Racial and Ethnic Differences in Endometrial Cancer

BY

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DISSERTATION

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This work is dedicated to all of the women and their families, who have suffered from endometrial cancer. Together we can beat this.

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LIST OF ABBREVIATIONS

95%CI	95% Confidence Interval
ACS	American Cancer Society
AIAN	American Indian Alaskan Native
APC	Annual Percentage Change
API	Asian Pacific Islanders
CCC	Clear Cell Carcinoma
CoC	Commission on Cancer
EC	Endometrial Cancer
FIGO	Federation of Gynecology and Obstetrics
HER-2	Human Epidermal Growth Factor Receptor 2 Oncogene
HGEC	High-Grade Endometrioid Carcinoma
HR	Hazard Ratios
HR_{adj}	Adjusted Hazard Ratios
HW	Hispanic White
IRR	Incidence Rate Ratio
KM	Kaplan Meier
LGEC	Low-Grade Endometrioid Carcinoma
NCDB	National Cancer Database
NHA	Non-Hispanic Asian
NHAIAN	Non-Hispanic American Indian Alaskan Native
NHB	Non-Hispanic Black
NHPI	Non-Hispanic Pacific Islanders
NHW	Non-Hispanic White
OR	Odds Ratios

LIST OF ABBREVIATIONS (CONTINUED)

OR_{adj}	Adjusted Odds Ratios
PTEN	Phosphatase and Tensin Homolog Tumor Suppressor Gene
RR	Relative Risk
SC	Serous Carcinoma
SE	Socio-Economic
SEER	Surveillance, Epidemiology and End Results
SES	Socio-Economic Status

SUMMARY

Endometrial cancer (EC) is the fourth most frequently diagnosed and the most common gynecologic cancer among American women (1). Past research suggests that racial/ethnic differences in EC outcomes exist (2-9); however these differences were almost exclusively examined in NHW and NHB women. Asians and Hispanics represent the fastest growing minority populations in the United States (U.S.) (10), yet most investigations have failed to include them in their analyses. In addition, previous research has generally presented results for overall EC, although recommended treatment regimens vary by histologic subtype (11) and there is evidence that subtype-specific survival differences exist (12).

The goal of this research was to assess whether racial/ethnic differences in stage at diagnosis, treatment modalities and 5-year overall survival existed and explore what factors mediated these differences. Our investigation focused on comparing EC outcomes stratified by four EC subtypes: (1) low-grade endometrioid carcinomas (LGEC), (2) high-grade endometrioid carcinomas (HGEC), (3) clear cell carcinomas (CCC) and (4) serous carcinomas (SC) between NHB, Hispanic, non-Hispanic Asian (NHA), non-Hispanic Pacific Islanders (NHPI), non-Hispanic American Indian/Alaskan Natives (NHAIAN) and NHW women. We were able to address these questions by performing cross sectional analyses of diagnosis stage and treatment modalities and a retrospective cohort survival study using data from the National Cancer Database (NCDB); one of the largest and most comprehensive dataset of EC in the U.S. and Puerto Rico (13).

Our findings demonstrated that the burden of EC is not equally distributed across racial/ethnic groups and that compared to NHW women, NHB women are significantly more likely to be diagnosed with aggressive EC subtypes. In addition, we found that NHPI and NHA women had higher odds of diagnosis with LGEC and NHB and NHA had higher odds of diagnosis with HGEC than NHW women.

In regards to treatment, the results from our investigation showed that racial/ethnic differences in receipt of surgery exist, after accounting for potential confounders. Notably, NHB women were the only minority group that had higher odds of not receiving surgical treatment than NHW, across all EC subtypes. Our results also demonstrated that Hispanic and NHAIAN women diagnosed with LGEC had significantly higher odds of not receiving surgery than NHW. Moreover, NHPI had five times higher odds of not receiving surgical treatment for SC than NHW. Additionally, our results showed that health insurance modified the relationship between race/ethnicity and receipt of surgical treatment in women diagnosed with LGEC and that those differences were almost exclusively present in only the 55.2% of patients with private health insurance. When assessing racial/ethnic differences in the receipt of radiation therapy and chemotherapy, we demonstrated that NHAIAN diagnosed with SC had higher odds of not receiving radiation therapy than NHW. Moreover, NHB women diagnosed with CCC had higher odds and NHA diagnosed with LGEC had lower odds of not receiving chemotherapy than NHW. Although chemotherapy is usually recommended for later-stage disease, no differences in receipt of chemotherapy were detected in stage-stratified models. Lastly, the results of the mediation analyses showed that racial/ethnic differences in receipt of surgical treatment in women diagnosed with LGEC, HGEC and SC were partially mediated by the socio-economic (SE) domain.

With respect to survival, NHB women diagnosed with LGEC, HGEC and SC had a lower overall 5-year survival than NHW, after accounting for potential confounders. In addition, NHA diagnosed with LGEC and Hispanics diagnosed with HGEC had a higher overall 5-year survival than NHW women. Lastly, the results from our mediation analyses demonstrated that receipt of surgical treatment and the SE domain contributed to NHB-NHW differences in overall 5-year survival in women diagnosed with LGEC and HGEC.

SUMMARY (CONTINUED)

The results from our study have some important implications as they showed that considering EC as a homogenous disease distorts the association between race/ethnicity and EC outcomes. In addition, our findings demonstrated that some results from unadjusted models differed substantially from adjusted models. Thus, caution is advised in evaluating previously published studies on racial/ethnic differences in EC that failed to individually evaluate associations for ED subtypes and to adjust for demographic, socio-economic and medical treatment factors.

To conclude, subtype-specific racial/ethnic differences in stage at diagnosis, receipt of treatment and 5-year overall survival in women diagnosed with EC exist. These differences can be attributed to several factors, including a lack of knowledge about EC symptoms, refusal of surgery by women of lower socio-economic status (SES), and structural and social barriers present in areas of lower SES. Interventions to address the detected disparities could consist of efforts to improve the timeliness of diagnosis by raising the awareness about EC symptoms, to increase knowledge about the necessity of EC surgery in women who are likely to refuse treatment, and to assist women of lower SES overcome barriers to accessing health services present in the area they live in. These interventions could be carried out within the framework of a patient navigation project or with the aid of community/social workers.

I. INTRODUCTION

A. Aims and Hypotheses

The overarching goal of this research was to assess whether racial/ethnic differences in stage at diagnosis, treatment modalities and overall 5-year survival existed and to identify factors mediating these differences.

This research used secondary data from the NCDB, representing approximately 70% or approximately 230,000 newly diagnosed EC cases in the U.S. and Puerto Rico between 2003 and 2012.

1. Specific Aim 1

We characterized racial/ethnic differences in tumor, socio-demographic and treatment facility factors. In addition, we assessed whether EC subtype-specific differences in stage at diagnosis existed between minority and NHW women. We hypothesized that there would be racial/ethnic differences in tumor, socio-demographic and treatment facility characteristics and that racial/ethnic differences in stage at diagnosis would vary by EC subtype.

2. Specific Aim 2

We assessed whether EC subtype-specific racial/ethnic differences in receipt of EC treatment, defined as surgery, radiation therapy and chemotherapy existed. In addition, we evaluated individual factors and domains of factors that could be mediating the detected racial/ethnic treatment differences. We hypothesized that there would be differences in receipt of each treatment modality and that these differences would vary by histologic subtype.

3. Specific Aim 3

We evaluated whether EC subtype-specific racial/ethnic differences in 5-year overall survival existed. In addition, we assessed what individual factors and domains of factors

mediated the detected racial/ethnic overall 5-year survival differences. We hypothesized that there would be differences in 5-year overall survival and that these differences would vary by histologic subtype.

B. Rationale for Proposed Research

Endometrial cancer is the most common gynecologic cancer and the fourth most commonly diagnosed cancer among U.S. women. It impacts the lives of many women and in the near future will impact many more (14). The incidence of EC is increasing, as are mortality rates (7, 14). The number of EC cases diagnosed annually is expected to significantly increase in the next two decades (25). It is estimated that the incidence of EC will nearly triple between 2015 and 2030, and that the mortality rate will increase by 18% (25).

Past research suggests that racial/ethnic differences in EC tumor presentation, treatment and survival exist (2-9). These differences were extensively documented among NHW and NHB women; however, a very limited number of studies characterized them in other minority groups. In recent years, the number of minority populations living in the U.S. has increased (15) especially those coming from Hispanic and Asian countries (10). Consequently, it is essential to understand factors related to EC diagnosis and treatment, particularly with respect to the changing demographics of the U.S. (10). Both the expected increase in the incidence of EC, and the increase in immigration support further investigation of tumor characteristics in minority populations, their treatment patterns as compared to NHW and their clinical outcomes. This additional knowledge will provide crucial information for the future planning of interventions to address potential differences in EC cancer outcomes.

There are two main types of EC characterized by the clinico-pathological and etiological characteristics. In the past, EC was analyzed as a homogenous disease, even though it had been established that the subtypes of EC significantly differed from each other (16).

Consequently, because 80% of women diagnosed with EC are diagnosed with Type 1 tumors (7, 17), the results of these studies were more likely to predominantly reflect the patterns of Type 1 EC. This important limitation is depicted in a comprehensive report on ovarian cancer released by the National Academy of Sciences in March 2016 (18). One of the main overarching recommendations of the Academy is to perform subtype-specific research and stop analyzing ovarian cancer as a homogenous disease. Doing so will help advance scientific understanding, thereby helping reduce ovarian cancer morbidity and mortality. This recommendation can be extended to EC research since, similar to ovarian cancer, EC is not a homogenous disease.

In addition, the current literature, with the exception of a single study that used the NCDB, is not generalizable to the entire population of the U.S. In fact, seven of the ten studies that included minority populations used Surveillance, Epidemiology and End Results data (SEER). The remaining three used, the data from a single institution in New York City, the Department of Defense centralized tumor registry data and the data from the NCDB (only for the 2000-2001 period) (5, 19, 20). Surveillance, Epidemiology and End Results data is limited because it only includes 18 population-based registries and covers approximately 28% of the U.S. population (21). While the SEER registry has almost complete ascertainment among regions captured, it is limited in the regions represented. (21) It fails to consider highly segregated cities, such as Chicago, Milwaukee and Philadelphia, in which racial differences in outcomes may differ due to segregation patterns (22). Another weakness of the SEER dataset is the lack of the availability of information regarding patients' health insurance and treatment with chemotherapy. This represents an important limitation as health insurance impacts access to care (23) and chemotherapy is one of the main treatments recommended for patients diagnosed with later-stage EC.

In summary, in addition to lack of generalizability, there are four important limitations of EC studies that included minority populations in their analyses and they include the lack of (1)

the description of current EC tumor characteristics by race/ethnicity other than black, (2) EC subtype-specific analyses, (3) adjustment for important demographic, socio-economic, tumor characteristic and treatment variables when assessing treatment and survival differences, and (4) information about factors mediating treatment and survival differences.

To the best of our knowledge, this study is the first to report the results of the relationship between race/ethnicity stage at diagnosis, three main EC treatment modalities, and 5-year overall survival after accounting for potential confounders. Moreover, this study is the first to compare women from five minority groups to NHW and explore factors mediating these differences.

C. Background

1. Burden of the Disease

Endometrial cancer is the fourth most frequently diagnosed and the most common gynecologic cancer among American women (1). The American Cancer Society (ACS) estimated that in 2015, 54,870 women were diagnosed with the disease, which roughly represents 3.3% of all cancer cases (1). The incidence of EC is 25.1 cases per 100,000 women a year and in 2012, there were an estimated 621,612 women living with the disease (1). At some point during her lifetime, a woman from the general population has a 2.8% chance to be diagnosed with EC (1).

2. Types of Endometrial Cancer and their Risk Factors

There are two major categorizations of EC, determined by the clinico-pathological characteristics of the tumors (16, 17, 24, 25). Eighty percent of women diagnosed with EC are diagnosed with Type 1 and twenty percent with Type 2 tumors. Histologically, Type 1 tumors represent the LGEC; a subtype of the malignant epithelial tumors. Type 2 tumors represent four

other subtypes of the malignant epithelial tumors; (1) HGEC, (2) CCC, (3) SC and (4) carcinosarcomas (CS). In addition to the epithelial tumors, Type 2 ECs also include four subtypes of the malignant mesenchymal tumors (sarcomas); (1) low-grade endometrial stromal sarcomas (ESS), (2) high grade ESS, (3) undifferentiated uterine sarcomas and (4) uterine leiomyosarcomas (7, 11, 26, 27).

Moreover, both types of tumors differ etiologically. While Type 1 tumors are estrogen-dependent, Type 2 tumors are characterized by genetic mutations (16, 17). The most common factors that affect a woman's risk of diagnosis with Type 1 EC are those that increase her exposure to circulating levels of estrogen or decrease her exposure to progesterone. (1, 28, 29). (TABLE I)

Because Type 2 EC are rare and therefore not studied as extensively as Type 1, the understanding about the epidemiology and biology of these types of tumors is limited. There is evidence that Type 2 tumors are not estrogen driven, but rather are characterized by the mutation of the p53 tumor suppression gene and the over expression of human epidermal growth factor receptor 2 (HER-2) oncogene (2, 17, 19, 27, 30). There is evidence that in comparison to Type 1 EC, Type 2 tumors are diagnosed more frequently in older, post-menopausal, normal weight and multiparous women (31).

3. Incidence

During the last decade, the incidence of EC has been increasing (1). This increase is believed to be due to a growing prevalence of obesity and to a lesser extent, an increased prevalence of diabetes (8, 32). Although these factors increase the risk for Type 1 EC, it is still unclear which type of EC is responsible for the overall increase in incidence.

TABLE I: HORMONAL FACTORS ASSOCIATED WITH ENDOMETRIOID CARCINOMA

RISK FACTORS	PROTECTIVE FACTORS
Use of estrogen replacement therapy	Use of birth control pills
Use of tamoxifen	Pregnancy
Increased total lifetime number of menstrual cycles	
Obesity	
Ovarian tumors that produce estrogen	
Polycystic ovary syndrome	

Some studies reported an increase in incidence for Type 1 (33, 34) and others for Type 2 tumors (7, 35). Furthermore, it is estimated that in the future, the overall incidence of EC is expected to rise even more and increase from approximately 55,000 in 2015 to 82,000 in 2020 and 122,000 in 2030 (14). By 2013, EC was projected to surpass colorectal cancer and become the sixth most frequently occurring cancer in terms of absolute cases (14). It is believed that this dramatic increase will occur as a result of an aging population, increased prevalence of obesity and other unknown factors associated with Type 2 EC (14).

4. Symptoms, Screening and Tumor Characteristics

The typical symptoms of EC are abnormal vaginal bleeding, spotting or discharge (28). Non-specific symptoms such as a pain in the pelvis, the detection of an abnormal mass and weight loss can also be associated with EC.

There are no effective screening tools for EC; however because the disease is symptomatic in most cases, it is often diagnosed at an early stage (1). It is estimated that in 67% of cases, EC is diagnosed at a localized, in 21% at a regional and in 8% at a distant stage (1). Diagnosis stage is one of the most important prognostic factors for survival as, for early stage tumors, surgery is considered to be curative (36). EC can be either diagnosed with an

ultrasound scan and/or a sampling of endometrial tissue that is usually performed with an endometrial biopsy, hysteroscopy or dilation and curettage (39). In most cases, endometrial tissue sampling allows determination of the clinical stage, grade and histology of the disease (40, 41).

Type 1 EC are usually diagnosed at an earlier stage and lower grade than Type 2 tumors and therefore have better prognosis (4, 7). Because of their histopathological properties, Type 1 tumors are usually confined to the uterus while Type 2 tumors, even if diagnosed at an early stage, may already have spread to the lymph nodes or other organs (42). It is estimated that 52–70% of Type 2 EC show extrauterine spread at the time of surgery, compared to 4.6% of Type 1 tumors (43-45).

Despite the lack of a screening test for EC, studies have demonstrated that having a regular source of medical care such as a primary care physician increases the chance of patients being diagnosed with early-stage tumors (40, 41).

5. Treatment Modalities

There are four main treatment types for EC: surgery, radiation therapy, hormonal therapy and chemotherapy. Treatment guidelines for EC are set by the National Comprehensive Cancer Network (NCCN), and represent the recognized standard for clinical policy in oncology (11). While surgery is recommended for every patient diagnosed with EC, regardless of the clinical diagnosis stage, grade and histology, the recommendations regarding adjuvant treatment such as radiation therapy, hormonal therapy, chemotherapy or clinical observation are not as straight forward. For example, an appropriate treatment for women diagnosed with stage IA SC or carcinosarcoma could include four options: (1) surgery and observation,(2) surgery and chemotherapy (3) surgery, chemotherapy and vaginal brachytherapy and (4) surgery and tumor directed radiation therapy (11). Overall, early-stage Type 1 EC are treated with surgery

alone; however risk factors such as the presence of the p53 mutation may alter the treatment protocol. Currently, there is no well-established treatment protocol for the use of adjuvant treatment for patients diagnosed with early and advanced-stage disease of any subtype. The adequate adjuvant treatment has yet to be determined (46-48).

Endometrial cancer tumors are pathologically staged during surgery. Hysterectomy and bilateral salpingo-oophorectomy are the underlying basis for treatment of EC. Surgery can be performed through laparotomy, vaginally or through less invasive techniques such as laparoscopy or robotic surgery (11). During surgery the peritoneal cavity is assessed and in some instances a lymphadenectomy is performed. Although the main route of the spread of EC is through the lymph nodes, two clinical trials have recently showed no survival benefits for patients who underwent lymphadenectomies (49, 50). Consequently, to avoid over-treatment, the National Comprehensive Cancer Network (NCCN) recommends a more selective and tailored lymphadectomy approach (11). For women who underwent pathological staging, adjuvant treatment can be recommended based on risk factors such as age, positive lymphovascular space invasion, tumor size, depth of invasion and lower uterine segment involvement (48, 51).

Radiation therapy is the most common adjuvant treatment used for EC. In addition, radiation therapy can be prescribed for recurrent tumors instead of surgery, when surgery is not feasible due to the extent of the disease or the presence of medical comorbidities such as obesity, diabetes, cardiovascular disease, and pulmonary disease (11). Radiation therapy includes tumor directed radiation therapy such as vaginal brachytherapy or external beam radiation therapy and pelvic radiotherapy.

Hormonal therapy can be considered for patients who are not candidates for surgery or radiation therapy. It is only indicated for grade 1 and 2 carcinomas and mainly involves the use of progestational agents, tamoxifen and aromatase inhibitors (52).

Chemotherapy is recommended for older patients or patients diagnosed with metastatic disease, i.e. advanced grade (grade III-IV) and stage tumors (stage II-IV) (53). Several randomized trials have shown that the use of multiple agent chemotherapy, as compared to single agent, was more effective because of the improved response rate and progression-free survival with negligible impact on overall survival (53-55). The two agents found to be the least toxic were the cisplatin and paclitaxel. Single agent chemotherapy is still used in patients who are believed to have unacceptable side-effects from the multiple agent treatment.

6. Mortality and 5-year Survival

According to the ACS, in 2015, out of the 54,870 women diagnosed, 10,170 women died of EC. This represents a case fatality rate of approximately 18.5%. There is evidence that because of the increase in incidence, mortality rates are expected to increase from 10,170 cases in 2015 to 12,000 in 2030 (7, 14). For all types of EC combined, the median age at death is 70 and the overall 5-year relative survival rate is 81.7% (1) The stage-specific 5-year relative survival rates are 95.3% for localized, 68.2% for regional and 16.9% for distant stages. Importantly, the 5-year relative survival rate for women diagnosed with a distant stage EC (16.9%) is lower than that for those diagnosed with distant stage ovarian cancer (28.8%) (56). These numbers illustrate how important the diagnosis stage is in the prognosis of the disease.

In addition to diagnosis stage, diagnosis grade and histologic subtypes are important prognostic factors for EC are diagnosis stage, grade and histology type. Type 2 ECs tend to have worse prognosis than Type 1 as they are often diagnosed at a later stage and are more aggressive (35). An analysis of the SEER data showed that although Type 2 EC tumors

accounted for only 28% of all EC diagnoses, they were responsible for 74% of all deaths (41). In addition, Type 2 tumors cause 50% of EC recurrences and their 5-year survival is significantly lower than for Type 1, 90% vs. 35% (41). (TABLE II)

TABLE II: DIFFERENCES BETWEEN TYPE 1 AND TYPE 2 ENDOMETRIOID CARCINOMAS (41)

TYPE 1 ENDOMETRIAL CANCERS:	TYPE 2 ENDOMETRIAL CANCERS:
70-80% of EC diagnoses	20-30% of EC diagnoses
26% of EC deaths	74% of EC deaths
50% of EC recurrences	50% of EC recurrences
5-year survival rate of 90%	5-year survival rate of 35%
4.6 % show extrauterine spread at the time of surgery	52-70% show extrauterine spread at the time of surgery

7. Analytic Methods Background: Mediation Analysis

Mediation analysis is a statistical method of estimating the underlying relationship between an independent and a dependent variable by quantifying the proportion of the disparity between the two explained by a mediator or group of mediators (57).

Previous studies have used mediation analyses to understand the effect of various important demographic, clinical, and treatment facility factors on the relationship between race/ethnicity and cancer outcomes (58-61). A recent study performed in Chicago found that the observed racial differences in receipt of mastectomy were primarily mediated by diagnosis stage and not patients' SES. The authors suggested that in order to attempt to decrease mastectomy treatment differences in this population, it would be necessary to act on factors that are associated with diagnosis stage rather than the SES differences that exist between the two populations. Importantly, the mediating effect of diagnosis stage was different when comparing

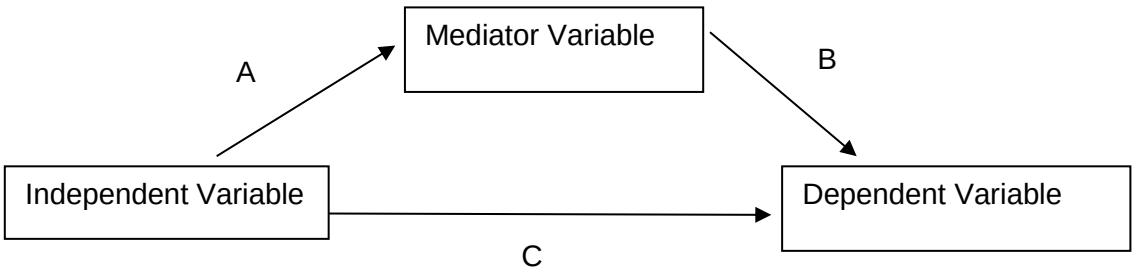
NHB to NHW and Hispanics to NHW (59). Another recent study estimated the mediating effect of treatment facility factors on racial/ethnic differences in delayed diagnosis for breast cancer. The authors found that all facility factors accounted for 43% of the disparity in diagnostic delay. The extent of mediation of facility factors was very similar when comparing NHB to NHW and non-Hispanics (NH) to NHW (62).

In the simplest form of a mediation analysis, the total effect of the independent variable on the dependent variable is estimated by the sum of the direct and indirect effects (A*B+C) (63). The direct effect is the effect of the independent variable on the outcome (C) (Figure 1). The total indirect effect is the product of the effect of the independent variable on the mediator (A) by the effect of the mediator on the dependent variable (B).

Mediators are usually selected based on current literature and conceptual frameworks. Statistically, three conditions need to be met for a variable to be considered a mediator (57): (1) the independent variable needs to be significantly associated with the mediator, (2) the mediator needs to be significantly associated with the dependent variable, (3) and the independent variable needs to be significantly associated with the dependent variable. Once the mediators have been tested, one can evaluate their effect on the relationship between the independent and dependent variables by comparing fully adjusted models with models unadjusted for the mediators and assess the change in the measure of association (57).

Mediation is a very useful addition to traditional multivariable analyses as it can help to determine to what extent, if at all, the hypothesized mediating factors are responsible for a disparity. In addition, if some factors are found to be mediators, performing a mediation analysis can help target key problems and design appropriate intervention to minimize inequalities.

Figure 1: Mediation analysis model showing the relationship between the independent and the dependent variable through a direct (C) pathway and indirect (A*B) pathway going through a mediator



II. RACIAL DIFFERENCES IN ENDOMETRIAL CANCER

Past research suggests that racial/ethnic differences in EC tumor presentation at diagnosis, treatment and survival exist (2-9). These differences are extensively documented among NHW and NHB women for overall EC and in some cases for Type 1 and Type 2 tumors; however, a very limited number of studies characterized them in other minorities.

In the last fifteen years, only ten studies assessed racial/ethnic differences in EC outcomes in minority populations. Seven of these studies analyzed Hispanics, two Asians, one Asians/Pacific Islanders (API) and one American Indians/Alaskan Natives (AI/AN) (3, 5, 7, 19, 20, 26, 64, 65). In seven out of the ten studies, EC was analyzed as a homogenous disease. Consequently, because 80% of women diagnosed with EC are diagnosed with Type 1 tumors, the results of these studies are more likely to predominantly reflect the patterns of Type 1 tumors. While all of the studies assessed survival, only three of them assessed treatment differences. In only four studies, in addition to the Kaplan-Meier (KM) curves, presenting the unadjusted estimates, the authors presented the results for the Cox-proportional hazard models adjusted for relevant confounders. However, none of the studies that reported racial/ethnic treatment differences presented results from adjusted models. Tumor aggressiveness and socio-economic variables were shown to be significantly associated with treatment and survival when comparing NHB to NHW women (26, 66, 67). Thus, models predicting treatment and survival should at least be adjusted for these variables in order to provide some meaningful information about treatment and survival differences in minority populations. (The summary of all studies is available in TABLE XXI, APPENDIX A)

A. Differences in Cancer Incidence

The incidence of EC is greatest among white women. The ACS estimates the 2008-2012 age-adjusted incidence rates of EC at respectively 25.8 cases per 100.000 women a year for

Whites and 24.0 for Blacks. However, the authors of a SEER and Behavioral Risk Factor Surveillance System study analyzing women 50 years and older, found that when accounting for a higher prevalence of hysterectomies among black women, since 2004, the incidence of EC among black exceeded that of white women (68). While the age-adjusted incidence for all types of EC combined is higher among NHW, NHB women have a higher age-adjusted incidence of Type 2 tumors and NHW have a higher age-adjusted incidence of LGEC (7). The results from the recent Annual Report to the Nation on the Status of Cancer estimates that after breast, lung and colon cancers, between 2005 and 2009, EC had the fourth highest cancer incidence among women of both races (40). Using SEER, a study found that for all types of EC, between 2000 and 2011, there was a positive 2.5 annual percentage change (APC) in the age-adjusted incidence for NHB and only 0.6 APC for NHW. (TABLE III) When stratifying by histology subtype, among NHB, this increase is primarily driven by an increase in Type 2 tumors and more specifically CS (APC=3.4) and SC (APC=3.8). Although the APC for overall EC seemed stable among NHW, there were also some variations in the age-adjusted incidence rates across different tumor subtypes. Over the years, among NHW, there was a decrease in incidence rates for LGEC (APC = -0.8) and HGEC (APC= -2.5) and an increase in incidence for other (APC = 5.4), SC (APC = 2.8) and CS (APC = 1.9). Across the whole study period, NHB women were 1.9 times more likely than NHW (iRR = 1.90; 95% CI 1.66-2.18) to be diagnosed with CCC 2.5 times more likely to be diagnosed with CS (iRR = 2.48; 95% CI 2.32-2.64) and 2.2 times more likely to be diagnosed with SC (iRR = 2.20; 95% CI 2.02-2.33) (7).

The 2008-2012 age-adjusted incidence rates of EC for all histologic subtypes for women of other racial/ethnic subgroups is lower than that of Whites and Blacks. It is estimated that the incidence rate per 100,000 women is respectively 19.9 for API, 19.8 for AI/AN and 20.7 for Hispanics (1, 7, 26). Similar to NHW and NHB women, data show that between 2005 and 2009,

EC had the fourth highest incidence of all cancers, among women of each racial/ethnic group except for API women, in whom thyroid cancer was the fourth most common cancer (40).

TABLE III: AGE-ADJUSTED INCIDENCE RATES FOR ENDOMETRIAL CANCER BY HISTOLOGIC SUBTYPE AND RACE/ETHNICITY, SEER 2000-2011

ENDOMETRIAL CANCER SUBTYPES	RACE/ETHNICITY ANNUAL PERCENTAGE CHANGE (APC)			
	NHW	**NHB**	**Hispanic**	**Asian**
All types	0.6*	2.5*	1.8*	2.5*
Low-grade endometrioid	-0.8*	1.0*	0.4	0.7
High-grade endometrioid	-2.5*	-0.5	-1.5	-0.8
Serous	2.8*	3.8*	4.5*	9.0*
Carcinosarcomas	1.9*	3.4*	2.2	3.3*
Clear Cell	1.4	0.4	1.4	Value could not be calculated
Other	5.4*	4.0*	7.4*	10.3*

* Statistically significant

The age-adjusted incidence of all types of EC increased as much for Asians as it did for Blacks (APC= 2.5) When stratifying by histologic subtype, in Asian women, the age-adjusted incidence rate dramatically increased for SC (APC= 9.0) and other tumors (APC= 10.3) and CS (APC= 3.3). Among Hispanics for all type EC, the APC increased by 1.8%, which was also driven by an increase in SC (APC= 4.5) and other tumors (APC= 7.4). The authors concluded that when compared with NHW women, Asians and Hispanics had the same or lower incidence rate ratios for all EC histologic subtypes. (TABLE III) (7)

B. Differences in Stage at Diagnosis and Histopathologic Factors

Diagnosis stage, grade and histology are the most important prognostic factors for women diagnosed with EC (11). SEER data shows that between 2002 and 2008, approximately 15.7% of black women and 7.7% of Whites were diagnosed with a distant stage of EC (1).

Black women's greater likelihood of diagnosis with later-stage EC is believed to be partially explained by diagnoses with more aggressive tumors such as the sarcomas, SC, CCC and CS (67).Using SEER, the authors found that 12% of NHB vs. 5% of NHW were diagnosed with SC and 13% vs. 4% diagnosed with CS. In addition, overall, in the whole sample, 81% of NHW women were diagnosed with Type 1 EC vs. only 62% for NHB (7). Differential genetic variations such as mutation of the p53 tumor suppression gene and the over expression of the HER-2 oncogene, between white and black women make them more likely to be diagnosed with more aggressive tumor subtypes. Past research found that p53 mutation and HER-2 over expressions are more commonly found in Type 2 cancers and are also significantly more common among black women (30). On the contrary, mutations in the phosphatase and tensin homolog (PTEN) tumor suppressor gene commonly associated with the endometrioid type tumors are more likely to occur in white women. Potential differential expression of other genes between both races have also been described; however because it is a new area of research none of them have been confirmed (69-72).

According to the ACS, approximately 9.5% of Hispanics, 9.0% of API and 7.0% of AI/AN were diagnosed with a distant stage of EC between 2002 and 2008 (1). In the single-institutional study performed in the Bronx neighborhood in New York City, the authors concluded that there were no differences in stage and grade at diagnosis between Hispanic and White women diagnosed with Type 1 EC. However, Hispanics had higher proportions of Type 2 tumors although of similar histologic subtypes when compared to Whites (20). Yet, when using the 1988-2009 SEER data, other authors found that when compared to Whites, a higher proportion

of Hispanics diagnosed with Type 2 EC were diagnosed with SC and CCC (50% vs. 46%, *P* = 0.03) and a later-stage disease (43.8% vs. 36.6% respectively, *P* = 0.04). (64). Among the patients who underwent a lymphadenectomy, the rate of positive lymph nodes was higher in Hispanics than in Whites (27.6% vs. 23.1%, *P* = 0.02). An older study that used the 1992-1998 SEER data found that when compared to NHW, Hispanics, had lower rates of CS, SC and CCC (26), and that Hispanics diagnosed with Type 1 tumors were less likely to be diagnosed with later stage and with undifferentiated or unknown grade tumors than NHW (26). Finally, the results of the most recent study that used the 2000-2010 SEER data showed no differences between Hispanic and NHW in any of the EC histologic subtypes (7).

A study that used the 1988-2009 SEER data found that a higher proportion of Asian women were diagnosed with later-stage EC (15.6% vs. 13.3% respectively, *P* = 0.04) and with a higher proportion of CCC and SC (10.6% vs. 9.6%, *P* = 0.041) than NHW. No differences were reported between AI/AN and NHW (3). However, another study using 2000-2010 SEER data demonstrated that the age-adjusted incidence rates for Type 2 tumors were lower in Asian women than in NHW (7). Finally, in a study using the Department of Defense centralized registry data, Asian-Pacific Islanders were diagnosed with the same stage, grade and histologic subtypes of EC as Blacks but with higher grade tumors and less favorable histologies than Whites (19).

C. Treatment Differences

Several older studies suggested that black women when compared to white were less likely to undergo pathologic staging at every stage of diagnosis and were less likely to be treated for advanced disease (4, 73). These treatment differences could potentially be explained by the fact that black women have a greater likelihood of being obese, diabetic and hypertensive when compared to whites (6, 74). According to the authors, these comorbidities are not only responsible for an increased probability of EC diagnosis, but can also explain a part

of the treatment differences as they might represent some contraindications for surgery. Moreover, the HER/neu oncogene more commonly found in Type 2 EC and more frequent in black women was found to be associated with chemotherapy resistance (30).

Yet, more recent studies showed that there were no white-black treatment differences in women diagnosed with EC (67, 75, 76). It is therefore hypothesized that treatment inequalities between both races have decreased or disappeared (77). However, even when women of both races receive the same treatment modalities, black women are still more likely to die when compared to their white counterparts (78, 79).

In a study that used SEER data, the authors concluded that among women diagnosed with EC, the proportion of Asians who underwent a lymphadenectomy was significantly higher (56.7% vs. 48.2%, *P* <.001) while the proportion of those treated with radiation therapy was significantly lower (21.8% vs. 26.0%, *P* <.001), when compared to NHW (3). In the same study, AI/AN were less likely that NHW to be treated with radiation therapy (21.7% vs. 26.0%, *P* < .001); but differences in receipt of lymphadenectomy were not evident. Yet in an older study using the Department of Defense tumor registry data, after adjusting for diagnosis stage, the authors did not see any differences in receipt of radiation therapy, chemotherapy or hormonal therapy between white, black and API women diagnosed with overall EC (19). In a study that used SEER data, among patients diagnosed with Type 2 EC, NHW women were more likely to be treated with radiation therapy than HW (42.3% vs. 39.5%, *P* = 0.04), but there were no differences in the reception of lymphadenectomy treatment between both races (64). None of the studies that analyzed minority populations accounted for potential confounders.

D. Mortality and Survival Differences

The EC mortality rate for black women is nearly twice as high as that of whites (7),overall age-adjusted EC mortality rates at 4.4 deaths per 100,000 women per year for all

races and respectively 4.1 for whites and 7.7 for blacks. A previous study demonstrated that while black women only represent 7% of newly diagnosed EC cases, they account for 14% of all EC deaths (80). A recent SEER study found that NHB women had lower Type 1 and higher Type 2 EC incidence-based mortality rates than NHW. NHB women were respectively 2.9, 2.6 and 2.4 times more likely to die from CS, SC and CCC than their NHW counterparts (7).

Several studies reported lower 5-year EC relative survival rates for black women when compared to whites (6, 67, 81). The most striking difference was reported in the recent SEER Cancer Statistics Review. Between 2005 and 2011, the 5-year survival rate for whites was 85.3% and 65.6% for blacks (60). This difference represents one of the largest survival differences by race among all cancer sites.

Between 2002 and 2008, the ACS estimates the overall age-adjusted EC mortality rates to be 2.8, 3.5 and 3.5 per 100.000 women per year for API, AI/AN, and Hispanics, respectively (1, 7). In addition, a study that used SEER data found that when compared to NHW women, Hispanic and Asian had lower age-adjusted mortality rates for Type 1 EC and either similar or lower rates for Type 2 tumor subtypes (7).

Evidence is inconclusive regarding Hispanic-NHW differences in 5-year EC survival. While some studies showed Hispanic-NHW differences, with Hispanics having poorer survival (5, 65) other studies reported no differences (64, 82). The results might be inconsistent because although the authors accounted for some potential confounding, three of the four studies presented results for overall EC. Two additional studies found that, in unadjusted models, there were no differences in survival between Hispanic and NHW women (7, 20).

A SEER study, that also treated EC as a homogenous disease, found that Asian women have significantly improved overall and cancer-specific survival than NHW. These results were computed using KM curves and confirmed with adjusted Cox proportional hazards regression

models (HR 0.92, 95% CI 0.84–1.00 p = 0.05) (3). The same study found that American Indian/Alaskan Native women had worse overall survival compared with Whites in adjusted models; however no differences were found for the cancer-specific survival. An analysis of the Department of Defense Centralized Registry data, found the crude overall EC 5-year survival rate for Asian-Pacific Islanders to be significantly lower than that of whites, 77% vs. 91% ($P < 0.01$). In the multivariable analyses, where only p-values were presented, race described as "Caucasian vs Asian-Pacific Islander" was determined to be a significant independent prognostic factor of survival. The models were only adjusted for age, stage, grade and histology (19). Another SEER study that presented crude results found no Asian-NHW 5-year survival differences for Type 1 and Type 2 EC (7).

E. Individual and Area –Level Socio-Economic Risk Factors

1. Individual-Level Socio-Economic Status

Genetic and biologic factors do not exclusively explain racial/ethnic differences in EC diagnosis stage, treatment and survival. In fact, black women's mortality rates are greater for every type and at every stage and grade of EC diagnosis. It is well established that independent of race, people with lower, as compared to those with higher individual-level SES, have a greater likelihood of cancer diagnoses and cancer deaths (83).

Previous studies showed that lower individual SES can explain some of the observed differences in EC outcomes. Even if there is no effective screening for EC, the disease is symptomatic and therefore can be detected at an early stage. However, women who are underinsured are less likely to have a medical care provider, such as a primary care physician, and therefore are less likely to share their symptoms in a timely manner. As a result they may be diagnosed with later-stage tumors (40, 41, 84). In fact, prior studies reported greater odds of diagnosis with advanced-stage EC for uninsured and Medicaid patients when compared to

those who were privately insured (85). Moreover, in women diagnosed with less aggressive EC subtypes, higher median family income was inversely associated with later-stage diagnoses (4). This association was not present among women diagnosed with more aggressive tumors. A possible explanation could be that while fast growing tumors have poor prognoses regardless of stage at diagnosis, women diagnosed with less aggressive tumors could benefit from better access to care.

Additionally, lower SES could play an important role in delaying a woman's treatment as less education can be associated with a lack of knowledge about EC symptoms. Women who are uninsured or underinsured, because of financial reasons, could wait longer to be referred to a specialist, thus resulting in the delay in diagnosis and treatment. A recent study showed that when compared to women with private health insurance, those who were uninsured, covered by Medicaid or Medicare were significantly more likely to die from EC (5).

It is well established that Blacks and Hispanics when compared to NHW are more likely to be poor (86, 87). They are also less likely to possess private health insurance, receive higher education and have a regular healthcare provider (5, 40). The specific differences in the SES of minority populations compared to NHW are depicted by the U.S. Census Bureau. Based on the 2014 report on Income and Poverty, the median household income in the U.S. was $53,657 with large variation by race, with Asians reporting the highest income at $74,297, NHWs at $60,256, Hispanics at $42,491 and Blacks the lowest at $35,398 (88). In addition, 12.0% of Asians, 10.0% of NHW, 23.6% of Hispanics and 26.2% of Blacks lived below the poverty level. The U.S. Census Bureau's report of Health Insurance Coverage indicated that the percentage of people without health insurance coverage decreased by 10.4%, or 33.0 million in 2014, compared to the number of uninsured in 2013. Despite efforts to provide health insurance for everyone, Blacks and Hispanics had still a higher rate of uninsured individuals compared to Asians and NHW (11.8% and 19.9% vs. 9.3% and 7.6%, respectively). The report also showed that 16.6%

of uninsured individuals earned <$25.000 per year (88, 89). Finally, the 2015 education attainment report showed that NHW were the most likely and Hispanics the least likely to have graduated from high school. Respectively, 93.3% of NHW, followed by 89.1% of Asians, 87.0% of Blacks and 66.7% of Hispanics finished high school in 2015. Previous EC studies have shown that when compared to blacks and Hispanics, NHW women tend to earn a higher income and be better educated (5, 82). They are also more likely to be privately insured (5).

