COMPARATIVE STUDY FOR HOSPITALIZATION CHARACTERISTICS AND PREDICTORS OF OVARIAN CANCER OF INPATIENTS IN THE UNITED STATES

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ABSTRACT

Ovarian cancer is the second most common type of gynecologic cancer, and it causes more death than any other female reproductive cancer. It is the 7th most common women's cancer. The objective of the present study is to highlight the risk factors of ovarian cancer related to hospitalization outcomes such as mortality, length of stay, and total medical charges when there is a presence of congestive heart failure (CHF) and other complications. The study implemented a cross-sectional design to achieve the primary objectives. Data were downloaded and extracted, with permission, from Nationwide Inpatient Sample (NIS). The collected data included patient demographic characteristics, such as age, gender, race, and income. Statistical Package for the Social Sciences (SPSS) version 28.0 was used to analyze the present study's data, and all outcomes with a p-value less than 0.05 were found to be significant. Overall mortality showed a higher incidence of epithelial ovarian cancer. The incidence of mortality increased with CHF and hypertension (HTN), in which the patients with HTN had a higher death rate with epithelial ovarian cancer than CHF. Regarding the length of stay, increasing age and being white results in an average decrease in length of stay. Those patients with weight loss comorbidities resulted in the greatest mean increase in length of stay. The increasing number of diagnoses, procedures, age, and being Hispanic results in an average increase in total cost. Being white or black results in an average decrease in total cost. The deceased risk of dying was associated with the number of procedures. Increased age and number of diagnoses were associated with an increased likelihood of dying. The increase in procedures and SES will increase the length of stay. And when it

comes to comorbidities, among those with hypertension, these predictors are significant. The predictors of mortality were assessed by age and number of diagnoses, which were associated with an increased likelihood of dying.

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CHAPTER I: INTRODUCTION

Background of Ovarian Cancer

Ovarian cancer refers to any cancerous growth that starts in the ovary. Ovaries are an integral part of the female body that produces reproductive eggs. Some scholars argue that ovarian cancer refers to abnormal cell growth that occurs in the ovary with the capability of multiplying quickly and destroying body tissues. Currently, ovarian cancer (OC) is the fifth most diagnosed cancer among females globally (Khazaei et al., 2021). There are three types of ovarian cancers: epithelial, germs and tumors, and trauma cell carcinoma (Stewart et al., 2019). Epithelial cancer is the most predominant pathologic type of cancer of the three types of ovarian cancer. Unlike other types, epithelial ovarian cancer has five key histotypes that vary in origination, pathogenesis, molecular alteration, risk factors, and prognosis (Khazaei et al., 2021). Genetic vulnerability usually manifests through rare inherited mutations ranging from high or moderate penetration. According to Grossman et al. (2018), Geno- related studies further identified additional susceptibility alleles related to ovarian cancer, such as the 14 subtypes specific alleles.

In terms of incidence and mortality, ovarian cancer accounts for a projected 259000 new cases and nearly 150000 deaths globally each year (Khazaei et al., 2021). The most alarming rate (11.3 per 100000 and 6.0 per 100000) are majorly reported in central and eastern Europe. In the United States, nearly 21000 cases and 14200 deaths are linked to ovarian cancer in women yearly (Grossman et al., 2018). In terms of severity and risk, a

female's lifetime risk of developing ovarian cancer is estimated as 1 in 75. The researchers found that the chances of a woman dying of the disease are estimated as 1 in 100.

Typically, ovarian cancer majorly manifests at a late stage with a five-year survival rate of only 29%. Few cases representing 15% of ovarian cancer are likely to be diagnosed with a localized tumor in stage one and a five-year survival rate of 92% (Verdoodt et al., 2017). In this case, ovarian cancer is considered one of the most prevalent and dangerous medical conditions globally (Khazaei et al., 2021). Researchers have shown that ovarian tumors may begin as noncancerous (Verdoodt et al., 2017). These malignant tumors may originate from epithelial surfaces, germ cells, sex codes, or stromal codes. The studies reviewed indicate that most ovarian cancer is likely to develop from inner cells in the lining of ovaries, commonly known as epithelial ovarian cancer.

Given that ovarian cancer starts deep in the pelvis, they mostly do not have any symptoms until they are in the advanced stages (Verdoodt et al., 2017). Additionally, most of the symptoms linked to ovarian cancer are difficult to differentiate from symptoms reported by women who are not diagnosed with ovarian cancer, including fatigue, constipation, and abdominal pain (Stewart et al., 2019). In view of the limited specificity of ovarian cancer symptoms, nearly 70% of women are constantly diagnosed with it in the advanced stage (Stewart et al., 2019). Over time, ovarian cancer is likely to spread to the abdominal cavity leading to the buildup of fluids inside the abdomen, commonly known as ascites.

Ovarian cancer has several symptoms and signs. Common ones include acute back pain, abnormal blotting, and constipation (Khazaei et al., 2021). Another blotting related to ovarian cancer is back abdominal pain, bowl movement, and other urinary symptoms.

Pathophysiology and Etiology of Ovarian cancer

Etiology refers to the cause and origin of a medical condition. This branch of medicine determines the cause of a disease or its pathology. Over the years, the etiology of ovarian cancer has remained poorly understood (Momenimovahed et al., 2019). In addition, the sores of epithelial cancer have increasingly become an issue of controversy among scholars (Shah et al., 2018). Historically, the ovarian surface underlying epithelium was considered the primary malignant source ((Sundar et al., 2021). The theory of incessant ovulation is based on the premise that recurring involvement of the ovarian surfaces during the ovulation process is a major factor for all ovulation cancer

According to the theory, the common factor linked to ovulation comprises injury and repair of the ovarian epithelium surface as a response to follicle inflammatory of ovarian environment, entrapment of ovarian surface in the ovary resulting in a cyst formation well, and hormonal steroid influence (Momenimovahed et al., 2019). However, according Shah et al. (2018), the accumulated evidence from different studies suggests that most epithelial ovarian cancer originates in the distal portion of fallopian tubes, more specifically from the fimbrial epithelium.

The first evidence links fimbrial epithelium obtained from risk-reducing salpingo-oophorectomies in women with either BRCA gene mutation or a family history of ovarian cancer (Sundar et al., 2021). After examining the entire fallopian tubes, the

researchers found foci of cymbal intraepithelial carcinoma. A similar lesion was also found in the fimbrial epithelium in women (Sundar et al., 2021). There are several classifications and new theories of ovarian cancer. For instance, some scholars have suggested two types of epithelial ovarian cancer: type I and type II (Shah et al., 2018). With time, fallopian tubes have been at the center of research and how they cause ovarian cancer. Researchers have noted that most ovarian cancer starts in the ovarian tubes (Sundar et al., 2021). The most common histological subtypes of ovarian epithelial carcinomas include serous (68%-71%), endometroid (9%-11%), clear cell (12%-13%), mucinous (3%), transitional (1%), and mixed histologist (6%) (Momenimovahed et al., 2019).

Most scholars have now convincingly reported two major types of ovarian carcinoma: type I and type II. Type I tumors may arise through well-recognized sequences from borderline serous tumors or endometriosis, including low-grade serous carcinoma, endometrioid, and clear cell carcinoma (Shah et al., 2018). The tumors are mainly early staged or low-grade tumors and have a relatively indolent disease cause. Type II carcinoma is common and severe histology (Momenimovahed et al., 2019). They are high grade and mainly originate from the fimbrial epithelium. The high-grade serous carcinoma may present clinically at stage three or four. This is consistent with the theory of peritoneal seeding by maligned cells from the fimbriated end of the tubes (Sundar et al., 2021). Most epithelial ovarian cancer is diagnosed in an advanced stage, is high grade, and has a poor prognosis compared to early-stage carcinomas.

Epidemiology of Ovarian cancer

Epidemiology is the branch of medicine that deals with understanding disease incidence, distribution, and possible control and analysis of factors relating to helping. Some scholars have defined epidemiology as the analysis of distribution patterns and determinants of health of disease conditions in a particular population. Ovarian cancer incidence displays a broad geographic variation (Sundar et al., 2021). The highest mortality rate and prevalence are reported in developed countries, including the United States and central Europe. In these countries, the prevalence of ovarian cancer is estimated to be 3 per 100000 women. However, in South America, the prevalence of ovarian cancer is intermediate, with 5.8 per 100000 women. The rate is lowest in other continents, such as Africa and Asia, with 3 per 100000 women. Researches suggested that migration of individuals from countries with low prevalence rates of ovarian cancer to those with higher rate increases the risk of an individual developing ovarian cancer, greatly underscoring the significance of nongenetic risk factors in the prevalence of ovarian cancer.

In the United States, racial differences in prevalence and mortality rates in ovarian cancer in women reflect the same observation reported at international levels (Momenimovahed et al., 2019). Additionally, white women have the highest prevalence of ovarian cancer, followed by Hispanic women and least among black and Asian women (Momenimovahed et al., 2019). In developed countries such as the United States, ovarian cancer mortality and prevalence rates have significantly declined since the early 1990s.

Genetic factors are another key risk factor for ovarian cancer in genetic epidemiology. For instance, researchers report that first-degree relative with a history of

cancer have nearly 3 to 7 increased chances of suffering from ovarian cancer (Reid et al. 2017). The common risk factors for ovarian cancer include hormonal and reproductive factors. Several epidemiological studies have implicated hormonal and reproductive factors in the pathogenesis of ovarian cancer. Age is another risk factor for ovarian cancer (Momenimovahed et al., 2019). Older women have a greater risk of suffering from ovarian cancer than younger women. Geographical location is also another risk factor for ovarian cancer. Individuals from different geographical locations have various incidences and mortality rates (Reid et al., 2017). Ovarian cancer occurs in four stages. In stage one, cancer affects one or both ovaries. Cancer spreads to other organs such as the uterus, fallopian tubes, or bowls in stage two (Momenimovahed et al., 2019). Cancer spreads beyond the pelvis to the abdomen or lymph nodes in the third stage. Finally, cancer spreads to different organs in stage four, including the lungs or liver (Reid et al. 2017). Treatment for ovarian cancer varies based on the type of cancer being targeted. In terms of epithelial cancer, surgery is the main form of treatment. Surgery removes the cancerous tumor from the body. The analysis revealed that stromal cell cancer is treated with surgery or thermotherapy.

Statement of the Problem

Different opinions are associated with ovarian cancer and other comorbidities like hypertension, overweight, and Congestive heart failure, and their impact on mortality in the United States (Khazaei et al., 2021). The incidence of this ovarian cancer increases with age, and old patients have other diseases; the chances are more. If the diagnosis is made in an advanced stage, this will cause a poor survival rate (Bouchard-Fortier et al., 2020). A few previous studies have examined the prevalence of individual cardiovascular

risk factors in women with ovarian cancer (Ahmed et al., 2020). However, none of these have considered hypertension in their assessment, and most have commented on known diagnoses only.

Goals and Objectives

The main objectives of this study are to find:

I. Is there an association between mortality and type of ovarian cancer?

II. Is there an association between mortality and type of ovarian cancer with CHF?

III. Is there an association between mortality and type of ovarian cancer patients with Hypertension?

IV. Are there predictors for the length of stay of patients with ovarian cancer?

V. Are there predictors for the length of stay of patients with ovarian cancer hypertension?

VI. Are there predictors for total charges of patients with ovarian cancer?

VII. Are there predictors for total charges of patients with ovarian cancer Congestive heart failure?

VIII. Are there predictors for total charges of patients with ovarian cancer hypertension?

IX. Are there predictors for mortality of patients with ovarian cancer?

X. Are there predictors for mortality of patients with ovarian cancer Congestive heart failure?

Research Hypothesis

Several hypotheses have been developed for this study. The hypotheses will be tested to prove or disprove the proposition made in the study. Both the null and alternate hypotheses have been developed for this study. The following are the study's hypotheses:

$H0_1$: There is no significant association between mortality and type of ovarian cancer

$H1_1$**:** There is a significant association between mortality and type of ovarian cancer

$H0_2$**:** There is a no significant association between mortality and type of ovarian cancer patient with Congestive heart failure.

$H1_2$ There is a significant association between mortality and type of ovarian cancer patient with Congestive heart failure.

$H0_3$: There is no association between mortality and type of ovarian cancer patients with HTN

$H1_3$: There is an association between mortality and type of ovarian cancer patients with HTN.

$H0_4$**:** There are no significant predictors for the length of stay of patients with ovarian cancer.

$H1_4$: There are a significant predictor for the length of stay of patients with ovarian cancer.

$H0_5$**:** There are no significant predictors for the length of stay of patients with ovarian cancer hypertension.

$H1_5$: There are significant predictors for the length of stay of patients with ovarian cancer hypertension.

$H0_6$: There are no significant predictors for total charges of patients with ovarian cancer

$H1_6$: There are significant predictors for total charges of patients with ovarian cancer.

$H0_7$: There are no significant predictors for total charges in patients with hyper- and hypothyroidism.

$H1_7$: There are significant predictors for total charges in patients with hyper- and hypothyroidism.

$H0_8$: There are no significant predictors for total charges of patients with ovarian cancer hypertension.

$H1_8$: There are significant predictors for total charges of patients with ovarian cancer hypertension.

$H0_9$: There are no significant predictors for mortality of patients with ovarian cancer.

$H1_9$: There are significant predictors for mortality of patients with ovarian cancer.

$H0_{10}$: There are no significant predictors for mortality of patients with ovarian cancer and Congestive heart failure.

$H1_{10}$: There are significant predictors for mortality of patients with ovarian cancer and Congestive heart failure.

Significance of study

Ovarian cancer happens when the ovary cells grow and produce a tumor. The risk of ovarian cancer increases as you grow old, especially after menopause. Ovarian cancer is the most deadly gynecologic cancer; it is called the silent killer, and it accounts for more deaths than any other cancer of the female reproductive system. The occurrence of ovarian cancer is more in old patients, and it is more if other diseases coexist. The present study will reveal the similarities and differences of risk factors and predictors of mortality, total

charges, and length of hospital stay for stages of different ovarian cancer in patients with comorbidities.

Ovarian cancer has several risk factors that contribute to its prevalence among women. In this study, I focused on exploring different predictors of ovarian cancer among women. In so doing, I identified, based on existing literature, age, gender, race, socioeconomic status (SES), number of procedures, number of diagnoses, and comorbidities as the major risk factors for ovarian cancer. Therefore, the current study findings can be used by stakeholders and at an individual level to understand how different factors cause ovarian cancer and possible mitigation strategies. In addition, the current study focused on ovarian cancer screening among women and mortality rates. The findings could be used to recommend appropriate policies to support early screening for ovarian cancer and reduce the high mortality rate, given that early screening and detection facilities timely treatment and reduced progression into advanced states that are more fatal.

CHAPTER II: LITERATURE REVIEW

The purpose of this study was to investigate the mortality of patients with an ovarian cancer diagnosis, length of stay, total charges, and their association with age, gender, race, socioeconomic status (SES), number of procedures, number of diagnoses, comorbidities, and ovarian cancer stage, in a cohort of inpatients with ovarian in the United States. In addition, the sections present an analysis of current literature on ovarian cancers. Each of the key themes related to the study is discussed below.

Causes of Ovarian Cancer

Previous studies were indifferent in identifying the cellular origin of ovarian cancer. Still, recent theories have hypothesized that it should not be considered a single disease entity but rather a diverse group of tumors with specific morphologic and genetic characteristics because of its historical differences. For instance, Reid et al. (2017) investigated the relationship between genetic abnormalities and syndromes, and Epithelial Ovarian Cancer (EOC) using qualitative methods. the investigators established that most patients who had EOC came from family backgrounds with a history of cancers from an early age. Over two primary cancers in a single individual have a higher risk of hereditary ovarian cancer syndromes. In addition, the findings revealed that the risk of ovarian cancer is higher in women with BRCA1 mutation than in BRCA2 mutation. Mutations within the central region of the *BRCA2* gene (the ovarian cancer cluster region) may be associated with a significantly higher risk of ovarian cancer in women.

Crosbie et al. (2021) conducted a qualitative study to explore hereditary causes of ovarian cancer. A sample of 261 women with ovarian cancer participated in the study. After

data analysis, the findings showed that mismatch repair deficiency by immunohistochemistry associated with Lynch syndrome (inherited pathogenic germline autosomal dominant mutation in one of the DNA mismatch repair genes) was common in most participants. In addition, most Lynch syndrome tumors were of endometrioid histological subtype. The findings show that Lynch syndrome is hereditary through family, and it may cause ovarian cancer. Liu et al. (2019) conducted a literature review using 36 articles to investigate the link between menopausal hormone replacement and ovarian cancer.

Data were analyzed, and the findings revealed a positive association of menopausal hormone replacement therapy (HRT) with the risk of ovarian cancer, which may increase the risk of serious and endometrioid tumors (Liu et al., 2019). In addition, high levels of gonadotropins during menopause act as a promoter on the affected ovarian tissue, and also estrogen-induced ovarian cell proliferation may stimulate the proliferation of ovarian surface epithelial cells, and progesterone could promote the apoptosis of ovarian cells, which may result in increased ovarian cancer tumors.

Park et al. (2021) conducted a qualitative study exploring the impact of obesity on women. A total of 2,708,938 participated in the research. Multivariate analyses revealed that the risk of ovarian cancer gradually increased as the body mass index (BMI) classification increased from underweight to class II obesity ovarian cancer. Class II obesity was significantly associated with increased risks in post- menopausal and pre-menopausal women. Dixon et al. (2018) pioneered a study investigating the link between height and ovarian cancer using a sample of 39 398 women. Dixon et al. (2018) established

that genetically predicted size was associated with increased ovarian cancer risk, and taller women with a genetic propensity had the highest risk of ovarian cancer.

