsequently reinterpreted and recoded by NHIS staff, possibly introducing additional error, and absence of specificity all diminish the reliability of the findings. Future studies to investigate this issue should be based on data collected with survey instruments that gather more specific and delineated (of primary payer) insurance information.

Access to Healthcare and Liver Cancer

The results of the third logistic regression analysis found no association between access to healthcare (as measured by a visit to a general practitioner in the last 12 months) and that of liver cancer. However, it should be noted that the information captured was limited as this variable represented a very incomplete picture of overall healthcare access, as it did not include visit to other medical professionals, nor did it measure the patient's actual history of healthcare access. While previous research has supported the efficacy of monitoring liver health and the benefits of liver cancer surveillance and screening in improving health and mortality outcomes (Beste et al., 2015b; Khalaf, 2017; Tillman et al., 2018) this study reports no link between recent general practitioner access and liver cancer development. It should be noted that the *p*-value of 0.095 (and the OR of 0.410), where 'no visit' as the reference, is indicative of a trend towards reduced likelihood for those who did visit a physician in the last year.

Findings Relative to the Conceptual Framework

The person-centered care theory was the theoretical framework used for this study and it advocated a best practice that focuses on the unique traits, the unmet needs, and the preferences of patients over the symptoms of their disease (Rogers, 1979). In instances when healthcare professionals employ this theory to their interaction with patients and in developing their treatment plan, it has led to a more responsive and compliant patients and by extension a more effective treatment outcome (Babilonia, 2016; Bayus, 2016; Pukrittayakamee et al., 2018). The proper application of a person-centered care theory requires informed policies and procedures that are developed based on meaningful research findings. This current study is an attempt at evidence-based policy and procedure development as it relates to liver cancer. Donabedian model focused on structural domain related to health-care system or context in which care is delivered which influence the processes and outcomes of health-care quality improvement (Santana et al., 2018). Structural domains were educational programs, health promotion and prevention programs with patients. Process domains cultivates communication, engaged patients in managing their care and integrates care and finally the outcome domains provide access to care and patient-reported outcomes. This current study used PCC constructs to linked Medicaid to liver disease, and healthcare access or clinics (structure and process) to liver cancer (outcome) with gender, race, and age (covariates or demographics) as controls, while PCC attributes such as structure, process, and outcome domains of the quality model with focused on the patient established interaction of the independent, dependent variables and covariate of this current study.

There exist already several studies that focus on the behavioral or lifestyle risk factors of liver cancer, such as alcohol consumption, smoking, or dietary or nutritional deficiencies. Other studies focus on the biological risk and comorbidity of liver cancer, such as cirrhosis, hepatis, biomarkers, or elevated liver enzymes. And yet other epidemiological studies have focused on the demographic characteristics, such as gender, race, and age to better understand and prevent liver cancer development. But there are very few studies, like the current one, that have focused on the "the unique health-driven needs" of the liver cancer patients and provide insight for the person-centered healthcare strategies.

There is a movement by healthcare organizations to make the US healthcare system more consumer-driven and this is requiring, among other factors, positioning for more meaningful relationships with clients (Land, 2019; McDowell, 2018; Sandoval, et al. 2020). This emphasis on 'customer satisfaction' has the potential for significant growth and profitability. Those who are taking the lead in these efforts and actively researching new and meaningful ways to provide treatment protocols and healthcare services in general. Studies that are designed on theories based on the person-centered care theory will provide the much sought-after information. According to the World Health Organization (WHO), person-centered or patient-centered care is based on the patient's views, experiences and needs and leads to empowering experience that leads to improved "patient satisfaction and outcomes—two key performance indicators for medical organizations" (Cloninger & Cloninger, 2015).