2. Area-Level Socio-Economic Status

Evidence is accumulating that the effect of SES on health and mortality cannot only be associated with the individual, but also with that of the individual's area SES (90, 91). Studies have shown that people who live in neighborhoods with the lowest SES (20 or 25th percentile) had a 17%-26% increased risk of all-cause mortality after adjusting for individual SES and disease risk factors (92, 93). Area-level SES can be perceived as the study of the environment in which people live and interact. Neighborhoods can influence one's health directly, through exposure to pollutants, walkability, transportation options, and crime or indirectly through, values placed on health, social position or support (91, 93). To capture the effect of how a neighborhood community can affect health, it became customary for researchers to use composite indices such as concentrated disadvantage and concentrated affluence (94, 95). Concentrated advantage and affluence can impact one's access to care (96, 97). Frequent contact with a medical provider has been shown to be associated with earlier stage at diagnosis and better treatment outcomes (40, 41, 84). Interestingly though, a recent study showed that in four major U.S. cities, area-based median family income captured the same dimensions of the neighborhood environment as did the composite indices measuring affluence and deprivation. In the future, the authors of this study recommend using the area-level based median household income instead of the composite indices given that most of the included factors are very highly inter-correlated (98).

3. Treatment Facility Characteristics

Treatment facility characteristics such as the type of facility and physician specialty were shown to be independent predictors of ovarian, breast and colon cancer staging (99, 100) and outcomes (101-104). In these studies, patients treated in high-volume academic research hospitals and by providers with advanced training had better outcomes than those treated in smaller or community hospitals and by physicians who were not specialists. A recent study, that used older SEER data (1991-1999), found that in the population of women who underwent surgical staging, when compared to whites, black women were more likely to be treated in high-volume hospitals and have their surgery performed by a gynecologic-oncologists. Yet, in fully adjusted models surgical specialty was not associated with decreased survival. The only variable that was significantly associated with better survival was hospital case volume (105). Although surprising, these results need to be considered in the proper context as the data used in this study is old, only representing 11 SEER sites from the 1990s and only including women who have undergone surgery. Additionally, these results may be due to the fact that in urban neighborhoods, minority populations are often clustered in proximity to major urban teaching hospitals that have higher volumes and better outcomes for many procedures than community hospitals (106, 107). Authors from this study reported that when compared to white women, blacks were still 10% more likely to die than NHW.

To conclude, there is evidence that individual/area-level socio-economic and treatment facility characteristics account for a part of racial/ethnic differences in diagnosis stage, EC treatment and survival (2, 4, 20, 26, 66, 67, 73, 108).

F. Overarching Research Methodology

1. Study Population and Study Design

Data for this study came from the NCDB which is a joint project of the ACS and the Commission on Cancer (CoC) of the American College of Surgeons. The NCDB received cases from over 1,500 hospitals with CoC-accredited cancer programs located in the U.S. and Puerto Rico (109). The centers reporting to the NCDB consisted of higher-tier community cancer hospitals, academic/research medical centers, and NCI-designated Comprehensive Cancer Centers (13).

This study used secondary data representing approximately 70% or 230,000 newly diagnosed EC cases in the U.S. and Puerto Rico between 2003 and 2012. Data was collected using nationally standardized definitions specified in the CoC's Facility Oncology Registry Data Standards, with standardized data transmission specifications coordinated by the North American Association of Cancer Registries (110).

These NCDB analyses were reviewed and approved by the institutional review board at the University of Illinois at Chicago as exempt given the de-identified nature of the data.

2. Analytic Variables

The variables used in this study follow NCDB categorizations.

a) Independent Variable: Race/Ethnicity

The variable "race/ethnicity" was based on patient's self-reported racial/ethnic identity. Its categories mirrored those defined by the Census(111): non-Hispanic White, non-Hispanic Black, Hispanics, non-Hispanic Asian, non-Hispanic Pacific Islanders/Hawaiian Native and non-Hispanic American Indian/ Alaskan Native. In order to stay consistent with existing literature, NHW women were considered as the reference group.

b) Covariates

For the purpose of this study, covariates were classified into three domains: 1) socio-demographic characteristics; 2) tumor characteristics; and 3) treatment facility characteristics.

Socio-demographic characteristics included age, zip-code level income, zip-code level education, health insurance, year of diagnosis and urbanicity. Age was modeled as a categorical variable: (1) <50 (2) 51-59, (3) 60-69 (4) ≥70 (112). The NCDB dataset contains zip code-level measures of income and education estimated by matching the zip code of the patient recorded at the time of diagnosis against files derived from 2010 U.S. Census data. They were categorized in quartiles; zip code-level median family income (<$38,000, $38,000-$47,999, $48,000-$62,999, ≥$63,000) and zip code-level education (≥ 21.0%, 13.0-20.0%, 7.0-12.9%, <7% of non-High School graduates). Health insurance was grouped into four categories: (1) not insured, (2) Medicaid, (3) Medicare and (4) private insurance. Private insurance plans included: health maintenance organization, preferred provider organization, managed care, private insurance, Civilian Health and Medical Program of the Uniformed Services (CHAMPUS) or TRICARE, military care, and insured- not otherwise specified. The private health insurance plans were grouped together by the NCDB because they represent either privately purchased insurance (i.e., purchased by the individual, a family member, or an employer) or insurance provided by the military, which functions in a similar manner as private insurance (i.e., CHAMPUS or TRICARE) (85).

Period of diagnosis was analyzed as a two-level category variable (2003-2007, 2008-2012). The NCDB estimated urbanicity by matching the state and county Federal Information Processing Standard code of the patient recorded at the time of diagnosis against 2012 files published by the United States Department of Agriculture Economic Research Service (109). It was used as a two category variable: urban vs. rural. Rural populations were defined as

populations of 20,000 people or less, living in cities or towns that were not adjacent to a metro area.

Tumor characteristic included diagnosis stage, grade and comorbidities. Tumor grade was obtained from the pathology reports. It was analyzed as a two and four-level category variable, respectively: high grade (well differentiated, moderately differentiated) vs. low grade (poorly differentiated, undifferentiated, anaplastic) and (1) well differentiated, (2) moderately differentiated, (3) poorly differentiated, (4) undifferentiated. Diagnosis stage was analyzed as a dichotomous variable: late (stage III, IV) vs. early (stage I, II). In order to minimize the quantity of missing data, when the pathologic stage group variable was not reported, the clinical stage group variable was used instead. Tumor subtype was created by combining histology (TABLE XXII, APPENDIX B) and diagnosis grade (26). It was analyzed as a four - level category variable: (1) Type 1: low-grade carcinomas (well and moderately differentiated), (2) Type 2: high-grade carcinoma (poorly and undifferentiated), (3) Type 2: serous carcinomas and (4) Type 2: clear cell carcinoma. All multivariable analyses were stratified by tumor subtype. The comborbidity variable represents the Charlson/Deyo comorbidity score. It was analyzed in three categories: 0, 1 and 2 and more comorbidities.

Facility characteristics included facility type, facility location and facility case volume. Facility type at diagnosis was analyzed as a three level-category variable; (1) academic/research programs, (2) community cancer programs and (3) comprehensive community cancer programs. Facility location at diagnosis represents nine census derived facility regions; (1) East-North Central including Illinois, Indiana, Michigan, Ohio and Wisconsin; (2) East South Central including Alabama, Kentucky, Mississippi, Tennessee; (3) West North Central including Iowa, Kansas, Minnesota, Missouri, North Dakota, Nebraska, South Dakota; (4) West South Central including Arizona, Louisiana, Oklahoma, Texas; (5) New England including Connecticut, Massachusetts, Maryland, New Hampshire, Rhode Island, Vermont; (6)

Middle Atlantic including New Jersey, New York, Pennsylvania; (7) South Atlantic including Washington DC, Delaware, Florida, Georgia, Maryland, North Carolina, South Carolina, Virginia, West Virginia; (8) Mountain including Arizona, Colorado, Idaho, Montana, New Mexico, Nevada, Utah, Wyoming and (9) Pacific including Alaska, Californian, Hawaii, Oregon, Washington.

In the multivariable analyses, facility location was used as a proxy for health care access. Previous studies showed that census-derived facility regions could potentially affect access to care, such as the earning threshold for Medicaid enrollment, physician availability, and reimbursement for cancer screening services among uninsured and Medicaid patients (85). Treatment facility case volume was used as a proxy for surgeon experience assuming that low institutional case volumes reflect a lack of gynecologic oncology subspecialty care (103). It represents the average annual number of patients diagnosed with EC at each facility. It was analyzed in quartiles of case volume. Quartile distribution of cases per year: 1^{st}= 1-19, 2^{nd}= 20-41, 3^{r}= 42 – 73, 4^{th} ≥74.

III. RACIAL/ETHNIC DIFFERENCES IN TUMOR AGRESSIVENESS AND PRESENTATION

A. Introduction

Endometrial cancer is the fourth most frequently diagnosed cancer and the most common gynecologic cancer among American women (1). The American Cancer Society (ACS) estimates that in 2015, 54,870 women got diagnosed with the disease and of those, 10,170 women died. (1). During the last decade, the incidence of EC has been rising and it is expected to rise even more in the future, increasing from approximately 55,000 in 2015 to 122,000 in 2030. This represents an increase of 121%. Because of the increase in the incidence rates, the mortality rates are also expected to increase (7, 14).

Past research suggests that racial/ethnic differences in EC tumor presentation exist (2-9). These differences were extensively documented among NHW and NHB women; however, a very limited number of studies characterized them in other minority groups (3, 5, 7, 19, 20, 26, 35, 64, 65). In recent years, the number of minority populations living in the U.S. has increased (15) especially those coming from Hispanic and Asian countries (10). Consequently, it is essential to understand factors related to EC stage at diagnosis with respect to the changing demographics of the U.S. (10). Both the expected increase in the incidence of EC, and the increase in immigration support further investigation of tumor characteristics in minority populations. This additional knowledge will provide crucial information for the future planning of interventions to address potential differences in EC cancer outcomes.

There are two main categorizations of EC based on the clinical, pathological and etiological characteristics of the tumor. Type 1 EC includes the LGEC, diagnosed in 80% of all EC cases (17). It is the least aggressive EC subtype associated with a survival of approximately 90%(7). The remaining 20% of EC cases are diagnosed with one of the four main histologic subtypes of the Type 2 tumors, listed in order from the most to the least common (113): (1)

HGEC, (2) SC, (3) CCC, or (4) CS. Type 2 tumors are referred to as high-risk tumors because of their tendency for recurrence, distant spread, and short survival time (12, 65). Studies demonstrate that Type 2 tumors are responsible for 50% of recurrences and in 52-70% of cases show extrauterine spread at the time of surgery (12). In addition, there is evidence that they account for 74% of all EC deaths and that women diagnosed with Type 2 tumors have a survival of only 35% (12).

Cancer grade is used as an indication of the likelihood of tumor's growth and spread. It is determined based on the histological morphology of the tumor tissue. There exist four main categorizations of the tumor grade, listed in order from the most aggressive to the least aggressive: (1) undifferentiated, (2) poorly differentiated, (3) moderately differentiated and (4) well differentiated (114).

Diagnosis stage is used as an indication of the size and spread of the tumor. Its categorization follows that of the Federation of Gynecology and Obstetrics (FIGO). If the tumor is confined to the uterus, it will be categorized as stage I, if the tumor extends beyond the uterus but is confined within the pelvis it will be categorized as stage II, if the tumor infiltrates abdominal tissues it will be categorized as stage III and lastly, if the tumor invades the bladder and rectum it will be categorized as stage IV (11). Generally, EC is symptomatic and, therefore, is usually diagnosed at an early stage (28). In 90% of cases, EC is diagnosed due to the presence of an abnormal vaginal bleeding (11). According to the ACS, for all EC cancer cases combined, 67% of cases are diagnosed with stage I, 21% with stages II and III and 8% with stage IV (1). Stage at diagnosis is a critical prognostic factor of EC as women who are diagnosed with early-stage disease (stages I and II) are offered additional treatment options (11). For example, young women diagnosed with stage I LGEC can be treated with a fertility sparing surgery rather than a bilateral salpingo-oophorectomy and hysterectomy. In addition, women who are diagnosed with early-stage tumors have better relative survival (7). The ACS

estimates that women diagnosed with stage I EC of any type, have a 95.3% relative survival rate vs. 68.8 for those diagnosed with stage II and III and 16.9% for women diagnosed with stage IV (1).

Previous studies showed that socio-economic indicators such as income, education and insurance status were associated with later-stage EC diagnosis and subsequently poorer survival rates (5). There is evidence that women who live in disadvantage neighborhoods have less access to care, which increases risk of late-stage EC diagnosis (4, 85). Similarly, women who do not possess private health insurance may be less likely to see a doctor and report symptoms such as abnormal bleeding resulting in diagnoses with later-stage disease (40, 41, 84).

The purpose of this analysis is to assess racial/ethnic tumor, socio-demographic and treatment facility characteristics for Type 1 (LGEC) and Type 2 (HGEC, CCC and SC) EC. In addition, this study aims to determine whether racial differences in stage at diagnosis exist between minority and NHW women. This study used the NCDB dataset which is the largest and most comprehensive dataset of EC in the U.S. It is based on registry data and includes 70% or approximately 230,000 stage-diagnosed EC cases in the U.S. and Puerto Rico between 2003 and 2012 (109).

B. Methods

First, tumor, socio-demographic and facility differences between minority and NHW women were assessed using the Chi-square test statistics. Second, the differences in the distribution of the categorical variables were tested using the Chi-square test and the distribution of the continuous variables using the t-test. The missingness for diagnosis stage, zip-code level income and zip-code level education was assessed with the Chi-square statistics. Lastly, multivariable logistic regressions were performed to estimate the relationship between

race/ethnicity and diagnosis stage for overall EC and for each EC tumor subtype: LGEC, HGEC and CCC. The outcome variable diagnosis stage was dichotomized; late (stage III, IV) vs. early (stages I, II). Urbanicity was not considered in the multivariable models because of the large numbers of missing values (4%). All of the other covariates were included in the multivariable models either because they were significantly associated with the outcome or because conceptually they were considered as important confounders. Odds ratios (OR) and 95% Confidence Intervals (95%CI) were estimated. All analyses were performed using SAS version 9.4.

C. Results

TABLE IV presents the characteristics of the study population by race/ethnicity, overall and by socio-demographic, tumor and facility covariates. A total of 252,785 women were diagnosed with EC in one of the CoC-approved hospitals between 2003 and 2012. Overall, 82.8% women self-identified themselves as NHW, 9.2% as NHB, 5.2% as Hispanic, 2.3% as NHA, 0.3% (n=666) as NHPI and 0.2% (n=597) as NHAIAN. In addition, 71.6% of women were diagnosed with LGEC, 15.9% with HGEC, 5.2% with SC, 1.3% with CCC and 1.3% with carcinosarcomas.

The distribution of race/ethnicity, grade at diagnosis and facility type in patients with missing values on stage at diagnosis, area-level income and area-level education was not substantially different from the distribution in patients with reported values. However, 41.0% of "other tumors" and 19.5% of carcinosarcomas had missing data on stage at diagnosis stage; as such women diagnosed with these tumor subtypes were deleted from the sample and were not explored in multivariable models.

Minority women statistically differed from NHW in all of the socio-demographic factors. The proportion of women diagnosed before the age of fifty was higher for all minorities

TABLE IV: SAMPLE CHARACTERISTICS BY RACE/ETHNICITY, OVERALL AND BY TUMOR, SOCIO-DEMOGRAPHIC AND TREATMENT FACILITY COVARIATES, NATIONAL CANCER DATABASE, 2003-2012, N=252,785

	Non-Hispanic White n=209,180	Non-Hispanic Black n=23,349	Hispanic n=13,066	Non-Hispanic Asian n=5,927	Non-Hispanic American Indian, Alaskan Native n=597	Non-Hispanic Pacific Islander / Hawaiian n=666	Total n=252,785
	%	%	%	%	%	%	%
Overall	82.8	9.2	5.2	2.3	0.2	0.3	
Socio-Demographic Characteristics							
Diagnosis Age							
<50	11.7	12.9#	27.8#	23.9#	27.5#	37.7#	13.1
51-59	28.4	23.8	28.5	35.0	28.1	30.2	28.2
60-69	31.1	35.5	25.4	24.6	26.5	20.4	31.0
70+	28.7	27.9	18.3	16.5	17.9	11.7	27.7
Age (mean)	63.0	63.0	57.0#	58.0#	57.0#	54.0#	59.0
Diagnosis Period							
2008-2012	54.9	58.9#	59.0#	61.1#	63.5#	60.1*	55.7
2003-2007	45.1	41.1	41.1	38.9	36.5	39.9	44.3
Zip-Code Level Income[a]							
$63.000+	34.9	14.2#	20.8#	52.9#	18.1#	41.0#	32.7
$48.000-62.999	27.2	18.7	25.7	24.9	18.1	35.9	26.3
$38.000-$47.999	23.1	22.1	25.2	12.9	22.8	14.9	22.8
<$38.000	12.9	42.8	26.7	7.2	39.2	6.6	16.3
Missing	2.0	2.1	1.6	2.1	1.8	1.7	2.0
Zip-Code Level Education[a]							
<7.0 without a high-school diploma	27.0	7.5#	8.9#	26.5#	12.2#	16.8#	24.2
7.0-12.9% without a high-school diploma	35.4	18.8	17.1	29.9	24.5	33.8	32.7
13.0-20.0% without a high-school diploma	23.9	36.9	22.1	20.1	28.6	26.7	24.9
≥21.0% without a high-school diploma	11.9	34.7	50.4	21.4	32.8	21.0	16.3
Missing	1.9	2.1	1.5	2.1	1.8	1.7	1.9
Health Insurance							
Private Insurance	52.3	39.9#	45.2#	62.3#	45.9#	55.9#	51.0
Medicare	41.3	44.2	27.9	22.7	32.7	20.7	40.3
Medicaid	3.5	9.9	14.4	9.1	17.4	17.1	4.9
Not Insured	3.0	6.0	12.5	5.8	4.0	6.3	3.8
Urbanicity							
Urban	90.0	94.0#	95.5#	93.8#	86.6#	88.0*	90.7
Rural	5.9	2.7	1.9	2.2	10.4	9.3	5.3
Missing	4.2	3.3	2.6	4.0	3.0	2.7	4.0
Tumor Characteristics							
Tumor Sub-Types							
Type 1: Low grade endometrioid	72.8	48.9#	70.8#	68.8#	70.5*	69.4	70.4
Type 2: High grade endometrioid	14.9	20.8	14.7	15.9	13.1	17.4	15.4
Serous	4.3	11.6	4.6	5.3	6.0	5.3	5.0
Clear Cell	1.1	2.3	1.2	1.4	0.8	1.4	1.2
Carcinosarcoma	2.8	8.3	2.9	3.0	4.0	2.9	3.3
Other Tumors	4.2	8.0	5.9	5.9	5.5	3.8	4.7

TABLE IV (CONTINUED): SAMPLE CHARACTERISTICS BY RACE/ETHNICITY, OVERALL AND BY TUMOR, SOCIO-DEMOGRAPHIC AND TREATMENT FACILITY COVARIATES, NATIONAL CANCER DATABASE, 2003-2012, N=252,785

	Non-Hispanic White n=209,180 %	Non-Hispanic Black n=23,349 %	Hispanic n=13,066 %	Non-Hispanic Asian n=5,927 %	Non-Hispanic American Indian, Alaskan Native n=597 %	Non-Hispanic Pacific Islander / Hawaiian n=666 %	Total n=252,785 %
Diagnosis Grade							
Low (Well/Moderately Differentiated)	75.2	52.7#	74.2#	71.9#	73.9	71.5#	73.0
High (Poorly/Undifferentiated)	24.8	47.4	25.8	28.1	26.1	28.5	27.0
Diagnosis Stage							
Early Stage (Stage I and II)	75.0	63.5#	73.4#	70.3#	71.9	67.9#	73.7
Late Stage (Stage III and IV)	15.8	24.8	17.1	19.0	17.3	22.5	16.8
Missing[b]	9.2	11.7	9.5	10.7	10.9	9.6	9.5
Charlson Comorbidity Score							
None	76.0	67.3#	73.7#	81.8#	63.3#	67.4	75.1
1	19.5	25.7	22.0	15.9	29.2	26.1	20.1
2 or more	4.6	7.0	4.3	6.5	7.5	6.5	4.7
Treatment Facility Characteristics							
Facility Type							
Academic/Research Programs	37.3	51.4#	43.8#	46.9#	44.9#	47.0#	39.2
Community Cancer Programs	7.4	5.9	6.6	6.4	5.5	14.3	7.2
Comprehensive Community Cancer Programs	55.2	42.7	49.6	46.7	49.6	38.7	53.5
Missing	0.1	0.0	0	0	0	0	0.1
Facility Location							
East North Central	19.8	16.0#	7.1#	9.2#	7.4#	3.8#	18.5
East South Central	6.3	9.7	0.5	1.3	0.7	1.1	6.2
Middle Atlantic	16.7	17.2	14.6	16.8	3.9	4.8	16.6
Mountain	5.1	0.9	7.4	3.2	32.0	10.2	4.8
New England	7.5	2.5	3.3	3.4	1.5	0.6	6.7
Pacific	10.8	4.2	27.1	48.7	15.9	70.1	12.1
South Atlantic	19.6	37.3	18.1	11.2	18.6	3.9	20.9
West North Central	8.2	2.7	1.5	1.9	7.5	2.4	7.2
West South Central	6.0	9.6	20.5	4.3	12.6	3.2	7.1
Treatment Facility Case-Volume							
≥74 average cases per year	25.5	24.5#	19.0#	20.7#	26.5*	8.9#	25.0
42-73 average cases per year	24.5	23.7	22.3	30.6	16.9	41.9	25.0
20-41 average cases per year	24.4	28.9	35.6	27.2	35.7	32.1	25.1
1-19 average cases per year	25.6	22.9	23.1	21.4	20.9	17.1	24.9

[a] Measure estimated by matching the zip code of the patient recorded at the time of diagnosis against files derived from year 2010 U.S. Census data. Variables were categorized as quartiles based on equally proportioned variable ranges among all U.S. zip codes.

[b] Missing values are reported only for variables with missing values.

* Significantly different from NHW (p_{value} <0.05).

Significantly different from NHW (p_{value} <0.001).

compared to NHW (11.7%) with the highest prevalence in NHPI (37.7%) and NHAIAN (27.5%) women. Similarly, the proportion of women living in areas where 21% or more of the population had no high-school diploma was higher for all minorities compared to NHW (11.9%). However, for area-level income and health insurance, NHA and NHPI were more likely than NHW to live in high-income areas and to have private health insurance. With respect to the tumor characteristics, NHW women were diagnosed with the least aggressive tumors when compared to all minorities. NHB women had the highest prevalence of diagnosis with any subtypes of Type 2 EC (43.0%), late-stage (24.8%) and high-grade tumors (47.4%). However, for the Charlson comorbidity score, NHA (81.8%) were more likely than NHW (76.0%) to have no comorbidities at the time of diagnosis.

Minority women differed from NHW in all of treatment facility characteristics including facility type, facility location and treatment facility-case volume. Treatment facility-case volume was used as a proxy for physician's specialization (115). The proportion of women treated in an academic/research program was higher for all minorities compared to NHW (37.3%) with the highest prevalence in NHB women (51.4%). When compared to minority women, NHW were the most likely to be treated in comprehensive community cancer programs. In regards to treatment facility case volume, NHPI women were the most likely (26.5%) and NHAIAN the least likely (8.9%) to receive care from high-volume hospitals when compared to NHW (25.5%).

TABLE V presents the distribution of socio-demographic, tumor and treatment facility characteristics by the primary outcome of the analysis, stage at diagnosis.

Late stage diagnosis was more prevalent in minorities; at older ages; in areas with higher income and education levels in women diagnosed between 2008 and 2012; in those with lower income and education levels; in women without private insurance and those living in the rural areas.

Late stage was also more prevalent in women diagnosed with LGEC, with high-grade tumors and those with two or more comorbidities. Finally, women diagnosed in academic/research centers and in the west south-central region were more likely to be diagnosed with later-stage EC. Urbanicity was the only variable that was not included in the multivariable models.

TABLE VI presents the results from the multivariable logistic regression models for the association between race/ethnicity and diagnosis stage for overall EC and stratified by EC tumor subtype. The NCDB dataset used for the multivariable analyses included 222,793 women with stage-diagnosed EC between 2003 and 2012. Because diagnosis stage was the outcome of these analyses, women with missing values for diagnosis stage were eliminated from the analytic sample (n=29,992).

1. Overall Endometrial Cancer

In the unadjusted models, NHB, Hispanic, NHA and NHPI had respectively 76% (OR=1.76; 95%CI 1.69-1.82), 11% (OR=1.11; 95%CI 1.05-1.17), 29% (OR=1.29; 95%CI 1.21-1.39) and 55% (OR=1.55; 95%CI 1.27-1.88) higher odds of diagnosis with late-stage overall EC than NHW.

In models adjusted for potential covariates, NHB, NHA and NHPI women had respectively 9% (OR_{adj}=1.09; 95%CI 1.04-1.13), 15% (OR_{adj}=1.15; 95%CI 1.05-1.24) and 31% (OR_{adj}=1.31; 95%CI 1.06-1.65) higher odds of being diagnosed with late-stage disease when compared to NHW.

TABLE V: DISTRIBUTION OF SOCIO-DEMOGRAPHIC, TUMOR AND FACILITY CHARACTERISTICS BY DIAGNOSIS STAGE (LATE VS EARLY), NATIONAL CANCER DATABASE, 2003-2012, N=228,793§

	Late Stage (III and IV)		Early Stage (I and II)		Chi-Square p_{value}
	n	%	n	%	
Overall	39,815	17.9	182,026	82.1	
Socio-Demographic Characteristics					
Race/Ethnicity					<.0001
Non-Hispanic White	32,996	17.4	156,924	82.6	
Non-Hispanic Black	5,327	27.2	14,268	72.8	
Hispanic	2,070	18.2	9,332	81.1	
Non-Hispanic Asian	1,057	20.7	4,053	79.3	
Non-Hispanic American Indian, Alaskan Native	98	19.1	414	80.9	
Non-Hispanic Pacific Islander/ Hawaiian	140	24.0	443	76.0	
Diagnosis Age					<.0001
<50	3,826	13.9	23,768	86.1	
51-59	9,582	15.2	53,323	84.8	
60-69	12,665	18.1	57,388	81.9	
70+	13,742	22.4	47,547	77.6	
Diagnosis Period					>.05
2008-2012	22,221	17.9	101,873	82.1	
2003-2007	17,594	18.0	80,153	82.0	
Zip-Code Level Income[a]					<.0001
$63.000+	12,003	16.5	60,562	83.5	
$48.000-62.999	10,290	17.6	48,226	82.4	
$38.000-$47.999	9,300	18.3	41,461	81.7	
<$38.000	7,773	21.0	29,336	79.1	
Zip-Code Level Education[a]					<.0001
<7.0 without a high-school diploma	8,936	16.6	44,885	83.4	
7.0-12.9% without a high-school diploma	12,547	17.2	60,238	82.8	
13.0-20.0% without a high-school diploma	10,176	18.5	44,989	81.6	
≥21.0% without a high-school diploma	7,207	20.0	28,793	80.0	
Health Insurance					<.0001
Private Insurance	16,891	14.9	96,532	85.1	
Medicare	18,565	20.7	70,995	79.3	
Medicaid	2,493	23.7	8,033	76.3	
Not Insured	1,866	22.4	6,466	77.6	
Urbanicity					<.05
Urban	35,872	17.8	165,424	82.2	
Rural	2,212	18.7	9,609	81.3	
Tumor Characteristics					
Tumor Sub-Types					<.0001
Type1: Low grade endometrioid	15,464	9.4	148,460	90.6	
Type2: High grade endometrioid	13,698	37.7	22,662	62.3	
Serous	6,232	52.3	5,691	47.7	
Clear Cell	1,199	41.8	1,672	58.2	
Carcinosarcoma	3,222	47.6	3,541	52.4	
Grade					<.0001
Low (well/moderately differentiated)	16,060	9.7	149,555	90.3	
High (poorly differentiated/undifferentiated)	23,755	42.3	32,471	57.8	
Charlson Comorbidity Score					<.05
None	29,881	18.0	136,446	82.0	
1	7,984	17.7	37,194	82.3	
2 or more	1,950	18.9	8,386	81.1	

TABLE V (CONTINUED): DISTRIBUTION OF SOCIO-DEMOGRAPHIC, TUMOR AND FACILITY CHARACTERISTICS BY DIAGNOSIS STAGE (LATE VS EARLY), NATIONAL CANCER DATABASE, 2003-2012, N=228,793§

	Late Stage (III and IV)		Early Stage (I and II)		Chi-Square p_{value}
	n	%	n	%	
Facility Characteristics					
Facility Type					<.0001
Academic/Research programs	16,796	19.0	71,488	81.0	
Community Cancer Programs	2,635	17.2	12,647	82.8	
Comprehensive Community Cancer Programs	20,356	17.2	97,739	82.8	
Facility Location					<.0001
East North Central	7,136	17.2	34,300	82.8	
East South Central	2,359	17.3	11,298	82.7	
Middle Atlantic	6,377	17.6	29,846	82.4	
Mountain	1,858	17.7	8,666	82.4	
New England	2,467	16.4	12,576	83.6	
Pacific	5,279	19.8	21,417	80.2	
South Atlantic	8,504	18.1	38,412	81.9	
West North Central	2,858	17.9	13,144	82.1	
West South Central	2,977	19.4	12,367	80.6	
Treatment Facility Case-Volume					>.05
≥74 average cases per year	9,493	17.8	43,811	82.2	
42-73 average cases per year	10,178	18.3	45,546	81.7	
20-41 average cases per year	10,015	17.8	46,407	82.3	
1-19 average cases per year	10,129	18.0	46,262	82.0	

[a] Measure estimated by matching the zip code of the patient recorded at the time of diagnosis against files derived from year 2010 U.S. Census data. Variables categorized as quartiles based on equally proportioned variable ranges among all U.S. zip codes.
[§] Women with missing values for diagnosis stage were eliminated from the analytic sample.

TABLE VI: MULTIVARIABLE LOGISTIC REGRESSION ODDS RATIOS (OR) RESULTS FOR THE ASSOCIATION BETWEEN RACE/ETHNICITY AND DIAGNOSIS STAGE (LATE VERSUS EARLY) BY HISTOLOGIC SUB-TYPE, NATIONAL CANCER DATABASE, 2003-2012, N=228,793[§]

	OR(95%CI)	OR(95%CI)	OR(95%CI)	OR(95%CI)	OR(95%CI)
	Overall EC	**Type 1: Low-grade Endometrioid**	**Type 2: High-grade Endometrioid**	**Type 2: Clear Cell**	**Type 2: Serous**
	n=228,793	**n=163,924**	**n=36,360**	**n=2,871**	**n=11,923**
Socio-Demographic Characteristics					
Race/Ethnicity					
Non-Hispanic White	Ref.	Ref.	Ref.	Ref.	Ref.
Non-Hispanic Black	**1.09 (1.04-1.13)**	0.97 (0.90-1.06)	**1.24 (1.15-1.32)**	1.06 (0.85-1.32)	1.06 (0.96-1.18)
Hispanic	0.97 (0.92-1.03)	0.95 (0.91-1.00)	0.99 (0.90-1.11)	0.79 (0.54-1.16)	0.97 (0.87-1.10)
Non-Hispanic Asian	**1.15 (1.05-1.24)**	**1.16 (1.04-1.29)**	**1.18 (1.03-1.37)**	0.60 (0.35-1.04)	1.09 (0.85-1.39)
Non-Hispanic American Indian, Alaskan Native	1.03 (0.79-1.33)	1.00 (0.71-1.42)	0.75 (0.45-1.26)	4.93 (0.54-38.15)	1.57 (0.76-3.22)
Non-Hispanic Pacific Islander/ Hawaiian	**1.31 (1.06-1.65)**	**1.42 (1.06-1.84)**	1.10 (0.74-1.64)	1.81 (0.39-8.50)	1.34 (0.66-2.69)
Diagnosis Age					
<50	Ref.	Ref.	Ref.	Ref.	Ref.
51-59	**0.93 (0.89-0.98)**	1.02 (0.97-1.08)	**0.77 (0.70-0.83)**	1.46 (0.97-2.19)	0.84 (0.65-1.10)
60-69	**0.86 (0.83-0.91)**	**0.93 (0.87-0.98)**	**0.71 (0.65-0.77)**	1.47 (0.99-2.18)	0.80 (0.62-1.03)
70+	**0.94 (0.89-0.99)**	1.03 (0.96-1.10)	**0.75 (0.68-0.82)**	**1.55 (1.03-2.33)**	0.86 (0.66-1.12)
Diagnosis Period					
2008-2012	Ref.	Ref.	Ref.	Ref.	Ref.
2003-2007	**1.05 (1.02-1.07)**	**1.06 (1.02-1.10)**	0.97 (0.93-1.01)	1.12 (0.97-1.30)	**1.22 (1.13-1.31)**
Zip-Code Level Income[a]					
$63.000+	Ref.	Ref.	Ref.	Ref.	Ref.
$48.000-62.999	1.03 (0.99-1.07)	1.03 (0.98-1.08)	0.99 (0.93-1.05)	1.09 (0.87-1.36)	1.07 (0.96-1.19)
$38.000-$47.999	**1.05 (1.01-1.10)**	1.05 (0.99-1.11)	0.99 (0.92-1.06)	1.09 (0.84-1.41)	**1.16 (1.02-1.31)**
<$38.000	1.06 (0.99-1.11)	1.04 (0.97-1.12)	1.01 (0.93-1.10)	1.05 (0.77-1.43)	1.14 (0.99-1.32)
Zip-Code Level Education[a]					
<7.0 without a high-school diploma	Ref.	Ref.	Ref.	Ref.	Ref.
7.0-12.9% without a high-school diploma	1.01 (0.98-1.05)	0.99 (0.94-1.04)	1.02 (0.96-1.09)	1.07 (0.85-1.34)	1.07 (0.96-1.20)
13.0-20.0% without a high-school diploma	1.01 (0.96-1.05)	0.96 (0.89-1.04)	1.03 (0.98-1.10)	1.13 (0.86-1.48)	1.05 (0.93-1.20)
≥21.0% a high-school diploma	1.00 (0.95-1.06)	0.98 (0.92-1.05)	1.03 (0.94-1.12)	1.26 (0.92-1.73)	1.08 (0.93-1.26)
Health Insurance					
Private Insurance	Ref.	Ref.	Ref.	Ref.	Ref.
Medicare	**1.06 (1.02-1.10)**	**1.06 (1.02-1.12)**	**1.10 (1.03-1.17)**	0.91 (0.74-1.12)	1.00 (0.91-1.10)
Medicaid	**1.45 (1.37-1.54)**	**1.49 (1.38-1.60)**	**1.41 (1.27-1.56)**	1.38 (0.96-1.97)	**1.44 (1.19-1.74)**
Not Insured	**1.43 (1.34-1.52)**	**1.44 (1.32-1.55)**	**1.46 (1.31-1.63)**	1.18 (0.77-1.82)	**1.34 (1.05-1.71)**
Tumor Characteristics					
Grade					
Moderately vs. well differentiated		**3.41 (3.29-3.53)**			
Poorly differentiated vs. undifferentiated			**0.75 (0.69-0.81)**		
Poorly differentiated undifferentiated vs. well/moderately differentiated	**1.82 (1.62-2.07)**			**2.00 (1.51-2.67)**	**1.86 (1.62-2.14)**
Charlson Comorbidity Score					
None	Ref.	Ref.	Ref.	Ref.	Ref.
1	**0.95 (0.92-0.98)**	**0.92 (0.88-0.96)**	0.97 (0.92-1.03)	1.10 (0.92-1.32)	1.07 (0.97-1.16)
2 or more	0.98 (0.92-1.04)	0.93 (0.85-1.00)	1.02 (0.93-1.13)	0.97 (0.70-1.34)	1.02 (0.87-1.21)
Treatment Facility Characteristics					
Facility Type					
Academic/Research Programs	Ref.	Ref.	Ref.	Ref.	Ref.
Community Cancer Programs	**0.91 (0.86-0.97)**	**0.85 (0.78-0.92)**	0.97 (0.87-1.08)	0.91 (0.63-1.31)	0.97 (0.80-1.18)
Comprehensive Community Cancer Programs	**0.92 (0.89-0.94)**	**0.88 (0.85-0.91)**	**0.94 (0.90-0.99)**	0.89 (0.75-1.05)	0.93 (0.85-1.00)
Facility Location					
West South Central	Ref.	Ref.	Ref.	Ref.	Ref.
West North Central	**0.93 (0.87-0.99)**	0.98 (0.90-1.06)	**0.83 (0.74-0.93)**	1.16 (0.78-1.73)	1.17 (0.96-1.42)
South Atlantic	**0.90 (0.85-0.94)**	**0.93 (0.86-0.99)**	0.91 (0.83-1.00)	0.91 (0.66-1.26)	0.96 (0.82-1.13)
Pacific	1.04 (0.99-1.11)	**1.16 (1.08-1.27)**	0.95 (0.85-1.05)	1.24 (0.86-1.77)	1.10 (0.92-1.32)
New England	**0.84 (0.79-0.90)**	**0.80 (0.73-0.88)**	0.91 (0.81-1.03)	1.01 (0.65-1.56)	0.83 (0.67-1.03)
Mountain	0.96 (0.89-1.03)	1.00 (0.91-1.10)	0.95 (0.83-1.07)	1.12 (0.70-1.80)	1.10 (0.87-1.39)
Middle Atlantic	**0.88 (0.83-0.93)**	0.93 (0.86-1.00)	**0.83 (0.75-0.92)**	1.00 (0.71-1.40)	0.94 (0.80-1.11)
East South Central	**0.84 (0.78-0.89)**	**0.84 (0.76-0.92)**	**0.81 (0.71-0.91)**	0.78 (0.51-1.19)	0.83 (0.68-1.02)
East North Central	**0.92 (0.87-0.97)**	0.96 (0.90-1.04)	0.97 (0.88-1.06)	1.07 (0.77-1.48)	0.95 (0.80-1.12)

TABLE VI (CONTINUED): MULTIVARIABLE LOGISTIC REGRESSION ODDS RATIOS (OR) RESULTS FOR THE ASSOCIATION BETWEEN RACE/ETHNICITY AND DIAGNOSIS STAGE (LATE VERSUS EARLY) BY HISTOLOGIC SUB-TYPE, NATIONAL CANCER DATABASE, 2003-2012, N=228,793[§]

	OR(95%CI)	**OR(95%CI)**	**OR(95%CI)**	**OR(95%CI)**	**OR(95%CI)**
	Overall EC	**Type 1: Low-grade Endometrioid**	**Type 2: High-grade Endometrioid**	**Type 2: Clear Cell**	**Type 2: Serous**
	n=228,793	**n=163,924**	**n=36,360**	**n=2,871**	**n=11,923**
Treatment Facility Case-Volume					
≥74 average cases per year	Ref.	Ref.	Ref.	Ref.	Ref.
42-73 average cases per year	0.99 (0.95-1.02)	0.96 (0.92-1.01)	1.04 (0.98-1.11)	0.88 (0.72-1.09)	0.99 (0.90-1.10)
20-41 average cases per year	1.03 (0.99-1.06)	1.04 (0.99-1.10)	**1.07 (1.01-1.15)**	0.98 (0.79-1.22)	1.04 (0.94-1.14)
1-19 average cases per year	**1.10 (1.06-1.15)**	**1.13 (1.06-1.19)**	**1.19 (1.10-1.28)**	0.98 (0.77-1.25)	1.07 (0.95-1.21)

[a] Measure estimated by matching the zip code of the patient recorded at the time of diagnosis against files derived from year 2010 U.S. Census data. Variables categorized as quartiles based on equally proportioned variable ranges among all U.S. zip codes.