Coleman et al. (2020) intended to investigate the relationship between family history and ovarian cancer using qualitative methods. The researchers found that a family history of ovarian cancer in first-degree biological (mother, sister) and other relatives increase a woman's risk of developing ovarian cancer. According to the researchers, inherited genetic mutations account for approximately 5% to 25% of all ovarian carcinomas. For example, women with a *BRCA1* mutation have a lifetime risk of 35% to 60% of developing ovarian cancer. *PALB2, BRIP1, BARD1, RAD51C*, and *RAD51D* are other germline mutations that present vulnerability to ovarian cancer because they encode DNA repair proteins in the Fanconi anemia BRCA pathway. Likewise, Rosenthal et al. (2017) pioneered a study exploring the effectiveness of ovarian cancer screening on patients with genetic causes of cancer through qualitative methods. A sample of 4,348 women underwent screening. The findings revealed that inherited mutations in *BRCA1* and *BRCA2* and Lynch syndrome (LS) are a significant risk of ovarian cancers, and annual screening of ovarian cancer that uses a cutoff for the serum tumor marker cancer antigen 125 (CA-125) was associated with improved survival (Rosenthal et al., 2017). Similar to Coleman, Menon et al. (2018) conducted a qualitative study to investigate the benefits of screening patients with inherited OC mutations. Menon et al. (2018) reported that BRCA1 and two mutations are the most common conferring a lifetime (cumulative) risk of invasive epithelial ovarian cancer. Women who underwent screening for serum CA 125 (35

units/mL or greater cutoff) and transvaginal ultrasonography had a higher five-year survival rate.

Torng (2017), exploring the association between endometriosis and ovarian cancer through a systematic review using 28 articles, found that endometriosis is associated with ovarian cancer (EAOC) because of particular histological subtypes of ovarian epithelial carcinoma to some specific molecular aberrations. Epithelial ovarian cancer cases reported in women with endometriosis may be because of high heterogeneity in a meta-analysis. Patients with endometriosis reported increased endometrioid carcinoma, clear cell carcinomas, and less serous carcinoma.

Bulun et al. (2019) investigated how mutations in patients with endometriosis cause ovarian cancer. After data analysis, Bulun et al. (2019) established that mutations in PIK3CA, KRAS, ARID1A, and other genes were found in the epithelium of intrauterine endometrial tissue, ovarian, and intraovarian pelvic endometriosis tissue, ovarian cancers linked to endometriosis (clear cell and endometrioid type), and other epithelial ovarian cancers. The investigators also found that a high concentration of estrogen in the ovary may exert an additional and direct genotoxic effect on DNA which may cause the accumulation of additional mutations and malignant transformation in already mutated endometriotic epithelial cells in an ovarian endometrioma. An additional mutation in already mutated endometriotic epithelial cells may initiate epithelial ovarian cancer. Temkin et al. (2019) performed a literature review using 52 articles to explore the role of menopausal hormone stimulation in ovarian cancer. Data analysis showed that ovarian cancer risk was significantly increased in current users of the menopausal hormone,

especially in women who used both estrogen-only and estrogen-progesteronal preparations.

Zhang et al. (2021) conducted a study to explore the association between estrogen and progesterone in menopausal hormones and ovarian cancer. The researchers established that exogenous estrogen and progesterone in the ovaries are associated with increased proliferation and apoptosis inhibition within the ovary. Fallopian tubes and estrogens provide a microenvironment conducive to tumor development by enhancing local vascular supply and favoring an immunosuppressive environment. Foong and Bolton (2017) conducted a systematic review using 43 articles to investigate the relationship between ovarian cancer and obesity. Obese women are at increased risk of ovarian cancer, which additional genetic and environmental factors may influence. Momenimovahed et al. (2019), using 125 articles, conducted a literature review exploring the association between ovarian cancer and age. The results revealed that epithelial ovarian cancer is an age-related disease mainly considered postmenopausal in women over 65 years. Older age in ovarian cancer is associated with more advanced disease and a lower survival rate.

Zheng et al. (2019) proposed exploring risks associated with age and ovarian cancer. Ovarian cancer was associated with a family history of ovarian cancer, especially where the mother and sister had a history of ovarian cancer. For others, concordant familial risks were highest for mucinous ovarian tumor cancer, with some discordant associations such as endometrioid cancer. Iversen et al. (2018) conducted a qualitative study investigating the relationship between hormonal contraceptives and ovarian cancer. A sample of 1 879 227 women took part in the research. Participants who frequently used

hormonal contraception reported cases of ovarian cancer. Still, contemporary combined hormonal contraceptives were associated with decreased ovarian cancer risk in women of reproductive age. As evidenced by the above literature, the significant causes of ovarian cancer include age, body mass, abnormal genetic syndromes, family history with cancer, height, and menopausal hormones, which have risk factors that may lead to different types of ovarian cancer.

Risk Factors All Three Ovarian Cancer

Ovarian cancers have several risk factors. Epithelial ovarian cancer is one of the most common types of ovarian cancer that starts in the surface layer covering the ovary. Epithelial ovarian cancer is a heterogeneous disease that comprises several histologic subtypes like serous, mucinous, endometrioid, clear cell, transitional cell, Brenner tumors, mixed and undifferentiated types Gadducci et al. (2019). In addition, germline mutations of the genes BRCA1 and BRCA2, which encode proteins required to restore double-strand DNA breaks through homologous recombination, may lead to increased cancer predisposition. As an illustration, Reid et al. (2017) conducted a qualitative study to investigate risk factors associated with EOC. According to study findings, hormonal and reproductive risk factors were common in EOC; the incessant ovulation hypothesis dictates that the number of ovulatory cycles increases the cellular division linked to repairing of the surface epithelium after each ovulation; this increases voluntary mutations, which may be a high risk of spread of EOC. In addition, old age at menopause was another high-risk factor in EOC; old age at menopause may increase risk by increasing the number of

ovulatory cycles according to the incessant ovulation hypothesis. According to the scholars, other risk factors include environmental.

Lifestyle factors such as asbestos, talc powder exposures in which genital exposure to talc increases the risk of EOC, cigarette smoking which may increase the risk for mucinous OC in a dose-response manner, and high risk was significant among pre-menopausal women and post-menopausal women who used hormonal therapy linked to estrogen (Reid et al., 2017). In another study, Chang et al. (2018) conducted a qualitative study exploring the clinicopathologic characteristics of patients with epithelial ovarian cancer. Data was collected from 2498 patients. The researcher used qualitative data analysis methods such as multivariate data analysis techniques to analyze data. Chang et al. (2018) established different types of EOC had different outcomes; for example, patients with clear cell carcinoma had significantly worse results than those with serous carcinoma in advanced stages of EOC.

Similarly, Lheureux et al. (2019) explored challenges experienced in treating epithelial ovarian cancer using qualitative study methods on 4036 patients with epithelial ovarian cancer. The researchers found that increased risk factors such as death were more prevalent in patients with advanced-stage EOC even after surgery. Other acute risk factors include pleural effusion, small bowel obstruction, and venous thromboembolism. Overall, the articles reviewed suggest that epithelial ovarian cancer is one of the riskiest types of cancer globally that may lead to the death of women regardless of their age and despite advanced treatments over the past few decades. In addition, EOC has increased risk factors like hormonal and reproductive risks, advanced stage EOC, andtherapy resistance, which

leads to death. In the next paragraph, a discussion of Stromal cell carcinoma cancer is presented.

Previous researchers have identified stromal cell carcinoma cancer as a rare type of cancer in the ovaries (Revathy & Kanchana, 2018). Ovarian stromal tumors develop in the ovaries' structural connective tissue cells where female hormones estrogen and progesterone are produced. They may lead to the production of estrogen that causes abnormal vaginal bleeding, resulting in stromal cell ovarian cancer

For instance, Fujisawa et al. (2019) conducted a qualitative study to explore how stromal cells contribute to cancer stroma in human epithelial ovarian cancer in 76 patients. Data were analyzed, and the findings showed that FOXL2-positive cells in the ovarian lesion indicated CAFs markers, such as alpha-smooth muscle actin and fibroblast activating protein which revealed that ovarian stromal cells are the primary source of cancer stroma in the ovaries. The scholars reported risk factors which include abnormal uterine bleeding, tumors that produce testosterone which can result in cessation of menstrual periods and facial and body hair growth, abdominal bloating and severe abdominal pain, and endometrial hyperplasia where the lining of the uterus is abnormally thick caused by too many cells.

In a separate study, Ray et al. (2018) conducted a qualitative study to explore different types of ovarian cancer. After data analysis using ESMO methods, the researchers established that patients with Stromal cell carcinoma had subacute pelvic pain and menstrual irregularities. The risk factors increased with age and the advanced stage of the

disease. In addition, the prognosis of small cell carcinomas of the ovary hypercalcemic type is very poor, and this may lead to a high risk of spread of cancer and rapid relapse.

Lan et al. (2019) pioneered a study investigating the relationship between micro-environment composition and recurrence of stromal cell carcinoma cancer using a sample of 91 patients through qualitative research technique. Multivariate logistic regression analysis was used to analyze data. The researchers found that a high ratio of stromal cells may create an increased risk of resistance when treating stromal cell carcinoma cancer, and this recurrence may result in death. The researchers also established micro environment factors that contain a lot of stromal cells and immune cells in a tumor may lead to chemoresistance within cancer because of the presence of fibroblasts and myofibroblasts associated with platinum resistance.

Likewise, Keyvani et al. 2019 conducted a qualitative study to investigate factors leading to stromal cell ovarian cancer resistance. Data were analyzed, and it was concluded that lack of early detection of cell ovarian cancer might lead to a high risk of its spread, resulting in tumor recurrence even after surgery and may result in death. In addition, peritoneal ascites associated with ovarian cancer, where spheroids reside in tumor cells and survive and later proliferate even in a non-adherent status, may cause treatment resistance of stem cells, resulting in a relapse of tumors which is a risk factor in continuous treatment. The researchers identified other risk factors, including abdominal pain, palpable mass, and heavy, irregular vaginal bleeding.

Given the above literature, stromal cell carcinoma is a rare type of ovarian cancer. It may cause abnormal vaginal bleeding, recurrence, and relapse without early detection

even after treatment and severe abdominal pain. According to researchers, earlier detection and treatment of this type of cancer may lead to a total recovery of patients (Zang et al., 2018). Researchers have identified germ cell tumor cancer as a type of ovarian cancer that may have adverse effects, and it is discussed in the next paragraph.

Previous studies identified Germ Cell tumor cancer as another type of ovarian cancer. Gershenson et al. (2019) define ovarian germ cell cancer tumors as tumors that develop from the ovaries' reproductive cells or germ cells. They can be benign (non-cancerous) or malignant, which means cancerous. In addition, Malignant ovarian germ cell tumors most often occur in teenage girls and younger women (Lockley et al., 2019). Germ cell tumor cancer is mainly inherited congenital disabilities or genetic conditions resulting from chromosomal abnormalities, which may increase the risk of developing the disease (Gershenson et al., 2019). For example, Lakshmanan et al. (2018) conducted a qualitative study to explore the experiences of germ cell tumor cancer patients. Data was collected from 39 patients. After analyzing participants' responses, the findings showed that dysgerminoma was common among the patients and caused dysregulation of the hormone beta-human chorionic gonadotropin in pregnant women. This may lead to unhealthy infants or the death of infants. Other risk factors established by the researchers include abdominal swelling and pain, abdominal mass, and vaginal bleeding after menopause.

Sadfa et al. (2021) intended to explore the characteristics of germ cell tumors in different age groups among women through a qualitative study with a sample of 100 participants. The researchers established that dysgerminoma and yolk sac tumor was the most common type of tumor among women characterized by risk factors like abdominal

pain and distention. In addition, the researchers identified pelvic discomfort, cramping, ovarian pain, swollen and bloated belly, nausea, irregular vaginal bleeding, and problems with bowels such as constipation.

Tamauchi et al. (2018) performed a study to explore the reproductive experiences of germ tumor cancer survivors. Data was collected through administered questionnaires from 135 patients. After data analysis, some participants reported miscarriages; a large percentage were fertile and gave birth to healthy babies, and very few reported infertilities. According to the researchers, other risk factors identified were pre- mature menopause and loss of 1 ovary because of chemotherapy. Derquin et al. (2020) conducted a qualitative study to investigate factors that cause germ cell cancer tumors. Data were collected from 147 patients. According to study findings, congenital disabilities that affect the nervous system, genitals, urinary tract, and genetic conditions that cause extra or missing sex chromosomes likely induce germ cell cancer tumors among women. In addition, there were increased relapse cases after treatment, and chemotherapy and disease progression caused death in patients. The above analysis shows that ovarian germ cell malignant tumors are rare, common among young women, and caused by abnormal genetic chromosomal abnormalities. However, germ cell ovarian cancer is not as lethal as epithelial ovarian cancer, and they mainly affect one ovary, which is curable if detected early.

Diagnosis of Three Types of Cancers

There are three different types of ovarian cancer diagnoses. The first method includes blood tests used to check for high levels of a marker called CA-125. Another diagnosis method is imaging tests, including transvaginal ultrasound, an MRI scan, or a

CT scan. The third approach used to diagnose ovarian cancers is laparoscopy. A healthcare professional inserts a thin tube with a camera attached through a small hole in the abdomen to see the ovaries and perhaps take a tissue sample for a biopsy. The last approach is a biopsy, which includes the microscopic examination of a tissue sample. Only a biopsy approach can confirm the presence of ovarian cancer.

Treatment of Three Ovarian Cancers

Epithelial Ovarian Cancer Treatment

There are three forms of treatment for epithelial ovarian cancer: surgery, chemotherapy, advanced drugs, and radiation, but radiation is rarely used. For example, Lheureux et al. (2019) conducted a qualitative study exploring methods of managing epithelial ovarian cancer. The researchers established that surgery is considered the most effective treatment method for epithelial ovarian cancer, and treatment is based on histologic subtype and the stage at diagnosis. Surgery enables accurate surgical staging, documented using the International Federation of Gynecology and Obstetrics (FIGO). There are several types of surgery: primary debulking surgery, interval debulking surgery, and secondary debulking surgery for recurrent debulking surgery for epithelial ovarian cancer. Primary debulking surgery is surgical staging done by a qualified gynecologic oncologist. It entails laparotomy through a midline incision, with a full exploration of the abdomen and pelvis, followed by at least total abdominal hysterectomy, bilateral salpingo-oophorectomy, and omentectomy (Chiofalo et al., 2019). Interval debulking surgery is done after three cycles of chemotherapy have begun because surgery cannot be done immediately due to the disease's extensiveness the clinical state of the patient, or logistic

reasons. Neoadjuvant chemotherapy and interval debulking surgery have been proposed to manage advanced EOC as they increase the rate of complete cytoreductive surgery and help reduce morbidity and mortality. Secondary debulking surgery through Desktop III/ENGOT OV20 trial or platinum-sensitive EOC showed a 5-month improvement in progression-free survival (PFS) from 14 to 19.6 months in patients.

Kurnit et al. (2021) conducted a qualitative study to investigate advanced methods of treating EOC. After data analysis, the researchers found standard chemotherapy as a treatment method using a combination of carboplatin and paclitaxel administered once every three weeks and linked to improved outcomes. The combined therapy of paclitaxel and carboplatin using a randomized EWOC-1 trial is mainly considered for older patients with poor performance. It may improve outcomes compared with the group that received single-agent carboplatin (Falandry et al., 2019). In addition, the researchers also found intraperitoneal chemotherapy that used the original GOG 172 protocol showed an a16-month overall survival benefit for women who underwent this type of chemotherapy compared to those who underwent intravenous chemotherapy (Kurnit et al. (2021). Furthermore, Intraperitoneal chemotherapy has been advanced to hyperthermic intraperitoneal chemotherapy, which is connected with an improved recurrence-free survival of 14 vs. 11 months, and overall survival of 46 vs. 34 months compared with the standard treatment arm with comparable complication rates (Lee & Wang, 2020).

Onda et al. (2020) conducted a qualitative study using a sample of 301 patients to investigate the impact of neoadjuvant chemotherapy. Neoadjuvant chemotherapy is treating a patient with cancer before their primary course of treatment to shrink cancerous

tumors using drugs bore administering other types of treatment. Onda et al. (2020) established that neoadjuvant chemotherapy permits the evaluation of tumor response to chemotherapy, the only precise predictor of outcome in osteosarcoma. Neoadjuvant chemotherapy could increase disease-free and overall survival through earlier treatment of microscopic metastatic foci if sufficient tumor shrinkage occurs. It may make a patient who would have required amputation eligible for limb-sparing surgery. In addition, neoadjuvant chemotherapy may improve postoperative healing because there is less urgency to resume chemotherapy.

In a different study, Osborne et al. (2017) conducted a qualitative study to explore the effect of radiation in treating EOC. Data were collected from 103 patients. The researchers established that patients with cervical cancer with para-aortic lymph node (PAN) metastases had improved concurrently with advances in treatment, including positron emission tomography (PET) and intensity-modulated radiation therapy (IMRT). Given the above literature, EOC has several types of treatment, and the treatments have advanced over the years, increasing patient survival rates. However, surgery was the most effective treatment method for epithelial cancer as it reduced the growth of the tumor, which may prevent the multiple spread of the disease.

Stromal cell carcinoma Treatment

Keyvani et al. 2019 conducted a qualitative study exploring the impact of targeted therapy treatment on patients with stromal cell carcinoma ovarian cancer. Targeted therapy of ovarian cancer stem cells to treat stromal cell carcinoma has proved to treat the disease through chemo signaling pathways and surface markers. (Keyvani et al., 2019). Chemo

signaling has several signaling pathways, including WNT, SONIC Hedgehog (SHH), NOTCH, PI3K/PTEN, and NF-kB, which are associated with stem cell properties through deregulation increases survival rates. According to the researchers, WNT signaling pathway is protective during embryogenesis, and tissue homeostasis as deregulation of the WNT pathway disrupts the natural growth and differentiation of colonic crypt stem cells. Disruption of the natural development of colonic crypt stem cells increases the expression of target genes such as c-myc and cyclin D, resulting in cancer stem cells (CSC) phenotype, which is an efficient approach to treating tumors. Furthermore, surface markers done through CD44+ SKOV3 cell lines were targeted by hyaluronic acid-paclitaxel (HA-TXL), resulting in decreased tumor weight and nodules and the addition of CD133+ OVCAR5-Luc cells was targeted, resulting in a considerable decrease in tumor progression. (Keyvani et al., 2019). Similarly, Ahmed et al. (2020) proposed investigating current treatment strategies for stromal cell carcinoma ovarian cancer. Data were analyzed, and the researchers reported the following advanced treatment for stromal cell carcinoma Folate Receptor

(FR), which targets the delivery of antibody-drug conjugate consisting of an anti-FRα antibody linked to a tubulin-disrupting maytansinoid DM4 drug where the potent antimitotic agent has shown promise in Phase 1 and 2 trials in several women who had moderate to high expression of FRα expression. Phase 1 and 2 trials showed tangible responses in patients with a median progression-free survival of 6.7 months. (Ahmed et al., 2020). Immunotherapy was another method reported by Ahmed et al. (2020) to have confirmed the presence of CD8+ and CD20+ TILs, which correlate positively with the

overall survival of cell carcinoma cancer patients. Also, the infiltration of both CD3+ and CD8+ tumor-associated lymphocytes (TILs) were linked with better overall survival, but CD8+ TILs were correlated with a more positive outcome. Analysis of CD8+ TILs in the tumor epithelium in some patients further revealed that the median survival for patients without TILs was 2.8 years.