Limitations of the Findings

The findings from this research, as important as they are, comes with several limitations that must be highlighted. These limitations included: the data set used, the many criteria applied, the nature of the statistical test employed, and how they all impacted the research results and its interpretation. Firstly, the NHIS data is based on self-reporting and this affects the reliability of the information gathered. For example, in the case of the outcome variable and others, no provision of proof of (or the absence of) a liver diagnosis is required. Also, as have been reported, that many responses to NHIS question can be misremembered and misreported for reasons of social pressure or misunderstanding of the question (Hanley, 2017). In this analysis, there was evidence of patient's insurance coverage and healthcare visits being dubious, whether it was the type of insurance coverage or doctor's visits, as contradicting answers were provided in separate questions. These and other reasons, inherent data based on response to questions in self-reporting survey, undermine the reliability of the current results.

The validity of the results is challenged by some of the inclusion and exclusion criteria that were applied to the data set, which added to the selection bias. The nature of survey research design introduces biases of some kind and the exclusion criteria that eliminated all those who did not remember, did not know, refused to answer, added more bias to the sample. Given that the incidence of the outcome in question (liver cancer) was already so low and was not affected by the exclusion criteria, this selection bias may not have been as critical. However, when there are only 40 cases of liver cancer, and having to excluded four participants who "refused" to answer and another nine whose

response was “don’t know,” those numbers can have a major impact on the results of the statistical analysis. Future research may need to strategically address and correct for any selection bias to improve the reliability of the results.

Thirdly, the use of binary logistic regression is an extremely valuable tool for assessing predictive relationship of certain various for disease outcome. However, logistic regression formula is dependent on the quality of the variables included. Some variables are strong predictors and others are not, and this can render the model very subjective. In this case, the measure of the validity lies not only in the precision of the significance and the odds ratio, but also in the classification power of the model (Field, 2017). Unfortunately, because the outcome percentage was so small (<1%), the classification for the blank model (without the variables) and that of the predictor model (with the variables) were not much different. So, adding the predictor variables, even the statistically significant one, did not have much effect on the power of the model to correctly reflect the data set. Ultimately, a data set with a higher percentage of the outcome being predicted for provides for more reliable results.

And finally, it should be mentioned that this analysis is based on cross-sectional data and therefore no causality interpretation can be made. Causality is derived from mostly from experimental research data, either randomized clinical research or lab/wet bench research. There is some causal information that can be gained from cross-sectional data, but that involves the use of structured equation modeling (SEM). The SEM path analysis allows for the interpretation of which conditions precede another in time and may be the underlying cause of the latter (Shi et al., 2016). An alternative is the use of

Cox-Hazard or Kaplan-Meier analysis of survival time data to investigate the association between certain predictors and the eventual disease outcome at a future date (Martínez-Camblor, 2019). These methods would require the use of sample data whose dependent variables are based on longitudinal data collection.

Recommendations for Future Research

This research has provided valuable insight into the risk factors that are associated with the development of liver cancer. The null results in two of the three research questions points to the need for future research with sample data that are more representative. The epidemiological research that is needed should focus mainly on the appropriate population and sample size, especially with a more suitable incidence of liver cancer patients. Because liver cancer is not as prevalent as some other cancers like breast or colon cancer, and the incident rate in the public is already low, a more deliberate effort should be made to collect relevant data. Additionally, here in the U.S., the low prevalence of hepatitis (A, B, or C) disease, relative to some other countries like China or Mongolia, has made liver cancer less of a threat and is unfortunately not as frequently studied. Regrettably, however there has been a steady incline in the liver cancer rates in the United States in recent years, placing emphasis on the need for appropriate data and related research efforts.

Future research should focus on the populations at highest risk (Native Americans and Pacific Islanders, and Asian Americans) with special efforts made to ensure adequate representation from these groups. These studies should be stratified prior to analysis so that the results present a clear understanding of the risk specific to each group being

assessed. This would be of great benefit in directing the efforts to reduce the threat of the disease among the respective groups. When they are not adequately included in the sample, it clouds the results, and a clear picture of the risk model is not obtained. When these groups are not sufficiently represented in the sample distribution, or even when they are combined with other groups that have much lower disease incidences, the strength of the risk factor as it pertains to them is not evident in the results. Consequently, the findings from these research samples can be misleading as it represents the measure of the risk factor for only the majority group that is reflected in the sample.