[§] Women with missing values for diagnosis stage were deleted from the analytic sample.

In addition, higher odds of late-stage diagnosis were found in women diagnosed during the earlier period (2003-2007) (OR_{adj}=1.05; 95%CI 1.02-1.07) as compared with the most recent period (2008-2012), those who lived in zip-code area where families reported having a median income between $38.000-$47.999 (OR_{adj}=1.05; 95%CI 1.01-1.10) as compared to those earning $63.000 and over, covered by Medicare (OR_{adj}=1.06; 95%CI 1.02-1.10), Medicaid (OR_{adj}=1.45; 95%CI 1.37-1.54), or those who were uninsured (OR_{adj}=1.43; 95%CI 1.34-1.52) as compared to those covered by private health insurance; diagnosed with poorly differentiated or undifferentiated tumors (OR_{adj}=1.82; 95%CI 1.62-2.07) as compared to those diagnosed with well and moderately differentiated tumors and treated in facilities seeing 1-19 EC cases a year (OR_{adj}=1.10; 95%CI 1.06-1.15) as compared to those seeing over 74 EC cases a year.

In contrast, lower odds of diagnosis with late-stage EC were found in women 50 and younger (OR_{adj}=0.93; 95%CI 0.89-0.98), between the ages of 60 and 69 (OR_{adj}=0.86; 95%CI 0.83-0.91) and those 70 and older 69 (OR_{adj}=0.94; 95%CI 0.89-0.99) as compared to those being 50 and younger, diagnosed with one comorbidity (OR_{adj}=0.95; 95%CI 0.92-0.98) as compared to those with none; treated in community cancer programs (OR_{adj}=0.91; 95%CI 0.86-0.97) and comprehensive community cancer programs (OR_{adj}=0.92; 95%CI 0.89-0.94) as opposed to academic/research programs and those treated in facility located in the West North Central (OR_{adj}=0.93; 95%CI 0.87-0.99), South Atlantic (OR_{adj}=0.90; 95%CI 0.85-0.94), New England (OR_{adj}=0.84; 95%CI 0.79-0.90), Middle Atlantic (OR_{adj}=0.88; 95%CI 0.83-0.93), and East South Central (OR_{adj}=0.84; 95%CI 0.78-0.89), East North Central (OR_{adj}=0.92; 95%CI 0.87-0.97) regions as compared to the West South Central.

2. Low-grade endometrioid carcinoma

In the fully adjusted model, NHPI and NHA women had respectively 42% (OR_{adj}=1.42; 95%CI 1.06-1.84) and 16% (OR_{adj}=1.16; 95%CI 1.04-1.29) higher odds of being diagnosed with late-stage disease when compared to NHW. In addition, higher odds of late-stage diagnosis

were found in women diagnosed during the earlier period (2003-2007) (OR_{adj}=1.06; 95%CI 1.02-1.10) as compared with the most recent period (2008-2012), covered by Medicare (OR_{adj}=1.06; 95%CI 1.02-1.12), Medicaid (OR_{adj}=1.49; 95%CI 1.38-1.60), or those who were uninsured (OR_{adj}=1.44; 95%CI 1.32-1.55) as compared to those covered by private health insurance; diagnosed with moderately differentiated tumors (OR_{adj}=3.41; 95%CI 3.29-3.53) as compared to those diagnosed with well differentiated tumors; treated in the Pacific region (OR_{adj}=1.16; 95%CI 1.08-1.27) as compared to those treated in the West South Central regions and treated in facilities seeing 1-19 EC cases a year (OR_{adj}=1.13; 95%CI 1.06-1.19) as compared to those seeing over 74 EC cases a year.

In contrast, lower odds of diagnosis with late-stage EC were found in women diagnosed between the ages of 60 and 69 (OR_{adj}=0.93; 95%CI 0.87-0.98) as compared to those being 50 and younger, diagnosed with one comorbidity (OR_{adj}=0.92; 95%CI 0.88-0.96) as compared to those with none; treated in community cancer programs (OR_{adj}=0.85; 95%CI 0.78-0.92) and comprehensive community cancer programs (OR_{adj}=0.88; 95%CI 0.85-0.91) as opposed to academic/research programs; and those living in the South Atlantic (OR_{adj}=0.93; 95%CI 0.86-0.99), New England (OR_{adj}=0.80; 95%CI 0.73-0.88) and East South Central (OR_{adj}=0.84; 95%CI 0.76-0.92) regions as compared to the West South Central.

3. High-grade endometrioid carcinoma

In fully adjusted models NHB and NHA women had respectively 24% (OR_{adj}=1.24; 95%CI 1.15-1.32) and 18% (OR_{adj}=1.18; 95%CI 1.03-1.37) higher odds of being diagnosed with late-stage disease when compared to NHW. In addition, significantly higher odds of diagnoses with late-stage EC were found in women covered by Medicare (OR_{adj}=1.10; 95%CI 1.03-1.17), Medicaid (OR_{adj}=1.41; 95%CI 1.27-1.56), or those uninsured (OR_{adj}=1.46; 95%CI 1.31-1.63) as compared to those who had private health insurance; and those treated in facilities seeing 1-19

(OR_{adj}=1.19; 95%CI 1.10-1.28) and 20-41 (OR_{adj}=1.07; 95%CI 1.01-1.15) EC as compared to those treating over 74 EC cases a year.

In contrast, significantly lower odds with late-stage diagnosis were found in women who were between the ages of 51 and 59 (OR_{adj}=0.77; 95%CI 0.70-0.83), 60 and 69 (OR_{adj}=0.71; 95%CI 0.65-0.77) and 70 and older (OR_{adj}=0.75; 95%CI 0.68-0.82) as compared to those being 50 and younger; were diagnosed with poorly differentiated tumors (OR_{adj}=0.75; 95%CI 0.69-0.81) as compared to those diagnosed with undifferentiated tumors; were treated at the comprehensive community cancer programs (OR_{adj}=0.94; 95%CI 0.90-0.99) as opposed to academic/research programs; and those living in the West North Central (OR_{adj}=0.83; 95%CI 0.74-0.93), Middle Atlantic (OR_{adj}=0.83; 95%CI 0.75-0.92) and East South Central (OR_{adj}=0.81; 95%CI 0.71-0.91) regions as compared to the West South Central.

4. **Clear Cell Carcinoma**

No racial/ethnic differences in diagnosis stage were detected in women diagnosed with CCC. Women who were 70 and older as compared to those who were 50 and younger and those diagnosed with poorly or undifferentiated tumors as opposed to those diagnosed with well and moderately well differentiated tumors had respectively 55% higher odds (OR_{adj}=1.55; 95%CI 1.03-2.33) and 100% higher odds (OR_{adj}=2.00; 95%CI 1.51-2.67) of being diagnosed with late-stage tumors.

5. **Serous Carcinoma**

Similarly to CCC, no racial/ethnic differences in diagnosis stage were detected in women diagnosed with SC. After adjusting for all of the confounders, higher odds of diagnosis with late-stage disease were found in women who were diagnosed during the earlier time period (2003-2008) (OR_{adj}=1.22; 95%CI 1.13-1.31) as compared to the most recent time period (2008-2012); lived in zip-code area where families reported having a median income between $38.000-

$47.999 ($OR_{adj}$=1.16; 95%CI 1.02-1.31) as compared to those earning $63.000 and over, were covered by Medicaid (OR_{adj}=1.44; 95%CI 1.19-1.74) or were uninsured (OR_{adj}=1.49; 95%CI 1.13-1.95) as compared to those covered by the private health insurance; and were diagnosed with poorly or undifferentiated tumors (OR_{adj}=1.86; 95%CI 1.62-2.14) as opposed to those diagnosed with well and moderately well differentiated tumors

D. Discussion

The findings of this study confirm the results from past research (7, 20, 26) by demonstrating that the burden of EC is not equally distributed between racial/ethnic groups. In the NCDB, NHB women were significantly more likely to be diagnosed with more aggressive EC subtypes than NHW. In addition, when compared to NHW, NHB, NHPI, NHA and Hispanics were more likely to be diagnosed with late-stage tumors.

Little is known about the risk factors for Type 2 EC subtypes, and the striking differences found in this study only emphasize the importance of understanding why these differences exist. A recent study suggested that risk factors such as a body mass index of more than 30, a personal history of diabetes and a lack of physical activity were associated with Type 2 tumors (116). Even if these factors may increase one's risk of diagnosis with more aggressive subtypes of EC, they cannot be exclusively responsible for it given that Hispanics are as likely as NHB to be obese and have a personal history of diabetes (117). Molecular and genetic factors may be able to shed some light on the racial/ethnic differences in tumor presentation.

In the unadjusted analyses assessing the relationship between the tumor, socio-demographic and treatment facility characteristics and late-stage diagnosis, race/ethnicity, diagnosis age, zip-code level income, zip-code level education, health insurance, urbanicity, tumor characteristics, facility type and facility location were significantly associated with the outcome. Overall, and consistent with previous literature, women diagnosed with SC, were

significantly more likely to present with extrauterine spread (stages III, IV) as compared to those diagnosed with other subtypes of EC(12). In addition, as expected, women diagnosed with higher grade tumors were significantly more likely to be diagnosed with later-stage EC than those diagnosed with lower grades.

1. Low-Grade Endometrioid Carcinoma

In the multivariable analyses, NHA and NHPI women had significantly higher odds of late-stage diagnosis with LGEC than NHW, after accounting for potential confounders. This study is the first to report the results of the relationship between race/ethnicity and late-stage diagnosis from fully adjusted models. It is also the first study to, in addition to NHB and Hispanic women, compare other minority populations to NHW women. Previous studies that presented unadjusted results, respectively, found no differences in Type 1 EC (LGEC and HGEC) between Black, Hispanic and White women (20) and found that Hispanics and Blacks were less likely than Whites to be diagnosed with Type 1 tumors at a localized stage (26). The NHPI-NHW and NHA-NHW differences in stage at diagnosis may be explained, in part, by the use of traditional remedies by NHPI and NHA. Previous studies showed that Asian women delay seeking medical care after noticing symptoms and may first turn to traditional remedies (119). In addition, NHPI women may live on remote islands, which could promote seclusion and, in turn, impact knowledge about the typical symptoms associated with EC and access to care, both of which may be associated with delays in diagnosis.

In addition, our study also shows that women who were uninsured and those covered by Medicaid had nearly 50% higher odds of diagnosis with late-stage EC when compared to those covered by private health insurance (85). It is not unexpected that women without health insurance and those covered by Medicaid had higher odds of diagnosis with late-stage disease, since they may be less likely to have a regular source of medical care such as a primary care

physician (118). This could prevent them from sharing their symptoms in a timely manner and, as a result, being diagnosed with later-stage disease (40, 41, 84, 85). Women with no health insurance are often of lower SES. Women of lower SES are more likely to have competing priorities in their everyday lives and are less likely to make the decision to take a day off to see a doctor because of abnormal bleeding (41). The findings, indicating more advanced-stage disease in women who are uninsured or underinsured, show that those without private health insurance likely do not receive optimal care in terms of timely diagnosis and follow-up with a health care specialist (85).

Moreover, the results of this study also show that women diagnosed at community cancer programs and comprehensive community cancer programs as compared to those diagnosed at the academic/research programs had lower odds of diagnosis with late-stage tumors. These differences might be explained by the fact that patients with advanced tumors are more likely to be referred to academic/research centers to receive more complex treatments. In addition, while the majority of women with private health insurance and those covered by Medicare were diagnosed at comprehensive community cancer programs, the majority of uninsured women were diagnosed at academic/research programs. In urban neighborhoods, minority populations are more likely to be uninsured and often live in the proximity of major city academic/research hospitals (106, 107). Interestingly though, most of the community cancer programs as opposed to the academic/research centers were low-case volume hospitals that, according to the results of our study and previous investigations, have higher odds of late-stage diagnosis (104).

2. High-grade Endometrioid Carcinoma

The results of the multivariable analyses showed that NHB and NHA women have higher odds of diagnosis with late-stage HGEC than NHW after adjusting for potential confounders. A

previous study that used SEER data reported that in crude models, Hispanics were more likely to be diagnosed with late-stage Type 2 EC than Whites (64). In contrast, another study found that Blacks and Hispanics were as likely as Whites to be diagnosed with late-stage tumors, in unadjusted models (20).

Similarly to women diagnosed with LGEC, those diagnosed with HGEC, who had no health insurance or were covered by Medicaid, had significantly higher odds of late-stage diagnosis than women who were covered by private health insurance. In addition, the results of our study showed that women diagnosed in a comprehensive community cancer program had lower odds of diagnosis with late-stage disease than those diagnosed in an academic research program. Moreover, women diagnosed in low-volume hospitals had higher odds of late-stage diagnosis when compared to those diagnosed in high-volume facilities.

Finally the results of this study show that younger women have significantly higher odds of diagnosis with late-stage HGEC than their older counterparts. This relationship was not found in other subtypes of the Type 2 tumors.

3. Clear-cell and serous carcinomas:

No racial/ethnic differences in the late-stage diagnosis for clear-cell and SC were detected in our study after adjusting for potential confounders.

However, in women diagnosed with SC, those who were uninsured or covered by Medicaid had higher odds of diagnosis with late-stage tumors than those covered by private health insurance.

Overall, while past studies have hypothesized that women who live in disadvantaged areas have worse access to care which subsequently could increase their likelihood of diagnosis with late-stage tumors (97, 120), our study did not show any significant relationships

between the zip-code level income, zip-code level education and late-stage diagnosis in any of the subtypes of EC.

This study adds to the literature on the differences between minority and NHW women because it shows that the unadjusted measures overestimated the association between race/ethnicity and diagnosis stage. Most importantly, in the NHB-NHW disparity, adjusting for important covariates significantly reduced the association between race/ethnicity and stage at diagnosis. These results suggest caution when evaluating unadjusted estimates in the literature.

In addition, considering EC as a homogenous disease distorts the association between race/ethnicity and diagnosis stage. Knowing that NHPI women have higher odds of late-stage diagnosis with LGEC, the least aggressive EC tumor, as opposed to SC could provide very important information for community programs. It could potentially mean that NHPI could be diagnosed at an earlier stage with increased education on early recognition of symptoms. Stage at diagnosis is an important predictive factor in survival and therefore it is critical to diagnose the disease at the earliest stage possible (2, 7). Finally, our results add to and extend the results from other studies on NHB-NHW differences. We showed that in contrast to previous data (85), NHB women only had higher odds of diagnosis with late-stage disease than NHW when diagnosed with HGEC. Differences in late-stage diagnosis in other EC tumor subtypes were not detected.

E. Limitations and Strengths

The results of this study should be interpreted in light of several limitations that primarily pertain to the variables available for analysis. Income and education are only available at the zip-code level. While zip-code level measures were important predictors of access care and consequently play a role in late-stage diagnosis, individual-level measures were also shown to be associated with late-stage disease (4, 40, 41). In addition, physician specialty, an important

independent predictor for staging (99, 100) and gynecologic cancer outcomes (99, 100, 103), was not available. However, we included average facility-case volume as a proxy to minimize bias, assuming that low case volumes reflect a lack of gynecologic oncology subspecialty care (103). The lack of these variables made impossible the assessment of these relationships. Finally, it is unclear whether the detected racial/ethnic differences in stage at diagnosis and tumor aggressiveness, reflect true biological variations or differences in lifestyle and socio-cultural risk factors. It is possible that the prevalence of these risk factors drives these differences as their prevalence is likely to differ between different racial/ethnic groups..

Despite these limitations, this study has several strengths. First, this study is the first to provide the results of the association between race/ethnicity and diagnosis stage from adjusted models. Second, this study is the first to, in addition to NHB, consider women of other minority populations. Third, as opposed to analyzing EC as a homogenous disease, or solely as Type 1 and Type 2, this study presents racial/ethnic differences in diagnosis stage by four histological subtypes. Data for carcinosarcomas and “other tumors” was incomplete, however, because these tumors are highly heterogeneous excluding them from our analyses does not represent a limitation for our study. Performing analyses by histologic subtypes was recommended by the comprehensive report on ovarian cancer released by the National Academy of Sciences in March 2016. This report stipulates that performing subtypes analyses will advance the science and help reduce cancer morbidity and mortality (18).

F. Conclusion

In conclusion, this study demonstrates that NHB women are significantly more likely to be diagnosed with any of the subtypes of Type 2 EC, than women of other racial/ethnic populations. This study also shows that NHA and NHPI are at higher odds of diagnosis with LGEC and that NHB and NHA have higher odds of diagnosis with late-stage HGEC when

compared to NHW. Finally, this study show that uninsured women and those covered by Medicaid have almost a 1.5 fold increase of diagnosis with late-stage LGEC, HGEC and SC than those covered by private health insurance.

IV. RACIAL/ETHNIC DIFFERENCES IN TREATMENT DEFINED AS SURGERY, RADIATION THERAPY AND CHEMOTHERAPY

A. Introduction

Differences in EC incidence and survival between NHB and NHW women have been well documented. Overall, while the incidence of the disease is higher in NHW women (1), survival is lower in NHB (5, 7, 26, 35, 67, 81). Treatment differences could potentially account for this survival disparity.

Surgery is the cornerstone of EC treatment and is recommended for every patient diagnosed with the disease, regardless the clinical stage, grade or histology of the tumor (11). Receiving surgical treatment is an important predictor of EC survival (3, 64). Using the Surveillance, Epidemiology, and End Results Program (SEER), Mahdi et al. demonstrated that in women diagnosed with overall EC, those who did not have surgery were three times more likely to die than those who did (3). Similarly, in women diagnosed with Type 2 EC tumors, those who did not have surgery had twice the risk of dying when compared to those who did (64).

While surgery is recommended for every patient, there is no well-established treatment protocol for the use of adjuvant treatment. Adjuvant treatment is the subject of a number of clinical trials; as such the adequate adjuvant therapy has yet to be determined (46-48). Radiation therapy is prescribed for recurrent tumors or used instead of surgery, when surgery is not feasible due to the extent of the disease or the presence of medical comorbidities (53). On the other hand, chemotherapy is recommended for older patients or patients diagnosed with metastatic disease, i.e. advanced grade (grade III-IV) and stage tumors (stage II-IV). Several randomized clinical trials have shown that the use of multiple agent chemotherapy, as compared to single agent, was more effective because of the improved response rate and progression-free survival with negligible impact on overall survival (53-55).

Previous studies examining factors associated with EC treatment have generally failed at presenting results for EC subtypes (4, 67, 73, 75, 76), although the recommended treatment regimens vary by histologic subtype (11). In addition, the National Academy of Sciences recommended performing subtype-specific analyses which would allow for scientific advancement and help reduce cancer morbidity and mortality (18). Furthermore, previous research has not accounted for important predictors that impact treatment such as tumor, socio-demographic and treatment facility characteristics. Past research suggests that racial/ethnic differences in EC treatment exist (2-9); however these differences were almost exclusively documented in NHW and NHB women. In fact, in the past sixteen years, only three studies have assessed treatment differences in nonblack minority women (e.g. Asian, Hispanic). Furthermore, while these studies found racial/ethnic treatment differences for overall EC, no studies have assessed whether these differences exist after accounting for potential confounders. Moreover, no studies have determined what factors are associated with potential differences.

Mediation analysis can be used to estimate the underlying relationship between race/ethnicity and treatment by quantifying what proportion of the disparity is explained by a mediator or group of mediators. Mediation analysis can be an important tool in cancer disparity research. It allows for the separation of the direct effect of race/ethnicity, on treatment, from the indirect effects mediated through variables pertaining to the socio-demographic, tumor or treatment facility characteristics. In a recent study performed in Chicago, the researchers found that the observed racial differences in having mastectomy were primarily mediated by diagnosis stage and not patients' socio-economic status (SES). Importantly, the mediating effect of diagnosis stage was different when comparing NHB to NHW and Hispanics to NHW (59). Another recent study estimated the mediating effect of treatment facility characteristics on racial/ethnic differences in delayed diagnosis for breast cancer. The authors found that all

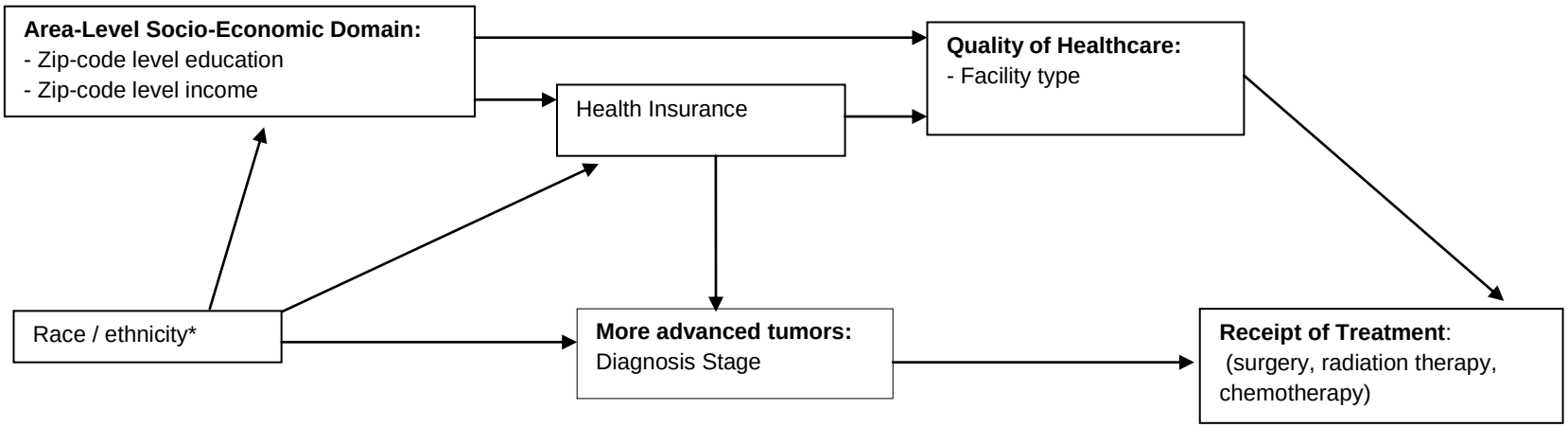
facility factors accounted for 43% of the disparity in diagnostic delay. The extent of the mediation of facility factors was very similar when comparing NHB to NHW and non-Hispanics to NHW (62). Mediation analysis has not been used to assess EC racial/ethnic differences and therefore it is unclear what factors could act as potential mediators. Based on our conceptual model (Figure 2), we hypothesized zip-code level income, zip-code level education, the socio-economic domain including both zip-code level measures, and stage at diagnosis to be potential mediators in the relationship between race/ethnicity and receipt of treatment. Treatment regimens are directly dependent on the tumor aggressiveness at the time of diagnosis (11) and the types of facilities where the patient gets treated (121). In addition, they are indirectly dependent on one's health insurance coverage (5) and patient's area-level SES (40, 41, 84).

The purpose of this analysis is to assess racial/ethnic differences in receipt of treatment (surgery, radiation therapy and chemotherapy) by EC tumor subtype using the NCDB. The NCDB is one of the largest and most comprehensive dataset of EC in the U.S. The NCDB is based on registry data and includes 70% or approximately 230,000 stage-diagnosed EC cases in the U.S. and Puerto Rico between 2003 and 2012 (109). The mediating effect of stage at diagnosis, area-level income, area-level education, health insurance status and treatment facility characteristics on racial/ethnic differences in the receipt of treatment was investigated. To the best of our knowledge, this study is the first to assess whether subtype-specific racial/ethnic differences in EC treatment modalities exist after adjusting for potential confounders and exploring factors that may mediate potential differences. Moreover, this study is the first to compare six racial/ethnic groups in models stratified by tumor subtype.

B. Methods

First, differences in receiving surgical treatment, radiation therapy and chemotherapy between NHW and women of other racial/ethnic groups were assessed using the Chi-square test statistics.

Figure 2: Conceptual framework for the relationship between race/ethnicity and receipt of treatment



* Non-Hispanic black, Hispanics, non-Hispanic Asians, non-Hispanic Pacific Islanders/Hawaiian Natives, Non-Hispanic American Indian/ Alaskan Natives vs. non-Hispanic Whites

Chemotherapy was defined as receipt of multi-agent chemotherapy. In the bivariate analyses, receiving surgical treatment, radiation therapy and chemotherapy were dichotomized as any vs. none. In addition, differences in receiving multi-agent chemotherapy were tested for each stage at diagnosis (I, II, III and IV).

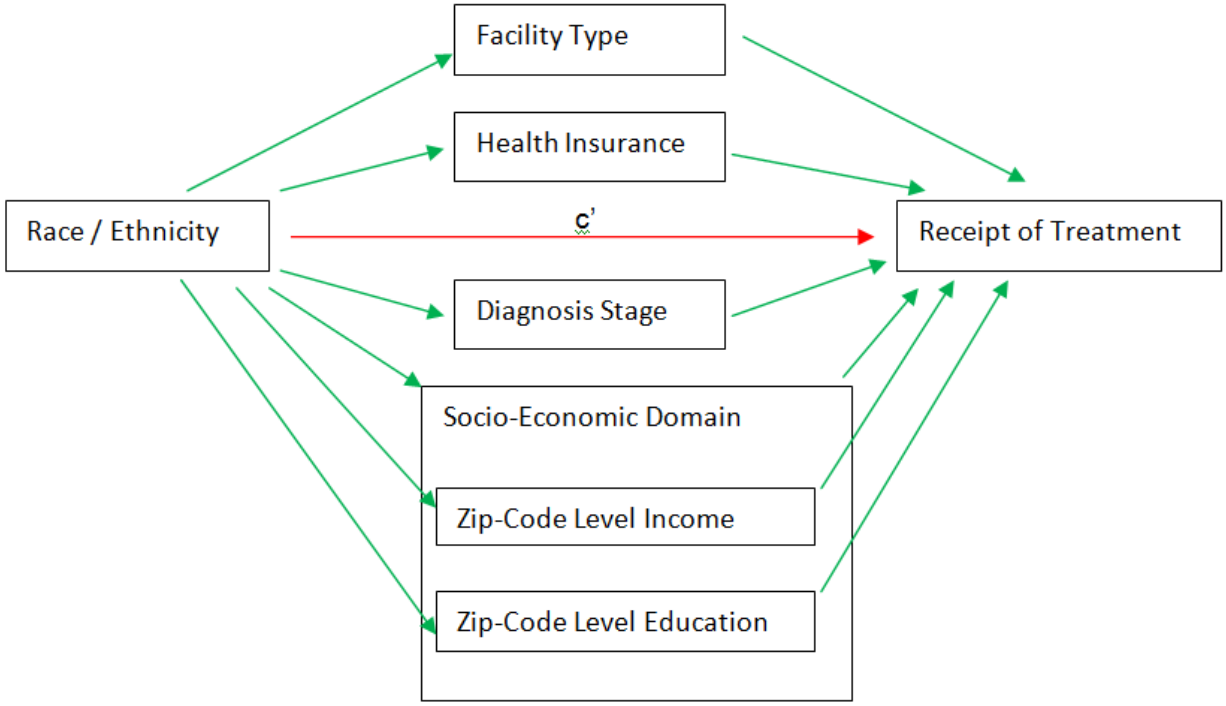
Second, three multivariable logistic regression models stratified by tumor subtype (LGEC, HGEC, CCC and SC) were fitted to estimate the relationship between race/ethnicity and receipt of surgery, radiation therapy and chemotherapy. All of the covariates were included in the multivariable models either because they were significantly associated with the outcome or because conceptually they were considered to be important confounders. The NCDB dataset used for the multivariable analyses included 208,247 women with stage-diagnosed EC between 2003 and 2012. Observations with missing values for any of the three outcome variables were excluded from the analyses: surgery (n=0), radiation therapy (n=3,226) and chemotherapy (n=5,592).

Third, because women of lower socio-economic status and those who were underinsured were shown to experience delayed treatment (112), effect modification was assessed for zip-code level income, zip-code level education and health insurance. Period of diagnosis was also considered as a potential effect modifier to determine if treatment differences have changed over time. Effect modification was assessed by including the pair-wise interaction term and two corresponding main effects into the final model. In addition, interaction between race/ethnicity and stage at diagnosis was tested in models predicting receipt of chemotherapy. The interaction between race/ethnicity and health insurance was statistically significant (P<0.0001) in the association between race/ethnicity and receiving surgical treatment, for women diagnosed with LGC; as such, the model was stratified by health insurance. Odds ratios and 95% confidence intervals were estimated.

Fourth, mediation analyses on racial/ethnic differences in receipt of surgery, radiation therapy and chemotherapy found in the multivariable models were performed. The socio-economic (SE) domain and five potential mediators were tested as intermediate variables: (1), zip-code level education, (2) zip-code level income, (3) health insurance, (4) diagnosis stage, (5) type of facility (Figure 3). The SE domain included zip-code level education and zip-code level income. Sixth indirect paths connecting race/ethnicity with the receipt of each treatment modality were estimated. The direct effect (c') is represented by a red arrow. In the primarily exploration of mediation, three tests were performed to confirm that a hypothesized mediator met the statistical criteria of mediation analysis. (1) Race/ethnicity was significantly associated with receipt of each treatment modality. (TABLE VIII) (2) Race/ethnicity was significantly associated with each mediator. (TABLE IV) (3) Each mediator was significantly associated with receipt of each treatment modality. (TABLE VIII) Next, OR were compared between the fully adjusted model and models unadjusted for the hypothesized mediator or the SE domain. The hypothesized mediator or the SE domain that altered the OR by a factor of 0.1 or more was further explored as an intermediate variable. Lastly, every intermediate variable or the SE domain was separately added to a fully adjusted multivariable model to calculate the mediated proportion and its 95%CI using the mediate SAS macro (122). The proportion of the effect of race/ethnicity mediated by intermediate variables (Figure 2) on each treatment modality was separately estimated for every minority women-NHW disparity detected in the multivariable models. The proportion mediated represented the excess or reduced odds in the receipt of treatment among the minority group as compared to NHW women that could be attributed to the SE domain or a mediator.

Bivariate, logistic and mediation analyses were performed using SAS software version 9.4 (SAS Institute, Inc., Cary, NC). *P*-values were two sided, with an α level of 0.05.

Figure 3: Conceptual model of potential mediators in the relationship between race/ethnicity and receipt of treatment



C. Results

TABLE IV describes the characteristics of the study population by race/ethnicity, overall, and by socio-demographic, tumor and facility covariates. A total of 252,785 women were stage-diagnosed with EC in one of the CoC-approved hospitals between 2003 and 2012. Overall, 83.7% women self-identified themselves as NHW, 8.4% as NHB, 5.2% as Hispanic, 2.3% as NHA, 0.3% as NHPI and 0.2% as NHAIAN. In addition, 71.6% of women were diagnosed with LGEC, 15.9% with HGEC, 5.2% with SC and 1.3% with CCC. (TABLE VII)

TABLE VII shows that, overall, 4.0% of women did not receive surgery, 72.7% did not receive radiation therapy and 84.9% did not receive multi-agent chemotherapy. In the stage-

stratified bivariate analyses, 95.2% of women diagnosed with early stage and 47.4% with late-stage tumors did not receive multi-agent chemotherapy.

NHB, Hispanic and NHAIAN women were significantly less likely than NHW to receive surgical treatment. In contrast, NHA were more likely to receive surgical treatment than NHW. In regards to radiation therapy, when compared to NHW, NHB were more likely and Hispanics, NHAIAN and NHPI were less likely to receive radiation therapy compared to NHW. Moreover, NHB, NHA and NHPI were more likely than NHW women to receive adjuvant chemotherapy. In the stage-stratified bivariate analyses, NHB women were more likely to receive multi-agent chemotherapy for early and late-stage diagnoses than NHW. NHB were more likely to receive chemotherapy for early-stage and Hispanic less likely to receive it for late-stage diagnoses than NHW.

TABLE VIII presents the distribution of socio-demographic, tumor and treatment facility characteristics, overall, and by the three primary outcomes of the analysis: surgical treatment, radiation therapy and chemotherapy and shows significant differences by race/ethnicity for all three types of treatments. Absence of surgical treatment was more prevalent in all minorities except in NHA; at older ages; in women diagnosed between 2008 and 2012; in areas with lower income and education levels and in women without private health insurance. In addition, women diagnosed with Type 2 EC; late-stage; EC with high-grade tumors and those with two or more comorbidities were less likely to have surgery. Lastly, absence of surgical treatment was more prevalent in women diagnosed in community cancer programs; in low-volume facilities and hospitals located in the Middle Atlantic regions.

Radiation therapy treatments were less prevalent in all minorities except in NHB; in women of younger ages; those diagnosed between 2008 and 2012; in areas with lower education levels; in women with private health insurance and those living in rural areas.

TABLE VII: DISTRIBUTION OF TREATMENT MODALITIES (SURGERY, RADIATION THERAPY, CHEMOTHERAPY) BY RACE/ETHNICITY, NATIONAL CANCER DATABASE, 2003-2012, N=215,078

	Non-Hispanic White n=179,922 %	Non-Hispanic Black n=18,037 %	Hispanic n=11,090 %	Non-Hispanic Asian n=4,968 %	Non-Hispanic American Indian, Alaskan Native n=492 %	Non-Hispanic Pacific Islander, Hawaiian n=569 %	Overall %
Overall	82.7	8.4	5.2	2.3	0.2	0.3	
Surgery							
Yes	96.4	92.0#	95.4#	96.9*	94.7*	96.0	96.0
No	3.6	7.9	4.6	3.0	5.3	4.0	4.0
Missing	0	0	0	0	0	0	0
Radiation Therapy							
Yes	25.7	28.4#	23.4#	25.3	19.7*	18.6#	25.8
No	72.8	70.1	75.2	72.9	79.3	80.1	72.7
Missing	1.5	1.5	1.4	1.9	1.0	1.2	1.5
Multi-Agent Chemotherapy							
Overall Yes	11.8	18.5#	12.3	16.0#	13.6	15.5*	12.5
Overall No	85.7	78.3	84.8	80.7	83.3	82.1	84.9
Missing	2.5	3.2	2.9	3.3	3.1	2.5	2.6
Multi-Agent Chemotherapy by Diagnosis Stage							
Early Stage (stage I, II)							
Yes	4.5	8.0#	4.9	5.7#	4.6	3.7	4.8
No	95.5	92.0	95.1	94.3	95.4	96.3	95.2
Late Stage (stage III, IV)							
Yes	52.6	52.3	50.1*	60.8#	59.0	57.6	52.7
No	47.4	47.7	49.9	39.2	41.0	42.4	47.4

* Significantly different from NHW (p_{value} <0.05).
# Significantly different from NHW (p_{value} <0.001).

In addition, women diagnosed with LGEC; at an early-stage; with low-grade tumors and with comorbidities were less likely to receive radiation therapy. Lastly, radiation therapy treatments were less prevalent in women diagnosed in comprehensive community cancer programs; facilities located in the West South Central regions and in higher-volume hospitals.

Finally, multi-agent chemotherapy treatments were the least prevalent in NHW; in women 50 and younger and those 70 and older; those diagnosed between 2003 and 2007; in areas with higher-income levels and in women with private health insurance. Women diagnosed with LGEC; at an early-stage; with low-grade tumors and with comorbidities were also less likely to be treated with multi-agent chemotherapy. Lastly, chemotherapy treatments were less prevalent in women diagnosed in comprehensive community cancer programs, facilities located in the Mountain regions and in lower-volume hospitals.

1. Receipt of Surgical Treatment

In the unadjusted models, NHB women had 2.1 (OR=2.08; 95%CI 1.98-2.18), Hispanic 1.3 (OR=1.27; 95%CI 1.19-1.37), and NHAIAN 1.4 (OR=1.38; 95%CI 1.01-1.89) times higher odds of not receiving surgical treatment for overall EC when compared to NHW.

In models adjusted for potential covariates, NHB had 60% (OR_{adj}=1.60; 95%CI 1.50-1.71) higher odds of not receiving surgical treatment for overall EC when compared to NHW. TABLE IX and TABLE X present the results from the multivariable logistic regression models for the association between race/ethnicity and receipt of surgical treatment, stratified by EC tumor subtype.

TABLE VIII: DISTRIBUTION OF SOCIO-DEMOGRAPHIC, TUMOR AND TREATMENT FACILITY CHARACTERISTICS OVERALL AND STRATIFIED BY RECEIPT OF TREATMENT (SURGERY, RADIATION THERAPY AND CHEMOTHERAPY), NATIONAL CANCER DATABASE, 2003-2012, n=208,247[a]

	Did not Receive Surgery (%) n=14,518	P_{value}	Did not Receive Radiation Therapy (%) n=180,691	P_{value}	Did not Receive Chemotherapy (%) n=210,685	P_{value}
Overall	5.9 %		74.0 %		86.3 %	
Socio-Demographic Characteristics						
Race/Ethnicity		<.0001		<.0001		<.0001
Non Hispanic White	3.6		73.9		87.9	
Non Hispanic Black	8.0		71.1		81.0	
Hispanic	4.6		76.3		87.3	
Non-Hispanic Asian	3.0		74.3		83.6	
Non-Hispanic American Indian, Alaskan Native	5.3		80.2		85.9	
Non-Hispanic Pacific Islander/Hawaiian	3.8		81.5		84.4	
Diagnosis Age		<.0001		<.0001		<.0001
<50	3.8		81.2		88.1	
51-59	2.5		76.4		87.8	
60-69	3.2		71.9		85.4	
70+	6.6		70.0		88.1	
Diagnosis Period		<0.05		<.0001		<.0001
2008-2012	4.2		75.1		85.0	
2003-2007	3.8		72.2		90.0	
Zip-Code Level Income[b]		<.0001		0.88		<0.05
$63.000+	3.2		73.8		87.3	
$48.000-62.999	3.6		73.7		87.3	
$38.000-$47.999	4.4		73.9		87.3	
<$38.000	5.5		74.0		86.7	
Zip-Code Level Education[b]		<.0001		<.0001		0.77
<7.0 without a high-school diploma	2.9		74.2		87.2	
7.0-12.9% without a high-school diploma	3.8		73.0		87.3	
13.0-20.0% without a high-school diploma	4.5		74.0		87.1	
≥21.0% without a high-school diploma	5.2		74.8		87.2	
Health Insurance		<.0001		<.0001		<.0001
Private Insurance	2.4		76.2		87.6	
Medicare	5.6		70.9		87.4	
Medicaid	6.9		72.2		83.4	
Not Insured	6.0		74.7		84.5	
Tumor Characteristics						
Tumor Sub-Types		<.0001		<.0001		<.0001
Type1: Low grade endometrioid	3.3		79.2		93.9	
Type2: High grade endometrioid	6.5		53.7		71.9	
Serous	5.3		65.1		47.1	
Clear Cell	5.9		60.2		62.6	
Diagnosis Stage		<.0001		<.0001		<.0001
Early (stage I, II)	2.9		77.6		95.2	
Late (stage III, IV)	9.6		55.4		47.4	
Grade		<.0001		<.0001		<.0001
Low (well, moderately differentiated)	3.3		79.1		93.6	
High (poorly differentiated, undifferentiated)	6.2		56.5		65.8	
Comorbidities		<.0001		<.0001		<.0001
None	3.8		73.4		86.9	
1	3.9		75.3		88.0	
2 or more	8.4		75.1		89.2	

TABLE VIII (CONTINUED): DISTRIBUTION OF SOCIO-DEMOGRAPHIC, TUMOR AND TREATMENT FACILITY CHARACTERISTICS OVERALL AND STRATIFIED BY RECEIPT OF TREATMENT (SURGERY, RADIATION THERAPY AND CHEMOTHERAPY), NATIONAL CANCER DATABASE, 2003-2012, n=208,247[a]

	Did not Receive Surgery (%) n=14,518	P_{value}	Did not Receive Radiation Therapy (%) n=180,691	P_{value}	Did not Receive Chemotherapy (%) n=210,685	P_{value}
Treatment facility characteristics						
Facility Type		<.0001		<.0001		<.0001
Academic/Research programs	4.0		73.2		85.3	
Community Cancer Programs	7.3		72.5		89.6	
Comprehensive Community Cancer Programs	3.6		74.5		88.3	
Facility Location		<.0001		<.0001		<.0001
East North Central	4.1		72.1		87.4	
East South Central	3.6		78.6		88.5	
Middle Atlantic	5.1		65.8		86.6	
Mountain	2.2		76.6		88.8	
New England	4.0		71.9		86.0	
Pacific	3.2		75.7		87.0	
South Atlantic	4.2		77.4		87.5	
West North Central	3.4		72.5		85.1	
West South Central	4.4		80.3		88.7	
Treatment Facility Case-Volume		<.0001		<.0001		<.0001
≥74 cases per year	3.2		75.3		85.3	
42 - 73 cases per year	3.0		75.2		87.0	
20 - 41 cases per year	3.4		74.2		87.6	
1 - 19 cases per year	6.6		70.5		88.9	

[a] Missing values for zip code-level income, zip code-level education, stage at diagnosis and facility type presented in Table IV are not shown and not used in the computations of the Chi-square statistic.