In contrast, with low, moderate, or high TILs, survival was enhanced to 3 years, 3.8 years, and 5.1 years respectively (Ahmed et al., 2020). Therefore, Gil et al. (2020) proposed exploring the effective methods of treating stromal cell carcinoma ovarian cancer using qualitative methods. The research findings showed that the adjuvant therapy method is chemotherapy with CP, cisplatin, ifosfamide, paclitaxel, ifosfamide, and gemcitabine is used in treating cell carcinoma cancer. (Gil et al., 2020). In addition, surgery in treating stromal cell carcinoma helps achieve no residual tumor, and hormonotherapy can be an alternative treatment for low-grade stromal cell carcinoma ovarian cancer. (Gil et al., 2020). Overall, the articles reviewed suggest that targeted therapy treatment methods played a significant role in treating stromal cell carcinoma ovarian cancer signaling pathways and surface markers, which disrupt the natural growth of colonic crypt stem cells and decrease tumor weight and nodules.

Germ cell tumor Treatment

Uccello et al. (2020) conducted a qualitative study to explore anti-cancer treatment options for malignant ovarian germ cell tumors (MOGCTs). The researchers established that MOGCTs mainly occur in young women and girls, so fertility-sparing surgery and platinum-based chemotherapy treatment were the best methods to ensure high chances of

curing malignant ovarian germ cell cancer in all stages of the disease. The researchers also found that surgical staging is the first step in managing MOGCTs which involves exploratory laparotomy, peritoneal washing for cytology, omental biopsy, and unilateral oophorectomy, and selective removal of enlarged lymph nodes. Furthermore, cisplatin-based chemotherapy with surgery might have positive outcomes even in advanced or incompletely resected disease when trying to do fertility-sparing surgery treatment.

Similar to Uccello et al. (2020), Zamani et al. (2021) proposed exploring the impact of fertility-sparing surgery and chemotherapy treatment on germ cell ovarian cancer patients using qualitative methods with a sample of 79 patients. According to study findings, fertility-sparing surgery with adjuvant chemotherapy was reported as a safe treatment for germ cell cancer, resulting in a high fertility rate. In addition, surgery may involve an oophorectomy to remove one or both of your ovaries or fallopian tubes or a total hysterectomy when cancer has spread beyond fallopian tubes and ovaries. The researchers also established that chemotherapy is likely to be done for weeks or months and it may involve infusing drugs into one of the veins, which may kill cancer cells and stop them from multiplying. As evidenced by the above analysis, treatment of germ cell cancer is possible through fertility-sparing surgery with adjuvant chemotherapy, making it possible for young women to get pregnant and give birth to healthy children.

Cardiac Complications of Three Ovarian Cancer

Ovarian cancer patients and survivors are exposed to increased cardiac complications like arrhythmia, coronary artery disease, stroke, valvar heart disease, and pericarditis. As an illustration, Chang et al. (2017) conducted a qualitative study exploring

preventive measures and treatments for cardiovascular complications during epithelial ovarian cancer treatment. After data analysis, the researchers found that cancer therapies like chemotherapy and radiation treatment may lead to cardiovascular complications. Cardiovascular complications include heart failure due to hypertension (HTN), pulmonary HTN, and radiation-induced cardiovascular diseases. High rates of heart failure or cardiomyopathy and venous thromboembolism were significant in younger patients and those without previous cardiovascular disease.

In another study, Slavchev et al. (2021) conducted a qualitative study using a sample of 104 patients with advanced epithelial cancer to explore the effect of cardiovascular disease on survival in advanced EOC. Data were analyzed using multivariate Cox proportional regression analysis, and the findings showed cardiovascular comorbidities such as Heart Failure, Arrhythmia, and Heart Valve Complications.

Cardiovascular diseases are likely to delay cancer diagnosis, and systemic therapy medications for EOC are associated with a potential risk of cardiovascular complications referred to as cardio-toxicity. These complications include heart failure, arrhythmias, myocardial ischemia, and pericardial diseases, reported using taxanes and platinum drugs (Polonsky & DeCara, 2019). In addition, bevacizumab drugs for EOC treatment may lead to the development of arterial thrombosis.

Likewise, Minlikeeva et al. (2017) conducted a literature review using 15 articles investigating the relationship between EOC, heart disease, and hypertension. Data was collected through questionnaires, telephone interviews, and face-to-face interviews. After data analysis, the researchers established that hypertension and diabetes in EOC patients

might lead to complications like heart disease and myocardial infarction during chemotherapy. Turco et al. (2020) conducted a qualitative study exploring outcomes of surgery and chemotherapy treatment of EOC patients using bevacizumab. A sample of 7096 participants was used in the research. According to study findings, several participants reported cardiovascular complications after using surgery and chemotherapy using bevacizumab. Cardiovascular system (CVS) complications include aortitis, heart failure, pulmonary hypertension, thromboembolism, right ventricular thrombus, and arterial thrombosis. Overall, the articles suggest that chemotherapy and radiation treatment of EOC have adverse effects as they may lead to cardiovascular complications like pulmonary HTN, pericardial diseases, and thromboembolism, which may result in the recurrence of EOC and death. In addition, drugs used in surgery and chemotherapy like bevacizumab are associated with toxicity. This may lead to severe outcomes of cardiovascular complications like aortitis, heart failure, and pulmonary hypertension.

Xu et al. (2020) conducted a qualitative study on the effects of debulking surgery on patients with EOC using a sample of 5223 patients. The researchers found that surgical complications were expected because of age, black race, higher comorbidity burden, unscheduled admission, stage IV disease, and extensive resection. Comorbidities linked with postoperative complications included congestive heart failure, chronic obstructive pulmonary disease (COPD), and renal failure. Bouchard et al. (2020) conducted a systematic review using 35 articles to explore the intraperitoneal impact of chemotherapy and surgery in EOC treatment. The researchers established that cardiovascular

complications were reported in several cases because of cytoreductive surgery and g heated intraperitoneal chemotherapy, which may result in increased morbidity.

Newton et al. (2019) explored the toxicity levels of methods used to treat germ cell ovarian cancer using qualitative methods and a sample of 130 patients. The researchers found that neoadjuvant/adjuvant chemotherapy caused both long-term and short-term toxicities like cardiac failure, kidney injuries, and rare death cases. Maozi et al. (2020) conducted a qualitative study exploring molecular sub-types for germ cell ovarian cancer for clinical trial purposes. The researchers established that adjuvant therapy treatment using bleomycin, etoposide, and cisplatin (BEP) might have toxicities that may have adverse effects on patients, which include cardiomyopathy, potentially fatal secondary malignancies, and bleomycin-associated lung injury.

Similar to Maozi et al. (2020), Chovanec et al. (2017) conducted a systematic review of 83 articles exploring the consequences of long-term toxicity on germ cell cancer patients. The findings showed germ cell ovarian cancer survivors who used cisplatin and platinum-based chemotherapy treatment reported neuro and ototoxicity, secondary malignancies, cardiovascular complications, renal and pulmonary toxicities, hypogonadism, low quality of life, and infertility. Gernier et al. (2021) proposed exploring the effects of chemotherapy on germ cell ovarian cancer patients using qualitative methods. Data were collected from 134 patients through self-reported questionnaires. The descriptive analysis technique was used to analyze data; the literature reviewed that chemotherapy treatment may have adverse effects, including cardiovascular and pulmonary disease and neurotoxicity. According to findings, cisplatin and bleomycin

induce endothelial function alterations and damage that may trigger vascular diseases in patients with germ cell ovarian cancer. Utama et al. (2021) conducted a qualitative study on the impact of radiotherapy treatment on germ cell ovarian cancer using a sample of 1 participant. The researchers established that resection of tumors invades major vascular structures like the abdominal aorta, leading to vascular complications and death.

Lee et al. (2019) conducted a qualitative study to explore the effects of recurrent germ cell ovarian cancer using a sample of 1 participant. Data were analyzed, and the scholars reported that chemotherapy treatment using bevacizumab conducted on recurrent germ cell ovarian cancer might have adverse effects like vascular complications. As evidenced by the above analysis, the use of bevacizumab during chemotherapy in treating germ cell ovarian cancer may have adverse effects, including cardiovascular complications like cardiovascular and pulmonary disease attributed to toxicity, which may have long-term implications on patients.

Henning and Harbison (2017) conducted a qualitative study to investigate the side effects of cancer drugs on patients. The researchers reported that trastuzumab drug for cancer treatment might cause cardiac stunning while tyrosine kinase inhibitors can increase systemic arterial pressure and impair myocyte contractility. In addition, radiation therapy on the left chest can exacerbate the cardiotoxicity of these anticancer drugs, resulting in accelerated atherosclerosis, myocardial infarction, heart failure, and arrhythmias. Oliveri et al. (2018) conducted a systematic review using 47 articles exploring the impact of cancer and cardiovascular disease on patients' psychological well-being. According to the researchers, ovarian cancer patients who developed cardiovascular complications and other

disorders during treatment through chemotherapy and radiation developed anxiety and high levels of stress, depression, suicidal thoughts, negative impact on quality of life, and hopelessness in gene carriers.

Bertero et al. (2018) conducted a study using qualitative methods to explore the relationship between ovarian cancer and heart failure. The study findings revealed that radiation and chemotherapy treatments that use antineoplastic agents might lead to cardiovascular toxicity, resulting in heart failure (Bertero et al., 2018). In addition, Bertero et al. (2018) found that neurohormonal activation might stimulate tumor growth in heart failure because of chronic stress. In a different study, Minasian et al. (2019) conducted a qualitative study investigating measures taken to address cardiovascular toxicity during and after cancer treatment. The researchers found that cancer chemotherapy treatment is a significant cause of cardiovascular (CV) toxicity, leading to left ventricular ejection fraction, aorta disease, heart attack, deep vein thrombosis, pulmonary embolism, fatigue, and arrhythmia. Given the literature above, drugs in treating stromal cell ovarian carcinoma may cause cardiac stunning and increase systemic arterial pressure and impair myocyte contractility, resulting in cardiovascular complications. In addition, radiation treatment using drugs may cause cardiotoxicity, resulting in heart failure, arrhythmias, and death in rare cases.

Hypertension and Ovarian Cancers

Ovarian cancer is linked to hypertension complications in women. For instance, Minlikeeva et al. (2017) conducted a qualitative study exploring the link between hypertension and antihypertensive medication. According to the study findings, beta-

blockers were among the most commonly prescribed medications for treating hypertension. It may reduce ovarian cancer risk by inhibiting beta-adrenergic signaling, which helps limit the growth of ovarian tumors. In addition, hypertension was not associated with ovarian cancer risk. In another study, Huang et al. (2021) conducted a quantitative study to investigate the effects of antihypertensive medication on ovarian cancer patients. After data analysis, it was established that polytherapy treatment involving calcium-channel blockers was associated with high ovarian mortality. According to findings, Use of thiazide diuretics was not linked to ovarian cancer mortality.

Yang et al. (2020) pioneered a study to explore the controversy related to ovarian cancer and hypertension using qualitative methods. Data were analyzed, and the findings showed that long-term ingestion of some oral anti-hypertensive drugs was linked with risks of incident cancer and a short survival period. In addition, the renin- angiotensin system (RAS) was involved in regulating specific cancer tumor microenvironments, which may promote cancer invasion and the development of tumors.

Staples et al. (2019) conducted a qualitative study using a sample of 593 women with EOC to explore the effect of hypertension medication on African American women with EOC. Data analysis was done, and the scholars established that hypertension was associated with an increased risk of EOC because of the use of anti-hypertensive medication like diuretics, ARBS, and ace inhibitors. Heitz et al. (2017) conducted a qualitative study to explore the effect of beta-blockers on EOC patients. Data was collected from 801 patients, and a Multivariate analysis technique was used to analyze data. The findings revealed that intake of beta-blockers did not affect patients with EOC.

Cho et al. (2020) conducted a qualitative study using 878 patients to explore the effects of four types of antihypertensive medications on the survival outcomes of EOC. The researchers established that angiotensin receptor blockers (ARBs) were associated with decreased risk of disease progression and linked with a lower recurrence rate in EOC patients. All the other three types of antihypertensive medications did not have any beneficial effect on EOC patients. Overall, the literature reviewed revealed that hypertension was associated with an increased risk of EOC because of the use of treatment drugs like diuretics, which alters treatment of ovarian cancer, and long-term use of some oral anti-hypertensive drugs was linked with risks of incident cancer the short survival period of patients with EOC.

Barone et al. (2019) conducted a systematic review using 31 articles to explore the benefits of the renin-angiotensin system in carcinoma. The researchers established a significant protective effect on carcinoma recurrence only when combined with vitamin K or branched-chain amino acids. Still, there was no increase in survival rates overall. Most of the literature reviewed the beneficial effects of renin-angiotensin system (RAS) inhibitors on hepatocarcinogenesis. Mohammed et al. (2021) conducted a qualitative study to investigate the role of hypertension in the development of cancer tumors. The researchers found that hypertension was associated with an increased likelihood of developing certain cancers like carcinoma ovarian cancer and higher cancer-related mortality. In addition, angiotensin II, common in hypertensive patients, may stimulate the production of vascular endothelial growth factor (VEGF), which augments cancer-related angiogenesis. Likewise, Seretis et al. (2019) conducted a systematic review using 148

articles to explore the relationship between cancer and blood pressure. A multivariable analysis technique was used to analyze data. The results showed a positive relationship between hypertension and the risk of esophageal adenocarcinoma, squamous cell carcinoma, liver, and endometrial cancer. conducted a qualitative study to explore the impact of drugs to treat ovarian cancer. Daniele et al. (2021) established that neither blood pressure, antihypertensive treatment, nor the development of hypertension during bevacizumab was prognostic.

Richardson et al. (2018) conducted a qualitative study to determine the survival rates of women with recurrent ovarian cancer using paclitaxel and pazopanib using a sample of 106 women. Data analysis revealed that severe hypertension was more common on the pazopanib plus paclitaxel arm, and more patients discontinued treatment on the paclitaxel arm because of ovary cancer disease progression. Liu et al. (2019) conducted a qualitative study to explore the effects of Olaparib in ovarian cancer treatment. Data was collected from 90 patients. The participants reported that a combination of cediranib/olaparib significantly extended progression-free survival compared with olaparib alone in relapsed platinum-sensitive ovarian cancer. Finally, Sommer et al. (2017) conducted a qualitative study exploring the effect of hypertension on ovarian cancer patients. The researchers found that patients with cancer are likely to have a high incidence of hypertension, and this may be attributed to chemotherapy which is an independent risk factor for hypertension because of the direct effects of many agents on endothelial function, sympathetic activity, renin-angiotensin system activity, and nephrotoxicity.

Similarly, Plummer et al. (2019) intended to explore the management of hypertension to facilitate bevacizumab treatment of cancer. However, the literature revealed that hypertension might be a barrier to the initiation of bevacizumab treatment because it is a side effect of all angiogenesis inhibitors, leading to premature discontinuation of effective anti-cancer treatment (Plummer et al., 2019). Therefore, Hong et al. (2021) conducted a qualitative study to investigate factors leading to hypertension during cancer treatment, and a sample of 1802 patients with various cancer types participated in the research. As a result, the researchers reported crisis-level hypertension in ovarian cancer patients, and chemotherapy exposure was linked with an increase in the risk of any degree of hypertension compared to periods of no chemotherapy.

Huang et al. (2018) conducted a quantitative study on the impact of antihypertensive medications on ovarian cancer. The researchers established that beta-blockers, an antihypertensive agent, may reduce ovarian tumor aggressiveness, inhibit angiogenesis and metastasis, and improve survival. In addition, hypertension was not associated with ovarian cancer mortality, and the associations between antihypertensive medications and ovarian cancer mortality were stronger among women with a history of hypertension. Jiang et al. (2021) conducted a systematic review using ten articles and a sample of 2106 patients investigating the consequences of treating cancer patients with Atezolizumab and Bevacizumab (A-B) and hypertension risk. The heterogeneity analysis technique was used to analyze data. The findings revealed that patients treated with A-B were associated with a significantly increased risk of all-grade hypertension compared with

patients treated with atezolizumab. Risk factors like age and obesity may also have adverse effects on hypertension in patients with cancer.

Zao et al. (2019) conducted a qualitative study to explore advanced strategies used ineffective treatment of ovarian cancer. The researchers established that the signaling axis with losartan, an angiotensin receptor blocker, may reduce the extracellular matrix in ovarian tumors and the associated physical barriers that typically hinder drug delivery like increased hypertension levels. In addition, the analysis revealed that patients receiving angiotensin system inhibitors simultaneously with standard treatment for ovarian cancer showed more prolonged overall survival than patients on other antihypertensives. Armbrust et al. (2018) proposed investigating the benefits of hypertension drug treatment on cancer patients using qualitative methods. A total of 808 patients participated in the research, and the Cox regression analysis technique was used in the data analysis. The researchers found that residual tumor burden was associated with worse progression-free survival because of hypertension. Still, the management of hypertension may lead to bevacizumab treatment being effective in treating ovarian cancer. Santala et al. (2021) conducted a qualitative study using a sample of 12 122 ovarian cancer patients to explore the effect of the antihypertensive drug on the survival rate of ovarian cancer patients. According to the researchers, hypertensive drugs not associated with ovarian cancer survive five years after OC diagnosis. ACE-inhibitors may lead to survival benefits in women with ovarian cancer. As evidenced by the above analysis, hypertension drugs benefit patients with ovarian cancer. The use of beta-blockers, a common antihypertensive

agent, may reduce ovarian tumor aggressiveness, inhibit angiogenesis and metastasis, and improve survival.