Race is not the only stratification process that could prove useful for liver cancer research. Even though most samples contain a mostly equal representation of both genders, stratification by gender could also prove insightful, as to the factors that cause risk of liver cancer is much greater for men than for women. Splitting samples along the genders and conducting separate risk analysis could be revealing as to what might risk factors for one gender be different for the other gender, or vice versa. The differences between the genders have resulted in separate risk models for each gender for other disease such cardiovascular diseases; neurological diseases, such as Parkinson's and Alzheimer's; and other types of cancer such as breast cancer and colon cancer (Bakeberg, 2019; Blenck, Harvey, Reckelhoff, & Leinwand, 2016; Etxeberria, Goicoa, & Ugarte, 2018). The current research results indicate that liver cancer research could benefit from a similar approach.

The risk models for cancer assessments are critical to the healthcare response to the patient's outcome whether identifying those at risk and who can benefit from

preventative methods, or those who are in early stages of the disease and may be responsive to treatment, or those who are in need of urgent further intervention such as chemotherapy, drugs, or surgery. For these screening models to be reliable, they must be developed based on research samples that are include adequate representation of the population as well as on analysis methods that generate models that be generalized. This study emphasizes the need for representation in distribution in the sample data and for use of statistical analysis that produce expedient models.

Finally, considering the person-centered theory approach, in the future researchers should look for personalized factors, other than insurance coverage and access to health. This may require some type of qualitative research or primary quantitative data collection, where such determination is from the patients themselves what these factors might be. Related research has found that in order to improve the quality of treatment that patients receive, the focus should go beyond obvious disease symptoms or general patient's characteristics. Incorporating emphatic understanding and emotional engagement and exchange in the research design requires knowledge of not just the physical and but the mental, emotional, and even spiritual toll of the disease (Van Leeuwen, 2018). This type of research in the future will provide the information needed to develop treatment protocol that includes these aspects of the patients lived experience and create an alliance between them and their caregiver and creating space for healing and real lasting change for these individuals.

Implication for Positive Social Change

The findings from this research, though limited, can be applied to bring about some positive changes in Public health and the healthcare delivery system. The results emphasize the complexity of the disease of liver cancer and the challenge of identifying related risk factors. What has been established is that given the distinctly different incidence across age groups and gender, public health promotion and screening resources should focus on the highest risk groups. Faced with limited resources, focusing on the high-risk groups will have a greater impact and bring about more meaningful changes in terms of health outcome and lives saved. The responsibility lies within the level of healthcare practitioners to take ownership for implementing and supporting these strategies. The nurses and clinicians should communicate the importance of liver health, being a part of a targeted surveillance program, and the need for getting regular liver blood tests done. They should share information to the public about annual and routine checkups for liver disease and establish the patient's confidence in early testing as crucial because research indicates that early diagnosis of liver cancer indicates easier treatment with more treatment options, and higher survival rates.

It is also important for all decision makers, healthcare providers, policy makers, and health administrators, to take ownership of implementing changes in the attitude and approach towards liver cancer. Like other liver cancer research, this study has highlighted the complexities involved in identifying the risk factors involved in the disease development. Study findings drives individuals at risk to make more informed lifestyle and health care choices to mitigate liver cancer risk, by encouraging a

holistic/person-centered approach with focus on the “the unique health-driven needs” of persons at risk of developing liver cancer.

Conclusion

Liver cancer is a deadly disease, whose early stages can go undetected for several years and cause rapid decline in the latter stages. Although epidemiological and clinical research have successfully identified many of the risk factors associated with the disease the exact etiology remains unclear. The results of this study confirmed age and gender as major risk factors, and it has also established a major role of an individual’s history of liver disease in predisposing him or her to the development of liver cancer. However, there were several limitations associated with the sample data on which these results are based, and as such further research is required in order to confirm the research findings and establish the generalizability of the risk model generated.

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