[b] Measures estimated by matching the zip code of the patient recorded at the time of diagnosis against files derived from year 2010 U.S. Census data. Variables categorized as quartiles based on equally proportioned variable ranges among all U.S. zip codes.

a) Low-Grade Endometrioid Carcinomas

In the fully adjusted model, Hispanic, NHB and NHAIAN women had respectively 16% (OR_{adj}=1.16; 95%CI 1.02-1.31), 82% (OR_{adj}=1.82; 95%CI 1.66-2.00) and 90% (OR_{adj}=1.90; 95%CI 1.21-2.98) higher odds of not receiving surgery when compared to NHW.

Higher odds of not having surgery were associated with lower zip-code level income, lower zip-code level education, lower treatment facility case volume and an increased number of comorbidities.

In addition, the odds of not receiving surgery were higher in women 70 and older (OR_{adj}=1.22; 95%CI 1.10-1.37) as compared to those 50 and younger; in women covered by Medicare (OR_{adj}=1.54; 95%CI 1.42-1.68), Medicaid (OR_{adj}=2.00; 95%CI 1.77-2.24), or those who were uninsured (OR_{adj}=1.94; 95%CI 1.70-2.22) as compared to those covered by the private health insurance and in those diagnosed with later-stage (OR_{adj}=3.10; 95%CI 2.89-3.33) as compared with earlier-stage tumors.

In contrast, lower odds for not having surgery were found in women diagnosed between the ages of 51 and 59 (OR_{adj}=0.61; 95%CI 0.55-0.67) and 60 and 69 (OR_{adj}=0.65; 95%CI 0.59-0.71) as compared to those being 50 and younger; those diagnosed between 2003 and 2007 (OR_{adj}=0.81; 95%CI 0.76-0.86) as compared to those diagnosed between 2008 and 2012 and in women diagnosed with moderately (OR_{adj}=0.71; 95%CI 0.67-0.76) as compared to those diagnosed with well-differentiated tumors. In addition, lower odds for not having surgery were also found in women treated in the comprehensive community cancer programs (OR_{adj}=0.79; 95%CI 0.74-0.90) as opposed to the academic/research programs; and those treated in facilities located in the Mountain (OR_{adj}=0.66; 95%CI 0.54-0.81) as compared to the West South Central regions.

The interaction term between and race/ethnicity and health insurance was highly significant at the level of *P*=0.001; as such results for women diagnosed with LGEC were also presented in insurance-stratified models. (TABLE IX) Among women with private health insurance, increased odds of not having surgery where found in Hispanic (OR_{adj}=1.52; 95%CI 1.24-1.86), NHB (OR_{adj}=1.73; 95%CI 1.46-2.06), NHA (OR_{adj}=1.35; 95%CI 1.02-1.78) and NHAIAN (OR_{adj}=2.33; 95%CI 1.13-4.82) women as compared to NHW. In women covered by Medicare only NHB (OR_{adj}=2.02; 95%CI 1.77-2.31) had increased odds of not having surgery when compared to NHW. However, in women with Medicaid, NHA (OR_{adj}=0.50; 95%CI 0.26-0.98) had lower odds of not having surgery when compared to NHW.

b) High-grade carcinomas

In the fully-adjusted model, NHB women had 48% higher odds (OR_{adj}=1.48; 95%CI 1.31-1.68) of not having surgery than NHW.

Higher odds of not having surgery were associated with older age, lower zip-code level education, lower treatment facility case volume and an increased number of comorbidities. In addition, the odds of not having surgery were higher in women with Medicare (OR_{adj}=1.38; 95%CI 1.21-1.59), Medicaid (OR_{adj}=1.79; 95%CI 1.47-2.18), or those who were uninsured (OR_{adj}=2.03; 95%CI 1.63-2.53) as compared to those with private health insurance. Higher odds of not having surgery were also found in women diagnosed with later-stage (OR_{adj}=4.14; 95%CI 3.76-4.55) as compared with earlier-stage tumors and those diagnosed in the Middle Atlantic regions (OR_{adj}=1.40; 95%CI 1.14-1.71) as compared to West South Central.

TABLE IX: MULTIVARIABLE LOGISTIC REGRESSION ODDS RATIOS (OR) FOR THE ASSOCIATION BETWEEN RACE/ETHNICITY AND LACK OF SURGICAL TREATMENT FOR LOW-GRADE CARCINOMAS, OVERALL AND STRATIFIED BY HEALTH INSURANCE, NATIONAL CANCER DATABASE, 2003-2012, n=208,247

	OR(95%CI)	OR(95%CI)	OR(95%CI)	OR(95%CI)	OR(95%CI)
	Type 1: Low-grade Carcinoma n=155,939	**Stratified Model[b]: Among Privately Insured n=86,064**	**Stratified Model: Among Insured by Medicare n=54,070**	**Stratified Model: Among Insured by Medicaid n=7,239**	**Stratified Model: Among Not Insured n=5,940**
Socio-Demographic Characteristics					
Race/Ethnicity					
Non-Hispanic White	Ref.	Ref.	Ref.	Ref.	Ref.
Hispanic	**1.16 (1.02-1.31)**	**1.52 (1.24-1.86)**	0.99 (0.78-1.25)	0.84 (0.62-1.15)	1.09 (0.76-1.55)
Non-Hispanic Black	**1.82 (1.66-2.00)**	**1.73 (1.46-2.06)**	**2.02 (1.77-2.31)**	1.13 (0.85-1.52)	1.38 (0.96-1.99)
Non-Hispanic Asian	1.00 (0.80-1.24)	**1.35 (1.02-1.78)**	0.80 (0.51-1.27)	**0.50 (0.26-0.98)**	0.48 (0.19-1.22)
Non-Hispanic American Indian, Alaskan Native	**1.90 (1.21-2.98)**	**2.33 (1.13-4.82)**	1.88 (0.91-3.90)	1.37 (0.47-4.01)	NA
Non-Hispanic Pacific Islander/ Hawaiian	1.07 (0.60-1.86)	1.18 (0.51-2.73)	1.70 (0.56-5.16)	0.57 (0.16-1.84)	0.47 (0.05-4.13)
Diagnosis Age					
<50	Ref.				
51-59	**0.61 (0.55-0.67)**				
60-69	**0.65 (0.59-0.71)**				
70+	**1.22 (1.10-1.37)**				
Diagnosis Period					
2008-2012	Ref.				
2003-2007	**0.81 (0.76-0.86)**				
Zip-Code Level Income[a]					
$63.000+	Ref.				
$48.000-62.999	1.01 (0.93-1.11)				
$38.000-$47.999	**1.16 (1.05-1.27)**				
<$38.000	**1.30 (1.15-1.46)**				
Zip-Code Level Education[a]					
<7.0 without a high-school diploma	Ref.				
7.0-12.9% without a high-school diploma	**1.15 (1.05-1.26)**				
13.0-20.0% without a high-school diploma	**1.16 (1.04-1.29)**				
≥21.0% without a high-school diploma	**1.15 (1.02-1.31)**				
Health Insurance					
Private Insurance	Ref.				
Medicare	**1.54 (1.42-1.68)**				
Medicaid	**2.00 (1.77-2.24)**				
Not Insured	**1.94 (1.70-2.22)**				
Tumor Characteristics					
Diagnosis Stage					
Early (Stages I, II)	Ref.				
Late (Stages III, IV)	**3.10 (2.89-3.33)**				
Grade					
Moderately vs. Well differentiated	**0.71 (0.67-0.76)**				
Comorbidities					
None	Ref.				
1	1.02 (0.95-1.10)				
2 or more	**2.20 (1.98-2.42)**				
Treatment facility characteristics					
Facility Type					
Academic/Research Programs	Ref.				
Community Cancer Programs	1.01 (0.90-1.13)				
Comprehensive Community Cancer Programs	**0.79 (0.74-0.85)**				
Facility Location					
West South Central	Ref.				
East North Central	0.94 (0.83-1.07)				
East South Central	0.87 (0.74-1.03)				
Middle Atlantic	**1.37 (1.21-1.56)**				
Mountain	**0.66 (0.54-0.81)**				
New England	1.11 (0.95-1.31)				
Pacific	0.91 (0.79-1.05)				
South Atlantic	1.07 (0.95-1.22)				
West North Central	0.89 (0.76-1.04)				

TABLE IX (CONTINUED): MULTIVARIABLE LOGISTIC REGRESSION ODDS RATIOS (OR) FOR THE ASSOCIATION BETWEEN RACE/ETHNICITY AND LACK OF SURGICAL TREATMENT FOR LOW-GRADE CARCINOMAS, OVERALL AND STRATIFIED BY HEALTH INSURANCE, NATIONAL CANCER DATABASE, 2003-2012, n=208,247

	OR(95%CI)
	Type 1: Low-grade Carcinoma n=155,939
Treatment Facility Case-Volume	
≥74 cases per year	Ref.
42 - 73 cases per year	1.00 (0.91-1.10)
20 - 41 cases per year	**1.15 (1.05-1.27)**
1 - 19 cases per year	**2.38 (2.17-2.62)**

[a] Measure estimated by matching the zip code of the patient recorded at the time of diagnosis against files derived from year 2010 U.S. Census data. Variables categorized as quartiles based on equally proportioned variable ranges among all U.S. zip codes.

[b] Model adjusted for all covariates, plus race/ethnicity*insurance interaction term added to test effect modification. Race/ethnicity*insurance interaction term significant at the level of $P<0.001$, stratified results are shown for the racial/ethnic disparity within each level of health insurance and facility type.

In contrast, women treated at the comprehensive community cancer programs (OR_{adj}=0.81; 95%CI 0.73-0.91) as opposed to those treated at the academic/research programs and those treated in facilities located in the Mountain (OR_{adj}=0.59; 95%CI 0.42-0.83), as compared to those located in the West South Central regions had significantly lower odds of having surgery.(TABLE X)

c) Clear Cell Carcinomas

NHB had 79% higher odds (OR_{adj}=1.79; 95%CI 1.15-2.79) of not having surgery when compared to NHW. In addition higher odds of not having surgery were found in women who were diagnosed with later-stage (OR_{adj}=2.94; 95%CI 2.07-4.18) as compared with earlier-stage tumors; those with two or more comorbidities (OR_{adj}=1.97; 95%CI 1.08-3.58) as compared to none and those treated in hospitals seeing 1-19 EC cases a year (OR_{adj}=3.15; 95%CI 1.83-5.40) as compared to hospitals seeing 74 and over. (TABLE X)

d) Serous Carcinomas

In the fully adjusted model, NHB and NHPI women had respectively 1.74 (OR_{adj}=1.74; 95%CI 1.40-2.17), and 5.86 times (OR_{adj}=5.86; 95%CI 2.02-16.97) the odds for not having surgery when compared to NHW. In addition, the odds of not having surgery were higher in women covered by Medicare (OR_{adj}=1.31; 95%CI 1.01-1.69) and Medicaid (OR_{adj}=2.07; 95%CI 1.40-3.06) as compared to those with private health insurance; in those diagnosed with later-stage (OR_{adj}=3.65; 95%CI 2.97-4.48) as compared with earlier-stage tumors, those diagnosed with two or more comorbidities (OR_{adj}=1.81; 95%CI 1.31-2.50) as compared to those with no comorbidities; in women diagnosed in the Middle Atlantic (OR_{adj}=1.93; 95%CI 1.29-2.91) and New England regions (OR_{adj}=1.89; 95%CI 1.16-3.08) as compared to the West South Central region and women treated in facilities seeing 1-19 EC cases a year (OR_{adj}=2.30; 95%CI 1.73-3.04) as compared to those seeing 74 and over.

In contrast, women treated at the comprehensive community cancer programs (OR_{adj}=0.74; 95%CI 0.60-0.91) as opposed to academic/research programs had significantly lower odds of having surgery. (TABLE X)

2. Receipt of Radiation Therapy

TABLE XI presents the results from the multivariable logistic regression models for the association between race/ethnicity and receipt of radiation therapy, stratified by EC tumor subtype.

a) Low-Grade Carcinoma

No racial/ethnic differences in receipt of radiation therapy were found in women diagnosed with LGEC.

Higher odds of not receiving radiation therapy were found in women treated in the community cancer programs (OR_{adj}=1.22; 95%CI 1.15-1.31) and comprehensive community cancer programs (OR_{adj}=1.05; 95%CI 1.02-1.08) as compared to the academic/research programs. (TABLE XI) In addition, higher odds of not receiving radiation therapy were associated with an increased number of comorbidities.

In contrast, lower odds of not receiving radiation therapy were associated with older age, with lower zip-code level income and a lower treatment facility case volume. In addition lower odds of not receiving radiation therapy were found in women diagnosed between 2003 and 2007 (OR_{adj}=0.92; 95%CI 0.90-0.95) as compared to those diagnosed between 2008 and 2012; living in areas where between 7.0% and 12.9% of people have no high-school diploma (OR_{adj}=0.94; 95%CI 0.90-0.98) as compared to areas where seven percent or less people have no-high-school diploma and in women covered by Medicare (OR_{adj}=0.93; 95%CI 0.89-0.96), Medicaid (OR_{adj}=0.87; 95%CI 0.81-0.93).

TABLE X: MULTIVARIABLE LOGISTIC REGRESSION ODDS RATIOS (OR) FOR THE ASSOCIATION BETWEEN RACE/ETHNICITY AND LACK OF SURGICAL TREATMENT FOR HIGH-GRADE CARCINOMA, CLEAR CELL AND SEROUS CARCINOMAS, NATIONAL CANCER DATABASE, 2003-2012, n=208,247

	OR(95%CI)	**OR(95%CI)**	**OR(95%CI)**
	Type 2: High-grade Carcinoma n=34,354	**Type 2: Clear Cell n=2,693**	**Type 2: Serous n=11,217**
Socio-Demographic Characteristics			
Race/Ethnicity			
Non-Hispanic White	Ref.	Ref.	Ref.
Hispanic	0.84 (0.66-1.07)	0.63 (0.21-1.83)	1.38 (0.91-2.10)
Non-Hispanic Black	**1.48 (1.31-1.68)**	**1.79 (1.15-2.79)**	**1.74 (1.40-2.17)**
Non-Hispanic Asian	0.88 (0.61-1.26)	0.90 (0.25-3.25)	0.96 (0.49-1.89)
Non-Hispanic American Indian, Alaskan Native	0.39 (0.05-2.90)	NA	1.72 (0.37-7.94)
Non-Hispanic Pacific Islander/ Hawaiian	0.48 (0.11-2.04)	NA	**5.86 (2.02-16.97)**
Diagnosis Age			
<50	Ref.	Ref.	Ref.
51-59	**1.35 (1.08-1.69)**	0.82 (0.28-2.42)	0.60 (0.30-1.22)
60-69	**1.48 (1.19-1.85)**	0.88 (0.32-2.45)	0.75 (0.39-1.45)
70+	**2.67 (2.12-3.37)**	1.49 (0.52-4.25)	1.51 (0.77-2.96)
Diagnosis Period			
2008-2012	Ref.	Ref.	Ref.
2003-2007	0.94 (0.85-1.03)	1.04 (0.73-1.47)	0.80 (0.67-0.96)
Zip-Code Level Income[a]			
$63.000+	Ref.	Ref.	Ref.
$48.000-62.999	0.95 (0.82-1.10)	0.81 (0.47-1.39)	1.03 (0.78-1.36)
$38.000-$47.999	1.06 (0.90-1.24)	0.87 (0.48-1.58)	1.20 (0.88-1.64)
<$38.000	1.19 (0.99-1.44)	0.65 (0.33-1.30)	1.20 (0.84-1.69)
Zip-Code Level Education[a]			
<7.0 without a high-school diploma	Ref.	Ref.	Ref.
7.0-12.9% without a high-school diploma	**1.15 (1.00-1.34)**	0.90 (0.52-1.57)	1.08 (0.81-1.44)
13.0-20.0% without a high-school diploma	**1.19 (1.00-1.41)**	1.17 (0.62-2.20)	1.14 (0.82-1.59)
≥21.0% without a high-school diploma	**1.27 (1.04-1.55)**	1.43 (0.69-2.97)	1.22 (0.83-1.80)
Health Insurance			
Private Insurance	Ref.	Ref.	Ref.
Medicare	**1.38 (1.21-1.59)**	1.23 (0.74-2.05)	**1.31 (1.01-1.69)**
Medicaid	**1.79 (1.47-2.18)**	0.94 (0.41-2.16)	**2.07 (1.40-3.06)**
Not Insured	**2.03 (1.63-2.53)**	1.61 (0.57-4.50)	1.65 (0.97-2.82)
Tumor Characteristics			
Diagnosis Stage			
Early (Stages I, II)	Ref.	Ref.	Ref.
Late (Stages III, IV)	**4.14 (3.76-4.55)**	**2.94 (2.07-4.18)**	**3.65 (2.97-4.48)**
Grade			
Moderately vs. Well differentiated Poorly differentiated vs undifferentiated	1.13 (0.95-1.33)		
Poorly differentiated undifferentiated vs. well/moderately differentiated		1.25 (0.62-2.51)	0.98 (0.69-1.37)
Comorbidities			
None	Ref.	Ref.	Ref.
1	0.91 (0.81-1.03)	0.91 (0.59-1.38)	0.81 (0.65-1.02)
2 or more	**1.75 (1.47-2.08)**	**1.97 (1.08-3.58)**	**1.81 (1.31-2.50)**

TABLE X (CONTINUED): MULTIVARIABLE LOGISTIC REGRESSION ODDS RATIOS (OR) FOR THE ASSOCIATION BETWEEN RACE/ETHNICITY AND LACK OF SURGICAL TREATMENT FOR HIGH-GRADE CARCINOMA, CLEAR CELL AND SEROUS CARCINOMAS, NATIONAL CANCER DATABASE, 2003-2012, n=208,247

	OR(95%CI)	**OR(95%CI)**	**OR(95%CI)**
	Type 2: High-grade Carcinoma n=34,354	**Type 2: Clear Cell n=2,693**	**Type 2: Serous n=11,217**
Treatment facility characteristics			
Facility Type			
Academic/Research Programs	Ref.	Ref.	Ref.
Community Cancer Programs	0.88 (0.72-1.06)	0.58 (0.28-1.20)	1.10 (0.75-1.62)
Comprehensive Community Cancer Programs	**0.81 (0.73-0.91)**	0.74 (0.49-1.10)	**0.74 (0.60-0.91)**
Facility Location			
West South Central	Ref.	Ref.	Ref.
East North Central	1.10 (0.90-1.35)	1.01 (0.48-2.14)	1.44 (0.95-2.19)
East South Central	0.88 (0.68-1.13)	0.90 (0.34-2.39)	0.68 (0.38-1.23)
Middle Atlantic	**1.40 (1.14-1.71)**	1.54 (0.75-3.17)	**1.93 (1.29-2.91)**
Mountain	**0.59 (0.42-0.83)**	0.99 (0.32-3.07)	0.60 (0.28-1.26)
New England	1.12 (0.87-1.44)	1.15 (0.44-3.02)	**1.89 (1.16-3.08)**
Pacific	0.81 (0.64-1.01)	0.82 (0.36-1.88)	0.78 (0.48-1.28)
South Atlantic	0.99 (0.81-1.20)	0.61 (0.29-1.29)	1.02 (0.67-1.54)
West North Central	0.84 (0.65-1.08)	1.08 (0.44-2.69)	1.04 (0.63-1.73)
Treatment Facility Case-Volume			
≥74 cases per year	Ref.	Ref.	Ref.
42 - 73 cases per year	0.92 (0.80-1.07)	1.13 (0.66-1.96)	1.13 (0.88-1.46)
20 - 41 cases per year	1.13 (0.97-1.30)	1.37 (0.81-2.33)	1.20 (0.93-1.55)
1 - 19 cases per year	**2.38 (2.06-2.76)**	**3.15 (1.83-5.40)**	**2.30 (1.73-3.04)**

[a] Measure estimated by matching the zip code of the patient recorded at the time of diagnosis against files derived from year 2010 U.S. Census data. Variables categorized as quartiles based on equally proportioned variable ranges among all U.S. zip codes.

or those who were uninsured (OR_{adj}=0.91; 95%CI 0.84-0.98) as compared to those covered by private health insurance. Moreover, lower odds of not receiving radiation therapy were found in women diagnosed with later-stage (OR_{adj}=0.24; 95%CI 0.23-0.25) as compared with earlier stage tumors and in women diagnosed with moderately (OR_{adj}=0.43; 95%CI 0.42-0.45) as compared to those diagnosed with well-differentiated tumors. Lastly, lower odds for not having surgery were found in women treated in all geographic regions when compared to the West South Central. (TABLE XI)

b) High-Grade Carcinomas

No racial/ethnic differences in receipt of radiation therapy were observed in women diagnosed with HGEC.

Higher odds of not receiving radiation therapy were found in women being 70 or older (OR_{adj}=1.19; 95%CI 1.09-1.32) as compared to 50 or younger, in women living in areas with a median income between $38.000 and $47.999 ($OR_{adj}$=1.10; 95%CI 1.02-1.19) as compared to areas with levels $63.000 or higher and women covered by Medicare (OR_{adj}=1.10; 95%CI 1.04-1.17), Medicaid (OR_{adj}=1.15; 95%CI 1.04-1.28), and those who were uninsured (OR_{adj}=1.17; 95%CI 1.05-1.32) as compared to those with private health insurance. Higher odds of not receiving radiation therapy were also found in women diagnosed with a higher number of comorbidities; and those treated in community cancer programs (OR_{adj}=1.21; 95%CI 1.09-1.35) as compared to the academic/research programs. (TABLE XI)

In contrast, lower odds of not receiving radiation therapy were found in women diagnosed between 2003 and 2007 (OR_{adj}=0.90; 95%CI 0.86-0.94) as compared to those diagnosed between 2008 and 2012; in women diagnosed with later-stage (OR_{adj}=0.88; 95%CI 0.84-0.92) as compared with earlier-stage tumors and in women treated in facilities located in all geographic regions when compared to the west south central region. Lastly, lower odds of not

receiving radiation therapy were associated with a lower treatment facility case volume. (TABLE XI)

c) Clear Cell Carcinomas

No racial/ethnic differences in the receipt of radiation therapy were observed in women diagnosed with CCC. Higher odds of not receiving radiation therapy were found in women being 70 or older (OR_{adj}=1.90; 95%CI 1.23-2.94) as compared to 50 or younger.(TABLE XI)

In contrast, lower odds of not receiving radiation therapy were found in women diagnosed between 2003 and 2007 (OR_{adj}=0.80; 95%CI 0.68-0.95) as compared to those diagnosed between 2008 and 2012; in women diagnosed with later-stage (OR_{adj}=0.82; 95%CI 0.69-0.96) as compared with earlier-stage tumors; in women treated in facilities located in all geographic regions besides New England when compared to the West South Central region and in those treated in facilities seeing 20 or less EC cases a year (OR_{adj}=0.65; 95%CI 0.50-0.84) as compared to 74 and over. (TABLE XI)

d) Serous Carcinomas

In the fully adjusted model, NHAIAN women had 3.8 times the odds (OR_{adj}=3.76; 95%CI 1.13-12.56) of not receiving radiation therapy when compared to NHW. In addition, higher odds of not receiving radiation therapy were found in women being 70 or older (OR_{adj}=1.37; 95%CI 1.01-1.85) as compared to those 50 and younger; in those diagnosed with later-stage (OR_{adj}=1.70; 95%CI 1.57-1.84) as compared with earlier-stage tumors, in women diagnosed with at least one comorbidity; and those treated in community cancer programs (OR_{adj}=1.30; 95%CI 1.04-1.62) and comprehensive community cancer programs (OR_{adj}=1.10; 95%CI 1.01-1.21) as compared to the academic/research programs. (TABLE XI)

In contrast, lower odds of not receiving radiation therapy were found in women diagnosed with low-grade (OR_{adj}=0.78; 95%CI 0.67-0.90) as compared to high-grade tumors; in women treated in facilities located in all geographic regions besides the East North Central when compared to the West South Central region and in those treated in facilities seeing 20 or less EC cases a year (OR_{adj}=0.64; 95%CI 0.56-0.73) as compared to 74 and over. (TABLE XI)

3. Receipt of Chemotherapy

TABLE XII presents the results from the multivariable logistic regression models for the association between race/ethnicity and receipt of chemotherapy, stratified by EC tumor subtype.

a) Low-Grade Carcinoma

No racial/ethnic differences in receipt of chemotherapy were observed in women diagnosed with LGEC.

Higher odds of not receiving chemotherapy were associated with older age, earlier year at diagnosis, lower zip-code level education, an increased number of comorbidities and a lower treatment facility case volume. In addition, the odds of not receiving chemotherapy were higher in women covered by Medicare (OR_{adj}=1.27; 95%CI 1.18-1.36) as compared to those covered by a private health insurance and in women treated in the community cancer programs (OR_{adj}=1.26; 95%CI 1.11-1.43), the comprehensive community cancer programs (OR_{adj}=1.14; 95%CI 1.07-1.21) as opposed to academic/research programs. (TABLE XII)

In contrast, lower odds of not receiving chemotherapy were found in NHA women (OR_{adj}=0.83; 95%CI 0.71-0.98) as compared to NHW, in women diagnosed with later-stage (OR_{adj}=0.02; 95%CI 0.02-0.02) as compared with earlier-stage tumors; in women diagnosed with moderate (OR_{adj}=0.58; 95%CI 0.55-0.61) as compared to well-differentiated tumors and

those treated in facilities located in all geographic regions besides the Mountain when compared to the West South Central region. (TABLE XII)

b) High-Grade Carcinoma

No racial/ethnic differences in receipt of chemotherapy were observed in women diagnosed with high-grade carcinomas.

Higher odds of not receiving chemotherapy were associated with older age, earlier year at diagnosis, lower zip-code level education, an increased number of comorbidities and a lower treatment facility case volume. In addition, higher odds of not receiving chemotherapy were found in women with Medicare (OR_{adj}=1.18; 95%CI 1.09-1.27), Medicaid (OR_{adj}=1.15; 95%CI 1.02-1.29) and those who were uninsured (OR_{adj}=1.21; 95%CI 1.06-1.38) as compared to those with a private health insurance; in those diagnosed with poorly differentiated (OR_{adj}=1.47; 95%CI 1.34-1.61) as compared to undifferentiated tumors and in women treated in the community cancer programs (OR_{adj}=1.17; 95%CI 1.02-1.35), the comprehensive community cancer programs (OR_{adj}=1.08; 95%CI 1.02-1.15) as opposed to academic/research programs. (TABLE XII)

In contrast, lower odds of not having surgery were found in women diagnosed with later-stage (OR_{adj}=0.12; 95%CI 0.11-0.13) as compared with earlier-stage tumors and in those treated in facilities located in all geographic regions with the exception of the Mountain region when compared to the West South Central region. (TABLE XII)

c) Clear Cell Carcinoma

In the fully adjusted model, NHB had 35% higher odds (OR_{adj}=1.35; 95%CI 1.05-1.75) of not receiving chemotherapy when compared to NHW.

TABLE XI: MULTIVARIABLE LOGISTIC REGRESSION ODDS RATIOS (OR) FOR THE ASSOCIATION BETWEEN RACE/ETHNICITY AND ABSENCE OF RADIATION THERAPY BY HISTOLOGIC SUB-TYPE, NATIONAL CANCER DATABASE, 2003-2012, n=208,247

	OR(95%CI)	OR(95%CI)	OR(95%CI)	OR(95%CI)
	Type 1: Low-grade Carcinoma n=155,939	**Type 2: High-grade Carcinoma n=34,354**	**Type 2: Clear Cell n=2,693**	**Type 2: Serous n=11,217**
Socio-Demographic Characteristics				
Race/Ethnicity				
Non-Hispanic White	Ref.	Ref.	Ref.	Ref.
Hispanic	1.03 (0.97-1.11)	1.06 (0.95-1.19)	1.46 (0.96-2.21)	1.08 (0.87-1.32)
Non-Hispanic Black	1.05 (0.99-1.12)	1.00 (0.94-1.08)	1.22 (0.96-1.55)	0.96 (0.85-1.07)
Non-Hispanic Asian	1.04 (0.95-1.15)	0.96 (0.83-1.11)	1.18 (0.68-2.05)	1.11 (0.84-1.46)
Non-Hispanic American Indian, Alaskan Native	0.97 (0.72-1.32)	1.64 (0.97-2.78)	0.42 (0.05-3.66)	**3.76 (1.13-12.56)**
Non-Hispanic Pacific Islander/ Hawaiian	1.26 (0.93-1.71)	1.53 (0.99-2.37)	2.59 (0.28-23.71)	1.77 (0.74-4.23)
Diagnosis Age				
<50	Ref.	Ref.	Ref.	Ref.
51-59	**0.74 (0.71-0.78)**	0.93 (0.85-1.01)	1.19 (0.77-1.83)	1.00 (0.74-1.36)
60-69	**0.59 (0.56-0.62)**	0.93 (0.85-1.01)	1.51 (0.99-2.30)	1.04 (0.77-1.40)
70+	**0.59 (0.56-0.63)**	**1.19 (1.09-1.32)**	**1.90 (1.23-2.94)**	**1.37 (1.01-1.85)**
Diagnosis Period				
2008-2012	Ref.	Ref.	Ref.	Ref.
2003-2007	**0.92 (0.90-0.95)**	**0.90 (0.86-0.94)**	**0.80 (0.68-0.95)**	1.02 (0.94-1.11)
Zip-Code Level Income[a]				
$63.000+	Ref.	Ref.	Ref.	Ref.
$48.000-62.999	0.97 (0.93-1.01)	1.05 (0.98-1.12)	0.95 (0.75-1.22)	0.91 (0.80-1.03)
$38.000-$47.999	**0.95 (0.91-0.99)**	**1.10 (1.02-1.19)**	1.15 (0.86-1.53)	0.89 (0.78-1.03)
<$38.000	**0.94 (0.89-0.99)**	1.02 (0.93-1.12)	0.87 (0.63-1.22)	1.04 (0.88-1.23)
Zip-Code Level Education[a]				
<7.0 without a high-school diploma	Ref.	Ref.	Ref.	Ref.
7.0-12.9% without a high-school diploma	**0.94 (0.90-0.98)**	0.99 (0.93-1.06)	0.94 (0.73-1.20)	1.12 (0.98-1.26)
13.0-20.0% without a high-school diploma	0.97 (0.93-1.02)	0.97 (0.90-1.05)	1.15 (0.86-1.55)	1.15 (0.99-1.32)
≥21.0% without a high-school diploma	1.00 (0.94-1.06)	1.03 (0.94-1.13)	1.19 (0.83-1.70)	1.16 (0.97-1.38)
Health Insurance				
Private Insurance	Ref.	Ref.	Ref.	Ref.
Medicare	**0.93 (0.89-0.96)**	**1.10 (1.04-1.17)**	0.98 (0.78-1.22)	1.05 (0.94-1.16)
Medicaid	**0.87 (0.81-0.93)**	**1.15 (1.04-1.28)**	0.79 (0.54-1.16)	1.16 (0.93-1.43)
Not Insured	**0.91 (0.84-0.98)**	**1.17 (1.05-1.32)**	1.05 (0.63-1.75)	1.06 (0.81-1.39)
Tumor Characteristics				
Diagnosis Stage				
Early (Stages I, II)	Ref.	Ref.	Ref.	Ref.
Late (Stages III, IV)	**0.24 (0.23-0.25)**	**0.88 (0.84-0.92)**	**0.82 (0.69-0.96)**	**1.70 (1.57-1.84)**
Grade				
Moderately vs. Well differentiated	**0.43 (0.42-0.45)**			
Poorly differentiated vs undifferentiated		1.04 (0.96-1.12)		
Low (Poorly differentiated undifferentiated) vs. High (well/moderately differentiated)			0.86 (0.65-1.14)	**0.78 (0.67-0.90)**
Comorbidities				
None	Ref.	Ref.	Ref.	Ref.
1	**1.11 (1.07-1.15)**	**1.15 (1.08-1.21)**	1.08 (0.88-1.32)	**1.20 (1.08-1.33)**
2 or more	**1.10 (1.03-1.17)**	**1.27 (1.14-1.41)**	1.03 (0.72-1.48)	**1.45 (1.19-1.78)**

TABLE XI (CONTINUED): MULTIVARIABLE LOGISTIC REGRESSION ODDS RATIOS (OR) FOR THE ASSOCIATION BETWEEN RACE/ETHNICITY AND ABSENCE OF RADIATION THERAPY BY HISTOLOGIC SUB-TYPE, NATIONAL CANCER DATABASE, 2003-2012, n=208,247

	OR(95%CI)	**OR(95%CI)**	**OR(95%CI)**	**OR(95%CI)**
	Type 1: Low-grade Carcinoma n=155,939	**Type 2: High-grade Carcinoma n=34,354**	**Type 2: Clear Cell n=2,693**	**Type 2: Serous n=11,217**
Treatment facility characteristics				
Facility Type				
Academic/Research Programs	Ref.	Ref.	Ref.	Ref.
Community Cancer Programs	**1.22 (1.15-1.31)**	**1.21 (1.09-1.35)**	1.04 (0.70-1.54)	**1.30 (1.04-1.62)**
Comprehensive Community Cancer Programs	**1.05 (1.02-1.08)**	1.05 (0.99-1.10)	1.05 (0.87-1.26)	**1.10 (1.01-1.21)**
Facility Location				
West South Central	Ref.	Ref.	Ref.	Ref.
East North Central	**0.54 (0.50-0.57)**	**0.54 (0.49-0.60)**	**0.46 (0.31-0.67)**	**0.48 (0.39-0.59)**
East South Central	**0.87 (0.80-0.94)**	**0.88 (0.77-0.99)**	**0.49 (0.31-0.79)**	0.86 (0.66-1.10)
Middle Atlantic	**0.36 (0.34-0.39)**	**0.42 (0.38-0.47)**	**0.45 (0.31-0.67)**	**0.41 (0.34-0.50)**
Mountain	**0.76 (0.70-0.84)**	**0.75 (0.65-0.86)**	**0.53 (0.31-0.91)**	**0.65 (0.49-0.86)**
New England	**0.51 (0.47-0.55)**	**0.59 (0.52-0.67)**	0.62 (0.39-1.00)	**0.60 (0.47-0.77)**
Pacific	**0.75 (0.70-0.80)**	**0.72 (0.64-0.80)**	**0.54 (0.35-0.81)**	**0.65 (0.52-0.80)**
South Atlantic	**0.79 (0.74-0.84)**	**0.76 (0.69-0.84)**	**0.66 (0.45-0.97)**	**0.77 (0.63-0.93)**
West North Central	**0.61 (0.57-0.66)**	**0.53 (0.47-0.59)**	**0.54 (0.34-0.86)**	**0.45 (0.35-0.57)**
Treatment Facility Case-Volume				
≥74 cases per year	Ref.	Ref.	Ref.	Ref.
42 - 73 cases per year	0.97 (0.93-1.01)	**0.90 (0.85-0.96)**	0.90 (0.71-1.13)	0.99 (0.89-1.11)
20 - 41 cases per year	**0.88 (0.84-0.91)**	**0.86 (0.81-0.92)**	0.81 (0.64-1.03)	1.06 (0.94-1.19)
1 - 19 cases per year	**0.70 (0.67-0.73)**	**0.64 (0.59-0.69)**	**0.65 (0.50-0.84)**	**0.64 (0.56-0.73)**

[a] Measure estimated by matching the zip code of the patient recorded at the time of diagnosis against files derived from year 2010 U.S. Census data. Variables categorized as quartiles based on equally proportioned variable ranges among all U.S. zip codes.