Mortality of Three Ovarian Cancers

Ovarian cancer is the leading cause of death among women in the US and globally (Grossman et al., 2018). Research findings estimate that women's risk of developing ovarian cancer is 1.4, corresponding to 1 in 78 women. In the United States, statistics show that the ovarian cancer prevalence rate is estimated to be 11.4 per 100000 women from 2014-to 2019. The incidence rate in non-Hispanic women is calculated to be 12 per 100000 women, considered the largest group with the highest incidence of ovarian cancer compared to non-Hispanic black and Asian women. Racial or ethnic differences in ovarian cancer incidences are better expressed by the prevalence of risk factors across demographic factors. This shows that minority women in the United States are the most affected by ovarian cancer.

In 2018, it was estimated that nearly 185 deaths in the United States occurred because of ovarian cancer, representing 4% of total cancer-related mortality among women (Grossman et al., 2018). According to the researchers, the mortality rate of ovarian cancer was 3.9% in 2018. While ovarian cancer incidences are much higher in the human development index, researchers have expressed concerns about the reversing mortality rate of ovarian cancer. The highest mortality rate of ovarian cancer is reported in India, while the rate has steadily decreased in the United States and Europe. Studies have shown that mortality to significant racial is significantly higher among Africa American women, signifying limited access to timely treatment (Verdoodt et al., 2017). In addition, nearly

two-thirds of ovarian cancer mortality rates are attributed to high-grade serous carcinoma (Verdoodt et al., 2017). Commodities and delayed diagnosis are the major predictors of an increasingly higher mortality rate linked to ovarian cancer.

Over the years, there have been trends in ovarian cancer mortality. For instance, current research evidence demonstrates a gradual decrease in nonovarian cancer incidence since the early 1980s. Khazaei et al. 92021) noted that the prevalence rate of ovarian cancer dropped from 29%, from 16.5 per 100000 women in 1985 to 11.7 per 100000 in 2019. However, of great importance is to emphasize the varying trends in ovarian cancer mortality based on age. In whites and African Americans aged 65 years and older, the incidence rate of ovarian cancer has increased from 1975 until 1990 before declining steadily. The increase in ovarian cancer prevalence between 1975 and 1990 could be linked to a decline in birthrate during the early 20th century. During the period, epithelia ovarian cancer incidence declined by 20%. The drop in ovarian cancer incidence in white women is attributed partly to the reduced use of menopausal hormones following a landmark report in early 2002 that linked the practice to breast cancer. Women who use menopausal hormones have an increased risk of developing ovarian cancer at least ten years after its discontinuation.

However, the prevalence of ovarian cancer among women below 65 years has generally decreased at a steady rate since late 1975. The decrease has been linked to oral contraceptives, which may confirm risk reduction and a recent decline in older women. Among females who use oral contraceptives above 5 to 9 years, the risk of developing

ovarian cancer is reduced by nearly 35% while increasing its occurrence for almost 30 years following the discontinuation of drugs.

Khazaei et al. (2021) also suggested the mortality rate of ovarian cancer has reduced by 33% from 1976, 10 per 100000 women, to 6.7 per 100000 in 2019, attributed to improvement in treatment. In addition, death linked to ovarian cancer has decreased in the United States from 2015 to 2020 across racial groups. However, the minority are the most affected groups due to their socioeconomic status, limiting their early access to treatment.

Epithelial ovarian cancer mortality rate significantly varies by race, age, and ethnicity (Torre et al., 2018). Age distribution in serous carcinoma is much older than epithelia suspects. As such, non-Hispanic women are at risk of nearly 5.2 per 100000 epithelia ovarian cancer incidence (Khazaei et al., 2021). Asia pacific islander women have the lowest rates of epithelial ovarian cancer, almost 3.4 per 100000 women (Khazaei et al., 2021). The highest mortality rate of epithelial ovarian cancer is reported in Asian women. Non-Hispanic black women have the lowest mortality rate for all epithelial cancer suspects. However, there has been no specific reason for the low rate.

Compared to epithelial ovarian cancer, nonepithelial one affects younger women. The common cell includes germ cell tumors (Torre et al., 2-018). Statistics show that tumor cells, ovarian cancer, and germ cells tumor have the highest mortality rate in non-Hispanic black women, with an overall rate of 0.5 per 100000 women, representing fivefold more significance than among Asia pacific islander women (Khazaei et al., 2021). In summary, the evidence reviewed in this section demonstrates that ovarian cancer, both types, has a higher mortality rate among women. The higher mortality rate could be attributed to

underlying mortality rate factors such as age, gender, and ethnicity. Timely access to treatment is another critical factor that influences the mortality rate of ovarian cancer in women. Women with access to early screening, diagnosis, and treatment are less likely to die from ovarian cancer than those who have no timely diagnosis treatment of ovarian cancer.

Research Gaps

Previously, scholars have dedicated much attention to investigating ovarian cancer and its mortality rates in different settings. For instance, some pioneering studies have focused on ovarian cancers cause or risk factors. For example, Momenimovahed et al. (2019) conducted a longitudinal study in the United States to investigate ovarian the mortality rate of ovarian cancer. After completing the analysis, the investigator found that ovarian cancer varies significantly based on age, race, and ethnicity. However, the investigators recommended additional research focused on establishing the mortality rate of different types of ovarian cancer, not from general perspectives. Grossman et al. (2018) also conducted a qualitative study to investigate risk factors of ovarian cancer in other geographical locations. Again, however, the investigators recommended additional research to focus on establishing the mortality rate of ovarian cancer, given that their studies focused on risk factors of ovarian cancer. Thus, suggesting a gap that the current research seeks to address.

Additionally, Stewart et al. (2017) also used a qualitative study to investigate risk factors and treatment of ovarian cancer using a heterogeneous sample. After conducting the analysis, the investigators established age, genetics, and environmental factors as the

major risk factors for ovarian cancer. Given their findings, the researcher recommended additional research to expand on their study focused on establishing the mortality rate of ovarian cancer. This provided a gap in the literature that the current research seeks to address.

Verdoodt et al. (2017) also conducted a qualitative study to investigate the risk factors of ovarian cancer in the United States. According to their findings, the researchers found age, gender, and race directly related to ovarian cancer. However, the investigators did not research how socioeconomic factors and ovarian cancer stage influenced the mortality rates of ovarian cancer. Therefore, a gap in the literature needs to address how socioeconomic factors, age, gender, race, comorbidities, and ovarian cancer stage relate to ovarian cancer mortality rates, which the current study seeks to address (Grossman et al., 2018). Torre et al. (2018) also noted that despite the improvement in screening and treatment of ovarian cancer, limited studies have focused on establishing mortality of ovarian cancer diagnosed patients, length of stay, total charges, and their link with demographic factors such as age, gender, race, and socioeconomic status.

While several studies have been conducted on ovarian cancer from different perspectives, current literature reveals that limited studies have focused on patients with an ovarian cancer diagnosis, length of stay, total charges, and their association with age, gender, race, and socioeconomic status the United States (Khazaei et al., 2021). This study intends to address the current gap in the literature by investigating the mortality of patients with an ovarian cancer diagnosis, length of stay, total charges, and their association with

age, gender, race, socioeconomic status, number of procedures, number of diagnoses, comorbidities, and ovarian cancer stage in women with ovarian cancer in United States.

Summary

Ovarian cancer is one of the leading causes of death among women in the United States. It is estimated that nearly 10 in 78 women with ovarian cancer will succumb to the disease (Grossman et al., 2018). Its prevalence remains an issue of concern in the United States. Despite the advancement in diagnosis and treatment of ovarian cancer, there still exist gaps in the literature regarding the mortality rate of ovarian cancer based on age, gender, race, and ethnicity (Grossman et al., 2018). This study intends to address this gap in the literature by investigating how age, gender, race, and socioeconomic status relate to the mortality rates of women diagnosed with ovarian cancer in the United States. In this section, several aspects of ovarian cancer were discussed. First, the researcher provided a brief overview of ovarian cancer, the risk factors, causes, and treatment. In addition, the researcher presented a discussion of cardiac complications related to ovarian cancer. Other sections discussed include hypertension and ovarian cancer and the mortality of the three ovarian cancers.

CHAPTER III: MATERIAL AND METHODS

Nationwide Inpatient Sample Data

Data from Nationwide Inpatient Sample (NIS) was used to achieve the objectives of the present study. Permission for downloading and approval of the use of these data was obtained. Most clinicians and researchers commonly used the NIS data in their studies, especially related to the influence of patients' information effects on the patients' length of stay, total charges, and mortality. The primary patients' information in the NIS database were demographics, hospital characteristics, types and years of admissions, and comorbidities.

Data And Methods

The NIS dataset used in the present study is related to patients with ovarian cancer. Therefore, the data from 2010-to 2012 is considered for the study. The main variables of NIS data included comorbidities, length of stay, SES (socio-economic status), age, race, number of procedures, number of chronic conditions, etc. The comorbidities mainly addressed in this study are hypertension and congestive heart failure. The variables in the data set are segregated into dependent and independent variables. The dependent variables of the present study are the length of hospital stay, total charges, and incidence of mortality. Patients' demographic characteristics (age, gender, race, etc.), household income, comorbidities, and other clinical variables were considered independent variables. SPSS version 28.0 analyzes the data by doing appropriate statistical tests. All results with p values less than 0.05 were deemed to be

significant. The statistical analysis is done by various tests like chi-square, multiple regression.

Data Variables, Research Questions, Statistical Analysis Procedures

All variables involved to achieve the objectives of this study are illustrated in Appendix 2.

Study hypotheses and statistical tests

To answer the research questions, 10 hypotheses were tested using different statistical tests. All research questions, hypotheses, outcomes, independent variables, and statistical tests are illustrated in Appendix 3. The analysis and results of the present study are fully outlined in the next chapter.

CHAPTER IV: RESULTS AND ANALYSIS

Introduction

The purpose of this study was to investigate the mortality of patients with an ovarian cancer diagnosis, length of stay, total charges, and their association with age, gender, race, socioeconomic status (SES), number of procedures, number of diagnoses, comorbidities, and ovarian cancer stage, in a cohort of inpatients with ovarian in the United States. The instrument for data collection of this study was archival data, specifically the patient records of the selected patients with ovarian cancer in the United States. In addition, this study collected and analyzed demographics, socioeconomic status (ZIPINC), gender, race, length of stay, DIED, and TOTALCHG from NEDS 2010, 2011, and 2012. What now follows are the demographic characteristics of the sample. This includes age, gender, race, socioeconomic status (SES), number of procedures, number of diagnoses, comorbidities, length of stay, risk of mortality, and ovarian cancer stage type.

Demographic characteristics and health information

Age

There were N = 62 768 patients with ovarian cancer in the dataset. The ages of patients ranged from 0 to 103 (M = 45.75, SD = 18.06). The ages appeared to follow a normal distribution as assessed by visual inspection of a histogram (Figure 1). Additionally, skewness and kurtosis values were computed with SPSS. All values were within acceptable ranges to assess normality. Hair et al. (2010) and Bryne (2010) argued

that data is considered normal if skewness is between -2 to +2 and kurtosis is between -7 to +7.

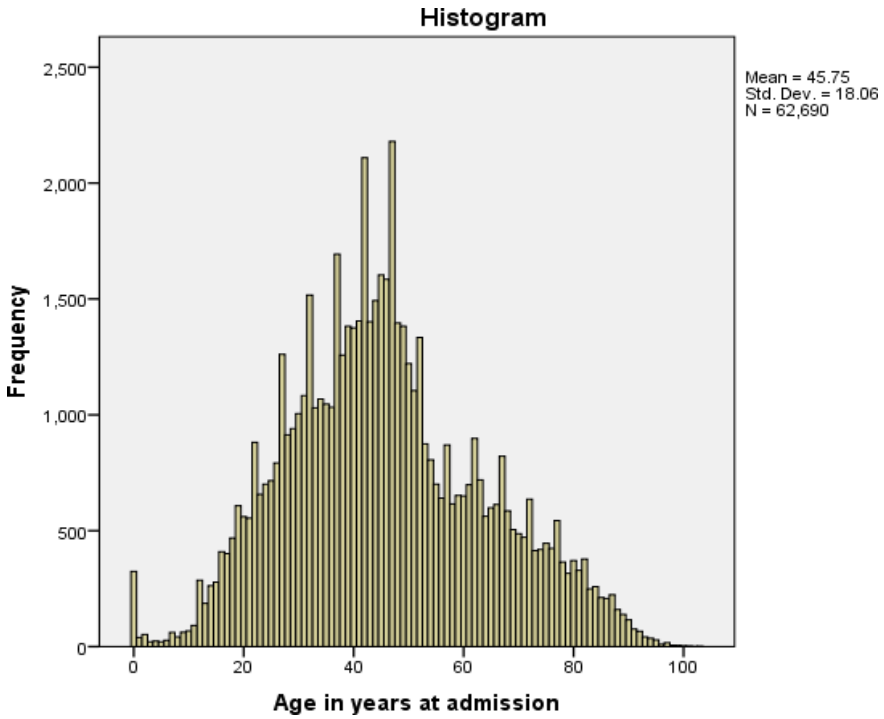

Figure 1: Histogram Depicting Distribution of Ages among Ovarian Cancer Patients

Gender

There were 62 319 (99.3%) females among ovarian cancer patients. There were 282 (0.4%) that identified with a male. Additionally, there were 167 (0.3%) no responses. Figure 2 below provides a bar chart that depicts this information.

Figure 2: Bar Chart Representing Gender of Ovarian Cancer Patients

SES

SES was measured by using the median household income national quartile for patients' zip code. Most were in the first quartile, 16,246 (25.9%). This was followed by the second quartile, 15,291 (24.4%); the third quartile, 15,397 (24.5%); and the fourth quartile, 14,488 (23.1%). There were 1346(2.1%) instances of no response. The bar chart in Figure 3 below depicts this information.

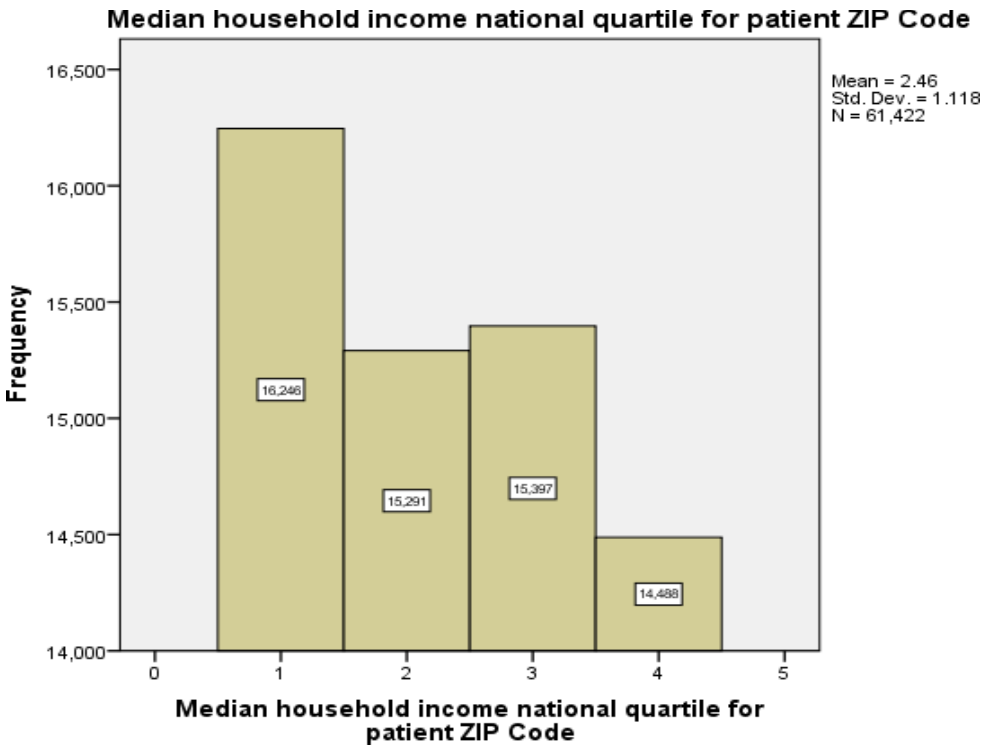

Figure 3: Median Household Income National Quartile of Ovarian Cancer Patients

Race

Regarding race, most were White, 36,201 (57.7%). This was followed by Black, 8414 (13.4%); Hispanic, 7209 (11.5%); Asian, 1692 (2.7%); some other race, 1660 (2.6%); and Native American, 459 (11.5%). This information is depicted in Figure 4 below.

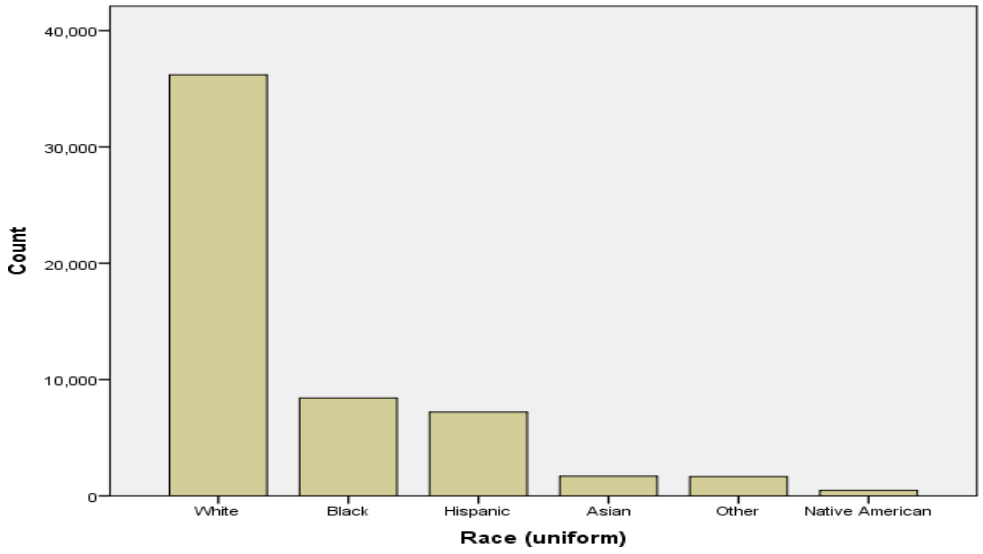

Figure 4: Bar Chart Depicting Race

Type of Ovarian Cancer

In this sample, there were three types of cancer under consideration: EOC (epithelial ovarian cancer), SCC (stromal cell carcinoma), and GCT (germ cell tumor). Most were SCC (76.2%). This was followed by EOC (23, 7%) and GCT (0.1%).