TABLE XII: MULTIVARIABLE LOGISTIC REGRESSION ODDS RATIOS (OR) FOR THE ASSOCIATION BETWEEN RACE/ETHNICITY AND ABSENCE OF CHEMOTHERAPY BY HISTOLOGIC SUB-TYPE, NATIONAL CANCER DATABASE, 2003-2012, n=208,247

	OR(95%CI)	OR(95%CI)	OR(95%CI)	OR(95%CI)
	Type 1: Low-grade Carcinoma n=155,939	**Type 2: High-grade Carcinoma n=34,354**	**Type 2: Clear Cell n=2,693**	**Type 2: Serous n=11,217**
Socio-Demographic Characteristics				
Race/Ethnicity				
Non-Hispanic White	Ref.	Ref.	Ref.	Ref.
Hispanic	0.98 (0.87-1.10)	0.98 (0.86-1.12)	0.87 (0.57-1.34)	1.01 (0.83-1.23)
Non-Hispanic Black	1.12 (0.99-1.25)	1.00 (0.92-1.10)	**1.35 (1.05-1.75)**	1.07 (0.96-1.19)
Non-Hispanic Asian	**0.83 (0.71-0.98)**	0.90 (0.76-1.07)	1.28 (0.68-2.41)	0.80 (0.61-1.04)
Non-Hispanic American Indian, Alaskan Native	0.72 (0.44-1.16)	0.66 (0.36-1.21)	0.77 (0.08-7.77)	1.35 (0.61-2.97)
Non-Hispanic Pacific Islander/ Hawaiian	0.93 (0.60-1.44)	1.37 (0.81-2.29)	1.23 (0.19-8.05)	0.97 (0.47-2.00)
Diagnosis Age				
<50	Ref.	Ref.	Ref.	Ref.
51-59	**1.39 (1.29-1.50)**	**1.13 (1.02-1.26)**	1.03 (0.66-1.63)	1.01 (0.74-1.37)
60-69	**1.60 (1.47-1.74)**	**1.11 (1.00-1.23)**	1.20 (0.78-1.87)	1.04 (0.78-1.40)
70+	**2.83 (2.54-3.14)**	**2.26 (2.01-2.53)**	**2.53 (1.59-4.02)**	**2.16 (1.60-2.93)**
Diagnosis Period				
2008-2012	Ref.	Ref.	Ref.	Ref.
2003-2007	**1.99 (1.88-2.10)**	**2.32 (2.19-2.46)**	**2.46 (2.05-2.96)**	**1.83 (1.69-1.99)**
Zip-Code Level Income[a]				
$63.000+	Ref.	Ref.	Ref.	Ref.
$48.000-62.999	1.00 (0.93-1.08)	0.97 (0.90-1.06)	0.97 (0.74-1.27)	0.99 (0.88-1.12)
$38.000-$47.999	1.05 (0.97-1.15)	1.01 (0.92-1.11)	**0.72 (0.53-0.98)**	0.87 (0.76-1.00)
<$38.000	1.05 (0.95-1.17)	1.05 (0.94-1.17)	**0.65 (0.45-0.94)**	0.89 (0.76-1.05)
Zip-Code Level Education[a]				
<7.0 without a high-school diploma	Ref.	Ref.	Ref.	Ref.
7.0-12.9% without a high-school diploma	1.02 (0.94-1.10)	1.06 (0.98-1.15)	0.88 (0.67-1.16)	1.00 (0.89-1.13)
13.0-20.0% without a high-school diploma	1.05 (0.96-1.15)	1.07 (0.97-1.18)	1.25 (0.91-1.73)	**1.22 (1.06-1.40)**
≥21.0% without a high-school diploma	**1.20 (1.08-1.35)**	**1.15 (1.02-1.29)**	**1.48 (1.01-2.18)**	**1.40 (1.18-1.66)**
Health Insurance				
Private Insurance	Ref.	Ref.	Ref.	Ref.
Medicare	**1.27 (1.18-1.36)**	**1.18 (1.09-1.27)**	1.27 (0.99-1.61)	**1.19 (1.08-1.33)**
Medicaid	1.02 (0.91-1.14)	**1.15 (1.02-1.30)**	1.33 (0.88-2.00)	**1.24 (1.01-1.52)**
Not Insured	0.99 (0.88-1.12)	**1.21 (1.06-1.38)**	1.44 (0.84-2.49)	1.24 (0.96-1.60)
Tumor Characteristics				
Diagnosis Stage				
Early (Stages I, II)	Ref.	Ref.	Ref.	Ref.
Late (Stages III, IV)	**0.02 (0.02-0.02)**	**0.12 (0.11-0.13)**	**0.20 (0.17-0.24)**	**0.31 (0.29-0.34)**
Grade				
Moderately vs. well differentiated	**0.58 (0.55-0.61)**			
Poorly differentiated vs. undifferentiated		**1.47 (1.34-1.61)**		
Low (Poorly differentiated undifferentiated) vs. High (well/moderately differentiated)			**0.61 (0.44-0.85)**	0.88 (0.76-1.02)
Comorbidities				
None	Ref.	Ref.	Ref.	Ref.
1	**1.10 (1.02-1.17)**	**1.20 (1.12-1.28)**	0.87 (0.70-1.08)	1.10 (1.00-1.21)
2 or more	**1.33 (1.17-1.52)**	**1.42 (1.25-1.62)**	1.20 (0.81-1.77)	**1.43 (1.18-1.72)**

TABLE XII (CONTINUED): MULTIVARIABLE LOGISTIC REGRESSION ODDS RATIOS (OR) FOR THE ASSOCIATION BETWEEN RACE/ETHNICITY AND ABSENCE OF CHEMOTHERAPY BY HISTOLOGIC SUB-TYPE, NATIONAL CANCER DATABASE, 2003-2012, n=208,247

	OR(95%CI)	OR(95%CI)	OR(95%CI)	OR(95%CI)
	Type 1: Low-grade Carcinoma n=155,939	**Type 2: High-grade Carcinoma n=34,354**	**Type 2: Clear Cell n=2,693**	**Type 2: Serous n=11,217**
Treatment facility characteristics				
Facility Type				
Academic/Research programs	Ref.	Ref.	Ref.	Ref.
Community Cancer Programs	**1.26 (1.11-1.43)**	**1.17 (1.02-1.35)**	0.91 (0.59-1.41)	1.03 (0.83-1.28)
Comprehensive Community Cancer Programs	**1.14 (1.07-1.21)**	**1.08 (1.02-1.15)**	0.96 (0.79-1.17)	1.08 (0.99-1.18)
Facility Location				
West South Central	Ref.	Ref.	Ref.	Ref.
East North Central	**0.77 (0.66-0.83)**	**0.63 (0.56-0.72)**	0.73 (0.50-1.09)	**0.66 (0.55-0.79)**
East South Central	**0.84 (0.73-0.98)**	**0.85 (0.73-0.99)**	0.88 (0.53-1.45)	**0.73 (0.58-0.92)**
Middle Atlantic	**0.81 (0.71-0.91)**	**0.65 (0.57-0.74)**	**0.59 (0.39-0.88)**	**0.62 (0.52-0.75)**
Mountain	0.90 (0.77-1.06)	0.95 (0.80-1.12)	1.00 (0.57-1.77)	1.09 (0.84-1.41)
New England	**0.64 (0.56-0.74)**	**0.56 (0.48-0.65)**	**0.38 (0.23-0.62)**	**0.46 (0.37-0.58)**
Pacific	**0.82 (0.72-0.93)**	**0.76 (0.67-0.87)**	0.98 (0.64-1.50)	**0.81 (0.67-0.99)**
South Atlantic	**0.81 (0.72-0.91)**	**0.72 (0.63-0.81)**	0.81 (0.55-1.18)	**0.78 (0.65-0.93)**
West North Central	**0.56 (0.49-0.64)**	**0.57 (0.49-0.66)**	0.94 (0.58-1.54)	**0.54 (0.43-0.67)**
Treatment Facility Case-Volume				
≥74 cases per year	Ref.	Ref.	Ref.	Ref.
42 - 73 cases per year	**1.13 (1.05-1.21)**	**1.08 (1.01-1.17)**	**1.62 (1.21-2.17)**	**1.17 (1.05-1.31)**
20 - 41 cases per year	**1.28 (1.19-1.38)**	**1.31 (1.21-1.42)**	1.21 (0.94-1.55)	**1.15 (1.03-1.29)**
1 - 19 cases per year	**1.23 (1.13-1.34)**	**1.35 (1.23-1.47)**	**0.65 (0.50-0.84)**	**1.35 (1.17-1.54)**

[a] Type 1 endometrial cancer defined as well and moderately differentiated endometrioid tumors.

[b] Measure estimated by matching the zip code of the patient recorded at the time of diagnosis against files derived from year 2010 U.S.Census data. Variables categorized as quartiles based on equally proportioned variable ranges among all U.S. zip

Higher odds of not receiving chemotherapy were associated with older age, earlier year at diagnosis, lower zip-code level education and a higher treatment facility case volume. (TABLE XII)

In contrast, lower odds of not receiving chemotherapy were associated with lower zip-code level income and a lower treatment facility case volume. In addition, lower odds of not receiving chemotherapy were found in women diagnosed with later-stage (OR_{adj}=0.20; 95%CI 0.17-0.24) as compared with earlier-stage tumors; in women diagnosed with low (OR_{adj}=0.61; 95%CI 0.44-0.85) as compared to high-grade tumors; those treated in the Middle Atlantic (OR_{adj}=0.59; 95%CI 0.39-0.88) and New England regions (OR_{adj}=0.38; 95%CI 0.23-0.62) as compared to the West South Central region. (Table XII)

b) Serous Carcinoma

No racial/ethnic differences in receipt of chemotherapy were observed in women diagnosed with SC.

Higher odds of not receiving chemotherapy were associated with older age, earlier year at diagnosis, lower zip-code level education, an increased number of comorbidities and a lower treatment facility case volume. In addition, higher odds of not receiving chemotherapy were found in women with Medicare (OR_{adj}=1.19; 95%CI 1.08-1.33) and Medicaid (OR_{adj}=1.24; 95%CI 1.01-1.52) as compared to those with a private health insurance. (TABLE XII)

In contrast, lower odds of not receiving chemotherapy were found in women diagnosed with later-stage (OR_{adj}=0.31; 95%CI 0.29-0.34) as compared with earlier-stage tumors and in those treated in facilities located in all geographic regions with the exception of the Mountain region when compared to the West South Central region. (TABLE XII)

TABLE XIII presents the proportion mediated by each hypothesized mediator and domains of mediators in the relationship between race/ethnicity and receiving surgical treatment in women diagnosed with LGEC, HGEC, CCC and SC.

In the initial assessment of hypothesized mediators, we found that in the NHB-NHW disparity in women diagnosed with LGEC the SE domain, altered the OR. No other hypothesized mediators meaningfully altered the OR. The SE domain significantly mediated 26.0% (95%CI 16.8 – 38.0) the effect between race/ethnicity and receipt of surgical treatment. No mediators were detected in either the disparity between Hispanic and NHW women or NHAIAN and NHW diagnosed with LGEC.

For disparity in the receipt of surgical treatment between NHB and NHW diagnosed with HGEC, only the SE domain and diagnosis stage meaningfully altered the OR. The SE domain and diagnosis stage respectively significantly mediated 23.9% (95%CI 16.0 – 34.1) and 13.9% (95%CI 5.5 – 31.1) of the total disparity. Together the SE domain and diagnosis stage mediated 36.1% (95%CI 27.4 – 45.8) of the effect between race/ethnicity and receipt of surgical treatment.

In the assessment of hypothesized mediators, we found that in the NHB-NHW disparity in women diagnosed with CCC, zip-code level income, zip-code level education and diagnosis stage altered the OR. No other hypothesized mediators meaningfully altered the OR. None of the effects mediated reached statistical significance.

In the disparity in receiving surgical treatment between NHB and NHW diagnosed with SC, the SE domain altered the odds ratios by at least 0.1. The mediating effect of the SE domain on receiving surgical treatment was not significant at the level of P=0.05. In the disparity between NHPI and NHW women diagnosed with SC, including the SE domain, insurance, diagnosis stage or the type of facility altered the OR by a factor of 0.1 or more when compared

to models unadjusted for the hypothesized mediators. However none of the effects mediated reached statistical significance.

TABLE XIV shows the proportion mediated by each hypothesized mediator and the SE domain in the disparity in receiving radiation therapy between NHAIAN and NHW women diagnosed with SC. In the initial assessment of hypothesized mediators, we found that the SE domain and diagnosis stage altered the OR for race/ethnicity by a factor of 0.1 or more when compared to models unadjusted for the hypothesized mediators. No other hypothesized mediators meaningfully altered the OR. However none of the effects mediated reached statistical significance.

No mediators were detected in the disparity between NHAIAN and NHW women diagnosed with HGEC. In addition, no mediators were detected in the racial/ethnic disparity in receiving chemotherapy.

D. Discussion

The results of this study demonstrate that, in the unadjusted analyses, NHB, Hispanic and NHAIAN women were less likely to undergo surgery than NHW. Similarly, previous studies showed that for overall EC, NHB and Hispanic women were less likely to have surgery than NHW (5, 20, 65, 77, 82). The only two previous analyses that studied other minority groups found that NHA women were more likely and API less likely to have surgery than NHW (3, 19). However, when adjusting for potential covariates, the disparity in receipt of surgical treatment for overall EC was only detected between NHB and NHW women. This demonstrates that results from unadjusted models differ from adjusted models and suggests caution when evaluating unadjusted estimates in the literature.

In regards to radiation therapy, our unadjusted results show that NHB women were more likely and Hispanics, NHAIAN and NHPI less likely to receive radiation therapy than NHW.

TABLE XIII: ESTIMATES OF THE PROPORTION MEDIATED FOR THE RACIAL/ETHNIC DIFFERENCES IN THE RECEIPT OF SURGICAL TREATMENT IN WOMEN DIAGNOSED WITH LOW-GRADE, HIGH-GRADE,CLEAR CELL AND SEROUS CARCINOMAS, NCDB, 2003-2007, n=208,247

Domains and Hypothesized Mediators[a]	**Proportion mediated %**	***P*-value**
Low-Grade Carcinomas - NHB vs. NHW		
Socio-Economic domain[b]	**26.0 (16.8-38.0)**	**<0.0001**
High-Grade Carcinomas - NHB vs. NHW		
Socio-Economic domain[b]	**23.9 (16.0-34.1)**	**<0.0001**
Diagnosis Stage	**13.9 (5.5 – 31.1)**	**0.03**
All mediators	**36.1 (27.4 - 45.8)**	**<0.0001**
Clear Cell Carcinomas - NHB vs. NHW		
Zip-code Level Income	0	-
Zip-code Level Education	10.8 (2.1 – 40.5)	0.20
Facility Type	12.7 (3.1 – 39.8)	0.14
All mediators	17.4 (2.1 – 67.5)	0.30
Serous Carcinomas - NHB vs. NHW		
Socio-Economic domain[b]	12.9 (4.1 – 33.8)	0.07
Serous Carcinomas - NHPI vs. NHW		
Socio-Economic domain[b]	0	-
Health Insurance	0	-
Diagnosis Stage	8.4 (2.9 – 22.5)	0.06
Facility Type	0	-
All mediators	8.3 (2.6 – 23.4)	0.08

[a] Each mediator and domain of mediators were separately assessed in fully-adjusted models.

[b] The socio-economic domain includes zip-code level income and zip-code level education.

TABLE XIV: ESTIMATES OF THE PROPORTION MEDIATED FOR THE NHAIAN-NHW DIFFERENCES IN THE RECEIPT OF RADIATION THERAPY IN WOMEN DIAGNOSED WITH SEROUS CARCINOMAS, NCDB, 2003-2012, n=208,247

Domains and Hypothesized Mediators[a]	**Proportion mediated %**	***P*-value**
Socio-Economic domain[b]	3.5 (0.1 – 67.4)	0.62
Diagnosis Stage	12.5 (0.8 – 71.9)	0.44
All mediators	15.5 (1.1 – 74.7)	0.40

[a] Each mediator and domain of mediators were separately assessed in fully-adjusted models. Zip-code level education, zip-code level income, health insurance and facility type did not meet the criteria of mediation analyses.

[b] The socio-economic domain includes zip-code level income and zip-code level education.

Our findings are inconsistent with previous studies that found that NHB women were less likely and Hispanic, Asian, API and American Indian/Alaskan Native more likely to receive radiation therapy than NHW (3, 19, 77, 82). The findings of previous studies likely differ from ours due to the nature of the data used (e.g. small and regional samples, short time-frames and different temporal periods).

Consistent with the literature, our unadjusted results demonstrate that NHB women are more likely to receive chemotherapy than NHW (19, 20). In addition, our results show that NHA and NHPI were more likely than NHW women to receive adjuvant chemotherapy. Our stage-specific unadjusted results demonstrate that NHB women were more likely than NHW to receive multi-agent chemotherapy for early-stage tumors. In contrast, when compared to NHW, Hispanic women were less likely to receive chemotherapy for late-stage tumors and NHA were more likely to receive it for earlier and later-stage tumors.

To the best of our knowledge, this study is the first to report the results of the relationship between six racial/ethnic groups and three main EC treatment modalities, from adjusted models stratified by tumor subtypes. The National Academy of Sciences strongly

recommends performing subtype-specific analyses allowing for scientific advancement and helping reduce cancer morbidity and mortality (18). Endometrial cancer tumor subtypes differ from each other based on their biological characteristics and the clinical course of the disease; as such they require different treatment regimens (11). Our study shows that considering EC as a homogenous disease distorts the association between race/ethnicity and receipt of surgery. For instance, while there appears to be no NHAIAN-NHW and NHPI-NHW disparities in the unadjusted estimates, the results from the subtype-specific analyses show that some important disparities exist.

Racial differences in receiving surgical treatment exist, after adjusting for diagnosis stage, diagnosis grade, Charlson Comorbidity Index, facility-level characteristics and area-level income and education. Notably, NHB women were the only minority group that had higher odds of not receiving surgical treatment, across all EC subtypes. The results also show that Hispanic and NHAIAN women diagnosed with LGEC had significantly higher odds of not having surgery than NHW. Finally, NHPI had five times higher odds than NHW of not having surgery for SC; one of the most aggressive types of EC (12).

A possible explanation for differences in receiving surgical treatment could be related to the patient's or family members' lack of acceptance of the recommended treatment. In our study, when compared to NHW, NHB, NHAIAN, NHA and NHPI patients or their family members and guardians were more likely to refuse recommended surgery. (TABLE XXIII, APPENDIX C) Even if the reasons behind the refusal of recommended surgery are not entirely understood, previous studies showed that NHB women are more likely to choose less aggressive, less invasive and more orthodox treatment methods than NHW (123, 124). They are also more likely to rely on their own spirituality for recovery, believing that prayers have the power to cure their cancer (125). In addition, black women are also shown to be more likely to believe that what happens to them is part of their destiny and perceive death as a natural event

coming after a cancer diagnosis (123). Lastly, black women also show more mistrust of the health care system and have misconceptions about cancer acquisition and spread (125, 126). Other factors that could also impact treatment decisions have been linked to patient-physician relationships. These relationships could be influenced by interpersonal communication problems resulting from poor mixed-race relationships (125, 127). In a recent ovarian cancer study, the authors reported that NHB women or their families were more likely to refuse the recommended surgery for every stage at diagnosis when compared to NHW (128).

Health insurance was found to be an effect modifier in the relationship between race/ethnicity and receiving surgical treatment in women diagnosed with LGEC. The results of our study show that racial/ethnic differences for LGEC are almost exclusively present in patients who are privately insured. These results could be potentially explained by the fact that while Medicare and Medicaid provide nearly uniform benefits for their enrollees, private health insurance plan category includes plans such as managed care, military care and TRICARE offering policies with significantly different benefits (85). As such, minority patients could be more likely to be covered by less expensive health plans that have higher co-pays and complex systems for referrals and authorizations. High co-pays could influence lower socio-economic status (SES) patients to refuse the recommended surgery. In other words, some patients could decide not to be treated because of the fear of potential medical debt (128). In addition, a complex system of referrals could delay a recommended treatment or the network of the health insurance plan could prevent patients from accessing higher-quality hospitals. In regards to radiation therapy and chemotherapy, our results show that NHAIAN women diagnosed with SC had higher odds of not receiving radiation therapy than NHW. Lastly, NHB women diagnosed with CCC have higher odds than NHW of not receiving chemotherapy. However, NHW women had higher odds of not receiving chemotherapy than NHA. No differences in receipt of chemotherapy were detected in stage-stratified models. The results from our study show that

unadjusted results differ from adjusted results demonstrating that, when accounting for potential confounders, NHB and NHPI women have the same odds of receiving radiation therapy than NHW. Similarly, although in unadjusted analyses, NHB women seem to be more likely to receive chemotherapy than NHW, the results from our adjusted models show that in fact NHB women have higher odds of not receiving chemotherapy than NHW.

The results from the mediation analyses demonstrate that the differences in receiving surgical treatment in women diagnosed with LGEC, HGEC and SC were partially explained by the SE domain. The SE domain significantly mediated a quarter of the disparity between NHB and NHW women diagnosed with LGEC and HGEC. In addition, the SE domain explained 12.9% of the disparity found between NHB and NHW women diagnosed with SC. One explanation for the mediating effect of the SE domain receiving surgical treatment could be related to the fact that, in the NCDB, a greater proportion of NHB women lived in underserved areas. Notably, nearly 43% of NHB when compared to only 13% of NHW lived in areas with a reported median family income level of $38.000 or lower. In addition, one third of NHB as compared to only 12% of NHW, lived in areas where 21% or more people did not finish high school. Lower neighborhood levels of education and income have been linked with reduced access to care (96, 129, 130). Findings from a previous study showed that after adjusting for individual-level SE characteristics, people residing in a disadvantaged area were less likely to have a regular healthcare provider, obtain preventive services and were more likely to have unmet medical needs (96). It has also been shown that women with less education were less likely to comply with complex courses of treatment and be familiar with the healthcare services available in their community (131). As mentioned above, our study also showed lower compliance with recommend treatment in minority groups, which could possibly due to financial reasons. In addition, studies have shown that neighborhoods can influence one's health indirectly, by the value the community places on health and the social support available to the

communities (91, 93). Women of lower SES are less likely to possess health insurance or are more likely to be underinsured, both of which could impact their access to high-quality hospitals, timely diagnoses and a better quality care in general (88, 89). Moreover, women who lack social support are more likely to wait longer before sharing their symptoms. Therefore, they are less likely to have an early-stage diagnosis which subsequently influences their course of treatment. Previous breast cancer studies found that stage at diagnosis mediated one third of the disparity in having a mastectomy (59) and overall survival (132) between NHB and NHW women. Our study shows that stage at diagnosis mediates a part of the disparity in receiving surgical treatment between NHB and NHW diagnosed with HGEC. More research will be needed in order to confirm and understand this association.

E. Limitations and Strengths

The results of this study should be interpreted in light of several limitations that primarily pertain to the variables available for analysis. Income and education are only available at the zip-code level. While zip-code level measures were shown to be important predictors of access care and subsequent receipt of treatment, previously individual-level measures were also shown to be associated with a delay in treatment due to the fact that less education may be associated with a lack of knowledge about EC symptoms (4). The lack of these variables made it impossible to assess these relationships and prohibited gaining a better understanding of the presence of effect modification in women diagnosed with LGEC. In addition, physician specialty, an important independent predictor for staging (99, 100) and gynecologic cancer outcomes (99, 100, 103), was not available. However, we included average facility-case volume as a proxy to minimize bias, assuming that low case volumes reflect a lack of gynecologic oncology subspecialty care (103). Lastly, the NCDB does not include any information about the completed number of chemotherapy cycles. The availability of this information could help explain some racial/ethnic differences in tumor aggressiveness and treatment.

Despite these limitations, this study has several strengths. First, it is the only study to provide the results of the association between race/ethnicity and the three main treatment modalities for EC from adjusted models. This demonstrated that results from unadjusted models differ from adjusted models and suggests caution when evaluating unadjusted estimates in the literature. Second, this study is the first to assess racial differences between five minority groups and NHW. Third, as opposed to analyzing EC as a homogenous disease, or solely as Type 1 and Type 2, this study presents racial/ethnic differences in receipt of treatment by four histological subtypes. Fourth, our study is the first study to explore factors mediating racial/ethnic differences in receipt of treatment. Lastly, an advantage of the NCDB over the commonly used SEER dataset is the availability of information about patients' health insurance status, treatment with chemotherapy and underlying comorbidities.

F. Conclusion

In conclusion, this study generally found that although surgery is a recommended first course of treatment for every patient diagnosed with EC, within the NCDB and across all histologic subtypes, racial/ethnic differences in surgical treatment exist. In addition, racial/ethnic differences in surgical treatment were found to differ by health insurance among women diagnosed with LGEC, with important racial/ethnic differences in surgical treatment only in women with private health insurance. Moreover this study shows that NHAIAN have higher odds than NHW for not receiving radiation therapy when diagnosed with SC. Additionally, when compared to NHW, NHB women had higher odds of not receiving chemotherapy when diagnosed with CCC. Lastly, the SE domain was found to mediate a part of the racial/ethnic differences in LGEC, HGEC and SC in receiving surgical treatment and in SC in the receiving radiation therapy.

V. RACIAL/ETHNIC DIFFERENCES IN OVERALL 5-YEAR SURVIVAL

A. Introduction

Endometrial cancer incidence, mortality and survival significantly vary by histologic subtype. Overall, LGEC have the highest incidence and the lowest mortality (7, 33, 133). Although CCC and SC occur less frequently, they are associated with the poorest survival (12, 133). In a study that used the SEER data, LGEC accounted for 72% of all EC diagnoses and 26% of total deaths. In contrast, SC accounted for 10% of diagnoses and 39% of EC deaths (12). High-grade endometrioid carcinomas, SC and CCC, typically categorized as Type 2 or high-risk tumors, are characterized by their tendency for recurrence, distant spread, and short survival time (12, 65). LGEC are usually referred to as Type 1 EC.

Non-Hispanic black women are more likely to be diagnosed with Type 2 EC when compared to nonblack women (7, 26). NHB women were 1.9 times more likely than NHW to be diagnosed with CCC and 2.2 times more likely to be diagnosed with SC (7). The incidence of tumor subtypes between Asian, Hispanic, American Indian, Alaskan Natives and White women seems to be similar (3).

Previous studies have observed lower EC survival in NHB than in NHW (5, 26, 35, 67, 81) with a recent study reporting a 5-year survival rate of 65.6% for NHB and 85.3% for NHW (81). Evidence is inconclusive regarding Hispanic - NHW EC differences in 5-year survival (5, 64, 65, 82). Asian women have a significantly improved overall and cancer-specific survival, for all types of EC combined than NHW, after accounting for potential confounders (3). The same study found that American Indian/Alaskan Native women had worse overall survival than NHW; however no differences were found for cancer-specific survival. Finally, a study that used the Department of Defense Centralized Registry data found the crude 5-year survival rate for overall EC to be significantly lower for Asian-Pacific Islander women than for white women (19).

The existing literature on EC survival has generally failed at examining survival rates by EC subtypes, even if there is evidence that subtype-specific survival differences exist (12). In addition, previous research on EC has been primarily directed towards studies assessing racial/ethnic differences between NHB and NHW women. Most of these studies have failed to include women from fast growing minority populations (e.g. Asian, Hispanic) (10). Lastly, previous research has not consistently controlled for important factors impacting survival, such as tumor, socio-demographic and treatment facility characteristics or whether the women received treatment.

Treatment differences may play a role in survival differences. Surgery is the cornerstone of treatment for women diagnosed with any grade and stage of EC (11). Previous studies showed that in women diagnosed with overall EC, those who did not undergo surgery were over three times more likely to die than those who received surgical intervention (3). Similarly, in women diagnosed with Type 2 tumors, those who did not receive surgery had twice the risk of dying when compared to those who did (64). There is evidence that racial/ethnic differences in receipt of surgery exist. In unadjusted models, Hispanic and Black women were less likely to receive surgery than NHW (5, 82). The results of our aim 2 showed that in models adjusted for potential confounders related to the receipt of treatment, NHB women diagnosed with any EC subtype had higher odds of not having surgery than NHW. In addition, our results demonstrated that Hispanic and non-Hispanic American Indian and Alaskan Native women diagnosed with LGEC had higher odds of not having surgery than NHW.

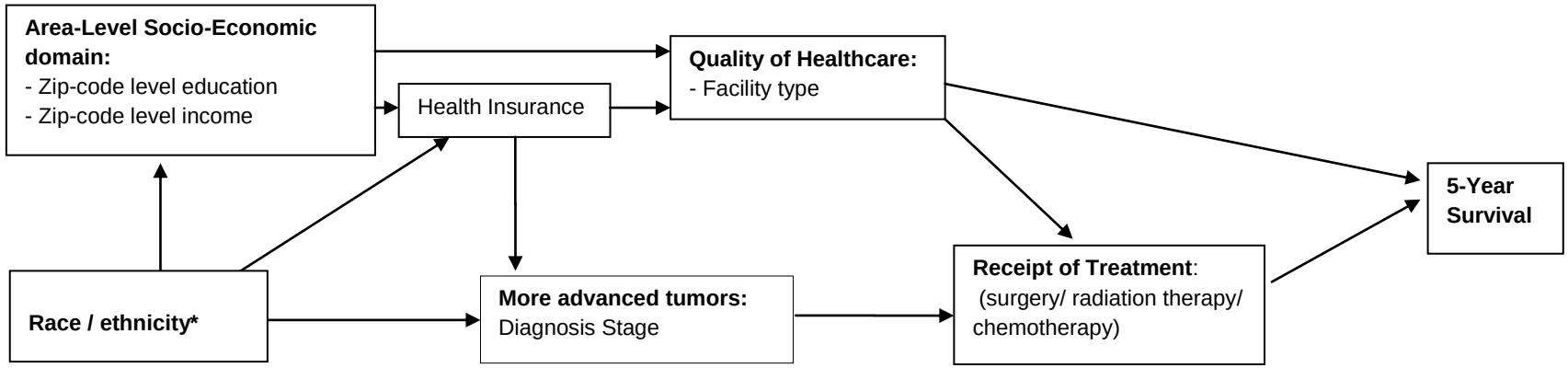
A part of the difference in subtype-specific survival can be attributed to the availability of effective treatments. Overall, LGEC are diagnosed as early-stage, whereas HGEC, CCC and SC, as late-stage tumors. It is estimated that between 52% and 70% of Type 2 tumors show extrauterine spread at the time of surgery, compared to only 4.6% of Type 1 (43-45). Surgery, when combined with local adjuvant therapy for early-stage tumors (stage I and II), is generally

curative (134). However, for women diagnosed with stage III or stage IV tumors, the prognosis remains poor and the effective treatment is yet to be determined (11, 134).

Previous studies have used mediation analyses to understand the effect of various important socio-demographic, tumor, and institutional prognostic factors in differences between minority and NHW women in regards to treatment outcomes such as the receipt and delay of treatment (58-61, 132). However, it is likely that because current mediation analysis techniques were difficult to implement for survival analyses, little attention has been paid to understanding racial differences in the context of survival. Using the National Comprehensive Cancer Network breast cancer data, the authors of a recent study found that the excess mortality in black women, when compared to white, was mediated by stage at diagnosis (132). In addition, the authors of this study assessed educational attainment, insurance status and treatment as potential mediators; however none of these variables were found to mediate the survival disparity. Mediation analysis has not been used to assess EC racial/ethnic differences and therefore it is unclear what factors could act as potential mediators. Based on our conceptual model (Figure 4), we hypothesized zip-code level income and the type of treatment facility to be potential mediators, in addition to stage at diagnosis, educational attainment, insurance status and treatment, selected in the National Comprehensive Cancer Network study (132). Survival is directly dependent on the treatment received (3, 64) and the types of facilities where the patient gets treated (121). In addition, it is indirectly dependent on the tumor aggressiveness at the time of diagnosis (11), health insurance coverage (5) and patient's area-level SES (40, 41, 84).

The purpose of this analysis is to examine racial/ethnic differences in 5-year overall survival by EC tumor subtype and explore potential mediators of these differences, using the NCDB. The NCDB is one of the largest and most comprehensive dataset of EC in the U.S.

Figure 4: Conceptual framework for the relationship between race/ethnicity and 5-year overall survival



* Non-Hispanic black, Hispanic, non-Hispanic Asian, non-Hispanic Pacific Islanders/Hawaiian Natives, Non-Hispanic American Indian/ Alaskan Native vs. non-Hispanic White

The NCDB is based on registry data and includes 70% or approximately 230,000 stage-diagnosed EC cases in the U.S. and Puerto Rico between 2003 and 2012 (109). The mediating effect of stage at diagnosis, area-level income, area-level education, health insurance status, treatment and treatment facility characteristics on 5-year survival was investigated in survival differences. To the best of our knowledge, this study is the first to assess whether racial/ethnic differences in overall five-year EC survival exist after adjusting for potential confounders and to explore factors that may mediate the potential differences. Moreover, this study is the first to compare six racial/ethnic groups in models stratified by tumor subtype.

B. Methods

First, vital status differences by histologic subtype between NHW and women of other racial/ethnic groups, diagnosed between 2003 and 2007, were assessed using the Chi-square test statistics. Vital status was reported through December 31st 2012. The CoC-accredited facilities are required to update vital status of patients reported to the NCDB in five-year cycle; such as women diagnosed in 2003 will be reported in 2005 and have their vital status updated in 2010. Consequently, because of the unavailability of the vital status, patients diagnosed after 2007 were excluded from the study sample.

Second, the overall and stage-stratified multivariable analyses for overall EC and by histologic subtypes were performed using the Cox-proportional hazard regression models. The NCDB does not include information about patients' cause of death and therefore EC specific mortalities could not be computed (109). Patients with incomplete follow-up were right censored based on the last day of follow-up. In addition, patients who died more than five years after their diagnosis were also right censored at five years. Five-year survival time was computed by subtracting the date of diagnosis from the last date of follow-up, the date of death or censoring at >5years. Hazard ratios (HR) and 95% Confidence Intervals (95%CI) were estimated. Third,

cumulative probability of survival was computed with the product limit estimate. Endometrial cancer subtype-specific Kaplan Meier (KM) curves were used to visually assess the assumption of proportion hazard between significant racial/ethnic differences found with the Cox-proportional hazard regression models. No departure from proportional hazard was observed in any of the racial/ethnic differences. Adjusted subtype-specific KM curves were created to compare racial differences in cumulative survival. KM curves for NHPI and NHAIAN diagnosed with CCC and SC were not presented because of the small sample sizes of both minority populations.

Fifth, effect modification between race/ethnicity and diagnosis stage (late vs. early stage) was assessed by including the pair-wise interaction term and two corresponding main effects into the fully adjusted models. Even if the interaction term was not statistically significant (P>0.05) in any of the subtype-stratified models, the HR for the stratified models were presented in the tables for comparison.

Sixth, mediation analyses on differences found in the Cox-proportional hazard models were performed. Two domains; zip-code level socio-economic factors and receipt of any treatment, and eight individual factors were tested as intermediate variables: (1), zip-code level education, (2) zip-code level income, (3) health insurance, (4) diagnosis stage, (5) facility type, (6) receipt of surgery, (7) receipt of radiation therapy and (8) receipt of chemotherapy (Figure 5) Ten indirect paths connecting race/ethnicity with 5-year overall survival by the way of two domains and eight factors were estimated. The direct effect (c') is represented by a red arrow. In the primarily exploration of mediation, we compared the hazard ratios of fully adjusted models with models unadjusted for the hypothesized factors and domains. Each factor or domain that altered the HR by a factor of 0.1 or more was further explored as an intermediate variable. Next, each intermediate variable or domain was separately added to the fully adjusted multivariable model to calculate the mediated proportion and its 95% CI using the mediate SAS macro (122).

The proportion of the effect of race/ethnicity mediated by intermediate variables (Figure 4) on 5-year survival was separately estimated for every minority women-NHW disparity detected in the multivariable models. The proportion mediated represents the excess or reduced EC overall 5-year mortality among the minority group as compared to NHW women that could be attributed to the domain of mediators or factor.

Analyses were performed using SAS software version 9.4 (SAS Institute, Inc., Cary, NC). *P*-values were two sided, with an α level of 0.05.

C. Results

1. Five-Year Overall Survival

TABLE IV describes the characteristics of the study population by race/ethnicity, overall and by socio-demographic, tumor and facility covariates. A total of 76,223 women were stage-diagnosed with EC in one of the CoC-approved hospitals between 2003 and 2007 with a follow-up until 2012. Overall, 84.2% women self-identified themselves as NHW, 8.1% as NHB, 5.1% as Hispanic, 2.1% as NHA, 0.3% (n=198) as NHPI and 0.2% (n=148) as NHAIAN. (TABLE XV) In addition, 71.6% of women were diagnosed with LGEC, 15.9% with HGEC, 5.2% with SC and 1.3% with CCC. (TABLE IV)

TABLE XV shows that, overall, the largest proportion of deaths occurred in women diagnosed with SC and the smallest in those diagnosed with LGEC, 55.4% vs. 11.0% respectively. NHB women diagnosed with any subtype of EC were significantly more likely to die than NHW. In contrast, Hispanic and NHA women diagnosed with LGEC were less likely to die than NHW.

Figure 5: Conceptual model of potential mediators in the relationship between race/ethnicity and 5-year overall survival.

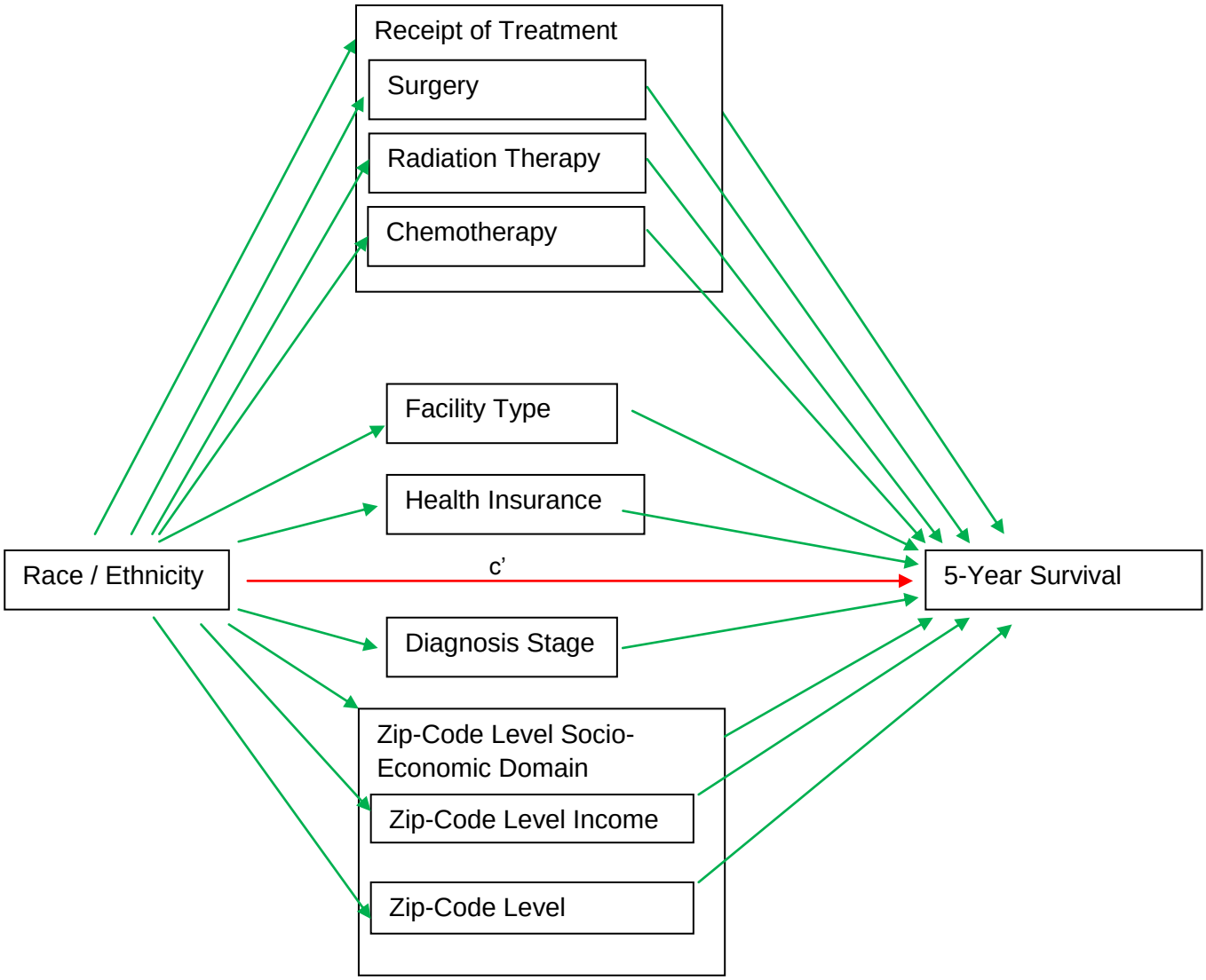


TABLE XV: DISTRIBUTION OF VITAL STATUS BY ENDOMETRIAL CANCER HISTOLOGIC SUBTYPE AND RACE/ETHNICITY, NATIONAL CANCER DATABASE, 2003-2012, n=76,223

	Non-Hispanic White n=64,196	Non-Hispanic Black n=6,173	Hispanic n=3,888	Non-Hispanic Asian n=1,620	Non-Hispanic American Indian, Alaskan Native n=148	Non-Hispanic Pacific Islander, Hawaiian n=198	Overall n=76,223
	%	%	%	%	%	%	%
Overall	84.2	8.1	5.1	2.1	0.2	0.3	
Low-Grade Carcinoma							
Dead	10.9	16.5#	9.0*	5.8#	10.8	10.8	11.0
Alive	89.1	83.5	91.0	94.2	89.2	89.2	89.0
High-Grade Carcinoma							
Dead	36.9	48.9#	35.1	27.0*	52.2 (n=12)	27.6 (n=8)	38.0
Alive	63.1	51.1	64.9	73.0	47.8 (n=11)	72.4 (n=21)	62.0
Clear Cell Carcinoma							
Dead	44.2	57.0*	30.0	26.1 (n=6)	0	0	45.5
Alive	55.8	43.0	70.0	73.9 (n=17)	0	100 (n=1)	54.5
Serous Carcinoma							
Dead	53.6	62.6#	47.6	54.6	20.0 (n=1)	54.6 (n=6)	55.4
Alive	46.4	37.4	52.4	45.5	80.0 (n=4)	45.4 (n=5)	44.6

* Statistically different from NHW (p_{value} <0.05).
# Statistically different from NHW (p_{value} <0.001).

The KM curves demonstrated that regardless of race/ethnicity, women diagnosed with LGEC had the highest ≥85% and those diagnosed with SC the lowest ≤50% survival.

Figure 6 and Figure 7 present the overall 5-year survival by race/ethnicity for women diagnosed with LGEC. NHB women had the lowest and NHA the highest survival. The survival for all women was higher than 85%.

Figure 6: Low-grade endometrioid carcinoma: 5-year overall survival by race/ethnicity

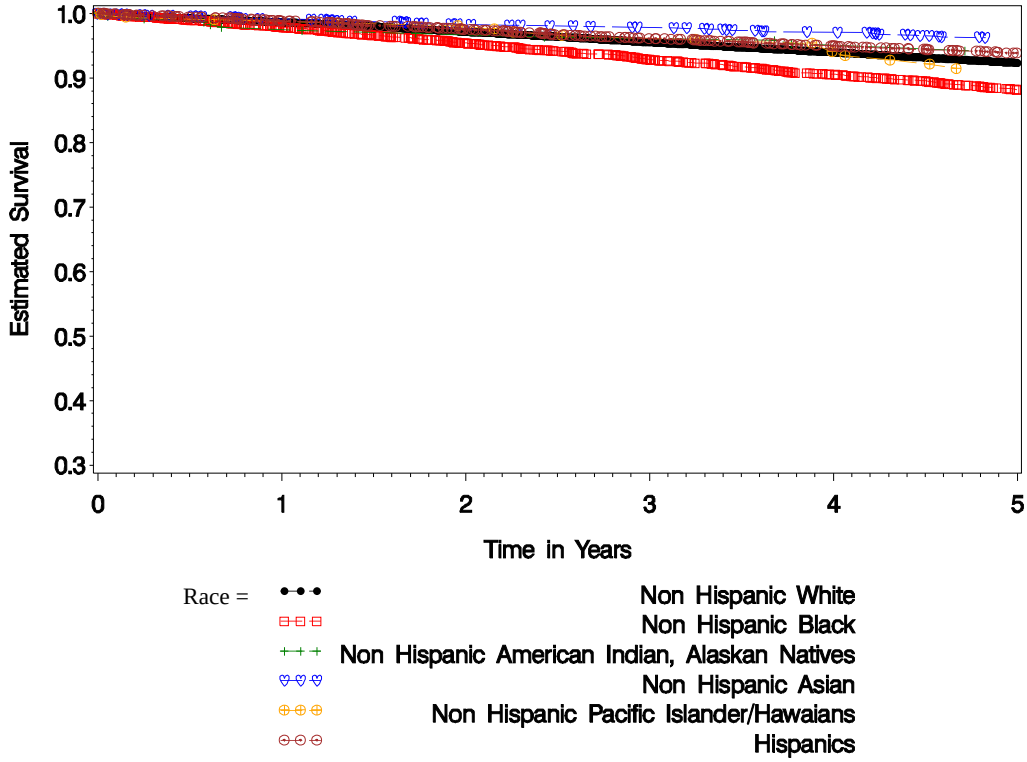


Figure 7: Low-grade endometrioid carcinoma: 5-year overall survival by race/ethnicity

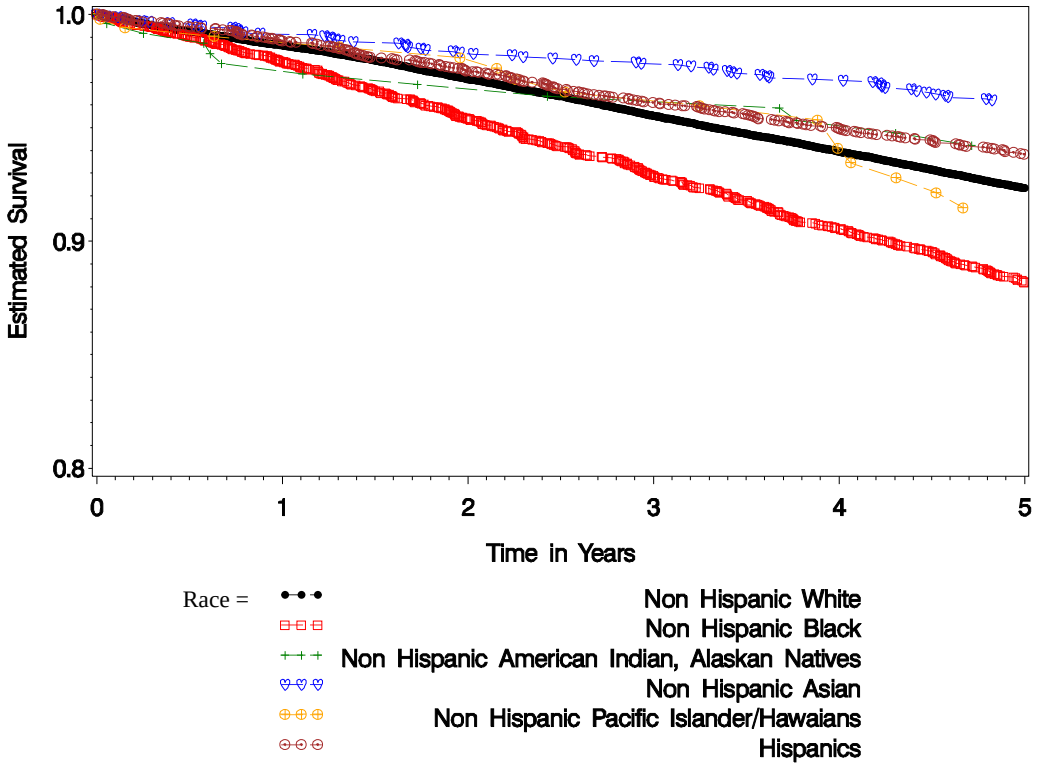
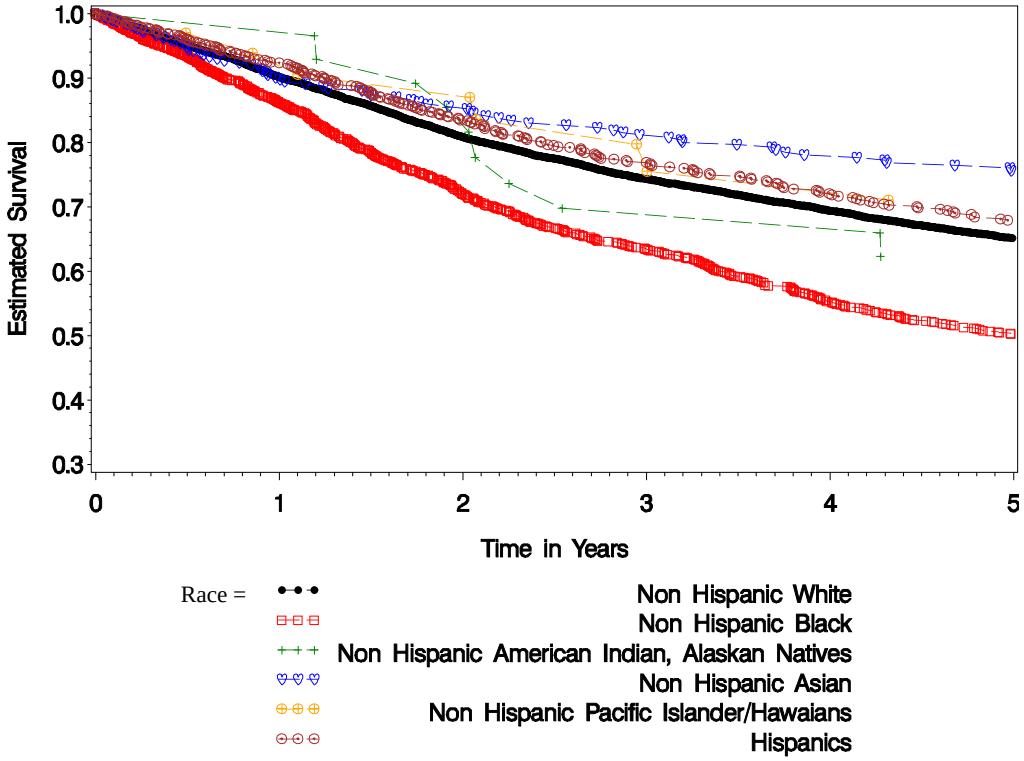


Figure 8 shows the overall 5-year survival by race/ethnicity for women diagnosed with HGEC. The survival was the lowest for NHB at approximately 50% and the highest for NHA at 75%. The survival for NHW women was approximately 65%.

Figure 9 presents the overall 5-year survival by race/ethnicity for women diagnosed with CCC. NHB women had the lowest survival at approximately 40% and NHA the highest at 74%. The survival for NHW women was approximately 58%.

Figure 10 shows the overall 5-year survival by race/ethnicity for women diagnosed with HGEC. The survival was the lowest for NHB at approximately 35% and the highest for NHA at 50%. The survival for NHW women was approximately 45%.

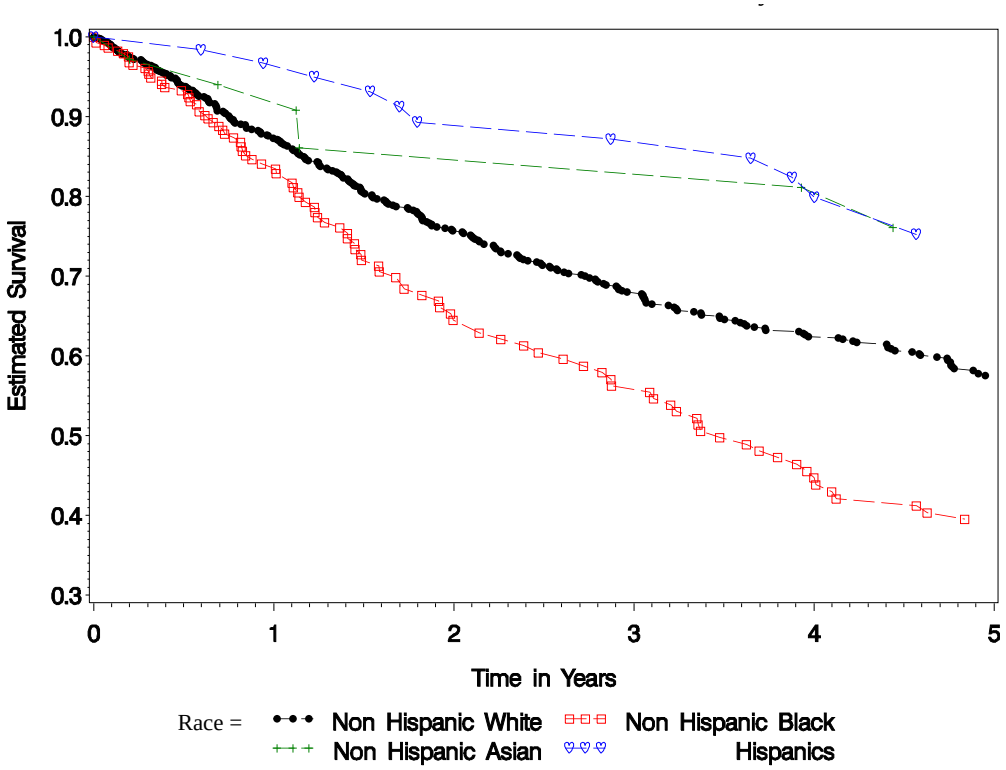
Figure 8: High-grade endometrioid carcinoma: 5-year overall survival by race/ethnicity



The unadjusted results from our study demonstrate that when diagnosed with overall EC, Hispanic (HR=0.85; 95%CI 0.78-0.93) and NHA (HR=0.79; 95%CI 0.69-0.92) women had a lower and NHB (HR=1.18; 95%CI 1.12-1.25) higher risk of death than NHW (results not shown).

TABLE XVI, TABLE XVII, TABLE XVIII and TABLE IX present the results from the multivariable Cox-proportional hazard models for the association between race/ethnicity and overall 5-year survival, stratified by EC tumor subtype and stage at diagnosis. In the fully adjusted models, racial differences were detected in women diagnosed with LGEC, HGEC and SC. (TABLE XVI)

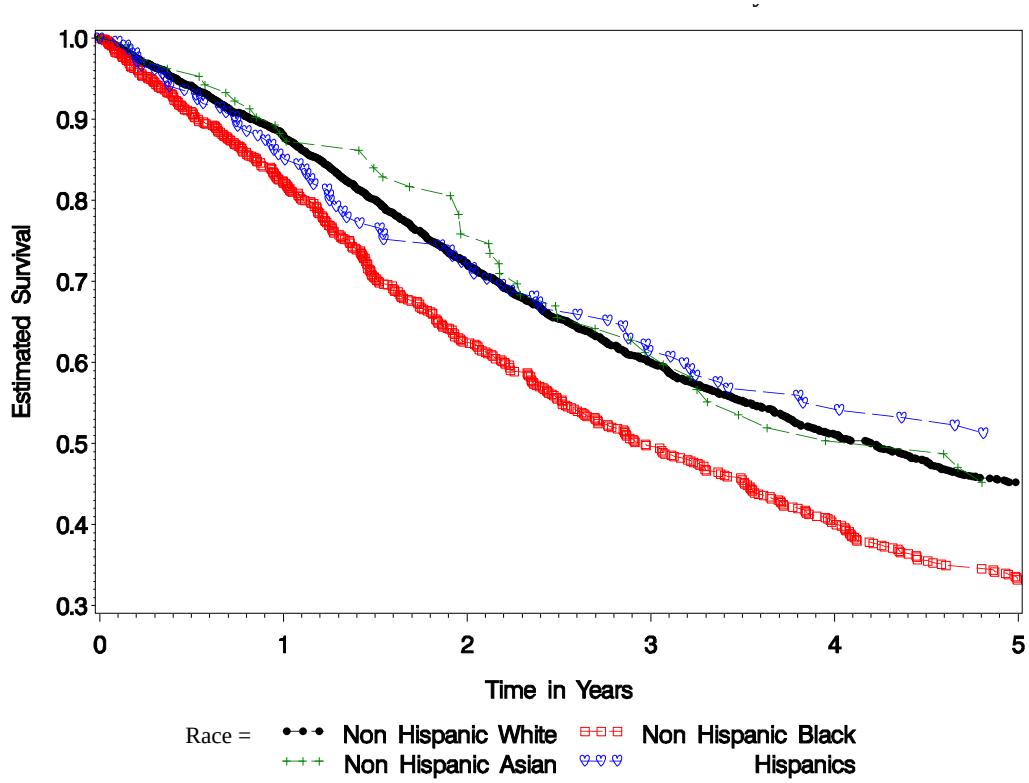
Figure 9: Clear cell carcinoma: 5-year overall survival by race/ethnicity



NHB women diagnosed with LGEC had 27% (HR_{adj}=1.27; 95%CI 1.16-1.39) higher risk of deaths than NHW. In contrast NHA women had 30% (HR_{adj}=0.70; 95%CI 0.54-0.89) lower risks of deaths when compared to NHW. The interaction term between race/ethnicity and stage at diagnosis was not significant; however stage-stratified results were presented. In women diagnosed with late-stage LGEC the differences are more pronounced than in those diagnosed with early stage. (TABLE XVI)

A higher risk of death was associated with older age, earlier year at diagnosis, lower zip-code level income and an increased number of comorbidities.

Figure 10: Serous carcinoma: 5-year overall survival by race/ethnicity



In addition, the risk of death was higher in women living in areas where between 7.0% and 12.9% (HR_{adj}=1.09; 95%CI 1.01-1.18), 13.0% and 20.0% (HR_{adj}=1.10; 95%CI 1.01-1.21) as compared to areas where less than seven percent of people had no high-school diploma, and in women covered by Medicare (HR_{adj}=1.78; 95%CI 1.65-1.92), Medicaid (HR_{adj}=2.18; 95%CI 1.94-2.46), and those who were uninsured (HR_{adj}=1.66; 95%CI 1.43-1.92) as compared to those with private health insurance. Higher risk of death was also found in women diagnosed with later-stage (HR_{adj}=4.04; 95%CI 3.78-4.32) as compared with earlier-stage tumors; those diagnosed with moderate as compared to well differentiated LGEC (HR_{adj}=1.57; 95%CI 1.49-1.66) and those who did not receive any surgery (HR_{adj}=6.05; 95%CI 5.61-6.53), and any radiation therapy (HR_{adj}=1.11; 95%CI 1.05-1.17) as compared to those who did. Lastly, higher

risk of death was observed in women who were treated in facilities located in the east south central (HR_{adj}=1.16; 95%CI 1.01- 1.32) as compared to the west south central regions and those treated in facilities seeing 1-19 (HR_{adj}=1.13; 95%CI 1.04-1.22) as compared to 74 and over cases of EC per year. (TABLE XVI)

NHB women diagnosed with HGEC had 16% (HR_{adj}=1.16; 95%CI 1.06-1.27) higher risk of death than NHW. (TABLE XVII) In contrast Hispanic women had 15% (HR_{adj}=0.85; 95%CI 0.73-0.98) lower risks of death when compared to NHW. The interaction term between race/ethnicity and stage at diagnosis was not significant; however stage-stratified results were presented. The disparity between Hispanic and NHW women was only detected for those diagnosed with late stage and the disparity between NHB and NHW in women diagnosed with early-stage tumors.

A higher risk of death was associated with older age, lower zip-code level education and an increased number of comorbidities. In addition, the risk of death was higher in women diagnosed in the year 2003 (HR_{adj}=1.21; 95%CI 1.11-1.33) as compared to 2007, in women covered by Medicare (HR_{adj}=1.25; 95%CI 1.15-1.36), Medicaid (HR_{adj}=1.40; 95%CI 1.22-1.60), and those who were uninsured (HR_{adj}=1.40; 95%CI 1.20-1.63) as compared to those with private health insurance.

Higher risk of death was also found in women diagnosed with later-stage (HR_{adj}=3.90; 95%CI 3.65-4.17) as compared with earlier-stage tumors; those diagnosed with undifferentiated as compared to poorly differentiated HGEC (HR_{adj}=1.16 95%CI 1.04-1.30) and those who did not receive any surgery (HR_{adj}=4.36; 95%CI 4.00-4.77), any radiation therapy (HR_{adj}=1.44; 95%CI 1.36-1.53) and any multi-agent chemotherapy (HR_{adj}=1.11; 95%CI 1.03-1.19) as compared to those who did.

TABLE XVI: RESULTS FOR THE EFFECT OF RACE/ETHNICITY ON OVERALL FIVE-YEAR SURVIVAL FOR WOMEN DIAGNOSED WITH LOW-GRADE CARCINOMAS, OVERALL, AND STRATIFIED BY STAGE AT DIAGNOSIS, NATIONAL CANCER DATABASE, 2003-2012, n=76,223

	HR(95%CI)	**HR(95%CI)**	**HR(95%CI)**
	Type 1: Low-grade Carcinoma n=55,265 deaths= 6,140	**Stratified Model[b]: Among Late-Stage n=5,389 deaths= 1,826**	**Stratified Model: Among Early Stage n= 49,876 deaths= 4,314**
Socio-Demographic Characteristics			
Race/Ethnicity			
Non-Hispanic White	Ref.	Ref.	Ref.
Hispanic	0.89 (0.78-1.01)	0.88 (0.70-1.11)	0.90 (0.77-1.06)
Non-Hispanic Black	**1.27 (1.16-1.39)**	**1.51 (1.28-1.78)**	**1.18 (1.06-1.32)**
Non-Hispanic Asian	**0.70 (0.54-0.89)**	**0.65 (0.43-0.97)**	**0.72 (0.53-0.99)**
Non-Hispanic American Indian, Alaskan Native	0.90 (0.51-1.60)	0.53 (0.07-3.76)	0.96 (0.53-1.74)
Non-Hispanic Pacific Islander/ Hawaiian	1.42 (0.87-2.34)	1.50 (0.71-3.20)	1.30 (0.67-2.52)
Diagnosis Age			
<50	Ref.		
51-59	**1.51 (1.34-1.70)**		
60-69	**2.10 (1.86-2.37)**		
70+	**4.24 (3.75-4.81)**		
Diagnosis Year			
2007	Ref.		
2006	1.06 (0.98-1.14)		
2005	**1.14 (1.05-1.23)**		
2004	**1.14 (1.05-1.24)**		
2003	**1.16 (1.07-1.25)**		
Zip-Code Level Income[a]			
$63.000+	Ref.		
$48.000-62.999	**1.08 (1.00-1.17)**		
$38.000-$47.999	**1.11 (1.02-1.21)**		
<$38.000	**1.24 (1.12-1.38)**		
Zip-Code Level Education[a]			
<7.0 without a high-school diploma	Ref.		
7.0-12.9% without a high-school diploma	**1.09 (1.01-1.18)**		
13.0-20.0% without a high-school diploma	**1.10 (1.01-1.21)**		
≥21.0% without a high-school diploma	1.06 (0.95-1.19)		
Health Insurance			
Private Insurance	Ref.		
Medicare	**1.78 (1.65-1.92)**		
Medicaid	**2.18 (1.94-2.46)**		
Not Insured	**1.66 (1.43-1.92)**		
Tumor Characteristics			
Diagnosis Stage			
Early (Stages I, II)	Ref.		
Late (Stages III, IV)	**4.04 (3.78-4.32)**		
Grade			
Well differentiated	Ref.		
Moderately differentiated	**1.57 (1.49-1.66)**		
Comorbidities			
None	Ref.		
1	**1.35 (1.28-1.44)**		
2 or more	**2.44 (2.23-2.66)**		
Receipt of Treatment			
Receipt of Surgery			
Yes	Ref.		
No	**6.05 (5.61-6.53)**		
Receipt of Radiation Therapy			
Yes	Ref.		
No	**1.11 (1.05-1.17)**		
Receipt of Chemotherapy			
Yes	Ref.		
No	0.93 (0.85-1.03)		

TABLE XVI (CONTINUED): RESULTS FOR THE EFFECT OF RACE/ETHNICITY ON OVERALL FIVE-YEAR SURVIVAL FOR WOMEN DIAGNOSED WITH LOW-GRADE CARCINOMAS, OVERALL, AND STRATIFIED BY STAGE AT DIAGNOSIS, NATIONAL CANCER DATABASE, 2003-2012, n=76,223

	HR(95%CI)
	Type 1: Low-grade Carcinoma n=55,265 deaths= 6,140
Treatment Facility Characteristics	
Facility Type	
Academic/Research Programs	Ref.
Community Cancer Programs	1.04 (0.94-1.16)
Comprehensive Community Cancer Programs	1.02 (0.96-1.08)
Facility Location	
West South Central	Ref.
East North Central	1.05 (0.94-1.18)
East South Central	**1.16 (1.01-1.32)**
Middle Atlantic	1.01 (0.90-1.14)
Mountain	1.12 (0.96-1.32)
New England	0.92 (0.80-1.07)
Pacific	0.93 (0.82-1.06)
South Atlantic	1.02 (0.91-1.14)
West North Central	1.01 (0.88-1.16)
Treatment Facility Case-Volume	
≥74 cases per year	Ref.
42 - 73 cases per year	0.98 (0.91-1.06)
20 - 41 cases per year	1.05 (0.97-1.14)
1 - 19 cases per year	**1.13 (1.04-1.22)**

[a] Measure estimated by matching the zip code of the patient recorded at the time of diagnosis against files derived from year 2010 U.S. Census data. Variables categorized as quartiles based on equally proportioned variable ranges among all U.S. zip codes.

[b] Model adjusted for all covariates, plus race/ethnicity*stage at diagnosis interaction term added to test effect modification. Race/ethnicity*stage at diagnosis interaction term was not significant at the level of $P<0.5$, however stratified results are shown for comparison for the racial/ethnic disparity within each level of stage at diagnosis.

Lastly, higher risk of death was observed in women who were treated in facilities located in the east north central (HR_{adj}=1.15; 95%CI 1.01- 1.30) and mountain regions (HR_{adj}=1.20; 95%CI 1.01- 1.44) as compared to the west south central. (TABLE XVII)

No racial/ethnic differences were found in women diagnosed with CCC. In the NCDB, between 2003 and 2007, there were no NHAIAN women and only one single NHPI woman diagnosed with CCC; as such HR between these racial/ethnic groups and NHW women were not computed. (TABLE XVIII)

The risk of death was higher in women who were seventy and older (HR_{adj}=2.05; 95%CI 1.08-3.92) as compared to fifty and younger, in those covered by Medicare (HR_{adj}=1.48; 95%CI 1.10-1.99) and Medicaid (HR_{adj}=1.77; 95%CI 1.13-2.75) as compared to those with private health insurance. In addition a higher risk of death was found in women diagnosed with later-stage (HR_{adj}=4.68; 95%CI 3.70-5.93) as compared with earlier-stage tumors; and those who did not have surgery (HR_{adj}=5.67; 95%CI 4.09-7.87), any radiation therapy (HR_{adj}=1.45; 95%CI 1.18-1.79) and any multi-agent chemotherapy (HR_{adj}=1.33; 95%CI 1.04-1.69) as compared to those who did. Lastly, higher risk of death was observed in women who were treated in facilities located in the west north central (HR_{adj}=1.86; 95%CI 1.08- 3.19) as compared to the west south central regions. (TABLE XVIII)

NHB women diagnosed with SC had 18% (HR_{adj}=1.18; 95%CI 1.04-1.33) higher risk of deaths than NHW. The interaction term between race/ethnicity and stage at diagnosis was not significant; however stage-stratified results were presented. In women diagnosed with early-stage SC, the differences are more pronounced than in those diagnosed with late stage. (TABLE XIX)

TABLE XVII: RESULTS FOR THE EFFECT OF RACE/ETHNICITY ON OVERALL FIVE-YEAR SURVIVAL FOR WOMEN DIAGNOSED WITH HIGH-GRADE CARCINOMAS, OVERALL, AND STRATIFIED BY STAGE AT DIAGNOSIS, NATIONAL CANCER DATABASE, 2003-2012, n=11,967

	HR(95%CI)	**HR(95%CI)**	**HR(95%CI)**
	Type 1: High-grade Carcinoma n= 11,967 deaths= 7,404	**Stratified Model[b]: Among Late-Stage n= 4,549 deaths= 2,807**	**Stratified Model: Among Early Stage n= 7,418 deaths= 1,756**
Socio-Demographic Characteristics			
Race/Ethnicity			
Non-Hispanic White	Ref.	Ref.	Ref.
Hispanic	**0.85 (0.73-0.98)**	**0.84 (0.70-0.99)**	0.89 (0.68-1.15)
Non-Hispanic Black	**1.16 (1.06-1.27)**	1.12 (0.99-1.25)	**1.23 (1.06-1.43)**
Non-Hispanic Asian	0.79 (0.63-1.00)	0.88 (0.67-1.16)	**0.64 (0.42-0.98)**
Non-Hispanic American Indian, Alaskan Native	0.83 (0.45-1.56)	0.62 (0.26-1.51)	1.32 (0.54-3.20)
Non-Hispanic Pacific Islander/ Hawaiian	1.05 (0.52-2.12)	1.35 (0.64-2.86)	0.71 (0.10-5.06)
Diagnosis Age			
<50	Ref.		
51-59	**1.22 (1.06-1.40)**		
60-69	**1.56 (1.37-1.79)**		
70+	**2.30 (2.00-2.66)**		
Diagnosis Period			
2007	Ref.		
2006	0.99 (0.90-1.08)		
2005	1.09 (1.00-1.19)		
2004	1.06 (0.97-1.17)		
2003	**1.21 (1.11-1.33)**		
Zip-Code Level Income[a]			
$63.000+	Ref.		
$48.000-62.999	1.04 (0.95-1.14)		
$38.000-$47.999	0.92 (0.83-1.02)		
<$38.000	1.00 (0.89-1.12)		
Zip-Code Level Education[a]			
<7.0 without a high-school diploma	Ref.		
7.0-12.9% without a high-school diploma	1.08 (0.98-1.18)		
13.0-20.0% without a high-school diploma	**1.19 (1.07-1.33)**		
≥21.0% without a high-school diploma	**1.24 (1.09-1.40)**		
Health Insurance			
Private Insurance	Ref.		
Medicare	**1.25 (1.15-1.36)**		
Medicaid	**1.40 (1.22-1.60)**		
Not Insured	**1.40 (1.20-1.63)**		
Tumor Characteristics			
Diagnosis Stage			
Early (Stages I, II)	Ref.		
Late (Stages III, IV)	**3.90 (3.65-4.17)**		
Grade			
Poorly differentiated	Ref.		
Undifferentiated	**1.16 (1.04-1.30)**		
Comorbidities			
None	Ref.		
1	**1.21 (1.12-1.30)**		
2 or more	**1.58 (1.40-1.77)**		
Receipt of Treatment			
Receipt of Surgery			
Yes	Ref.		
No	**4.36 (4.00-4.77)**		
Receipt of Radiation Therapy			
Yes	Ref.		
No	**1.44 (1.36-1.53)**		
Receipt of Chemotherapy			
Yes	Ref.		
No	**1.11 (1.03-1.19)**		

TABLE XVII (CONTINUED): RESULTS FOR THE EFFECT OF RACE/ETHNICITY ON OVERALL FIVE-YEAR SURVIVAL FOR WOMEN DIAGNOSED WITH HIGH-GRADE CARCINOMAS, OVERALL, AND STRATIFIED BY STAGE AT DIAGNOSIS, NATIONAL CANCER DATABASE, 2003-2012, n=11,967

	HR(95%CI)
	Type 1: High-grade Carcinoma n= 11,967 deaths= 7,404
Treatment Facility Characteristics	
Facility Type	
Academic/Research Programs	Ref.
Community Cancer Programs	1.04 (0.91-1.20)
Comprehensive Community Cancer Programs	1.05 (0.98-1.12)
Facility Location	
West South Central	Ref.
East North Central	**1.15 (1.01-1.30)**
East South Central	1.02 (0.87-1.20)
Middle Atlantic	1.13 (0.99-1.29)
Mountain	**1.20 (1.01-1.44)**
New England	0.99 (0.84-1.16)
Pacific	0.95 (0.83-1.09)
South Atlantic	1.08 (0.95-1.22)
West North Central	1.11 (0.94-1.29)
Treatment Facility Case-Volume	
≥74 cases per year	Ref.
42 - 73 cases per year	0.98 (0.90-1.07)
20 - 41 cases per year	0.99 (0.91-1.09)
1 - 19 cases per year	1.08 (0.98-1.19)

[a] Measure estimated by matching the zip code of the patient recorded at the time of diagnosis against files derived from year 2010 U.S. Census data. Variables categorized as quartiles based on equally proportioned variable ranges among all U.S. zip codes.

[b] Model adjusted for all covariates, plus race/ethnicity*stage at diagnosis interaction term added to test effect modification. Race/ethnicity*stage at diagnosis interaction term was not significant at the level of $P<0.5$, however stratified results are shown for comparison for the racial/ethnic disparity within each level of stage at diagnosis.

A higher risk of death was associated with older age and an increased number of comorbidities. In addition, the risk of death was higher in women diagnosed in the year 2003 (HR_{adj}=1.17; 95%CI 1.01-1.36) as compared to 2007, in women diagnosed with later-stage (HR_{adj}=4.53; 95%CI 4.03-5.10) as compared with earlier-stage disease; those diagnosed with poorly and undifferentiated (HR_{adj}=1.24; 95%CI 1.04-1.48) as compared to well and moderately differentiated tumors and those who did not have surgery (HR_{adj}=3.25; 95%CI 2.73-3.87), radiation therapy (HR_{adj}=1.58; 95%CI 1.42-1.75) and multi-agent chemotherapy (HR_{adj}=1.46; 95%CI 1.32-1.62) as compared to those who did. Lastly, higher risk of death was observed in women treated in facilities that saw 1-19 cases (HR_{adj}=1.17; 95%CI 1.00-1.37) as compared to those that saw 74 and more cases of EC per year. (TABLE XIX)

2. Mediation of Racial/Ethnic Differences in 5-Year Survival

In the initial assessment of hypothesized mediators, we found that for the disparity between NHB and NHW women diagnosed with LGEC, receipt of surgery, zip-code level income and the SE domain altered the hazard ratio. No mediators were detected in the disparity between NHA and NHW women diagnosed with LGEC. TABLE XX shows that in the 5-year survival disparity between NHB and NHW women diagnosed with LGEC, receipt of surgery, the SE domain and zip-code level income respectively accounted for 22.7% (95%CI 11.2 – 40.6), 26.4% (95%CI 16.9 – 38.8) and 10.4% (95%CI 5.9 – 17.4) of the disparity. When all identified mediators were assessed together they accounted for 44.1% (95%CI 29.8 – 59.4) of the total disparity.

Similarly, in the 5-year survival disparity between NHB and NHW diagnosed with HGEC, only receipt of surgery and the SE domain altered the hazard ratios by a factor of 0.1 or more. No mediators were detected in the disparity between Hispanic and NHW women diagnosed with HGEC.

TABLE XVIII: RESULTS FOR THE EFFECT OF RACE/ETHNICITY ON OVERALL FIVE-YEAR SURVIVAL FOR WOMEN DIAGNOSED WITH CLEAR CELL CARCINOMAS, OVERALL, AND STRATIFIED BY STAGE AT DIAGNOSIS, NATIONAL CANCER DATABASE, 2003-2012, n=877

	HR(95%CI)	HR(95%CI)	HR(95%CI)
	Type 1: Clear Cell Carcinoma n=877 deaths= 401	**Stratified Model[b]: Among Late-Stage n=367 deaths= 262**	**Stratified Model: Among Early Stage n=510 deaths= 139**
Socio-Demographic Characteristics			
Race/Ethnicity			
Non-Hispanic White	Ref.	Ref.	Ref.
Hispanic	0.56 (0.30-1.06)	0.54 (0.24-1.25)	0.47 (0.16-1.37)
Non-Hispanic Black	1.15 (0.87-1.52)	1.07 (0.75-1.52)	1.14 (0.69-1.89)
Non-Hispanic Asian	0.71 (0.30-1.68)	0.90 (0.28-2.91)	0.41 (0.09-1.89)
Non-Hispanic American Indian, Alaskan Native	NA	NA	NA
Non-Hispanic Pacific Islander/ Hawaiian	NA	NA	NA
Diagnosis Age			
<50	Ref.		
51-59	1.18 (0.61-2.30)		
60-69	1.40 (0.74-2.64)		
70+	**2.05 (1.08-3.92)**		
Diagnosis Period			
2007	Ref.		
2006	1.29 (0.93-1.79)		
2005	1.06 (0.75-1.48)		
2004	1.12 (0.82-1.55)		
2003	1.17 (0.84-1.63)		
Zip-Code Level Income[a]			
$63.000+	Ref.		
$48.000-62.999	1.11 (0.78-1.56)		
$38.000-$47.999	1.23 (0.84-1.81)		
<$38.000	1.01 (0.65-1.56)		
Zip-Code Level Education[a]			
<7.0 without a high-school diploma	Ref.		
7.0-12.9% without a high-school diploma	0.76 (0.54-1.07)		
13.0-20.0% without a high-school diploma	0.89 (0.60-1.33)		
≥21.0% without a high-school diploma	1.08 (0.70-1.68)		
Health Insurance			
Private Insurance	Ref.		
Medicare	**1.48 (1.10-1.99)**		
Medicaid	**1.77 (1.13-2.75)**		
Not Insured	1.47 (0.73-2.95)		
Tumor Characteristics			
Diagnosis Stage			
Early (Stages I, II)	Ref.		
Late (Stages III, IV)	**4.68 (3.70-5.93)**		
Grade			
Low (well, moderately differentiated)	Ref.		
High (poorly differentiated, undifferentiated)	1.17 (0.82-1.66)		
Comorbidities			
None	Ref.		
1	0.98 (0.76-1.26)		
2 or more	**2.47 (1.64-3.73)**		
Receipt of Treatment			
Receipt of Surgery			
Yes	Ref.		
No	**5.67 (4.09-7.87)**		
Receipt of Radiation Therapy			
Yes	Ref.		
No	**1.45 (1.18-1.79)**		
Receipt of Chemotherapy			
Yes	Ref.		
No	**1.33 (1.04-1.69)**		

TABLE XVIII (CONTINUED): RESULTS FOR THE EFFECT OF RACE/ETHNICITY ON OVERALL FIVE-YEAR SURVIVAL FOR WOMEN DIAGNOSED WITH CLEAR CELL CARCINOMAS, OVERALL, AND STRATIFIED BY STAGE AT DIAGNOSIS, NATIONAL CANCER DATABASE, 2003-2012, n=877

	HR(95%CI)
	Type 1: Clear Cell Carcinoma n=877 deaths= 401
Treatment Facility Characteristics	
Facility Type	
Academic/Research Programs	Ref.
Community Cancer Programs	1.03 (0.63-1.70)
Comprehensive Community Cancer Programs	1.06 (0.83-1.34)
Facility Location	
West South Central	Ref.
East North Central	1.09 (0.70-1.71)
East South Central	1.26 (0.72-2.21)
Middle Atlantic	1.11 (0.70-1.76)
Mountain	1.14 (0.58-2.23)
New England	1.53 (0.90-2.60)
Pacific	1.10 (0.67-1.81)
South Atlantic	1.07 (0.70-1.65)
West North Central	**1.86 (1.08-3.19)**
Treatment Facility Case-Volume	
≥74 cases per year	Ref.
42 - 73 cases per year	0.98 (0.73-1.32)
20 - 41 cases per year	0.96 (0.71-1.30)
1 - 19 cases per year	1.18 (0.86-1.63)

[a] Measure estimated by matching the zip code of the patient recorded at the time of diagnosis against files derived from year 2010 U.S. Census data. Variables categorized as quartiles based on equally proportioned variable ranges among all U.S. zip codes.

[b] Model adjusted for all covariates, plus race/ethnicity*stage at diagnosis interaction term added to test effect modification. Race/ethnicity*stage at diagnosis interaction term was not significant at the level of $P<0.5$, however stratified results are shown for comparison for the racial/ethnic disparity within each level of stage at diagnosis.