Mortality

Out of the *N* = 62, 768 ovarian cancer patients, 762 (1.2%) died and 61,998 (98.88%) did not die. The bar chart in Figure 5 depicts this information.

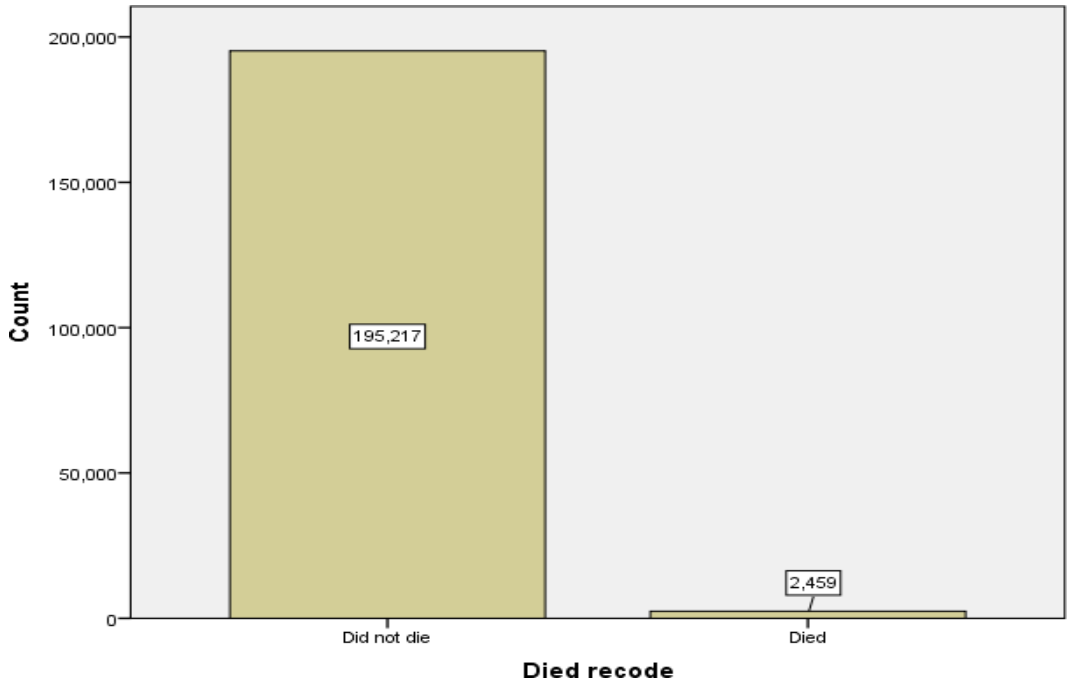

Figure 5: Bar chart Depicting Mortality of Ovarian cancer Patients

Length of Stay and Total Charge

Length of stay of patients ranged from zero to 29 days (M = 3.91, SD = 5.27). The total charge for services ranged from $108.00 to $1,401,187 (M = $32,738, SD = $43,109.00). Both length of stay and total charges were highly positively skewed as depicted in Figure 6 and 7 histograms.

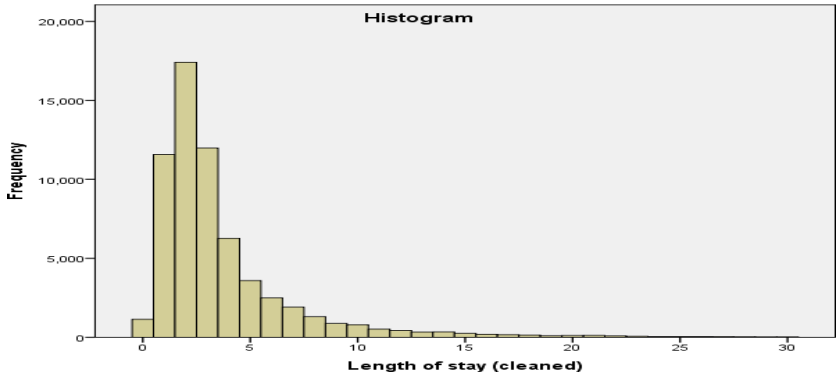

Figure 6: Histogram of Length of Stay of Ovarian Cancer Patients

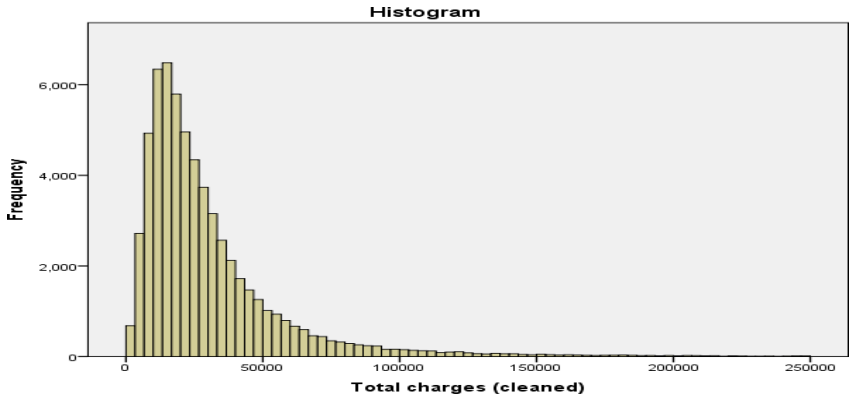

Figure 7: Histogram of Total Charge for Ovarian Cancer Patients

Number Of Procedures

The number of procedures ranged from zero to 31 (M = 2.47, SD = 2.26). The skewness and kurtosis values suggested that the deviation from normality, as shown in Figure 8, is not severe. As skewness and kurtosis values were in acceptable ranges.

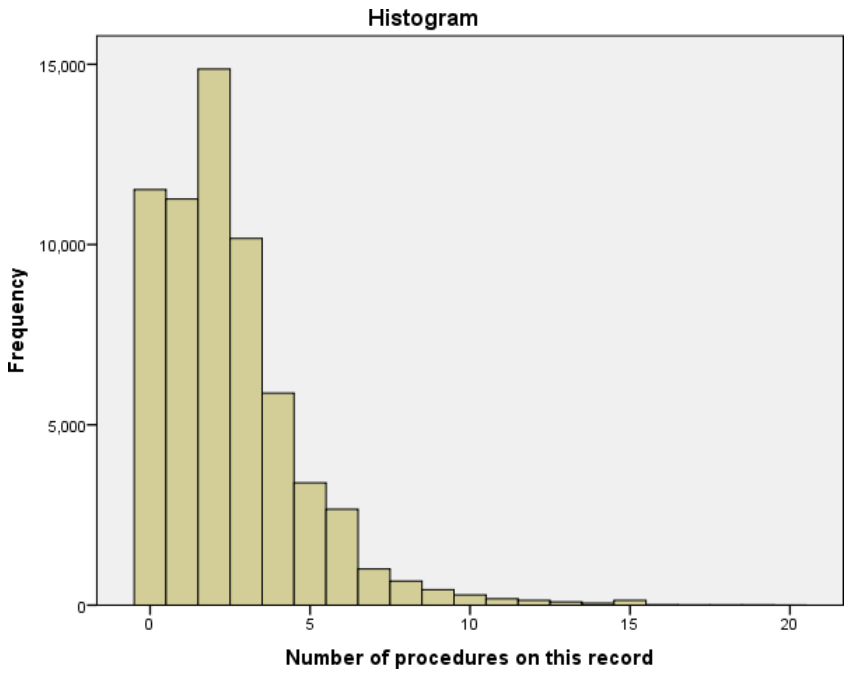

Figure 8: Histogram of the Number of Procedures

Comorbidities

There were several comorbidities measures included in the NIS data set. The top five were hypertension, 16,995 (27.1%); deficiency anemia, 9335 (14.9%); Fluid/Electrolyte disorders, 9318 (14.8%); Chronic pulmonary disease, 6956 (11.1%); and Obesity, 6481 (10.3%). The complete list of comorbidities is provided in Table 1.

Table 1: Comorbidity Measures

	N	%
Hypertension	16995	27.1%
Deficiency anemia	9335	14.9%
Fluid /electrolyte disorders	9318	14.8%
Chronic pulmonary disease	6956	11.1%
Obesity	6481	10.3%
Depression	5893	9.4%
Hypothyroidism	5700	9.1%
Diabetes, uncomplicated	5682	9.1%
Metastatic cancer	4199	6.7%
Solid tumor without metastasis	4041	6.4%
Weight loss	2254	3.6%
Other neurological disorders	2006	3.2%
Chronic blood loss anemia	1833	2.9%
Psychoses	1768	2.8%
Coagulopathy	1661	2.6%
Renal failure	1595	2.5%
Congestive heart failure	1314	2.1%
Valvular disease	1248	2.0%
Drug abuse	1128	1.8%
Rheumatoid arthritis/collagen vascular diseases	1123	1.8%
Liver disease	1045	1.7%
Pulmonary circulation disorders	838	1.3%
Alcohol abuse	677	1.1%
Peripheral vascular disorders	672	1.1%
Diabetes with chronic complications	643	1.0%
Paralysis	401	0.6%
Lymphoma	93	0.1%
Acquired immune deficiency syndrome	55	0.1%
Peptic ulcer disease excluding bleeding	17	0.0%

Mortality And Type Of Ovarian Cancer

The association between mortality and type of ovarian cancer (EOC -epithelial ovarian cancer, SCC- stromal cell carcinoma, GCT - germ cell tumor) was assessed by conducting Chi-square tests of association to address this first research question:

RQ1: Is there an association between mortality and type of ovarian cancer?

The results of the Chi-square test was significant, $\chi 2(2) = 505.628$, $p < .001$ (Table 2). There was a significant association between mortality and type of ovarian cancer. Specifically, as depicted in Table 3, more people died in the EOC category than in other types of ovarian (EOC- 213, SCC- 5, GCT-0).

Table 2: Chi-Square Tests

	$\chi 2$	*df*	*P*
Pearson Chi-Square	505.628	2	<.001
Likelihood Ratio	488.849	2	<.001
Linear-by-Linear Association	504.647	1	<.001
N of Valid Cases	20075		

Table 3: Mortality by Cancer Stage Tabulation

		EOC	SCC	GCT	Total
Died during hospitalization	No	5606	14243	8	19857
	Yes	213	5	0	218
Total		5819	14248	8	20075

Mortality And Type Of Ovarian Cancer Patient With Congestive Heart Failure (CHF)

The association between mortality and type of ovarian cancer with CHF was assessed by conducting Chi square tests of association to address this second research question:

RQ2: Is there an association between mortality and type of ovarian cancer patients with Congestive heart failure?

The Chi-square test results were significant, $\chi 2(2) = 9.115$ p =.003 (Table 4). There was a significant association between mortality and type of ovarian cancer among patients with CHF. Specifically, as depicted in Table 5, among those patients that died, there were more in the EOC group than in any other group.

Table 4: Chi-Square Tests

	$\chi 2$	*df*	*P*
Pearson Chi-Square	9.115	2	.003
Continuity Correction[b]	7.841	2	.005
Likelihood Ratio	11.195	2	.001
Fisher's Exact Test			
Linear-by-Linear Association	9.089	2	.003
N of Valid Cases	356		

Table 5: Mortality by Cancer Stage of Patients with CHD patients with CHF

		EOC	SCC	GCT	Total
Died during hospitalization	No	202	130	0	332
	Yes	22	2	0	24
Total		224	132	0	356

Mortality And Type of Ovarian Cancer Patient With Hypertension (HTN)

The association between mortality and type of ovarian cancer with HTN was assessed by conducting Chi-square tests of association to address this third research question:

RQ3: Is there an association between mortality and type of ovarian cancer patients with HTN?

The results of the Chi-square test was significant, $\chi 2(2) = 104.946$, $p < .001$ (Table 6). There was a significant association between mortality and type of ovarian cancer among patients with HTN. Specifically, as depicted in Table 7, among those patients that died, there were more in the EOC group than any other group.

Table 6: Chi-Square Tests

	$\chi 2$	*df*	*P*
Pearson Chi-Square	104.946[a]	2	<.001
Likelihood Ratio	122.761	2	<.001
Linear-by-Linear Association	104.709	1	<.001
N of Valid Cases	5695		

a. 2 cells (33.3%) have expected count less than 5. The minimum expected count is .04.

Table 7: Mortality by Cancer Stage of Patients with HTN

		EOC	SCC	GCT	Total
Died during hospitalization	No	2301	3310	3	5614
	Yes	79	2	0	81
Total		2380	3312	3	5695

Predictors of The Length Of Stay Of Patients With Ovarian Cancer

Multiple linear regression was conducted in order to address this fourth research question:

RQ4: Are there predictors for the length of stay of patients with ovarian cancer? Multiple regression was conducted with SPSS software which included the independent variables of age, race, SES, comorbidities, number of diagnoses, and number of procedures. The dependent variable was the length of stay. A forward selection process was chosen to determine the best combination of significant predictors.

There was approximate normality of regression residuals (Figure 9) and homoscedasticity and collective linearity (Figure 10). Figure 9 shows an approximate symmetric distribution mound-shaped distribution, which justifies approximate normality. Additionally, the non-random pattern in the scatter plot of Figure 10 suggests homoscedasticity and collective linearity between the independent variables and the dependent variable. There were no significant outliers in the regression residuals and no multicollinearity, as indicated by all variance inflation factors below 5.0.

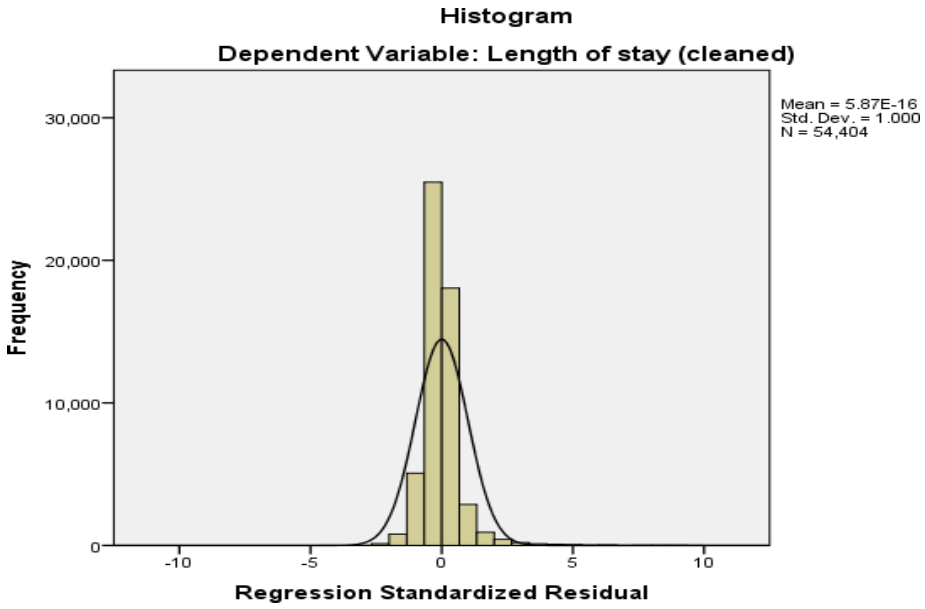

Figure 9: Histogram of Length of Stay

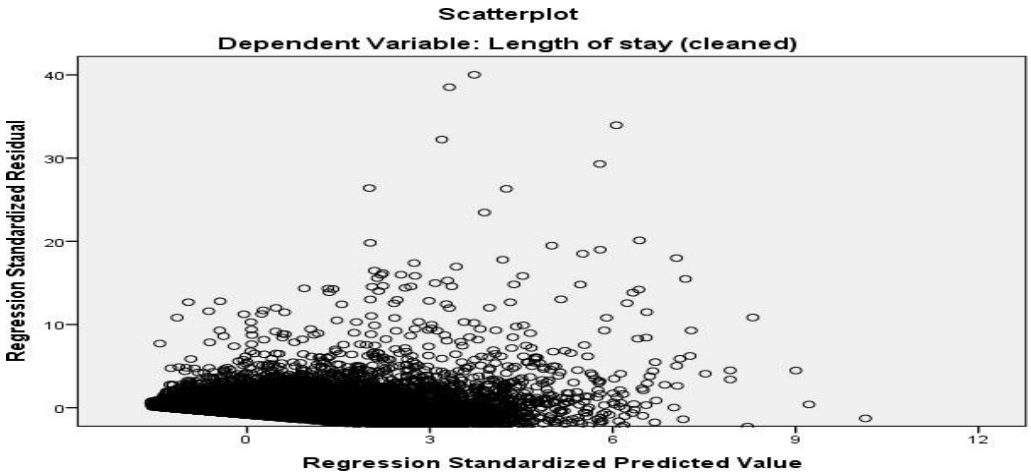

Figure 10: Scatter Plot of Predicted Versus Regression Residuals

The overall model was significant, $F(31, 54403) = 686.809$, $p < .001$. There were significant predictors of number of diagnoses ($b = 0.300$, $p < .001$); number of procedures ($b = 0.649$, $p < .001$); age ($b = -.012$, $p < .001$); Race (White: $b = -.419$, $p < .001$); SES ($p < .01$); and comorbidities ($p < .001$). The increasing number of diagnoses ,procedures, and

SES results in an average increase in length of stay. Increasing age and being White results in an average decrease in length of stay. Regarding comorbidities, there were several that were significant predictors which are listed in Appendix 1. The comorbidity that had that most significant effect was weight loss which had the largest standardized regression coefficient ($b = 3.519$, $p < .001$). Those patients with weight loss comorbidities resulted in the greatest mean increase in length of stay.

Predictors of the Length of Stay of Patients with Ovarian Cancer Hypertension

Multiple linear regression was conducted in order to address this fifth research question

RQ5: Are there predictors for the length of stay of patients with ovarian cancer hypertension?