TABLE XIX: RESULTS FOR THE EFFECT OF RACE/ETHNICITY ON OVERALL FIVE-YEAR SURVIVAL FOR WOMEN DIAGNOSED WITH SEROUS CARCINOMAS, OVERALL, AND STRATIFIED BY STAGE AT DIAGNOSIS, NATIONAL CANCER DATABASE, 2003-2012, n=3,279

	HR(95%CI)	HR(95%CI)	HR(95%CI)
	Type 1: Serous Carcinoma n=3,279 deaths= 1,826	**Stratified Model[b]: Among Late-Stage n=1,882 deaths= 1,402**	**Stratified Model: Among Early Stage n=1,397 deaths= 424**
Socio-Demographic Characteristics			
Race/Ethnicity			
Non-Hispanic White	Ref.	Ref.	Ref.
Hispanic	0.88 (0.68-1.13)	0.94 (0.71-1.25)	0.72 (0.42-1.24)
Non-Hispanic Black	**1.18 (1.04-1.33)**	**1.16 (1.01-1.34)**	**1.31 (1.02-1.68)**
Non-Hispanic Asian	0.97 (0.71-1.32)	1.03 (0.73-1.44)	0.59 (0.24-1.46)
Non-Hispanic American Indian, Alaskan Native	0.31 (0.04-2.22)	0.29 (0.04-2.11)	NA
Non-Hispanic Pacific Islander/ Hawaiian	1.25 (0.56-2.83)	1.83 (0.80-4.17)	NA
Diagnosis Age			
<50	Ref.		
51-59	1.49 (0.99-2.25)		
60-69	**1.69 (1.13-2.52)**		
70+	**2.16 (1.44-3.25)**		
Diagnosis Period			
2007	Ref.		
2006	1.05 (0.91-1.22)		
2005	1.07 (0.92-1.23)		
2004	1.08 (0.93-1.26)		
2003	**1.17 (1.01-1.36)**		
Zip-Code Level Income[a]			
$63.000+	Ref.		
$48.000-62.999	1.03 (0.89-1.19)		
$38.000-$47.999	0.94 (0.80-1.11)		
<$38.000	0.97 (0.81-1.18)		
Zip-Code Level Education[a]			
<7.0 without a high-school diploma	Ref.		
7.0-12.9% without a high-school diploma	0.98 (0.85-1.13)		
13.0-20.0% without a high-school diploma	1.02 (0.86-1.21)		
≥21.0% without a high-school diploma	0.93 (0.76-1.13)		
Health Insurance			
Private Insurance	Ref.		
Medicare	1.10 (0.97-1.25)		
Medicaid	1.20 (0.94-1.52)		
Not Insured	1.07 (0.78-1.46)		
Tumor Characteristics			
Diagnosis Stage			
Early (Stages I, II)	Ref.		
Late (Stages III, IV)	**4.53 (4.03-5.10)**		
Grade			
Low (well, moderately differentiated)	Ref.		
High (poorly differentiated, undifferentiated)	**1.24 (1.04-1.48)**		
Comorbidities			
None	Ref.		
1	**1.25 (1.11-1.40)**		
2 or more	**1.35 (1.10-1.65)**		
Receipt of Treatment			
Receipt of Surgery			
Yes	Ref.		
No	**3.25 (2.73-3.87)**		
Receipt of Radiation Therapy			
Yes	Ref.		
No	**1.58 (1.42-1.75)**		
Receipt of Chemotherapy			
Yes	Ref.		
No	**1.46 (1.32-1.62)**		

TABLE XIX (CONTINUED): RESULTS FOR THE EFFECT OF RACE/ETHNICITY ON OVERALL FIVE-YEAR SURVIVAL FOR WOMEN DIAGNOSED WITH SEROUS CARCINOMAS, OVERALL, AND STRATIFIED BY STAGE AT DIAGNOSIS, NATIONAL CANCER DATABASE, 2003-2012, n=3,279

	HR(95%CI)
	Type 1: Serous Carcinoma n=3,279 deaths= 1,826
Treatment Facility Characteristics	
Facility Type	
Academic/Research Programs	Ref.
Community Cancer Programs	0.90 (0.71-1.15)
Comprehensive Community Cancer Programs	1.03 (0.92-1.14)
Facility Location	
West South Central	Ref.
East North Central	0.89 (0.72-1.10)
East South Central	1.06 (0.82-1.37)
Middle Atlantic	1.01 (0.82-1.25)
Mountain	1.08 (0.80-1.45)
New England	0.80 (0.62-1.03)
Pacific	0.79 (0.63-1.00)
South Atlantic	1.09 (0.89-1.33)
West North Central	1.01 (0.79-1.30)
Treatment Facility Case-Volume	
≥74 cases per year	Ref.
42 - 73 cases per year	1.12 (0.99-1.27)
20 - 41 cases per year	1.06 (0.93-1.21)
1 - 19 cases per year	**1.17 (1.00-1.37)**

[a] Measure estimated by matching the zip code of the patient recorded at the time of diagnosis against files derived from year 2010 U.S. Census data. Variables categorized as quartiles based on equally proportioned variable ranges among all U.S. zip codes.

[b] Model adjusted for all covariates, plus race/ethnicity*stage at diagnosis interaction term added to test effect modification. Race/ethnicity*stage at diagnosis interaction term was not significant at the level of $P<0.5$, however stratified results are shown for comparison for the racial/ethnic disparity within each level of stage at diagnosis.

In the overall 5-year survival disparity between NHB and NHW, receipt of surgery and the SE domain respectively accounted for 40.9% (95%CI 21.6 - 63.5) and 33.1% (95%CI 16.4 – 55.5) of the disparity. (TABLE XX) When assessed together, receipt of surgery and the SES domain accounted for 59.1% (95%CI 37.1 – 78.0) of the total disparity.

No mediators were detected in the 5-year survival disparity between NHB and NHW women diagnosed with SC.

TABLE XX: ESTIMATES OF THE PROPORTION MEDIATED FOR THE OVERALL 5-YEAR SURVIVAL DISPARITY BETWEEN NHB AND NHW WOMEN DIAGNOSED WITH LOW-GRADE AND HIGH-GRADE CARCINOMAS, NCDB, 2003-2012, n=76,223

Domains and Hypothesized Mediators[a]	**Proportion mediated % (95%CI)**	***P*-value**
Low-Grade Carcinomas		
Receipt of Surgery	22.7 (11.2 - 40.6)	<0.05
Socio-Economic domain[b]	26.4 (16.9 - 38.8)	<0.05
Zip-code Level Income	10.4 (5.9 - 17.4)	<0.05
All mediators[c]	44.1 (29.8 – 59.4)	<0.05
High-Grade Carcinomas		
Receipt of Surgery	40.9 (21.6 – 63.5)	<0.05
Socio-Economic domain[b]	33.1 (16.4 – 55.5)	<0.05
All mediators[c]	59.1 (37.1 – 78.0)	<0.05

[a] Each mediator and domain of mediators were separately assessed in fully-adjusted models. The treatment domain, zip-code level education, health insurance, diagnosis stage, facility type, radiation therapy and chemotherapy did not meet the criteria of mediation analyses.
[b] The socio-economic domain includes zip-code level income and zip-code level education.
[c] All mediators include receipt of surgery, zip-code level income and zip-code level education.

D. Discussion

Racial differences in EC survival between NHB and NHW women are well documented (5, 26, 35, 67, 81). The current study confirms and extends the findings from previous

investigations by presenting the results of subtype-specific overall 5-year survival differences between NHB, Hispanic, NHA, NHPI, NHAIAN and NHW women from the NCDB, which is the largest and most comprehensive dataset of EC cases in the U.S. The National Academy of Sciences strongly recommends performing subtype-specific analyses which would allow for scientific advancement and help reduce cancer morbidity and mortality (18). Endometrial cancer tumor subtypes differ from each other based on their biological characteristics and the clinical course of the disease; as such they require different treatment regimens and have different prognosis (11).

This study demonstrates that NHB women diagnosed with LGEC, HGEC and SC, between 2003 and 2007, had a lower overall 5-year survival than NHW, after adjusting for potential confounders. However, this study also shows that NHA diagnosed with LGEC and Hispanic diagnosed with HGEC had a higher overall 5-year survival than NHW. The results from our mediation analyses suggested that (1) receipt of surgery and (2) the socio-economic domain, which includes zip-code level income and education, contribute to NHB-NHW differences in overall 5-year survival in women diagnosed with LGEC and HGEC. However, NHB-NHW survival differences persist after adjusting for these factors. While NHB women were the most likely to be diagnosed with Type 2 tumor subtypes (aim 1), the largest 5-year survival disparity was observed in those diagnosed with LGEC and especially in women diagnosed with late-stage tumors. However, the survival curves for LGEC show a 5-year overall survival of more than 85% for women of any racial/ethnic group. The overall 5-year survival as shown by the KM curves is significantly lower for women diagnosed with any other subtype of EC and is the lowest for those diagnosed with SC: approximately 52% for NHA and 34% for NHB.

Racial/ethnic disparities in 5-year overall survival may be more likely to be detected in women diagnosed with less aggressive tumors, characterized by better survival rated, because their death may be due to factors unrelated with their cancer diagnosis. These factors could

represent various comorbid conditions resulting from lifestyle habits, such as an unhealthy diet, smoking and lack of physical activity, related to race/ethnicity. In addition, less aggressive tumors, characterized by a lower grade, are likely to recur after a period of time longer than five years after diagnosis. Therefore the 5-year survival may predominantly capture deaths due to comorbidities in women with less aggressive tumors.

The results of our study confirm those of previous investigations that found NHB women to have a lower EC survival than NHW (5, 26, 35, 67, 81). However, none of the previous studies presented survival differences by histologic subtype. In addition, all of the previous studies analyzed historic data with Wright et al using the most recent cases, including women diagnosed through 2004 (67). In our analysis, we included women diagnosed between 2003 and 2007 with a vital status reported through 2012 and found that for overall EC, NHB women had 18% higher risk of dying than NHW. Using SEER data, Wright et al found that Black women were 60% more likely to die from EC than White women. The reason for the difference in the magnitude of the hazard ratios between this study and our current analysis may be explained by the fact the Wright et al did not adjust for receipt of surgery, chemotherapy and any of the socio-demographic variables. Differences in findings may also be due to the time and place of diagnosis. In the analysis of NCDB data, Fedewa et al found that NHB women diagnosed with overall EC between 2000 and 2001 were 28% more likely of dying than NHW (5).

Consistent with the only existing study, our results demonstrate that NHA women have a higher overall survival than NHW and that there are no survival differences between NHAIAN and NHW (3). Mahdi et al. found that NHA diagnosed with EC had a higher overall survival rate and marginally higher cancer-specific survival rate than NHW. In this study, the marginal effect of race/ethnicity on survival might be due to the fact that the authors failed to present subtype-specific differences. In our study, higher overall 5-year survival in NHA women was only found in those diagnosed with LGEC.

The results of this study partially confirm the results from previous research on Hispanic-NHW 5-year survival differences. Two previous studies found that that for overall EC, Hispanic women were more likely to die than NHW (64, 65). Differences in the finding may be due to differences in time and place of diagnosis. Both studies used SEER data that only represented 26% of the entire population of the U.S. and did not collect information about receipt of chemotherapy and comorbidities or most importantly, health insurance (21). Health insurance was found to be an important prognostic factor for overall 4-year survival. Patients covered by a health insurance plan other than a private plan have an increased risk of death (5). In the same study, using the NCDB, Fedewa et al. demonstrated that there were no 4-year overall survival differences between Hispanic and NHW women diagnosed with EC (5). Our study showed a marginally lower survival rate for Hispanic women diagnosed with HGEC. No Hispanic-NHW differences were detected in women diagnosed with other EC subtypes.

Some potential explanations for the NHB-NHW survival differences include delayed receipt of surgery (112) and NHB women's resistance to chemotherapy treatments (30). The greatest NHB-NHW disparity was found for the least aggressive EC tumor subtype almost exclusively diagnosed at an early stage. For early-stage tumors the receipt of surgery is believed to be curative (134) and therefore, the fact that NHB women are more likely to die of LGEC likely represents a failure of the system. A recent study using the 2003-2011 NCDB data showed that NHB women were 30% more likely to wait longer than 6 weeks for surgery when compared to NHW women. In addition, the authors showed that after adjusting for potential confounders, a wait time for surgery of more than 6 weeks was associated with an increased hazard of death (112). Delays in treatment have been shown to be associated with worse survival for other cancer sites (100). NHB women are more likely than NHW to be poor, less educated, live in disadvantaged areas and be underinsured (88, 89). Survival differences between NHB and NHW women may be also due to biological differences. NHB women are

more likely than NHW to possess an up regulated HER/neu oncogene which was found to be associated with chemotherapy resistance (30). In addition, the HER/neu oncogene expression was found to be associated with more aggressive EC tumors and earlier death. These biological differences may also explain why we did not detect any differences in the stage-specific survival analyses. Cultural practices could account for the higher survival rate in NHA than NHW. When compared to NHW, NHA are more likely to have a lower body mass index, more likely to eat diets that include vegetables, soy and less fat (122, 135). Notably, their diet might have an impact on estrogen-dependent tumors such as LGEC. Research showed that diets rich in soy and fiber were associated with a reduced incidence of EC (134). It could be hypothesized that the anti-estrogenic effect of soy could have an impact on survival of women diagnosed with LGEC (3). In addition, there is evidence that NHA women are less likely to be exposed to endogenous and exogenous estrogen during their lifespan. As compared to NHW, NHA women are more likely to be younger at childbirth, older at menarche, have more children, breastfeed, are less likely to use birth control pills and be prescribed hormonal replacement therapy after menopause (136).

The results from the mediation analyses demonstrate that the NHB-NHW differences in 5-year survival in women diagnosed with LGEC and HGEC were partially explained by the SE domain and receipt of surgery. NHB women are more likely to live in areas of lower SES, which could explain the mediating effect of the SE domain. Notably, 43% of NHB and 13% of NHW lived in areas where people reported a median family income level of $38,000 or less. Moreover, 33% or NHB and only 12% of NHW lived in areas where 21% or more of the people did not finish high school. Neighborhoods with lower SES have been characterized by reduced access to care (96, 129, 130). In addition, women of lower SES may be less likely to possess health insurance or more likely to be underinsured, both of which could impact their access to high-quality hospitals and the likelihood of receipt of a timely and guideline-adherent treatment

(88, 89). Previous research showed that people residing in a disadvantaged area were less likely to have a regular healthcare provider, obtain preventive services and were more likely to have unmet medical needs, after accounting for individual-level SES characteristics (96). There is evidence that women with less education were unlikely to be familiar with the healthcare services available in their community and to comply with complex courses of treatment (131).

The findings from the current study also show that receipt of surgery mediated respectively 22.7% and 40.9% of the 5-year survival disparity between NHB-NHW diagnosed with LGEC and HGEC. These results could be potentially explained by the fact that NHB patients, or their families, were more likely to refuse recommended surgery. (TABLE XXII, APPENDIX B) The reasoning motivating the refusal is not entirely understood; however research shows that NHB women are more likely to choose less aggressive, less invasive and more orthodox treatment methods than NHW (123, 124). Moreover, NHB are more likely to consider their disease to be a part of their destiny and perceive death as a natural event coming after a cancer diagnosis (123). Lastly, research shows that black women are more likely than NHW to mistrust the health care system and have misconceptions about cancer acquisition and spread (125, 126). Previous studies have linked poor patient-physician relationships to problems with interpersonal communication, resulting from mixed-race relationships (125, 127). Our results show the importance of first course treatment. Women diagnosed with any EC subtypes, who did not have surgery, were over 3 times more likely to die when compared to those who had surgery. These results show that receiving surgical treatment is an extremely important factor in EC survival.

E. Limitations and Strengths

The results of this study should be interpreted in the light of several limitations that primarily pertain to the variables available for analysis. The NCDB does not include information

about patients' cause of death and therefore EC specific mortalities were not computed (109). Women diagnosed with less aggressive tumors may be dying of other conditions unrelated to their EC diagnosis; as such this limitation is more important for women diagnosed with LGEC than those diagnosed with clear cell and serous carcinomas. However, using the NCDB, Fedewa et al. showed that the results of all cause overall EC survival approached those of EC relative survival and differed by only 7%-8% by race/ethnicity. When compared to the relative survival, all cause-survival rates were 2%-4% lower in patients with Medicaid, private insurance, Medicare (<65) and uninsured and 14% lower for patients ≥65 covered by Medicare (5). Income and education are only available at the zip-code level. While zip-code level measures were shown to be important predictors of access to care and subsequently play a role in the receipt of treatment and survival, individual-level measures were also shown to be associated with a delay in treatment, as less education can be associated with a lack of knowledge about EC symptoms (4). We acknowledge the presence of some residual confounding due to the absence of these variables. In addition, the lack of information about patients' exact comorbidities prevents us from understanding the role of individual disease in the detected racial differences. Lastly, the NCDB does not include any information about the completed number of chemotherapy cycles. The availability of this information could help explain some racial/ethnic differences in survival.

Despite these limitations, this study has several strengths. First, it is the only study to assess whether racial/ethnic differences in overall five-year EC survival exist after adjusting for potential confounders and to explore factors mediating these differences. Second, this study is the first to assess racial differences between five minority groups and NHW. Third, as opposed to analyzing EC as a homogenous disease, or solely as Type 1 and Type 2, this study presents racial/ethnic differences in 5-year survival by four histological subtypes. Fourth, our study is the first study to explore factors mediating racial/ethnic differences in 5-Year survival. Lastly, an

advantage of the NCDB over the commonly used SEER dataset is the availability of information about patients' health insurance status, chemotherapy treatment and underlying comorbidities.

F. Conclusion

In conclusion, this study generally found that considering EC as a homogenous disease distorts the association between race/ethnicity and 5-year overall survival, suggesting caution when evaluating estimates for overall EC in the literature. Within the NCDB, NHB women diagnosed with any subtype of EC have a higher risk of death than NHW. The disparity was the most significant in women diagnosed with LGEC, which is the least aggressive type of EC. Moreover, this study also shows that NHA women diagnosed with LGEC and Hispanic women diagnosed with HGEC, are less likely to die than NHW women. Additionally, in women diagnosed with any EC subtype, those who did not have surgery were significantly more likely to die than those who did. Lastly, the SE domain and receipt of surgery were found to mediate a part of the differences in the overall 5-year survival rates for LGEC and HGEC between NHB and NHW women.

VI. DISCUSSION

This dissertation work was inspired by the recent increase in the incidence of EC (14) and the future impact of this increase on the growing number of immigrating minority populations and changing demographics of the U.S. (10). The purpose was to assess whether racial/ethnic subtype-specific differences in stage at diagnosis, treatment modalities and 5-year overall survival existed and, if found, to explore factors mediating these differences. We were able to answer these questions by performing cross sectional analyses of diagnosis stage and treatment modalities and a retrospective cohort survival study using data from the NCDB, which is one of the largest and most comprehensive dataset of EC in the U.S. and Puerto Rico.

A. Summary and Discussion of Aims

The purpose of the first aim was to assess racial/ethnic differences in tumor, socio-demographic and treatment facility characteristics for Type 1 (LGEC) and Type 2 EC (HGEC, CCC and SC). In addition, the goal of this aim was to determine whether subtype-specific racial/ethnic differences in stage at diagnosis between minority women and NHW existed. The results of our investigation showed that the burden of EC is not equally distributed across racial/ethnic groups and that compared to NHW women, NHB women are significantly more likely to be diagnosed with aggressive EC subtypes. In addition, the results of our study showed that NHPI had higher odds of diagnosis with LGEC and NHB with HGEC than NHW women. Lastly, our study showed that when compared to NHW, NHA women had higher odds of diagnosis with LGEC and HGEC. Past research that analyzed EC as a homogenous disease demonstrated that, in unadjusted models, NHB women were more likely than NHW to be diagnosed with EC (2, 85).

The results from the first aim added significantly to the literature because we demonstrated that because subtype-specific racial/ethnic differences exist, analyzing EC as a

homogenous disease does not allow for a complete depiction of the underlying relationship between race/ethnicity and stage at diagnosis. Endometrial cancer tumor subtypes differ from each other based on their biological characteristics and the clinical course of the disease; as such they should be analyzed separately (11, 18). In addition, our study demonstrated that results from unadjusted models differ from adjusted models and suggest caution when evaluating unadjusted estimates in the literature. The racial/ethnic disparities in stage at diagnosis detected in our study are likely due to a combination of genetic predispositions and differences in lifestyle and socio-cultural risk factors. It is possible that EC risk factors drive these differences as their prevalence is likely to differ among racial/ethnic groups.

The main purpose of our second aim was to assess whether subtype-specific racial/ethnic differences existed in receipt of EC treatment, defined as surgery, radiation therapy and chemotherapy. We found racial/ethnic differences in receipt of surgery, after accounting for important covariates. Notably, NHB women were the only minority group that had higher odds of not receiving surgery than NHW, across all EC subtypes. Our results also show that Hispanic and NHAIAN women diagnosed with LGEC had significantly higher odds of not receiving surgery than NHW. Finally, NHPI had five times higher odds of not receiving surgery for SC than NHW. These disparities could be due to a lack of receipt of guideline-adherent treatment, prevalence of comorbidities preventing surgery or the refusal of treatment by the patient or patient's family members. Similarly, previous research showed that NHB and Hispanic and Asian Pacific Islanders women were less likely to receive surgery than NHW (5, 20, 65, 77, 82). However, all of the previous studies on racial/ethnic differences in receipt of surgery presented results from unadjusted models where EC was analyzed as a homogenous disease. Our study demonstrated variation in racial/ethnic differences in treatment across EC subtypes and that results from unadjusted models differ from adjusted models.

In addition, our results show that health insurance modified the relationship between race/ethnicity and receipt of surgery in women diagnosed with LGEC and that those differences were almost exclusively present in patients covered by a private health insurance. These results could suggest that while Medicare and Medicaid provide nearly uniform benefits for their enrollees, the private health insurance category includes plans such as managed care, military care and TRICARE offering policies with significantly different benefits (85). As such, minority patients could be more likely to be covered by less expensive health plans that have higher co-pays and complex system or referrals and authorizations. High co-pays could influence a patient or a patient's family refuse the recommended surgery. In other words, some patients could decide not to be treated because of the fear of potential medical debt (128). In addition, a complex system of referrals could delay the receipt of a recommended treatment and the limitations related to the health insurance provider network could prevent patients from accessing higher-quality hospitals.

Our findings of differences in receipt of surgery in women diagnosed with LGEC have important clinical implications. Low-grade endometrioid carcinomas are the most common subtype of EC and are usually diagnosed at an early stage. Surgery performed on early-stage tumors is believed to be curative (134) and therefore new interventions should be developed with the objectives of insuring universal access to surgery. Further research is also indicated to understand SES and cultural factors that may lead to refusal of surgery in minority women with LGEC.

In regards to radiation therapy and chemotherapy, the results of our study showed that NHAIAN diagnosed with SC had higher odds of not receiving radiation therapy than NHW. Moreover, NHB women diagnosed with CCC had higher odds and NHA diagnosed with LGEC had lower odds of not receiving chemotherapy than NHW. No differences in the receipt of chemotherapy were detected in stage-stratified models. Our findings are inconsistent with

previous studies that found that NHB women were less likely and Hispanic, Asian, API and American Indian/Alaskan Native more likely to receive radiation therapy than NHW (3, 19, 77, 82). However, previous studies did not adjust for potential confounders and analyzed EC as a homogenous disease. Consistent with the literature, in our unadjusted models, NHB women are more likely to receive chemotherapy than NHW (19, 20). However after accounting for potential confounders, only the disparity for NHB women diagnosed with CCC remained significant. These results suggest that there may be substantial confounding in published literature, and that the adjusted and stage-specific analyses from this study will significantly add to the field.

The secondary goal of aim 2 was to assess the relative contribution of hypothesized mediators related to tumor characteristics, socio-economic and treatment facility factors on the detected racial/ethnic differences in receipt of treatment. The results of this mediation analyses demonstrated that the differences in receipt of surgery in women diagnosed with LGEC, HGEC and SC were partially mediated by the SE domain. The SE domain significantly explained a quarter of the disparity between NHB and NHW women diagnosed with LGEC and HGEC. These results could be explained by the fact that, in the NCDB, a greater proportion of NHB women lived in underserved areas. Lower neighborhood levels of education and income have been linked with a reduced access to care (96, 129, 130). A previous study showed that after adjusting for individual-level SE characteristics, people residing in a disadvantaged area were less likely to have a regular healthcare provider, obtain preventive services and were more likely to have unmet medical needs (96). Women with less education were less likely to comply with complex courses of treatment and be familiar with the healthcare services available in their community (131). In addition, previous research has shown that neighborhoods can influence one's health indirectly, by the mean of values placed on health and the social support available (91, 93). Women who lack social support are likely to wait longer before sharing their symptoms

which hinders their likelihood of diagnosis at an early stage and subsequently influences their course of treatment.

In our final aim, we assessed whether subtype-specific racial/ethnic differences in overall five-year EC survival existed and explored whether the relative contribution of hypothesized mediators related to tumor characteristics, socio-economic factors, receipt of treatment and treatment facility factors on the detected differences. The results from our study demonstrated that NHB women diagnosed with LGEC, HGEC and SC had a lower overall 5-year survival than NHW, after adjusting for important covariates. In addition, our study showed that NHA diagnosed with LGEC and Hispanic diagnosed with HGEC had a higher overall 5-year survival than NHW. Lastly, the results from our mediation analyses demonstrated that (1) receipt of surgery and (2) the SE domain contributed to NHB-NHW differences in overall 5-year survival in women diagnosed with LGEC and HGEC.

The results of our study confirmed those from previous investigations that found that NHB women had a lower EC survival than NHW (5, 26, 35, 67, 81). However, none of the previous studies presented survival differences by histologic subtype. In addition, all of the previous investigations analyzed historic data with Wright et al using the most recent, including women diagnosed through 2004 (67). In our analysis, we included women diagnosed between 2003 and 2007 with a vital status reported through 2012. Some potential explanations for the NHB-NHW survival differences include delayed receipt of surgery (112) and resistance of NHB women to chemotherapy treatments (30). The greatest NHB-NHW disparity was found in women diagnosed with LGEC, which is the most common and least aggressive EC tumor subtype (17), and almost exclusively diagnosed at an early stage. For early-stage tumors, the receipt of surgery is believed to be curative (134) and therefore, the fact that NHB women are more likely to die of LGEC likely represent a failure of the system.

Consistent with the only existing study, our results demonstrate that NHA women have a higher overall survival than NHW and that there are no survival differences between NHAIAN and NHW (3). The reason why NHA women have a higher survival rates than NHW could be explained by the fact that during their lifetime, NHA women are less likely to be exposed to endogenous and exogenous estrogen (135), which is associated with a reduced incidence of EC (134). In addition they are more likely to eat anti-estrogenic diets containing ingredients such as soy and fiber (122, 134, 135). It could be hypothesized that, in addition to the incidence, reduced exposure to estrogen has an impact on survival for women diagnosed with LGEC (3).

The results from the mediation analyses demonstrate that the NHB-NHW differences in 5-year survival in women diagnosed with LGEC and HGEC were partially mediated by the SE domain. These findings may be related to the fact that NHB women are more likely to live in areas of lower SES. Women of lower SES are less likely to possess a health insurance or are more likely to be underinsured both of which could impact their access to high-quality hospitals and the likelihood of receipt of a timely and guideline adherent primary treatment (88, 89). Previous research showed that people residing in a disadvantaged area were less likely to have a regular healthcare provider, obtain preventive services and were more likely to have unmet medical needs after accounting for individual-level SES characteristics (96).

Lastly, the findings from the current study also show that receipt of surgery mediated respectively 22.7% and 40.9% of the 5-year survival disparity between NHB-NHW diagnosed with LGEC and HGEC. NHB patients or their families may be more likely to refuse recommended surgery and to choose less aggressive, less invasive and more unorthodox treatment methods than NHW (123, 124). Moreover NHB are more likely to consider their disease to be a part of their destiny and perceive death as a natural event coming after a cancer diagnosis (123).

B. Overarching limitations and strengths of the National Cancer Database

The two main overarching limitations of this study relate to the generalizability of the results and the nature of the data. The NCDB is the largest and most comprehensive dataset of EC cases in the U.S.; however it does not include patients reported by non CoC-approved hospitals, notably, small community hospitals that serve minorities and women from lower socio-economic populations. It is likely that because of their lower SES, these women are more likely to be underinsured or have insurance plans with a complex system of referrals or authorizations, are less likely have a medical care provider and in general may have less knowledge about the symptoms of the disease. All of these factors are associated with later stage at diagnosis and a delay in or lack of appropriate treatment (40, 41, 84, 85). Consequently, the results of this study may underestimate the gap seen between minority women and NHW in real life. Another limitation of the NCDB is the lack of incidence data, which prevented us from estimating the changes in the incidence of EC subtypes over time.

Despite these limitations, several overarching strengths related to the nature of the dataset exist; the most important being its size. The NCDB includes 70% or approximately 230,000 EC cases diagnosed in the U.S. and Puerto Rico between 2003 and 2012. The availability of such a large sample size allowed us to analyze minority populations such as the NHPI and NHAIAN that respectively only represent 0.2% and 1.2% of the entire populations (10). Performing such analyses is nearly impossible for researchers using local registries or single-institution datasets. An additional advantage of such a large national dataset was the possibility of exploring racial/ethnic differences in EC outcomes for the very rare but at the same time very aggressive EC subtypes such as CCC and SC. Previous EC disparity research has primarily analyzed EC as a homogenous disease or in some cases as Type 1 and Type 2 tumors. Type 2 EC represent a very heterogeneous group of tumors and therefore future

research should analyze them as such in order to gain a better understanding of the characteristics of these tumors (17). The results from our study have some important implications as they show that considering EC as a homogenous disease distorts the association between race/ethnicity and EC outcomes, suggesting caution when evaluating unadjusted estimates in the literature. Our analyses follow the recommendations of the National Academy of Sciences that strongly recommends performing subtype-specific analyses in order to advance the science and help reduce cancer morbidity and mortality (18).

C. Public Health Significance and Future Directions

Endometrial cancer impacts the lives of many women and in the near future will impact that of many more (14). There are known racial/ethnic differences in incidence, treatment and survival. Consequently, it is essential to understand factors related to EC diagnosis and treatment, particularly with respect to the changing demographics of the U.S. It is also critical to identify racial/ethnic differences in clinical outcomes and potential factors that contribute to these differences. In the future, the number of minorities living in the U.S. is expected to increase (10), as is the incidence of EC (14). Therefore the additional knowledge gained about EC tumor presentation, receipt of treatment and survival in women from minority populations will provide crucial information for the future planning of interventions to decrease racial/ethnic disparities in EC cancer outcomes.

Potential interventions that could reduce these disparities could consist of efforts that would aim at improving the timeliness of diagnosis by raising the awareness about EC symptoms, increasing the knowledge about the necessity of EC surgery in women who are likely to refuse treatment and helping women of lower SES overcome the barriers to accessing health services in the area in which they live. These interventions could be carried out within the framework of a patient navigation project or with the aid of community/social workers.

This study has provided insight into subtype-specific racial/ethnic differences in EC outcomes between minority population and NHW women. However, additional areas should be investigated in order to obtain a more comprehensive understanding of the detected differences. First, the risk factors associated with LGEC, which is the most common EC subtype, are related to increased exposure to estrogen or decreased exposure to progesterone. Future studies analyzing hormonal factors in the context of racial/ethnic differences could help explain further why differences in LGEC exist. In addition to endogenous hormones, exposure to environmental endocrine disrupters, dietary estrogens and pharmaceuticals are of interest. Second, the risk factors for Type 2 EC subtypes are yet to be determined, as is the adequate adjuvant treatment regimen (46-48). However, there is evidence that Type 2 EC subtypes are characterized by the over expression of human epidermal growth factor receptor 2 (HER-2) oncogene associated with chemotherapy resistance (30). In addition, the over expression of HER-2 gene was found to be more prevalent in NHB as compared to NHW (30). As such, further genetic studies are necessary to determine whether other genetic mutations are related to treatment responses and whether these mutations are differentially expressed by race or ethnic group. Third, our study showed that the receipt of surgery is an important predictor of survival in women diagnosed with any subtype of EC. Moreover, our results showed that minority women are less likely to receive the recommended surgery. It is critical to conduct future studies to understand if access to surgery and/or refusal to undergo surgery underlies this gap in order to develop effective interventions. Lastly, this study used area-level measures as proxies for individual-level characteristics. Future studies should assess whether and how individual-level socio-economic characteristics contribute to the racial/ethnic differences in EC outcomes.

VII. REFERENCES

1. Surveillance Epidemiology and End Results Program (SEER). SEER Stat Fact Sheets: Endometrial Cancer. [Available from: http://seer.cancer.gov/statfacts/html/corp.html.]

2. Long B, Liu FW, Bristow RE. Disparities in uterine cancer epidemiology, treatment, and survival among African Americans in the United States. Gynecologic oncology. 2013;130(3):652-9.

3. Mahdi H, Schlick CJ, Kowk LL, Moslemi-Kebria M, Michener C. Endometrial cancer in Asian and American Indian/Alaskan Native women: tumor characteristics, treatment and outcome compared to non-Hispanic white women. Gynecologic oncology. 2014;132(2):443-9.

4. Madison T, Schottenfeld D, James SA, Schwartz AG, Gruber SB. Endometrial cancer: socioeconomic status and racial/ethnic differences in stage at diagnosis, treatment, and survival. American journal of public health. 2004;94(12):2104-11.

5. Fedewa SA, Lerro C, Chase D, Ward EM. Insurance status and racial differences in uterine cancer survival: a study of patients in the National Cancer Database. Gynecologic oncology. 2011;122(1):63-8.

6. Hill HA, Eley JW, Harlan LC, Greenberg RS, Barrett RJ, 2nd, Chen VW. Racial differences in endometrial cancer survival: the black/white cancer survival study. Obstetrics and gynecology. 1996;88(6):919-26.

7. Cote ML, Ruterbusch JJ, Olson SH, Lu K, Ali-Fehmi R. The Growing Burden of Endometrial Cancer: A Major Racial Disparity Affecting Black Women. Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology. 2015;24(9):1407-15.

8. Cote ML, Alhajj T, Ruterbusch JJ, Bernstein L, Brinton LA, Blot WJ, et al. Risk factors for endometrial cancer in black and white women: a pooled analysis from the Epidemiology of Endometrial Cancer Consortium (E2C2). Cancer causes & control : CCC. 2015;26(2):287-96.

9. Allard JE, Maxwell GL. Race disparities between black and white women in the incidence, treatment, and prognosis of endometrial cancer. Cancer control : journal of the Moffitt Cancer Center. 2009;16(1):53-6.

10. Sandra L. Colby JMO. Projections of the size and composition of the US population: 2014 to 2060. U.S. Department of Commerce, Economics and Statistics Administration, U.S. CENSUS BUREAU, 2015 March 2015.

11. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) Uterine Neoplasms 2016. [Available from: https://www.tri-kobe.org/nccn/guideline/gynecological/english/uterine.pdf.]

12. Hamilton CA, Cheung MK, Osann K, Chen L, Teng NN, Longacre TA, et al. Uterine papillary serous and clear cell carcinomas predict for poorer survival compared to grade 3 endometrioid corpus cancers. British journal of cancer. 2006;94(5):642-6.

13. Winchester DP, Stewart AK, Phillips JL, Ward EE. The national cancer data base: past, present, and future. Annals of surgical oncology. 2010;17(1):4-7.

14. Rahib L, Smith BD, Aizenberg R, Rosenzweig AB, Fleshman JM, Matrisian LM. Projecting cancer incidence and deaths to 2030: the unexpected burden of thyroid, liver, and pancreas cancers in the United States. Cancer research. 2014;74(11):2913-21.

15. Smith BD, Smith GL, Hurria A, Hortobagyi GN, Buchholz TA. Future of cancer incidence in the United States: burdens upon an aging, changing nation. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2009;27(17):2758-65.

16. Bokhman JV. Two pathogenetic types of endometrial carcinoma. Gynecologic oncology. 1983;15(1):10-7.

17. Ryan AJ, Susil B, Jobling TW, Oehler MK. Endometrial cancer. Cell and tissue research. 2005;322(1):53-61.

18. National Academies of Sciences E, and Medicine., 2016. Ovarian cancers: Evolving paradigms in research and care. Washington D, 10.17226/21841. TNAPd.

19. Kost ER, Hall KL, Hines JF, Farley JH, Nycum LR, Rose GS, et al. Asian-Pacific Islander race independently predicts poor outcome in patients with endometrial cancer. Gynecologic oncology. 2003;89(2):218-26.

20. Smotkin D, Nevadunsky NS, Harris K, Einstein MH, Yu Y, Goldberg GL. Histopathologic differences account for racial disparity in uterine cancer survival. Gynecologic oncology. 2012;127(3):616-9.

21. NCI SEER Public-Use Data: . Applications and Limitations in Oncology Research | Cancer Network. [Available from: http://www.cancernetwork.com/oncology-journal/nci-seer-public-use-data-applications-and-limitations-oncology-research.]

22. Surveillance E, and End Results Program ,. Surveillance, Epidemiology, and End Results Program Turning Cancer Data Into Discovery. [Available from: http://seer.cancer.gov/registries/terms.html.]

23. Morgan MA, Behbakht K, Benjamin I, Berlin M, King SA, Rubin SC. Racial differences in survival from gynecologic cancer. Obstetrics and gynecology. 1996;88(6):914-8.

24. Lauchlan SC. Tubal (serous) carcinoma of the endometrium. Archives of pathology & laboratory medicine. 1981;105(11):615-8.

25. Hendrickson M, Ross J, Eifel P, Martinez A, Kempson R. Uterine papillary serous carcinoma: a highly malignant form of endometrial adenocarcinoma. The American journal of surgical pathology. 1982;6(2):93-108.

26. Sherman ME, Devesa SS. Analysis of racial differences in incidence, survival, and mortality for malignant tumors of the uterine corpus. Cancer. 2003;98(1):176-86.

27. Soslow RA. High-grade endometrial carcinomas - strategies for typing. Histopathology. 2013;62(1):89-110.

28. American Cancer Society (ACS). Endometrial cancer risk factors. [Available from: http://www.cancer.org/cancer/endometrialcancer/detailedguide/endometrial-uterine-cancer-risk-factors#top.]

29. Kandoth C, Schultz N, Cherniack AD, Akbani R, Liu Y, Shen H, et al. Integrated genomic characterization of endometrial carcinoma. Nature. 2013;497(7447):67-73.

30. Santin AD, Bellone S, Siegel ER, Palmieri M, Thomas M, Cannon MJ, et al. Racial differences in the overexpression of epidermal growth factor type II receptor (HER2/neu): a major prognostic indicator in uterine serous papillary cancer. American journal of obstetrics and gynecology. 2005;192(3):813-8.

31. Felix AS, Weissfeld JL, Stone RA, Bowser R, Chivukula M, Edwards RP, et al. Factors associated with Type I and Type II endometrial cancer. Cancer causes & control : CCC. 2010;21(11):1851-6.

32. Sheikh MA, Althouse AD, Freese KE, Soisson S, Edwards RP, Welburn S, et al. USA endometrial cancer projections to 2030: should we be concerned? Future oncology (London, England). 2014;10(16):2561-8.

33. Evans T, Sany O, Pearmain P, Ganesan R, Blann A, Sundar S. Differential trends in the rising incidence of endometrial cancer by type: data from a UK population-based registry from 1994 to 2006. British journal of cancer. 2011;104(9):1505-10.

34. Duong LM, Wilson RJ, Ajani UA, Singh SD, Eheman CR. Trends in endometrial cancer incidence rates in the United States, 1999-2006. Journal of women's health. 2011;20(8):1157-63.

35. Ueda SM, Kapp DS, Cheung MK, Shin JY, Osann K, Husain A, et al. Trends in demographic and clinical characteristics in women diagnosed with corpus cancer and their potential impact on the increasing number of deaths. American journal of obstetrics and gynecology. 2008;198(2):218.e1-6.

36. Rauh-Hain JA, Gonzalez R, Bregar AJ, Clemmer J, Hernandez-Blanquisett A, Clark RM, et al. Patterns of care, predictors and outcomes of chemotherapy for ovarian carcinosarcoma: A National Cancer Database Analysis. Gynecologic oncology. 2016.

37. Singh P, Smith CL, Cheetham G, Dodd TJ, Davy ML. Serous carcinoma of the uterus-determination of HER-2/neu status using immunohistochemistry, chromogenic in situ hybridization, and quantitative polymerase chain reaction techniques: its significance and clinical correlation. International journal of gynecological cancer : official journal of the International Gynecological Cancer Society. 2008;18(6):1344-51.

38. Baker J, Obermair A, Gebski V, Janda M. Efficacy of oral or intrauterine device-delivered progestin in patients with complex endometrial hyperplasia with atypia or early endometrial adenocarcinoma: a meta-analysis and systematic review of the literature. Gynecologic oncology. 2012;125(1):263-70.

39. National Cancer Insitute (NIH). Uterine Cancer-Patient Version. [Available from: http://www.cancer.gov/types/uterine.]

40. Reid BC, Rozier RG. Continuity of care and early diagnosis of head and neck cancer. Oral oncology. 2006;42(5):510-6.

41. Kirsner RS, Wilkinson JD, Ma F, Pacheco H, Federman DG. The association of Medicare health care delivery systems with stage at diagnosis and survival for patients with melanoma. Archives of dermatology. 2005;141(6):753-7.

42. DeVita VTHS, S. A. M. U. E. L. Hellman, and S. Rosenberg,. Cancer: Principles and Practice of Oncology 1997 [volume 2:]

43. Goff BA. Uterine papillary serous carcinoma: what have we learned over the past quarter century? Gynecologic oncology. 2005;98(3):341-3.

44. Yoon JH, Yoo SC, Kim WY, Chang SJ, Chang KH, Ryu HS. Para-aortic lymphadenectomy in the management of preoperative grade 1 endometrial cancer confined to the uterine corpus. Annals of surgical oncology. 2010;17(12):3234-40.

45. Thomas M, Mariani A, Wright JD, Madarek EO, Powell MA, Mutch DG, et al. Surgical management and adjuvant therapy for patients with uterine clear cell carcinoma: a multi-institutional review. Gynecologic oncology. 2008;108(2):293-7.