Multiple regression was conducted with SPSS software which included the same independent variables as RQ4. However, only those that had hypertension were selected. A forward selection process was chosen to determine the best combination of significant predictors. There was approximate normality of regression residuals (Figure 11) and homoscedasticity and collective linearity (Figure 12). Figure 11 shows an approximate symmetric distribution mound-shaped distribution, which justifies approximate normality. Additionally, the nonrandom pattern in the scatter plot of Figure 12 suggests homoscedasticity and collective linearity between the independent variables and the dependent variable. There were no significant outliers in the regression residuals and no multicollinearity, as suggested by all variance inflation factors below 5.0.

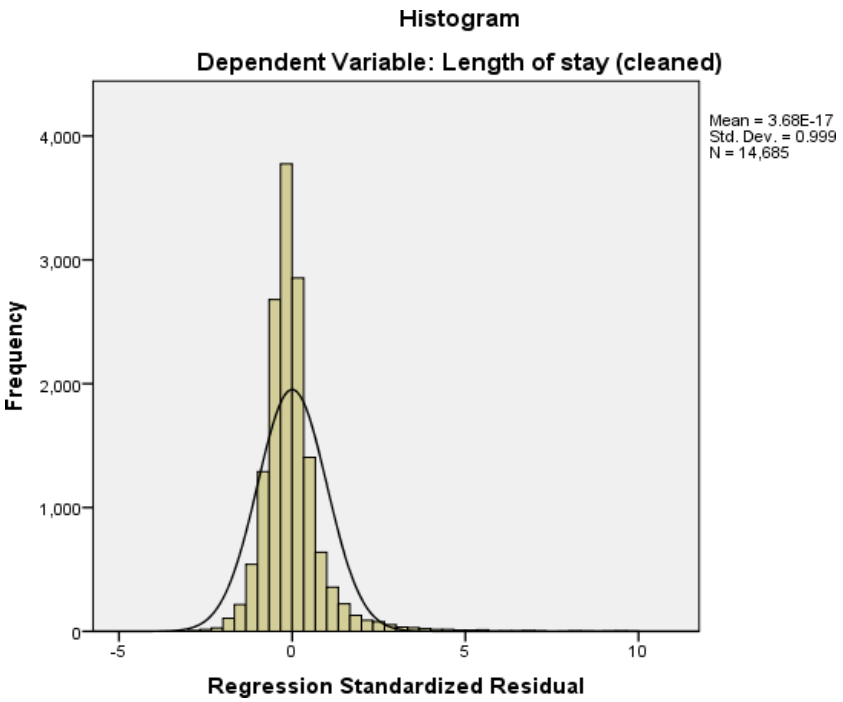

Figure 11: Histogram of Length of Stay

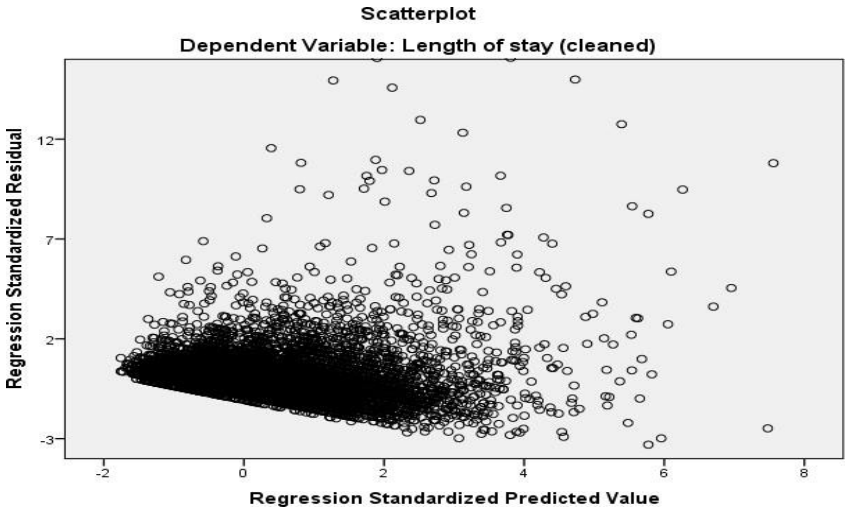

Figure 12: Scatter Plot of Predicted and Regression Residuals

The overall model was significant, $F(16, 14684) = 442.684$, $p < .001$. There were significant predictors of number of diagnoses ($b = 0.245$ $p < .001$); number of procedures ($b = 0.706$, $p < .001$); age ($b = .009$, $p < .001$); Race (White: $b = -.594$, $p < .001$); SES (First quartile: $b = 0.398$, $p < .001$)); and comorbidities ($p < .001$). The increasing number of diagnoses, procedures, age, and SES results in an average increase in length of stay. Being White results in an average decrease in length of stay. Regarding comorbidities, there were several that were significant predictors which are listed in Table 8. The comorbidity that had that most significant effect was weight loss which had the largest standardized regression coefficient ($b = 3.145$, $p < .001$). Those patients with weight loss comorbidities resulted in the greatest mean increase in length of stay.

Table 8: Comorbidities

Variable	B	SE	β	*t*	*p*	Tolerance	VIF
(Constant)	-.945	.166		-5.711	.000		
NDX	.245	.010	.226	25.743	.000	.595	1.680
NPR	.706	.015	.324	45.865	.000	.918	1.089
CM_WGHTLOSS	3.145	.174	.129	18.065	.000	.902	1.109
CM_LYTES	1.344	.098	.103	13.753	.000	.817	1.223
CM_TUMOR	1.284	.127	.072	10.121	.000	.899	1.112
CM_METS	1.257	.130	.070	9.645	.000	.879	1.137
White	-.594	.083	-.052	-7.164	.000	.887	1.127
CM_PARA	2.817	.404	.048	6.972	.000	.985	1.016
CM_OBESE	-.544	.104	-.037	-5.229	.000	.899	1.112
CM_PULMCIRC	1.564	.265	.041	5.900	.000	.961	1.040
CM_CHF	.759	.179	.030	4.238	.000	.908	1.102
FirstQuartile	.398	.083	.033	4.782	.000	.957	1.045
CM_COAG	.843	.203	.029	4.158	.000	.950	1.053
CM_ANEMDEF	.385	.097	.029	3.987	.000	.890	1.124
AGE	.009	.003	.028	3.578	.000	.770	1.299
CM_NEURO	.463	.186	.017	2.489	.013	.973	1.028

Multiple linear regression was conducted in order to address this sixth research question

RQ6: Are there predictors for total charges of patients with ovarian cancer?

Multiple regression was conducted with SPSS software which included the independent variables of age, race, SES, comorbidities, number of diagnoses, and number of procedures. The dependent variable was a total charge. A forward selection process was chosen to determine the best combination of significant predictors. There was approximate normality of regression residuals (Figure 13) and homoscedasticity and collective linearity (Figure 14). Figure 13 shows an approximate symmetric distribution mound-shaped distribution, which justifies approximate normality. Additionally, the nonrandom pattern in the scatter plot of Figure 14 suggests homoscedasticity and collective linearity between the independent and dependent variables. There were no significant outliers in the regression residuals and no multicollinearity, as indicated by all variance inflation factors below 5.0.

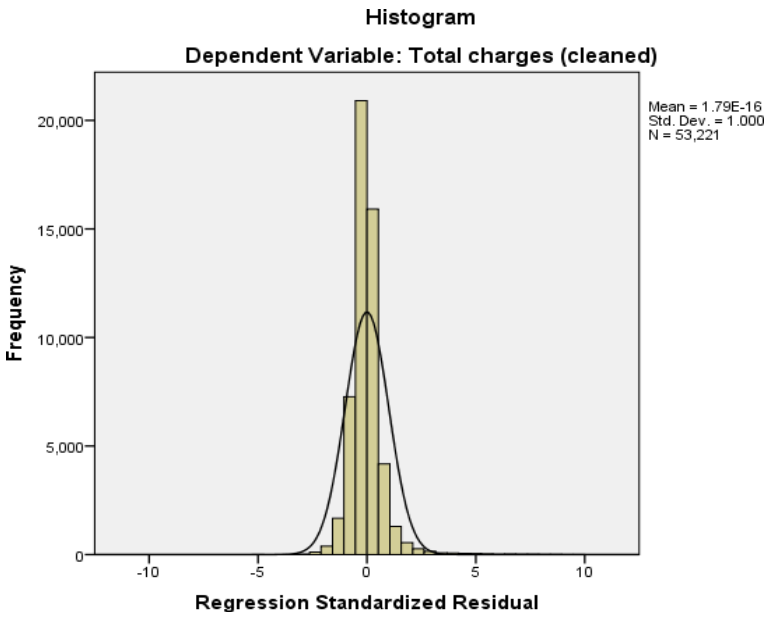

Figure 13: Histogram of Total Charges

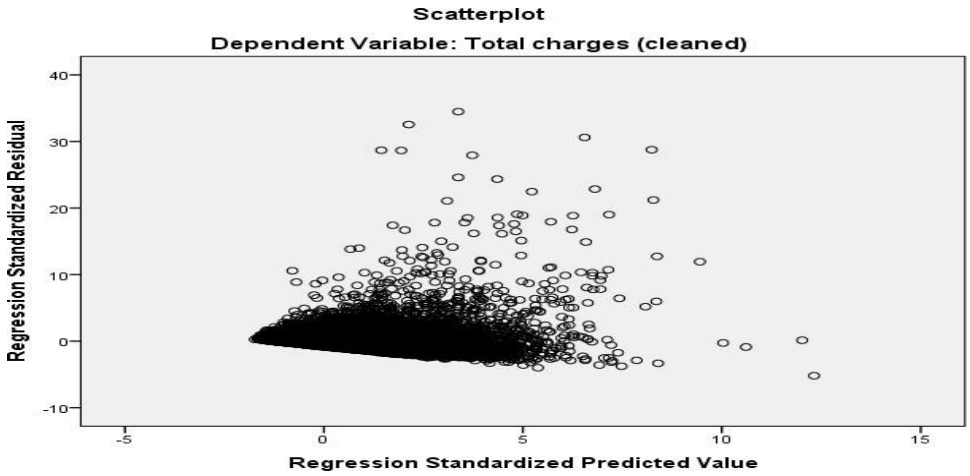

Figure 14: *Scatter Plot of Predicted and Regression Residuals*

The overall model was significant, $F(27, 53221) = 442.684$, $p < .001$. There were significant predictors of number of diagnoses ($b = 1817.379$, $p < .001$); number of procedures ($b = 7696.833$, $p < .001$); age ($b = -134.790$, $p < .001$); Race (White: $b = -5657.613$, $p < .001$; Black:$b = -2636.244$, $p < .001$; Hispanic: $b = 4256.601$; $p < .001$);

SES (First quartile: b = -2189.839, p < .001; Second quartile: b = -1622.247); and comorbidities (p < .001). The increasing number of diagnoses, procedures, age, and being Hispanic results in an average increase in total cost. Being White or Black results in an average decrease in total cost. Regarding comorbidities, there were several that were significant predictors which are listed in Table 9. The comorbidity that had that most significant effect was weight loss which had the largest standardized regression coefficient (b = 21352.657, p < .001). Those patients with weight loss comorbidities resulted in the greatest mean increase in total charge.

Table 9: Regression Coefficients for RQ 6

Variable	B	SE	B	*t*	*p*	Tolerance	VIF
(Constant)	8164.474	799.633		10.210	.000		
NPR	7696.833	75.926	.396	101.372	.000	.874	1.144
NDX	1817.379	50.097	.194	36.277	.000	.465	2.150
CM_WGHTLOSS	21352.657	930.096	.089	22.957	.000	.885	1.130
CM_LYTES	8411.445	506.080	.068	16.621	.000	.798	1.253
Hispanic	4256.601	777.362	.032	5.476	.000	.384	2.603
CM_METS	9128.324	707.276	.051	12.906	.000	.846	1.182
AGE	-134.790	11.379	-.055	-11.846	.000	.617	1.619
CM_CHF	11443.593	1185.986	.037	9.649	.000	.908	1.101
CM_TUMOR	6517.147	702.620	.036	9.275	.000	.884	1.131
CM_PARA	18036.682	2079.138	.032	8.675	.000	.974	1.027
CM_COAG	9283.202	1040.581	.034	8.921	.000	.943	1.060
White	-5657.613	665.740	-.061	-8.498	.000	.261	3.831
CM_PULMCIRC	11400.553	1453.321	.029	7.844	.000	.956	1.046
CM_BLDLOSS	-6981.640	978.537	-.026	-7.135	.000	.977	1.023
CM_DEPRESS	-3473.728	578.020	-.023	-6.010	.000	.935	1.069
First Quartile	-2189.839	399.397	-.022	-5.483	.000	.839	1.192
CM_OBESE	-2173.089	561.983	-.015	-3.867	.000	.922	1.085
CM_NEURO	4037.118	944.809	.016	4.273	.000	.954	1.048
Second Quartile	-1622.247	402.247	-.016	-4.033	.000	.879	1.138
CM_VALVE	-4769.757	1157.516	-.015	-4.121	.000	.958	1.044
CM_HTN_C	-1452.361	428.878	-.015	-3.386	.001	.723	1.383
Black	-2636.244	766.836	-.021	-3.438	.001	.348	2.873
CM_CHRNLUNG	-1604.648	537.949	-.011	-2.983	.003	.935	1.070
CM_HYPOTHY	-1605.472	584.700	-.010	-2.746	.006	.931	1.074
CM_LYMPH	-9968.235	4157.408	-.009	-2.398	.017	.997	1.003
CM_AIDS	12443.809	5577.497	.008	2.231	.026	.996	1.004
CM_ALCOHOL	3408.956	1603.295	.008	2.126	.033	.980	1.020

Multiple linear regression was conducted in order to address this seventh research question

RQ7: Are there predictors for total charges of patients with ovarian cancer Congestive heart failure?

Multiple regression was conducted with SPSS software which included the same independent variables as RQ6. However, those individuals that had congestive heart failure were selected. The dependent variable was a total charge. A forward selection process was chosen to determine the best combination of significant predictors. There was approximate normality of regression residuals (Figure 15) and homoscedasticity and collective linearity (Figure 16). Figure 15 shows an approximate symmetric distribution mound-shaped distribution, which justifies approximate normality. Additionally, the nonrandom pattern in the scatter plot of Figure 16 suggests homoscedasticity and collective linearity between the independent and dependent variables. There were no significant outliers in the regression residuals and no multicollinearity, as indicated by all variance inflation factors below 5.0.

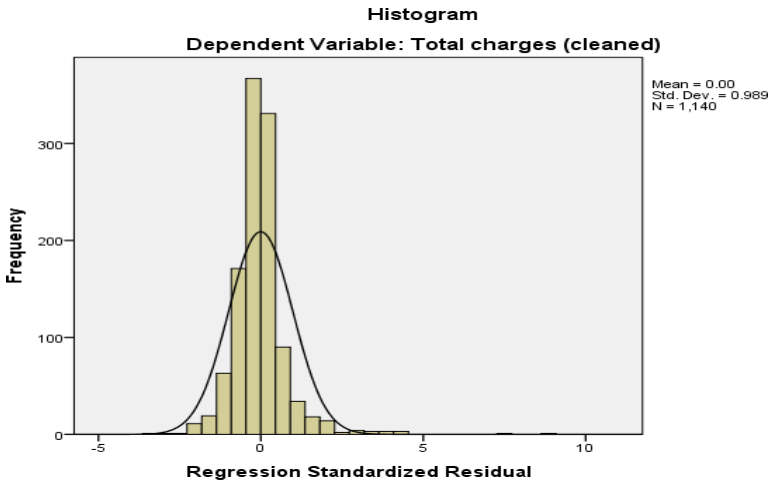

Figure 15: Histogram of Total Charges

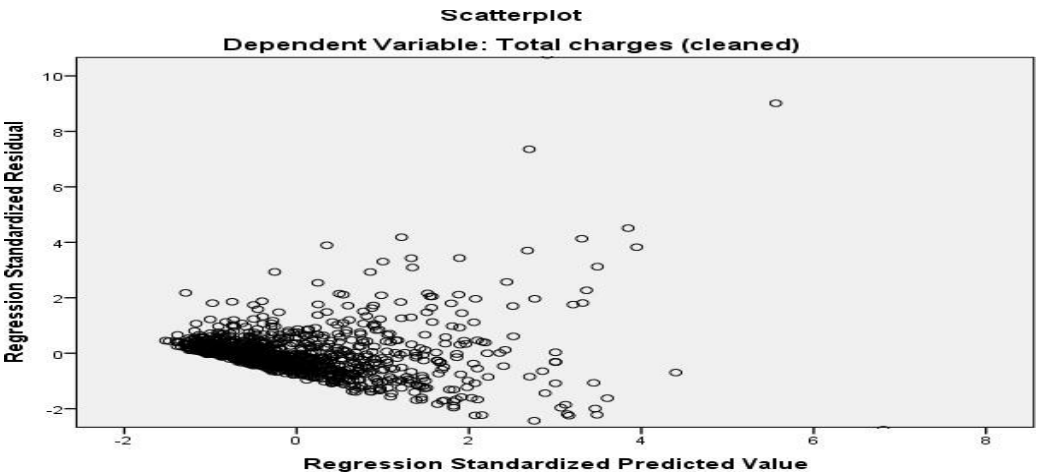

Figure 16: Scatter Plot of Predicted Versus Regression Residuals

The overall model was significant, $F(10, 1103) = 70.536$, $p < .001$. There were significant predictors of number of diagnoses ($b = 2566.123$, $p < .001$); number of procedures ($b = 14123.750$, Race (Hispanic: $b = 45497.149$, $p < .001$); and comorbidities ($p < .001$). The increasing number of diagnoses, procedures, and being Hispanic results in an average increase in total cost. Regarding comorbidities, there were several that were significant predictors, which are listed in Table 11. The comorbidity that had the most significant effect was weight loss which had the largest standardized regression coefficient ($b = 22286.352$, $p < .001$). Those patients with weight loss comorbidities resulted in the greatest mean increase in total charge.

Table 11: Regression Coefficients for RQ 7

Variables	B	SE	B	*t*	*p*	Tolerance	VIF
(Constant)	-15499.988	6394.448		-2.424	.016		
NPR	14123.750	720.045	.496	19.615	.000	.864	1.157
NDX	2566.123	428.663	.162	5.986	.000	.753	1.329
Hispanic	45497.149	8475.871	.127	5.368	.000	.989	1.011
CM_WGHTLOSS	22286.352	6500.030	.084	3.429	.001	.913	1.095
CM_COAG	25131.287	7925.645	.076	3.171	.002	.951	1.052
CM_RENLFAIL	-16487.463	5640.587	-.071	-2.923	.004	.943	1.061
CM_DEPRESS	-13286.334	6300.953	-.050	-2.109	.035	.972	1.029
CM_DM	-10609.607	4945.732	-.051	-2.145	.032	.968	1.033
CM_BLDLOSS	-23533.933	11448.640	-.049	-2.056	.040	.984	1.017
CM_PERIVASC	-16499.922	8180.814	-.048	-2.017	.044	.959	1.043

Multiple linear regression was conducted in order to address this eighth research question

RQ8: Are there predictors for total charges of patients with ovarian cancer hypertension?

Multiple regression was conducted with SPSS software which included the same independent variables as RQ7. However, those individuals that had hypertension were selected. The dependent variable was a total charge. A forward selection process was chosen to determine the best combination of significant predictors. There was approximate normality of regression residuals (Figure 17) and homoscedasticity and collective linearity (Figure 18).

Figure 17 shows an approximate symmetric distribution mound-shaped distribution, which justifies approximate normality. Additionally, the nonrandom pattern in the scatter

plot of Figure 18 suggests homoscedasticity and collective linearity between the independent variables and the dependent variable. There were no significant outliers in the regression residuals and no multicollinearity, as indicated by all variance inflation factors below 5.0.

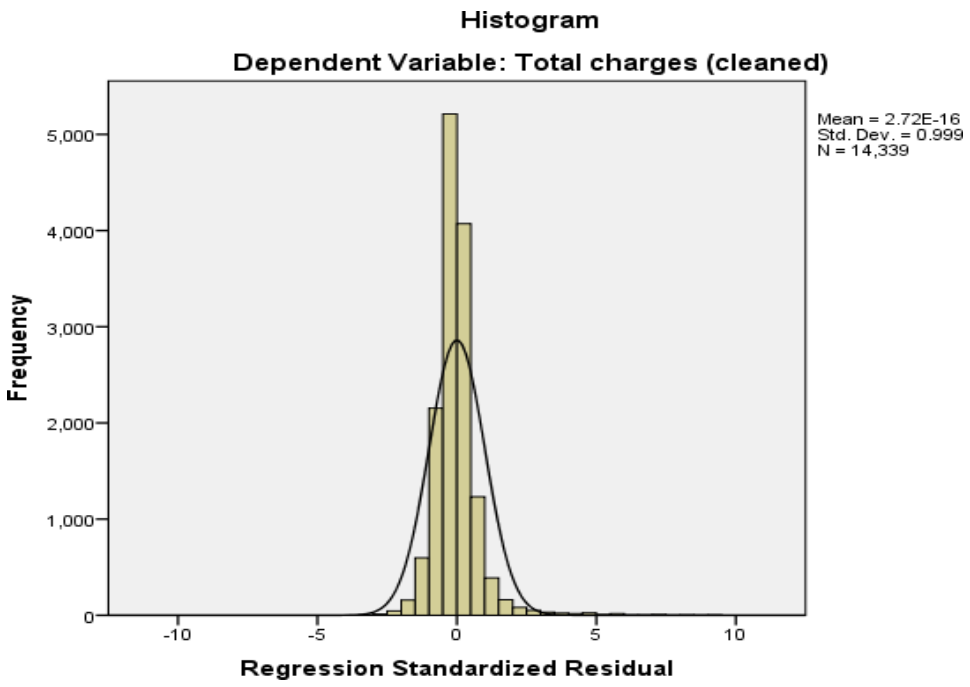

Figure 17: Histogram of Total Charges

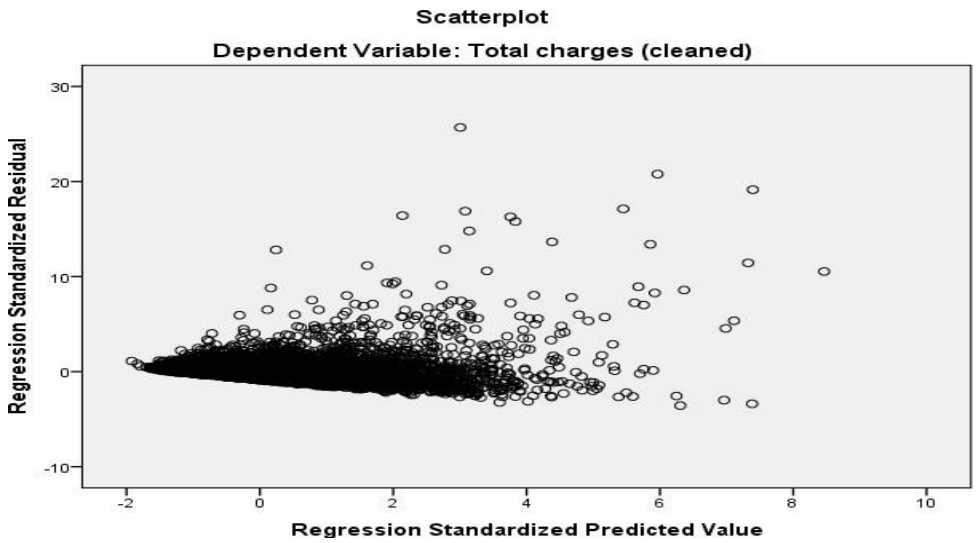

Figure 18: Scatter Plot of Predicted Versus Regression Residuals

The overall model was significant, $F(22, 14338) = 314.942$, $p < .001$. There were significant predictors of number of diagnoses ($b = 1937.566$, $p < .001$); number of procedures ($b = 8308.308$, $p < .001$); Age ($b = -60.774$, $p < .001$); Race (White: $b = -11863.915$, $p < .001$; Black: $b = -8431.323$, $p < .001$; Native America: $b = -13966.029$, $p = .002$); SES (Third quartile: $b = 2488.888$, $p = .002$) and comorbidities ($p < .001$). The increasing number of diagnoses, procedures, and being Hispanic results in an average increase in total cost. Regarding comorbidities, there were several that were significant predictors which are listed in Table 10. The comorbidity that had that most significant effect was weight loss which had the largest standardized regression coefficient ($b = 18801.359$, $p < .001$). Those patients with weight loss comorbidities resulted in the greatest mean increase in total charge.

Table 10: Regression Coefficients for RQ 8

Variable	B	SE	β	t	p	Tolerance	VIF
(Constant)	3176.988	1682.226		1.889	.059		
NPR	8308.308	140.451	.425	59.155	.000	.913	1.096
NDX	1937.566	89.175	.197	21.728	.000	.570	1.753
CM_WGHTLOSS	18801.359	1597.544	.085	11.769	.000	.900	1.111
White	-11863.915	1013.037	-.114	-11.711	.000	.494	2.022
CM_LYTES	7721.019	892.217	.066	8.654	.000	.813	1.231
Black	-8431.323	1193.148	-.068	-7.066	.000	.505	1.980
CM_COAG	9156.759	1853.703	.035	4.940	.000	.949	1.054
CM_PARA	21307.849	3695.908	.040	5.765	.000	.986	1.014
CM_CHF	8868.939	1633.669	.039	5.429	.000	.906	1.104
CM_TUMOR	6264.793	1156.186	.039	5.418	.000	.899	1.112
CM_METS	4779.454	1195.228	.029	3.999	.000	.878	1.140
Third Quartile	2488.888	795.638	.022	3.128	.002	.993	1.007
Native American	-13966.029	4574.205	-.021	-3.053	.002	.963	1.038
CM_PULMCIRC	7428.285	2398.865	.022	3.097	.002	.959	1.042
CM_ANEMDEF	2428.551	883.354	.020	2.749	.006	.884	1.131
CM_LYMPH	-19160.662	6970.833	-.019	-2.749	.006	.997	1.003
CM_AIDS	23592.049	9592.915	.017	2.459	.014	.993	1.007
CM_ALCOHOL	6749.191	3190.264	.015	2.116	.034	.984	1.016
CM_DEPRESS	-2453.154	1041.578	-.017	-2.355	.019	.937	1.067
AGE	-60.774	24.006	-.020	-2.532	.011	.752	1.329
CM_OBESE	-2239.257	957.545	-.017	-2.339	.019	.897	1.115
CM_BLDLOSS	-4562.094	2191.883	-.014	-2.081	.037	.977	1.024

Binary logistic regression was conducted in order to address this ninth research question:

RQ9: Are there predictors for mortality of patients with ovarian cancer?

Binary logistic regression was conducted in order to assess the relationship between mortality, age, race, SES, comorbidities, type of ovarian cancer, number of diagnoses, and number of procedures Binary logistic regression analysis is used to predict a dichotomous dependent variable, mortality (died or not died) in this case, based on

independent variables. Table 11 provides the results of the binary logistic regression conducted. Increased age (b = 0.029, OR = 1.029, p < .001), and number of diagnoses (b = 0.123, OR = 1.31, p < .001) were associated with increased likelihood of dying. Additionally, anemia (b = .552, OR = 1.737, p < .001); depression (b = 1.303, OR = 3.679, p < .001); Hypertension (b = 0.605, OR = 2.390, p < .001); hypothyroidism (b = 0.605, OR = 1.832, p = .009); and obesity (b = 0.782, OR = 2.186, p = .024) were associated with increased likelihood of dying. Deceased risk of dying was associated with the number of procedures (b = -0.186, OR = 0.830, p < .001). Appendix B and C provides these results.

Table 11: Binary Logistic Regression Coefficients and Odds Ratios for RQ 9

Variable	B	SE	Wald	df	*p*	*OR*
AGE	.029	.005	27.717	1	.000	1.029
NPR	-.186	.025	57.763	1	.000	.830
NDX	.123	.016	58.004	1	.000	1.131
CM_ANEMDEF(1)	.552	.185	8.899	1	.003	1.737
CM_DEPRESS(1)	1.303	.358	13.209	1	.000	3.679
CM_HTN_C(1)	.871	.162	28.822	1	.000	2.390
CM_HYPOTHY(1)	.605	.231	6.861	1	.009	1.832
CM_LYTES(1)	-.790	.160	24.473	1	.000	.454
CM_OBESE(1)	.782	.345	5.130	1	.024	2.186
CM_PULMCIRC(1)	-.972	.240	16.440	1	.000	.379
CM_WGHTLOSS(1)	-.443	.188	5.560	1	.018	.642
Constant	-24.503	13613.289	.000	1	.999	.000

Binary logistic regression was conducted in order to address this tenth research question:

RQ10: Are there predictors for mortality of patients with ovarian cancer Congestive heart failure?

The results of the binary regression are depicted in Appendix A. Increasing age (*b* = .038, *OR* = 1.038, *p* = .045) and EOC type of ovarian cancer (*b* = 1.609, *OR* = 4.996) are associated with increased likelihood of dying among those patients with congestive heart failure. Table 12 provides this information.

Table 12: Binary Logistic Regression Coefficients and Odds Ratios for RQ 10

	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
							Lower	Upper
AGE	.038	.019	4.012	1	.045	1.038	1.001	1.077
TypeOvarianOV_DX1_10(1)	1.609	.758	4.501	1	.034	4.996	1.130	22.081
CM_PULMCIRC(1)	-1.005	.526	3.658	1	.056	.366	.131	1.025
Constant	-5.837	1.612	13.107	1	.000	.003		

CHAPTER V: DISCUSSION AND LIMITATION

Introduction

Ovarian cancer is the thirteen-leading cause of death in the United States. The Epidemiology and End Results Programs survey estimates that around 222,000 women are living with cancer in the US. This thesis has presented findings on mortality of patients with an ovarian cancer diagnosis, length of stay, total charges, and their association with age, gender, race, socioeconomic status (SES), number of procedures, number of diagnoses, comorbidities, and ovarian cancer stage, in a cohort of inpatients with ovarian in the United States. Expanding on the discussion sections of the previous chapters, this chapter: summarizes the key findings of the work presented in the thesis; comments on how the work has contributed to filling the knowledge gaps, including a discussion of its strengths and limitations.

Sociodemographic Characteristics and Medical Information

The data for this study was obtained from the HCUP NIS database for evaluation of socio-demographic and medical information as predictors of length of the hospital, total charges, and mortality. There were 62768 patients with ovarian cancer in the dataset. For purposes of this study, male patients were excluded, leaving 62 319 (99.3%) females. Descriptive statistics were used to measure frequency. The ages of patients ranged from 0 to 103 (M = 45.75, SD = 18.06). The ages appeared to follow a normal distribution as assessed by visual inspection of a histogram (Figure 1). There were three types of cancer under consideration: epithelial ovarian cancer (EOC (23.7%), stromal cell carcinoma

(SCC) (76.2%), and germ cell tumor (GCT) (0.1%). Among the 62, 768 ovarian cancer patients, 762 (1.2%) died and 61,998 (98.88%) did not die.

Length of stay of patients ranged from zero to 29 days (M = 3.91, SD = 5.27). The total charge for services ranged from $108.00 to $1,401,187 (M = $32,738, SD = $43,109.00). Both lengths of stay and total charges were highly positively skewed. The number of procedures showed a deviation from normality, ranging from zero to 31 (M = 2.47, SD = 2.26). The top five comorbidities measures included hypertension, 16,995 (27.1%); deficiency anemia, 9335 (14.9%); Fluid/Electrolyte disorders, 9318 (14.8%); Chronic pulmonary disease, 6956 (11.1%); and Obesity, 6481 (10.3%). Collectively, the group of tumors known as ovarian cancer is the tenth most common cancer and the fifth most common cause of cancer death among women in high-income countries (gross national income per capita over US$12,235 (The World Bank 2020), where incidence rates age-standardized to the standard world population are 8.2 per 100,000 and mortality rates are 4.2 per 100,000 (IARC Global Cancer Observatory 2020).

In 2018, over 295,000 women were diagnosed in absolute terms, and there were nearly 185,000 deaths from cancer worldwide (IARC Global Cancer Observatory 2020). Age-standardized incidence varies from over 12 per 100,000 (in several eastern and north-eastern European countries) to less than 3 per 100,000 (in a number of African countries) (IARC Global Cancer Observatory 2020), although for some regions, low rates may reflect incomplete population coverage by the cancer registry (Dixon et al., 2014).

Ovarian cancer accounts for a disproportionately high number of cancer deaths (given its incidence) due to its poor prognosis. Survival rates are low; only about 45% of

women are still alive five years after diagnosis in developed countries (Parkin et al., 2014). Modest improvements have been seen over recent decades. For example, five-year survival in the early 1980s was 25-39% in the UK, USA, and Australia (Felix et al. 2017). Nevertheless, ovarian cancer survival remains far poorer than for many better-known cancers affecting women, such as breast cancer, with a five-year survival rate of 91% (Felix et al. 2017).

In addition, some populations have not experienced this improvement in survival, for instance, black women in the USA, who currently have similar or worse survival rates than they did 30 years ago (Parkin et al., 2014). Most women with ovarian cancer (for instance, 79% in the USA (Parkin et al., 2014) are not diagnosed until their cancer is advanced, having spread beyond the ovary. The stage measures the degree of spread of cancer within the body, ranging from local (stage I) to distant (stage IV) spread. Women whose cancers are diagnosed at a late (advanced) stage have far poorer survival than women whose cancers were at an earlier stage at diagnosis (for instance, 29% vs. 92% five-year survival for women diagnosed with stage III-IV vs. IA-IB cancers (11)), but improving early detection is challenging.

Mortality, the length of stay, total charges, and type of ovarian cancer

Mortality

The study developed a Chi-square test to determine whether there was an association between mortality and type of ovarian cancer (EOC -epithelial ovarian cancer, SCC- stromal cell carcinoma, GCT - germ cell tumor). The results of the Chi-square test was significant, $\chi 2(2) = 505.628$, $p < .001$ as demonstrated in table 2. There was a

significant association between mortality and type of ovarian cancer. Specifically, as depicted in Table 3, more people died in the EOC category than in other types of ovarian (EOC- 213, SCC- 5, GCT-0). The Chi-square test results were significant, $\chi 2(2) = 9.115$ p =.003 (Table 4). There was a significant association between mortality and type of ovarian cancer among patients with CHD. The results of the Chi-square test was significant, $\chi 2(2) = 104.946$, $p < .001$ (Table 4). There was a significant association between mortality and type of ovarian cancer among patients with HTN. Specifically, as depicted in Table 5, among those patients that died, there were more in the EOC group than in any other group. Binary logistic regression was conducted in order to assess the relationship between mortality, age, race, SES, comorbidities, type of ovarian cancer, number of diagnoses, and number of procedures. Binary logistic regression analysis is used to predict a dichotomous dependent variable, mortality (died or not died) in this case, based on independent variables.

Table 11 provides the results of the binary logistic regression conducted. Increased age ($b = 0.029$, OR = 1.029, $p < .001$), and number of diagnoses ($b = 0.123$, OR = 1.31, $p < .001$) were associated with increased likelihood of dying. Additionally, anemia ($b = .552$, OR = 1.737, $p < .001$); depression ($b = 1.303$, OR = 3.679, $p < .001$); Hypertension ($b = 0.605$, OR = 2.390, $p < .001$); hypothyroidism ($b = 0.605$, OR = 1.832, $p = .009$); and obesity ($b = 0.782$, OR = 2.186, $p = .024$) were associated with increased likelihood of dying. Deceased risk of dying was associated with the number of procedures ($b = -0.186$, OR = 0.830, $p < .001$)

These results support the introduction of universal screening for previously unrecognized cardiovascular risk factors and assessment of glycemic, blood pressure, and lipid control for those already diagnosed. After that, several treatment options are available to optimize these risk factors to reduce the incidence of subsequent cardiovascular disease. Weight loss has been shown to improve insulin resistance, lower blood pressure and normalize cholesterol levels and has the additional benefits of being low cost and associated with minimal risk of harm (Vidal 2002; Look and Wing 2010). Traditionally, it has been reported to be notoriously difficult to achieve by diet and exercise alone, even within clinical trials, and especially hard to sustain in the long term (Laskey et al. 2016). The recent DiRECT study conducted in primary care in Scotland and Tyneside have contested this, finding that significant weight loss of ≥15kg at 12 months is possible in motivated individuals and can lead to remission of type 2 diabetes (Lean et al. 2017). Some may require initiation of antihypertensive medication and statin therapy and could be combined with metformin treatment, which has similarly been shown to improve multiple cardiovascular risk factors.