46. Hogberg T. Adjuvant chemotherapy in endometrial carcinoma: overview of randomised trials. Clinical oncology (Royal College of Radiologists (Great Britain)). 2008;20(6):463-9.

47. Secord AA, Geller MA, Broadwater G, Holloway R, Shuler K, Dao NY, et al. A multicenter evaluation of adjuvant therapy in women with optimally resected stage IIIC endometrial cancer. Gynecologic oncology. 2013;128(1):65-70.

48. Group SGOCPECW, Burke WM, Orr J, Leitao M, Salom E, Gehrig P, et al. Endometrial cancer: a review and current management strategies: part II. Gynecologic oncology. 2014;134(2):393-402.

49. Kitchener H, Swart AM, Qian Q, Amos C, Parmar MK. Efficacy of systematic pelvic lymphadenectomy in endometrial cancer (MRC ASTEC trial): a randomised study. Lancet (London, England). 2009;373(9658):125-36.

50. Benedetti Panici P, Basile S, Maneschi F, Alberto Lissoni A, Signorelli M, Scambia G, et al. Systematic pelvic lymphadenectomy vs. no lymphadenectomy in early-stage endometrial carcinoma: randomized clinical trial. Journal of the National Cancer Institute. 2008;100(23):1707-16.

51. Creutzberg CL, van Stiphout RG, Nout RA, Lutgens LC, Jurgenliemk-Schulz IM, Jobsen JJ, et al. Nomograms for prediction of outcome with or without adjuvant radiation therapy for patients with endometrial cancer: a pooled analysis of PORTEC-1 and PORTEC-2 trials. International journal of radiation oncology, biology, physics. 2015;91(3):530-9.

52. Colombo N, Preti E, Landoni F, Carinelli S, Colombo A, Marini C, et al. Endometrial cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2013;24 Suppl 6:vi33-8.

53. Fleming GF, Brunetto VL, Cella D, Look KY, Reid GC, Munkarah AR, et al. Phase III trial of doxorubicin plus cisplatin with or without paclitaxel plus filgrastim in advanced endometrial carcinoma: a Gynecologic Oncology Group Study. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2004;22(11):2159-66.

54. Fleming GF, Filiaci VL, Bentley RC, Herzog T, Sorosky J, Vaccarello L, et al. Phase III randomized trial of doxorubicin + cisplatin versus doxorubicin + 24-h paclitaxel + filgrastim in endometrial carcinoma: a Gynecologic Oncology Group study. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO. 2004;15(8):1173-8.

55. Thigpen JT, Brady MF, Homesley HD, Malfetano J, DuBeshter B, Burger RA, et al. Phase III trial of doxorubicin with or without cisplatin in advanced endometrial carcinoma: a gynecologic oncology group study. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2004;22(19):3902-8.

56. Surveillance Epidemiology and End Results Program (SEER). SEER Stat Fact Sheets: Ovarian Cancer. [Available from: http://seer.cancer.gov/statfacts/html/ovary.html.]

57. Tyler J. Vanderweele. Explanation in Causal Inference, Mathods for Mediation and Interaction: Oxford University Press 2015.

58. Jung SY, Vitolins MZ, Paskett ED, Chang S. Exogenous estrogen as mediator of racial differences in bioactive insulin-like growth factor-I levels among postmenopausal women. The journals of gerontology Series A, Biological sciences and medical sciences. 2015;70(4):495-502.

59. Dookeran KA, Silva A, Warnecke RB, Rauscher GH. Race/ethnicity and disparities in mastectomy practice in the Breast Cancer Care in Chicago study. Annals of surgical oncology. 2015;22(1):66-74.

60. Meghani SH, Kang Y, Chittams J, McMenamin E, Mao JJ, Fudin J. African Americans with cancer pain are more likely to receive an analgesic with toxic metabolite despite clinical risks: a mediation analysis study. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2014;32(25):2773-9.

61. Russell E, Kramer MR, Cooper HL, Thompson WW, Arriola KR. Residential racial composition, spatial access to care, and breast cancer mortality among women in Georgia. Journal of urban health : bulletin of the New York Academy of Medicine. 2011;88(6):1117-29.

62. Kohler U KK, Holm A.,. Comparing coefficients of nested nonlinear probability models. Stata journal. 2011;11(3):420-38.

63. Hafeman DM, Schwartz S. Opening the Black Box: a motivation for the assessment of mediation. International journal of epidemiology. 2009;38(3):838-45.

64. Mahdi H, Hou H, Kowk LL, Moslemi-Kebria M, Michener C. Type II endometrial cancer in Hispanic women: tumor characteristics, treatment and survival compared to non-Hispanic white women. Gynecologic oncology. 2014;133(3):512-7.

65. Rodriguez AM, Schmeler KM, Kuo YF. Disparities in endometrial cancer outcomes between non-Hispanic White and Hispanic women. Gynecologic oncology. 2014;135(3):525-33.

66. Setiawan VW, Pike MC, Kolonel LN, Nomura AM, Goodman MT, Henderson BE. Racial/ethnic differences in endometrial cancer risk: the multiethnic cohort study. American journal of epidemiology. 2007;165(3):262-70.

67. Wright JD, Fiorelli J, Schiff PB, Burke WM, Kansler AL, Cohen CJ, et al. Racial disparities for uterine corpus tumors: changes in clinical characteristics and treatment over time. Cancer. 2009;115(6):1276-85.

68. Jamison PM, Noone AM, Ries LA, Lee NC, Edwards BK. Trends in endometrial cancer incidence by race and histology with a correction for the prevalence of hysterectomy, SEER 1992 to 2008. Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology. 2013;22(2):233-41.

69. Maxwell GL, Risinger JI, Hayes KA, Alvarez AA, Dodge RK, Barrett JC, et al. Racial disparity in the frequency of PTEN mutations, but not microsatellite instability, in advanced endometrial cancers. Clinical cancer research : an official journal of the American Association for Cancer Research. 2000;6(8):2999-3005.

70. Basil JB, Goodfellow PJ, Rader JS, Mutch DG, Herzog TJ. Clinical significance of microsatellite instability in endometrial carcinoma. Cancer. 2000;89(8):1758-64.

71. Kohler MF, Carney P, Dodge R, Soper JT, Clarke-Pearson DL, Marks JR, et al. p53 overexpression in advanced-stage endometrial adenocarcinoma. American journal of obstetrics and gynecology. 1996;175(5):1246-52.

72. Clifford SL, Kaminetsky CP, Cirisano FD, Dodge R, Soper JT, Clarke-Pearson DL, et al. Racial disparity in overexpression of the p53 tumor suppressor gene in stage I endometrial cancer. American journal of obstetrics and gynecology. 1997;176(6):S229-32.

73. Hicks ML, Phillips JL, Parham G, Andrews N, Jones WB, Shingleton HM, et al. The National Cancer Data Base report on endometrial carcinoma in African-American women. Cancer. 1998;83(12):2629-37.

74. Cossrow N, Falkner B. Race/ethnic issues in obesity and obesity-related comorbidities. The Journal of clinical endocrinology and metabolism. 2004;89(6):2590-4.

75. Fleury AC, Ibeanu OA, Bristow RE. Racial disparities in surgical care for uterine cancer. Gynecologic oncology. 2011;121(3):571-6.

76. Trimble EL, Harlan LC, Clegg LX, Stevens JL. Pre-operative imaging, surgery and adjuvant therapy for women diagnosed with cancer of the corpus uteri in community practice in the United States. Gynecologic oncology. 2005;96(3):741-8.

77. Olson SH, Atoria CL, Cote ML, Cook LS, Rastogi R, Soslow RA, et al. The impact of race and comorbidity on survival in endometrial cancer. Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology. 2012;21(5):753-60.

78. Collins Y, Holcomb K, Chapman-Davis E, Khabele D, Farley JH. Gynecologic cancer disparities: a report from the Health Disparities Taskforce of the Society of Gynecologic Oncology. Gynecologic oncology. 2014;133(2):353-61.

79. Maxwell GL, Tian C, Risinger JI, Hamilton CA, Barakat RR. Racial disparities in recurrence among patients with early-stage endometrial cancer: is recurrence increased in black patients who receive estrogen replacement therapy? Cancer. 2008;113(6):1431-7.

80. Ghafoor A, Jemal A, Cokkinides V, Cardinez C, Murray T, Samuels A, et al. Cancer statistics for African Americans. CA: a cancer journal for clinicians. 2002;52(6):326-41.

81. Howlader N NA, Krapcho M, Garshell J, Miller D, Altekruse SF, Kosary CL, Yu M, Ruhl J, Tatalovich Z,Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds),. SEER Cancer Statistics Review, 1975-2012, National Cancer Institute. November 2014 SEER data submission. [Available from: http://seer.cancer.gov/csr/1975_2012/.]

82. Cook LS, Nelson HE, Cockburn M, Olson SH, Muller CY, Wiggins CL. Comorbidities and endometrial cancer survival in Hispanics and non-Hispanic whites. Cancer causes & control : CCC. 2013;24(1):61-9.

83. Harlan LC, Greene AL, Clegg LX, Mooney M, Stevens JL, Brown ML. Insurance status and the use of guideline therapy in the treatment of selected cancers. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2005;23(36):9079-88.

84. Agency for Healthcare Research and Quality. National Healthcare Quality & Disparities Reports. [Available from: http://www.ahrq.gov/research/findings/nhqrdr/index.html.]

85. Halpern MT, Ward EM, Pavluck AL, Schrag NM, Bian J, Chen AY. Association of insurance status and ethnicity with cancer stage at diagnosis for 12 cancer sites: a retrospective analysis. The Lancet Oncology. 2008;9(3):222-31.

86. DeNavas-Walt C PB. Income and Poverty in the United States: 2014: United States Census Bureau; 2015. [Available from: https://www.census.gov/content/dam/Census/library/publications/2015/demo/p60-252.pdf.]

87. Wen M, Browning CR, Cagney KA. Poverty, affluence, and income inequality: neighborhood economic structure and its implications for health. Social science & medicine (1982). 2003;57(5):843-60.

88. Carmen DeNavas-Walt and Bernadette D. Proctor. Income and Poverty in the United States: 2014. U.S. Department of Commerce, Economics and Statistics Administration, U.S. CENSUS BUREAU, 2015 September 2015.

89. Jessica C. Smith and Carla Medalia. Health Insurance Coverage in the United States: 2014. U.S. Department of Commerce, Economics and Statistics Administration, U.S. CENSUS BUREAU, 2015 September 2015.

90. Diez Roux AV. Neighborhoods and Health: What Do We Know? What Should We Do? American journal of public health. 2016;106(3):430-1.

91. Mode NA, Evans MK, Zonderman AB. Race, Neighborhood Economic Status, Income Inequality and Mortality. PloS one. 2016;11(5):e0154535.

92. Major JM, Doubeni CA, Freedman ND, Park Y, Lian M, Hollenbeck AR, et al. Neighborhood socioeconomic deprivation and mortality: NIH-AARP diet and health study. PloS one. 2010;5(11):e15538.

93. Signorello LB, Cohen SS, Williams DR, Munro HM, Hargreaves MK, Blot WJ. Socioeconomic status, race, and mortality: a prospective cohort study. American journal of public health. 2014;104(12):e98-e107.

94. Peterson CE, Rauscher GH, Johnson TP, Kirschner CV, Freels S, Barrett RE, et al. The effect of neighborhood disadvantage on the racial disparity in ovarian cancer-specific survival in a large hospital-based study in cook county, illinois. Frontiers in public health. 2015;3:8.

95. Browning CR, Cagney KA. Neighborhood structural disadvantage, collective efficacy, and self-rated physical health in an urban setting. Journal of health and social behavior. 2002;43(4):383-99.

96. Kirby JB, Kaneda T. Neighborhood socioeconomic disadvantage and access to health care. Journal of health and social behavior. 2005;46(1):15-31.

97. Gornick ME. A decade of research on disparities in medicare utilization: lessons for the health and health care of vulnerable men. American journal of public health. 2008;98(9 Suppl):S162-8.

98. Oka M. Measuring a neighborhood affluence-deprivation continuum in urban settings: Descriptive findings from four US cities. Demographic Research. Demographic Research 2015;32:pp.1469-86.

99. Vernooij F, Heintz AP, Coebergh JW, Massuger LF, Witteveen PO, van der Graaf Y. Specialized and high-volume care leads to better outcomes of ovarian cancer treatment in the Netherlands. Gynecologic oncology. 2009;112(3):455-61.

100. Aune G, Torp SH, Syversen U, Hagen B, Tingulstad S. Ten years' experience with centralized surgery of ovarian cancer in one health region in Norway. International journal of gynecological cancer : official journal of the International Gynecological Cancer Society. 2012;22(2):226-31.

101. Breslin TM, Morris AM, Gu N, Wong SL, Finlayson EV, Banerjee M, et al. Hospital factors and racial disparities in mortality after surgery for breast and colon cancer. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2009;27(24):3945-50.

102. Keating NL, Kouri E, He Y, Weeks JC, Winer EP. Racial differences in definitive breast cancer therapy in older women: are they explained by the hospitals where patients undergo surgery? Medical care. 2009;47(7):765-73.

103. Cliby WA, Powell MA, Al-Hammadi N, Chen L, Philip Miller J, Roland PY, et al. Ovarian cancer in the United States: contemporary patterns of care associated with improved survival. Gynecologic oncology. 2015;136(1):11-7.

104. Bristow RE, Palis BE, Chi DS, Cliby WA. The National Cancer Database report on advanced-stage epithelial ovarian cancer: impact of hospital surgical case volume on overall survival and surgical treatment paradigm. Gynecologic oncology. 2010;118(3):262-7.

105. Armstrong K, Randall TC, Polsky D, Moye E, Silber JH. Racial differences in surgeons and hospitals for endometrial cancer treatment. Medical care. 2011;49(2):207-14.

106. Williams DR, Collins C. Racial residential segregation: a fundamental cause of racial disparities in health. Public health reports (Washington, DC : 1974). 2001;116(5):404-16.

107. Rosenthal GE, Harper DL, Quinn LM, Cooper GS. Severity-adjusted mortality and length of stay in teaching and nonteaching hospitals. Results of a regional study. Jama. 1997;278(6):485-90.

108. Oliver KE, Enewold LR, Zhu K, Conrads TP, Rose GS, Maxwell GL, et al. Racial disparities in histopathologic characteristics of uterine cancer are present in older, not younger blacks in an equal-access environment. Gynecologic oncology. 2011;123(1):76-81.

109. American College of Surgeons. National Cancer Data Base. [Available from: https://www.facs.org/quality-programs/cancer/ncdb.]

110. American College of Surgeons Commision on Cancer. Cancer Program Standards 2012. [Available from: https://www.facs.org/~/media/files/quality%20programs/cancer/coc/programstandards2012.ashx .]

111. United States Census Bureau. Race. [Available from: http://www.census.gov/topics/population/race/about.html.]

112. Strohl AE, Feinglass JM, Shahabi S, Simon MA. Surgical wait time: A new health indicator in women with endometrial cancer. Gynecologic oncology. 2016.

113. Doll A, Abal M, Rigau M, Monge M, Gonzalez M, Demajo S, et al. Novel molecular profiles of endometrial cancer-new light through old windows. The Journal of steroid biochemistry and molecular biology. 2008;108(3-5):221-9.

114. National Cancer Insitute (NIH). Tumor Grade. [Available from: http://www.cancer.gov/about-cancer/diagnosis-staging/prognosis/tumor-grade-fact-sheet.]

115. Baldwin LA, Huang B, Miller RW, Tucker T, Goodrich ST, Podzielinski I, et al. Ten-year relative survival for epithelial ovarian cancer. Obstetrics and gynecology. 2012;120(3):612-8.

116. Yang HP, Wentzensen N, Trabert B, Gierach GL, Felix AS, Gunter MJ, et al. Endometrial cancer risk factors by 2 main histologic subtypes: the NIH-AARP Diet and Health Study. American journal of epidemiology. 2013;177(2):142-51.

117. Rodriguez F, Stefanick ML, Greenland P, Soliman EZ, Manson JE, Parikh N, et al. Racial and ethnic differences in atrial fibrillation risk factors and predictors in women: Findings from the Women's Health Initiative. American heart journal. 2016;176:70-7.

118. Institute of Medicine Committee on U, Eliminating R, Ethnic Disparities in Health C. In: Smedley BD, Stith AY, Nelson AR, editors. Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care. Washington (DC): National Academies Press (US). Copyright 2002 by the National Academy of Sciences. All rights reserved.; 2003.

119. Kumar K, Greenfield S, Raza K, Gill P, Stack R. Understanding adherence-related beliefs about medicine amongst patients of South Asian origin with diabetes and cardiovascular disease patients: a qualitative synthesis. BMC endocrine disorders. 2016;16(1):24.

120. Clegg LX, Reichman ME, Miller BA, Hankey BF, Singh GK, Lin YD, et al. Impact of socioeconomic status on cancer incidence and stage at diagnosis: selected findings from the surveillance, epidemiology, and end results: National Longitudinal Mortality Study. Cancer causes & control : CCC. 2009;20(4):417-35.

121. Bristow RE, Chang J, Ziogas A, Anton-Culver H. Adherence to treatment guidelines for ovarian cancer as a measure of quality care. Obstetrics and gynecology. 2013;121(6):1226-34.

122. Gomez SL, Clarke CA, Shema SJ, Chang ET, Keegan TH, Glaser SL. Disparities in breast cancer survival among Asian women by ethnicity and immigrant status: a population-based study. American journal of public health. 2010;100(5):861-9.

123. George M, Margolis ML. Race and lung cancer surgery--a qualitative analysis of relevant beliefs and management preferences. Oncology nursing forum. 2010;37(6):740-8.

124. Hardy D, Liu CC, Xia R, Cormier JN, Chan W, White A, et al. Racial disparities and treatment trends in a large cohort of elderly black and white patients with nonsmall cell lung cancer. Cancer. 2009;115(10):2199-211.

125. Mehta RS, Lenzner D, Argiris A. Race and health disparities in patient refusal of surgery for early-stage non-small cell lung cancer: a SEER cohort study. Annals of surgical oncology. 2012;19(3):722-7.

126. Rawaf MM, Kressin NR. Exploring racial and sociodemographic trends in physician behavior, physician trust and their association with blood pressure control. Journal of the National Medical Association. 2007;99(11):1248-54.

127. Mead EL, Doorenbos AZ, Javid SH, Haozous EA, Alvord LA, Flum DR, et al. Shared decision-making for cancer care among racial and ethnic minorities: a systematic review. American journal of public health. 2013;103(12):e15-29.

128. Otoo M, Beckmeyer-Borowko A, Brewer K, Peterson C, Davis F, Hoskins K, et al. Racial differences in reasons for failure to receive ovarian cancer treatment. Gynecologic oncology. 2015;137:48-50.

129. Andersen RM, Davidson, P.L. Improving Access to Care in America: Individual and Contextual Indicators. Working Paper 8328. 2001.

130. Berk ML, Schur CL, Cantor JC. Ability to obtain health care: recent estimates from the Robert Wood Johnson Foundation National Access to Care Survey. Health affairs (Project Hope). 1995;14(3):139-46.

131. Goldman DP, Lakdawalla, D. Understanding Health Disparities Across Education Groups. Working Paper 8328. 2001.

132. Warner ET, Tamimi RM, Hughes ME, Ottesen RA, Wong YN, Edge SB, et al. Racial and Ethnic Differences in Breast Cancer Survival: Mediating Effect of Tumor Characteristics and Sociodemographic and Treatment Factors. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2015;33(20):2254-61.

133. Mary McGunigal JL, MD, Manjeet Chadha, MD, Vishal Gupta, MD,. Is There a Difference in Survival Between Patients With Uterine Papillary Serous, Clear Cell, and Grade 3 Endometrial Cancers? A National Cancer Data Base Analysis. Oncology (Williston Park, NY). 2016;30(4 Suppl 1).

134. Myung SK, Ju W, Choi HJ, Kim SC. Soy intake and risk of endocrine-related gynaecological cancer: a meta-analysis. BJOG : an international journal of obstetrics and gynaecology. 2009;116(13):1697-705.

135. Wu AH, Ziegler RG, Horn-Ross PL, Nomura AM, West DW, Kolonel LN, et al. Tofu and risk of breast cancer in Asian-Americans. Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology. 1996;5(11):901-6.

136. Wu AH, Ziegler RG, Pike MC, Nomura AM, West DW, Kolonel LN, et al. Menstrual and reproductive factors and risk of breast cancer in Asian-Americans. British journal of cancer. 1996;73(5):680-6.

VIII. APPENDICES

APPENDIX A:

TABLE XXI: PUBLISHED LITERATURE FOR THE ASSOCIATION OF RACE/ETHNICITY IN MINORITY POPULATIONS AND ENDOMETRIAL CANCER TUMOR CHARACTERISTICS, RECEIPT OF TREATMENT AND SURVIVAL. ALL OF THE BELOW PRESENTED STUDIES ARE RETROSPECTIVE COHORT STUDIES[1].

Author	Publication Year	Period of time	Registry	Races[2] (%)	Outcome	Endometrial cancer types	Adjustment for variables	Sample Size	Results (OR, 95%CI) , (HR, 95%CI) or p-value
Kost et al. (19)	2002	1988-1995	Department of defense centralized registry	W: 90 AA:4.4 API: 5.5	-5-year survival -Treatment assessed in bivariate analyses	Overall EC	-Survival analyses adjusted for age, diagnosis stage, grade and histology. - Treatment analyses were unadjusted	1,811	**Treatment**: No significant treatment differences were reported **Survival**: W vs AA: NS[3] W vs API : 0.033 (HR are not presented)
Sherman et al. (26)	2003	1992-1998	SEER	W: 81.8 AA: 9.1 H: 9.1 Results presented for whites (W+H) and blacks (AA)	Relative survival	Both types	No-Kaplan Meier curves presented instead	20,192	Worse survival for AA when compared to whites for every age, grade and stage group
Ueda et al.(35)	2008	1988-2001	SEER	W:85.5 AA: 5.6 H:3.6 Asian: 3.7 (race was analyzed as a dichotomous variable: AA vs. other races)	5 year-survival	Overall EC	Adjusted for age, race, stage, grade, histology, primary surgery and lymphadenecto-my	48,150	AA vs others: 1.41 (1.30-1.53) Worse survival for AA when compared to other races. The authors only talk about AA and do not mention Hispanics or Asians.

APPENDIX A (CONTINUED):

TABLE XXI (CONTINUED): PUBLISHED LITERATURE FOR THE ASSOCIATION OF RACE/ETHNICITY IN MINORITY POPULATIONS AND ENDOMETRIAL CANCER TUMOR CHARACTERISTICS, RECEIPT OF TREATMENT AND SURVIVAL. ALL OF THE BELOW PRESENTED STUDIES ARE RETROSPECTIVE COHORT STUDIES[1].

Author	Publication Year	Period of time	Registry	Races[2] (%)	Outcome	Endometrial cancer types	Adjustment for variables	Sample Size	Results (OR, 95%CI) , (HR, 95%CI) or p-value
Fedewa et al. (5)	2011	2000-2001	NCDB	W: 77.2 H: 3.8 AA:7.8 O:2.6	4-year survival	Overall EC stratified by diagnosis stage(stages I, II & III)	Yes	39,510	W: ref. H: 0.96 (0.82-1.13) AA:1.28 (1.17-1.40) O:0.81 (0.62-1.05)
Smotkin et al. (20)	2012	1999-2009	Montfiore Hospital, Bronx, NYC	W: 39.0 AA: 31.0 H: 24.0 O: 6.3 (excluded in analyses)	-Treatment -Survival	Overall EC	Treatment: unadjusted Survival: Adjusted for histology	984	Treatment: The authors do not say if differences in receipt of treatment where statistically significant. They only provide percentages. Survival: W:ref. AA:1.12 (0.84-1.48) H: 0.93 (0.67-1.29)
Cook et al(82).	2012	1992-2004	SEER	HW:9.8 NHW:90.2 (Medicare population)	10-year survival	Overall EC	Adjusted for age, diagnosis year, stage, histology, surgery, radiation therapy, chemotherapy, comorbidities and education	3,286	Cancer specific mortality: HW vs NHW: 0.95 (0.74-1.21) Overall mortality HW vs NHW: 1.00 (0.79-1.27)

APPENDIX A (CONTINUED):

TABLE XXI (CONTINUED): PUBLISHED LITERATURE FOR THE ASSOCIATION OF RACE/ETHNICITY IN MINORITY POPULATIONS AND ENDOMETRIAL CANCER TUMOR CHARACTERISTICS, RECEIPT OF TREATMENT AND SURVIVAL. ALL OF THE BELOW PRESENTED STUDIES ARE RETROSPECTIVE COHORT STUDIES[1].

Author	Publication Year	Period of time	Registry	Races[2] (%)	Outcome	Endometrial cancer types	Adjustment for variables	Sample Size	Results (OR, 95%CI) , (HR, 95%CI) or *P*-value
Mahdi et al. (3)	2014	1988-2009	SEER	NHW:93 AS:6.4 AI/AN:0.6	-Treatment -Survival	Overall EC	Treatment: unadjusted Survival: Adjusted for age, grade, histology, surgery, lymphadenectomy and radiation	105,083	**Treatment:** *Lymphadenectomy:* NHW: 48.2% AS: 56.7%, *P*<0.001 AI/AN: 46.5% *P*=0.4 *Radiation therapy:* NHW: 26.0% AS: 21.8%, *P*<0.001 AI/AN: 21.7% *P*=0.014 **Overall survival:** NHW: ref. AS: 0.83 (0.73-0.94) AI/AN: 0.66 (0.54-0.80) **Cancer specific survival:** NHW: ref. AS: 1.06 (0.80-1.40) AI/AN: 1.35 (1.15-1.59)

TABLE XXI (CONTINUED): PUBLISHED LITERATURE FOR THE ASSOCIATION OF RACE/ETHNICITY IN MINORITY POPULATIONS AND ENDOMETRIAL CANCER TUMOR CHARACTERISTICS, RECEIPT OF TREATMENT AND SURVIVAL. ALL OF THE BELOW PRESENTED STUDIES ARE RETROSPECTIVE COHORT STUDIES[1].

Author	Publication Year	Period of time	Registry	Races[2] (%)	Outcome	Endometrial cancer types	Adjustment for variables	Sample Size	Results (OR, 95%CI) , (HR, 95%CI) or *P*-value
Rodriguez et al(65).	2014	2000-2010	SEER	H:9.4 NHW:90.6	Treatment Survival	Overall EC	Treatment: unadjusted Survival: Adjusted for age, marital status, SEER region, stage, histology, grade, lymphadenectomy, surgery and radiation	69,764	Treatment: no treatment was significantly higher for Hispanics than NHW. Survival results presented for US born Hispanics and non-US born Hispanics: NHW: ref US born Hispanics: 1.61 (1.44-1.79) Non-US born Hispanics: 1.27 (1.13-1.43)
Mahdi et al. (64)	2014	1988-2009	SEER	NHW:90.2 HW:9.8	-Treatment -Survival	Type 2	Adjusted for age, grade, histology, surgery, lymphadenectomy and radiation	14,434	**Treatment:** *Lymphadenectomy:* NHW: 67.9% HW: 65.8% *P*=0.1 *Radiation therapy:* NHW: 42.3% HW: 39.5% *P*=0.04 **Overall survival:** NHW: ref. HW: 1.06 (0.97-1.16) **Cancer specific survival:** NHW: ref. HW: 1.02 (0.91-1.14)

APPENDIX A (CONTINUED):

TABLE XXI (CONTINUED): PUBLISHED LITERATURE FOR THE ASSOCIATION OF RACE/ETHNICITY IN MINORITY POPULATIONS AND ENDOMETRIAL CANCER TUMOR CHARACTERISTICS, RECEIPT OF TREATMENT AND SURVIVAL. ALL OF THE BELOW PRESENTED STUDIES ARE RETROSPECTIVE COHORT STUDIES[1].

Author	Publication Year	Period of time	Registry	Races[2] (%)	Outcome	Endometrial cancer types	Adjustment for variables	Sample Size	Results (OR, 95%CI) , (HR, 95%CI) or *P*-value
Cote et al. (7)	2015	2000-2011	SEER	NHW: 75.2 HW: 9.4 NHB:8.6 AS:6.8	5-year relative survival	Both types	No, results stratified by histology type and stage	120,513	NHW:ref. H: not-significant NHB: significant

[1] Articles that solely compare NHB to NHW are not included.

[2] W: White, AA: African American, API: Asian-Pacific Islanders, H: Hispanics, NHW: non-Hispanic White, AS: Asian, AI/AN: American Indian/Alaskan Natives, HW: Hispanic White.

[3] NS:Non-significant.

APPENDIX B:

TABLE XXII: CATEGORIZATION OF HISTOLOGY CODES BY ENDOMETRIAL CANCER SUBTYPE

ENDOMETRIAL CANCER SUBTYPE	**HISTOLOGY CODES**
1.Low-grade endometrioid carcinomas	8050,8140,8141,8143,8210,8211,8260,8261,8262,8263,8323,8340,8380, 8381,8382,8383,8384,8440,8470,8471,8480,8481,8490,8550,8560,8570,8571,8572,8573
2.High-grade endometrioid carcinomas	8005,8084,8310,8313
3. Serous carcinomas	8441,8460,8461,8462
4. Clear cell carcinomas	8950,8951,8980,8981

APPENDIX C:

TABLE XXIII: REASON FOR NO SURGERY ON PRIMARY SITE BY RACE, NATIONAL CANCER DATABASE, 2003-2012, n=208,247

	Non-Hispanic White n=6,290 %	Non-Hispanic Black n=1,380 %	Hispanic n=487 %	Non-Hispanic Asian n=145 %	Non-Hispanic American Indian, Alaskan Native n=25 %	Non-Hispanic Pacific Islander / Hawaiian n=21 %	Total n=8,348 %
Surgery of the primary site was performed	2.5	1.9	3.1	3.5	4.0	0	2.4
Surgery not performed because it was not part of the planned first course treatment	64.7	66.7	67.6	73.1	48.0	52.4	65.3
Surgery was not recommended/performed, contraindicated due to patient risk factors	19.2	15.1	11.1	6.2	36.0	9.5	17.9
Surgery not performed because the patient died prior to planned or recommended surgery	0.9	1.1	0.6	0	0	4.8	0.9
Surgery was recommended by physician but not performed, No reason was noted in patient record	1.6	3.0	3.7	2.8	0	0	2.0
Surgery was recommended but was refused by the patient, patient's family member or guardian	5.8	7.7	5.3	9.7	8.0	23.8	6.2
Surgery was recommended, but unknown if performed	2.2	2.0	5.8	3.5	0	0	2.4
Unknown if surgery was recommended or performed, Diagnosed at autopsy or death certificate only	3.0	2.3	2.9	1.4	4.0	9.5	2.9

UNIVERSITY OF ILLINOIS
AT CHICAGO

Office for the Protection of Research Subjects (OPRS)
Office of the Vice Chancellor for Research (MC 672)
203 Administrative Office Building
1737 West Polk Street
Chicago, Illinois 60612-7227

Determination Notice
Research Activity Does Not Involve "Human Subjects"

June 17, 2016

Anna B. Beckmeyer-Borowko, MBA, MPH
School of Public Health
1747 W Roosevelt Rd
Chicago, IL 60612
Phone: (312) 257-5836

RE: Research Protocol # 2016-0616
"Racial and ethnic differences in endometrial cancer"

Sponsor(s): None

Dear Ms. Beckmeyer-Borowko:

The above proposal was reviewed on June 15, 2016 by OPRS staff/members of IRB #7. From the information you have provided, the proposal does not appear to involve "human subjects" as defined in 45 CFR 46. 102(f).

The specific definition of human subject under 45 CFR 46.102(f) is:

> *Human subject* means a living individual about whom an investigator (whether professional or student) conducting research obtains
>
> (1) data through intervention or interaction with the individual, or
> (2) identifiable private information.
>
> *Intervention* includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. *Interaction* includes communication or interpersonal contact between investigator and subject. *Private information* includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

All the documents associated with this proposal will be kept on file in the OPRS.

If you have any questions or need further help, please contact the OPRS office at (312) 996-1711 or me at (312) 355-2908.

Sincerely,

Charles W. Hoehne, B.S., C.I.P.

Assistant Director, IRB #7
Office for the Protection of Research Subjects

cc: Mark I. Rosenblatt, Ophthalmology, M/C 648
Charlotte E. Joslin (faculty sponsor), Ophthalmology, M/C 648

IX. VITA

NAME: ANNA B. BECKMEYER-BOROWKO

EDUCATION

Ph.D. in Epidemiology, School of Public Health, University of Illinois at Chicago (UIC) **2012-2016**

- Cumulative GPA 3.94

M.P.H. Master in Public Health, University of Kentucky, **GPA 4.0** **2009-2011**

- Concentration: Health Services Management

M.B.A. in International Business Development, University of Neuchâtel, Switzerland **2007-2009**

B.A. Economics and Management, University of Neuchâtel, Switzerland **2004-2007**

RESEARCH EXPERIENCE

Research Assistant - Data Analyst - Racial Differences in Ovarian Cancer Survival Project, UIC **2014-present**

- Using SAS and STATA software has performed various type of multivariable analyses having for goal to explain racial/ethnic differences in ovarian cancer stage at diagnosis, treatment and survival using large cohort data
- Wrote and submitted manuscripts to peer-reviewed journals
- Presented the results of research at multiple national conferences in the US, including the American Public Health Association that took place in Chicago in November 2015
- Keeps the documents for the Institutional Review Board of the grant current and reapplies for future cycles

Research Assistant - Bridging the Gap – Community Obesity Measures Project, UIC **Fall 2013-Spring 2014**

- Statistical analyses using SAS and STATA (including use of commands for survey data analysis)
- Documentation of datasets, programs, and outputs

Research Assistant - Data Analyst - Chicago Prostate and Colorectal Project, UIC **Fall 2012-Spring 2013**

- Using SAS, performed survival analyses having for goal to explain racial/ethnic disparities in prostate and colorectal cancer survival with various variables such as socio-economic disadvantage and stage at diagnosis
- Utilized SatScan to detect the tracts as being potential hot spots for advanced-stage tumors and ArcGIS to map them

Research Assistant, Kentucky Injury Prevention & Research Center, Lexington, KY **2008-2011**

- Performed a cost-benefit analysis of the injury center
- Utilized SAS, SatScan, ArcGIS to look for trends and hot spots of unexpected rates of suicides and homicides
- Responsible for managing and updating the reporting system by maintaining contacts with coroners, the police and universities

WORK EXPERIENCE

Pre-Doctoral Fellow, National Institute of Health Cancer Research Education Grant, UIC **2015-2016**

French Teacher, Alliance Française de Chicago **2013-2014**

Teaching Assistant, Department of Epidemiology and Biostatistics, UIC **2012-2015**

- Taught Master students intermediate and introductory epidemiology
- Taught Master students introductory SAS class

Sales Coordinator, Luxury Swiss Watch Manufacturer Ulysse Nardin, Switzerland **2012**

- Sales coordinator for over 15 countries in Eastern Europe and Central Asia
- Monitored the financial status of Ulysse Nardin's distributors in overseas competitive markets
- Prepared reports, presentations and companywide statistics

Marketing Assistant, Haute école de gestion Arc, Neuchâtel, Switzerland **2009**

- Responsible for promotion, marketing and communications of the business school
- Coordinated guest lectures and an educational conference series
- Organized the 'Forum HEG' career fair for students and big enterprises such as KPMG and Apple

Substitute Teacher, Canton of Neuchâtel, Switzerland **2004-2009**

- Substitute teacher at the high school and middle school levels for mathematics, languages and science

PUBLICATIONS & PRESENTATIONS

Manuscripts and Oral Presentations:

- **Beckmeyer-Borowko, A. B**., Peterson, C. E., Brewer, K. C., Otoo, M. A., Davis, F. G., Hoskins, K. F., & Joslin, C. E. (2016). The effect of time on racial differences in epithelial ovarian cancer (OVCA) diagnosis stage, overall and by histologic subtypes: a study of the National Cancer Database. *Cancer Causes & Control*, 1-11.
- Otoo, M. A., **Beckmeyer-Borowko, A**.**B**, Brewer, K. C., Peterson, C. E., Davis, F., Hoskins, K., & Joslin, C. E. (2015). Racial differences in reasons for failure to receive ovarian cancer treatment. Gynecologic Oncology, 137, 48-50.
- Saman, D. M., Walsh, S., & **Borówko, A.B** (2012). Does place of residence affect risk of suicide? A spatial epidemiologic investigation in Kentucky from 1999 to 2008. BMC public health, 12(1), 1.
- Oral presentation: **Beckmeyer-Borowko A. B.**, Peterson, C. E., Brewer, K. C., A., Otoo, M. A., Davis, F., Hoskins, K., & Joslin, C. E. The effect of time on racial differences in epithelial ovarian cancer stage at diagnosis among cases identified through the National Cancer Database.*143rd Annual meeting of the American Public Health Association, Chicago IL, 01-04. 11. 2015*

Poster Presentations:

- **Beckmeyer-Borowko A. B.**, Peterson, C. E., Brewer, K. C., A., Otoo, M. A., Davis, F., Hoskins, K., & Joslin, C. E. The effect of time on racial differences in epithelial ovarian cancer stage at diagnosis among cases identified through the National Cancer Database*. Society of Gynecologic Oncology Conference, Chicago IL 28-31.03.2015*
- **Beckmeyer-Borowko A. B.**, Peterson, C. E., Brewer, K. C., A., Otoo, M. A., Davis, F., Hoskins, K., & Joslin, C. E. The effect of time on racial differences in epithelial ovarian cancer stage at diagnosis among cases identified through the National Cancer Database*. UIC, School of Public Health Research and Awards Day, Chicago IL 07.04.2015*

- **Beckmeyer-Borowko A. B.**, Racial/ethnic differences in endometrioid endometrial cancer treatment among women identified through the National Cancer Database (1998-2012)**.** *UIC Cancer Research Forum, Chicago IL 20.10.2015*
- **Beckmeyer-Borowko A. B.**, Peterson, C. E., Brewer, K. C., A., Otoo, M. A., Davis, F., Hoskins, K., & Joslin, C. E. Racial/ethnic differences in endometrioid endometrial cancer treatment types among women identified through the National Cancer Database. *American Society of Preventive Oncology Conference, Columbus OH 12-15.03.2016*

VOLUNTEER WORK

Medical Volunteer, Shoulder to Shoulder Global, Ecuador **May 2011**

- Medical assistant and translator in Spanish on a team of doctors and health officials providing aid to indigenous communities in western Ecuador
- Conducted pre-screening of both children and adults during clinics and provided support at the nursing station

AIDS Outreach Volunteer, AIDS volunteers (AVOL), Lexington, KY **2010**

- Helped the executive director research and write grants
- Involved in the review of AVOL's budget to allow for the expansion of services

Junior Enterprise Volunteer, Jeune Consulting, Neuchâtel, Switzerland **2004**

- Organized a tennis tournament for 120 members comprised of students and employers
- Raised over $15,000 for the event. Conducted the reception as well as dinner after the event

AWARDS & RECOGNITIONS

University of Illinois in Chicago **2012-2015**

- Won the 2015 Award in Excellence of Doctoral Research in a poster presentation
- Won the 2014 Public Health Student Association Travel Award

University of Kentucky, Master of Public Health **2010-2011**

- Cumulative 4.0 GPA
- Received a "high pass" from the thesis committee responsible for assessing final examinations.
- Awarded a $3,500 scholarship by the College of Public Health for academic excellence.
- Recipient of a $1,000 scholarship by the Office of International Affairs (OIA) for exemplifying strong academics.

University of Neuchatel, Master in International Business Development **2009**

- Received "cum laude" distinction.

National League Handball Player, Switzerland **2002-2003**

- Played for the Handball Swiss Nationalmannschaft
- Played for the A National Handball League team: DHB Rotweiss Thun / Uni Bern