This is the first study to investigate the risk of cardiovascular events in women diagnosed with ovarian cancer. A few previous studies have examined the prevalence of individual cardiovascular risk factors in women with ovarian cancer. However, none of these have considered hypertension in their assessment, and most have commented on known diagnoses only. When non-selective screening for diabetes was performed by Burzawa et al. (2011), they described a prevalence of available type 2 diabetes of 30.3% in women newly diagnosed with ovarian cancer. In addition, they made a new finding of

insulin resistance in a further 36% of women, similar to the prevalence of 27.1% of hypertension seen in the current study. The lower rate of chronic pulmonary disease (11.3%) may reflect the different ethnic backgrounds of included women and different healthcare systems, with differing access to opportunistic screening.

Within the SEER database, Felix et al. (2017) found significantly more deaths from cardiovascular disease in women with a history of ovarian cancer than in the general population. In contrast, a retrospective analysis of participants within the Iowa Women's Health Study noted that ovarian cancer survivors had a 25% lower risk of cardiovascular mortality compared with age and BMI-matched controls (Felix et al. 2017a). However, this latter study was reliant upon information obtained from death certificates to determine disease-specific mortality rates and is thus at risk of the inherent inaccuracies associated with the use of these types of data.

In addition, the median BMI of women included in the study at 28kg/m2 was lower than our cohort's. Still, BMI matching of cases to controls also eliminated the impact of obesity on other cardiovascular risk factors, all intimately related. Involvement in a longitudinal study of lifestyle factors on cancer incidence may have also influenced participant behavior, encouraging women to make positive changes to their diet and activity levels. This could explain why there was no difference in the rate of non-fatal cardiovascular events in women with and without a history of ovarian cancer in the Women's Health Initiative (Felix et al. 2017). As with the Iowa Women's Health Study, participants were healthier, with a lower prevalence of obesity and hypertension than in the

current study, potentially due to the 'healthy bias associated with the selective recruitment of women into clinical trials.

Length of Stay

This study determined the association between length of stay and ovarian cancer. Multiple regression was conducted with SPSS software which included the independent variables of age, race, SES, comorbidities, number of diagnoses, and number of procedures. The dependent variable was the length of stay. A forward selection process was chosen to determine the best combination of significant predictors. The mean hospital length of stay remained consistent among the ovarian cancer population, with an average length of 2.1 days. Patients who elected immediate reconstruction stayed an additional .397 days. This value compared to the findings by Wang et al., where the length of stay was 2.32 to 2.84 days based on the type of reconstruction performed. The overall model was significant, $F(31, 54403) = 686.809$, $p < .001$. There were significant predictors of number of diagnoses ($b = 0.300$, $p < .001$); number of procedures ($b = 0.649$, $p < .001$); age ($b = -.012$, $p < .001$); Race (White: $b = -.419$, $p < .001$); SES ($p < .01$); and comorbidities ($p < .001$). The increasing number of diagnoses, procedures, and SES results in an average increase in length of stay. Increasing age and being White results in an average decrease in length of stay. Regarding comorbidities, several were significant predictors, which are listed in Table 6 .The most significant effect of the comorbidity was weight loss, which had the largest standardized regression coefficient ($b = 3.519$, $p < .001$).

Ovarian cancer is an illness in older women who mostly experience various medical commodities such as heart failure, pulmonary diseases, diabetes mellitus, and

hypertension. There were significant predictors of number of diagnoses (b = 2566.123, p < .001); number of procedures (b = 14123.750, Race (Hispanic: b = 45497.149, p < .001); and comorbidities (p < .001). The increasing number of diagnoses, procedures, and being Hispanic results in an average increase in total cost. Regarding comorbidities, several were significant predictors, which are listed in Table 9. The comorbidity that had the most significant effect was weight loss which had the largest standardized regression coefficient (b = 22286.352, p < .001). Those patients with weight loss comorbidities resulted in the greatest mean increase in total charge.

Total Charges

Multiple regression was conducted with SPSS software which included the independent variables of age, race, SES, comorbidities, number of diagnoses, and number of procedures. The dependent variable was total charge. The mean total charges for the current study was $35,303.76. This finding is similar to the findings of Smith et al. ($26,399 and $36,367), respectively. These variations in cost of total charges are due to type of cancer and whether the patient elected immediate reconstruction. The overall model was significant, F(27, 53221) = 442.684, p < .001. There were significant predictors of number of diagnoses (b = 1817.379, p < .001); number of procedures (b = 7696.833, p < .001); age (b = -134.790, p < .001); Race (White: b = -5657.613, p < .001; Black:b = -2636.244, p < .001; Hispanic: b = 4256.601; p < .001); SES (First quartile: b = -2189.839, p < .001; Second quartile: b = -1622.247); and comorbidities (p < .001). The increasing number of diagnoses, procedures, age, and being Hispanic results in an average increase in total cost. Being White or Black results in an average decrease in total cost. Regarding

comorbidities, there were several that were significant predictors which are listed in Table 8.

It was shown that the excessive burden experienced by patients with gynecologic cancer is multifaceted. In Australia, Lew et al. modeled the natural history of HPV infection and cervical intraepithelial neoplasia to simulate the progression and regression of women's underlying health state those infected with HPV. The estimated cost per case of cervical cancer prevented was $69,400(~52,773USD), including screening, diagnostic, treatment, management, and vaccine use costs. In our study, the estimated mean direct treatment cost per ovarian cancers patient was $2,312. Our study's estimated annual direct treatment cost was $70.1 million USD. However, Brown et al. estimated the total annual cost for cervical cancer screening, management, and treatment was USD 259.5 million. Compared to Lew and Brown's research, their research included more health services, such as screening, management, or vaccine use. Therefore, the total cost of their studies was much more.

There were significant predictors of number of diagnoses ($b = 1937.566$, $p < .001$); number of procedures ($b = 8308.308$, $p < .001$); Age ($b = -60.774$, $p < .001$); Race (White: $b = -11863.915$, $p < .001$; Black: $b= -8431.323$, $p < .001$; Native America: $b = -13966.029$, $p = .002$); SES (Third quartile: $b = 2488.888$, $p = .002$) and comorbidities ($p < .001$). The increasing number of diagnoses, procedures, and being Hispanic results in an average increase in total cost. Regarding comorbidities, several were significant predictors, which are listed in table 1. The comorbidity that had the most significant effect was weight loss which had the largest standardized regression coefficient ($b = 18801.359$, $p < .001$). Those

patients with weight loss comorbidities resulted in the greatest mean increase in total charge.

The median household income showed similar values across the four quartiles. However, when we looked at normalized ratios with a total number of discharges by income and race, Whites and Asians had the highest income in 2008, 2009, and 2011 ($64,000+). In 2009, Whites had the highest income across all four income quartiles. The normalized ratios with a total number of discharges by race across the four years showed Whites and Asians had the highest number of discharges from 2008 through 2011, with Asians dominating in 2008 and 2011 with (.39%) and (.43%) respectively. These findings are consistent with the 2020 U.S. Census bureau. The Census Bureau reported the average income for Asian Americans is among the highest in America. By 2020, the median Asian American household income will be approximately $80,000, compared to the median U.S. household income of approximately $64,000.00.

Study Limitations

The main limitations of this study are related to the use of a National Inpatient Sample. The National Inpatient Sample provides benefits but does impose limitations. Consolidating information into one extensive United States database offers valuable information on current medical practices. However, the accuracy of the data relies on data being entered and coded correctly by the practitioner. Coding errors and missing data can result in data that is difficult to interpret, producing inaccurate analysis. In addition, the 2008 through 2011 dataset utilizes ICD-9 codes, broad for many diagnoses and procedures.

Due to the broad nature of specific codes, using particular diagnoses and methods during the patient encounter can be limited.

Additionally, the NIS contains a snapshot of the inpatient encounter, and patient information is reported at the discharge level. There is no information contained in the dataset on post-surgical outcomes. While the beginning stages of reconstruction may occur during the inpatient encounter, the data related to delayed reconstruction, if elected, is not captured in this dataset. The NIS contains not only clinical but also resource use information and does not include the psychological information of the patient relating to the impact of mastectomy and overall satisfaction. Ideally, having post-surgical data that occurs within 30 to 60 days post-discharge would provide useful information regarding complications, overall decision satisfaction, and any increases in total charges.

CHAPTER VI: CONCLUSION AND FUTURE RESEARCH

Study Summary

The purpose of this study was to investigate the mortality of patients with an ovarian cancer diagnosis, length of stay, total charges, and their association with age, gender, race, socioeconomic status (SES), number of procedures, number of diagnoses, comorbidities, and ovarian cancer stage, in a cohort of inpatients with ovarian in the United States. The instrument for data collection of this study was archival data, specifically the patient records of the selected patients with ovarian cancer in the United States.

There was a significant association between mortality and type of ovarian cancer. Specifically, more people died in the EOC category than other types of ovarian cancer. This relationship was also the same in those specifically with congestive heart failure or hypertension. Predictors of the length of stay of patients with ovarian cancer were assessed. There were significant predictors of number of diagnoses ($b = 0.300$, $p < .001$); number of procedures ($b = 0.649$, $p < .001$); age ($b = -.012$, $p < .001$); Race (White: $b = -.419$, $p < .001$); SES ($p < .01$); and comorbidities ($p < .001$). The increasing number of diagnoses, procedures, and SES results in an average increase in length of stay. Those patients with weight loss comorbidities resulted in the greatest mean increase in length of stay. Among those with hypertension, these predictors were also significant.

Predictors for total charges of patients with ovarian cancer were assessed. There were significant predictors of number of diagnoses ($b = 1817.379$, $p < .001$); number of procedures ($b = 7696.833$, $p < .001$); age ($b = -134.790$, $p < .001$); Race (White: $b = -5657.613$, $p < .001$; Black: $b = -2636.244$, $p < .001$; Hispanic: $b = 4256.601$; $p < .001$);

SES (First quartile: b = -2189.839, p < .001; Second quartile: b= -1622.247); and comorbidities (p < .001). The increasing number of diagnoses, procedures, age, and being Hispanic results in an average increase in total cost. These same relationships were found among the congestive heart failure and hypertensive patients.

Lastly, predictors of mortality were assessed by conducting binary logistic regression. Increased age (b = 0.029, OR = 1.029, p < .001), and number of diagnoses (b = 0.123, OR = 1.31, p < .001) were associated with increased likelihood of dying. Additionally, anemia (b = .552, OR = 1.737, p < .001); depression (b = 1.303, OR = 3.679, p < .001); Hypertension (b = 0.605, OR = 2.390, p < .001); hypothyroidism (b = 0.605, OR = 1.832, p = .009); and obesity (b = 0.782, OR = 2.186, p = .024) were associated with increased likelihood of dying.

Future Research

The consequences of ovarian cancer research are much expected in larger populations. This will initiate the influence of cardiovascular comorbidities and diabetes on ovarian cancer outcomes in isolation from other comorbidities. Therefore, more risk factors need to be studied to find their association with mortality, length of stay, and total medical charges. Furthermore, the spectrum of risk factors should be considered, including genetics, hormonal and environmental factors, and behavioral and social factors.

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APPENDIX A: REGRESSION COEFFICIENTS FOR RQ 4

Variable	*B*	SE	B	*t*	*p*	Tolerance	VIF
(Constant)	5.072	.294		17.280	<.001		
NDX	.300	.006	.265	47.589	<.001	.425	2.351
NPR	.649	.009	.275	70.506	<.001	.869	1.151
CM_WGHTLOSS	3.519	.112	.121	31.394	<.001	.883	1.133
CM_LYTES	1.262	.061	.084	20.567	<.001	.796	1.256
FEMALE	-4.841	.291	-.061	-16.659	<.001	.977	1.023
CM_METS	1.622	.085	.075	19.015	<.001	.843	1.186
CM_TUMOR	1.356	.085	.062	15.972	<.001	.884	1.132
AGE	-.012	.001	-.040	-8.635	<.001	.602	1.661
CM_PULMCIRC	2.039	.176	.043	11.557	<.001	.957	1.045
White	-.442	.045	-.039	-9.898	<.001	.845	1.183
CM_OBESE	-.585	.068	-.033	-8.671	<.001	.909	1.100
CM_PARA	1.841	.251	.027	7.345	<.001	.974	1.027
CM_CHF	1.042	.144	.028	7.260	<.001	.909	1.100
CM_DRUG	.839	.152	.021	5.524	<.001	.937	1.067
First Quartile	.411	.056	.034	7.285	<.001	.620	1.613
CM_HTN_C	-.323	.052	-.027	-6.175	<.001	.710	1.409
CM_COAG	.713	.126	.021	5.656	<.001	.939	1.065
CM_BLDLOSS	-.735	.117	-.023	-6.272	<.001	.976	1.024
CM_CHRNLUNG	-.381	.065	-.022	-5.895	<.001	.933	1.071
CM_ALCOHOL	1.155	.197	.022	5.851	<.001	.940	1.064
CM_DEPRESS	-.387	.070	-.021	-5.542	<.001	.936	1.069
CM_NEURO	.463	.114	.015	4.050	<.001	.955	1.047
CM_VALVE	-.547	.141	-.014	-3.888	<.001	.958	1.044
CM_HYPOTHY	-.257	.071	-.014	-3.639	<.001	.931	1.074
CM_LIVER	-.571	.155	-.014	-3.678	<.001	.958	1.044
Second Quartile	.212	.056	.017	3.758	<.001	.657	1.522
Asian	-.351	.119	-.011	-2.948	.003	.921	1.086
CM_ANEMDEF	.129	.058	.009	2.234	.026	.889	1.125
Third Quartile	.119	.056	.010	2.137	.033	.655	1.526
CM_DM	-.145	.073	-.008	-1.997	.046	.884	1.131
CM_ARTH	-.292	.147	-.007	-1.988	.047	.984	1.016

APPENDIX B: DATA VARIABLES USED FOR THE ANALYSIS

Study variables	NIS variables	Variables description
1)AGE	AGE	Age in years; Numerical Variable
2)MORTALITY	DIED	The patient did not die during hospitalization (DIED=0);The patient died during hospitalization (DIED=1), Categorical Variable
3)GENDER	FEMALE	Gender of patient FEMALE = 1 is Female;FEMALE= 0 is Male; Categorical Variable
4)TOTAL CHARGE	TOTCHG	Total charges, Numerical Variable
5)RACE	RACE	1 = White, 2 = Black, 3 = Hispanic, 4 =Asian/Pacific, 5 = Native Am., 6 = Other; Categorical Variable
6)NUMBER OF PROCEDURES	NPR	The number of procedures performed while the patient was hospitalized; Numerical Variable
7)SOCIO_ECONOMIC STATUS	ZIPINC_QRTL	Median household income for patient's ZIP Code, 1= 76th to 100th percentile, 2= 26th to 50th percentile, 3= 51st to 75th percentile, 4= 0-25th percentile; Categorical Variable
8)COMORBIDITIES	CM_AIDS, CM_ALCOHOL, CM_ANEMDEF, CM_ARTH, CM_BLDLOSS, CM_CHF, CM_CHRNLUNG, CM_COAG, CM_DEPRESS, CM_DM, CM_DMCX, CM_DRUG, CM_HTN_C, CM_HYPOTHY, CM_LIVER, CM_LYMPH,	Acquired immune deficiency syndrome, alcohol abuse, deficiency anemias, rheumatoid arthritis/collagen diseases, chronic blood loss anemia, congestive heart failure, chronic pulmonary disease, coagulopathy, depression, diabetes uncomplicated, diabetes with chronic complications, drug abuse, hypertension , hypothyroidism, liver disease, lymphoma, fluid and electrolyte disorders, metastatic cancer, other neurological disorders, obesity, paralysis, peripheral vascular disorders, psychoses, pulmonary circulation disorders, renal failure, solid tumor without metastasis, peptic ulcer disease excluding bleeding, valvar disease, weight loss; Categorical variable

	CM_LYTES, CM_METS, CM_NEURO, CM_OBESE, CM_PARA, CM_PERIVASC, CM_PSYCH, CM_PULMCIRC, CM_RENLFAIL, CM_TUMOR, CM_ULCER, CM_VALVE, CM_WGHTLOSS	
9)LENGTH OF STAY	LOS	The number of days the patient was hospitalized; Numerical Variable
10)Number of chronic conditions	CHRONIC	Number of chronic conditions; Numerical variable

linear regression, and Multinomial logistic regression.

APPENDIX C: STUDY HYPOTHESES, RESEARCH QUESTIONS, AND APPROPRIATE STATISTICAL TESTS

Research question	Hypothesis	Independent variables	Outcomes variables	Inferential statistical analysis
Is there an association between mortality and type of ovarian cancer?	Hypothesis 1	Type of ovarian cancer	Mortality	Chi-square
Is there an association between mortality and type of ovarian cancer patient with Congestive heart failure?	Hypothesis 2	Type of ovarian cancer	Mortality	Chi-square
Is there an association between mortality and type of ovarian cancer patients with HT?	Hypothesis 3	Type of ovarian cancer	Mortality	Chi-square
Are there predictors for the length of stay of patients with ovarian cancer?	Hypothesis 4	Patients' information & comorbidities	Length of stay	Multiple linear regression
Are there predictors for the length of stay of patients with ovarian cancer hypertension?	Hypothesis 5	Patients' information & comorbidities	Length of stay	Multiple linear regression
Are there predictors for total charges of patients with ovarian cancer?	Hypothesis 6	Patients' information & comorbidities	Total charges	Multiple linear regression
Are there predictors for total charges of patients with ovarian cancer Congestive heart failure?	Hypothesis 7	Patients' information & comorbidities	Total charges	Multiple linear regression
Are there predictors for total charges of patients with ovarian cancer hypertension?	Hypothesis 8	Patients' information & comorbidities	Total charges	Multiple linear regression

Are there predictors for mortality of patients with ovarian cancer?	Hypothesis 9	Patients' information & comorbidities	Mortality	Multinomial logistic regression
Are there predictors for mortality of patients with ovarian cancer Congestive heart failure?	Hypothesis 10	Patients' information & comorbidities	Mortality	Multinomial logistic regression