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Impact of Race and Ethnicity on Short-term Surgical Outcomes in Women Treated for Cervical Cancer: American College of Surgeons National Surgical Quality Improvement Program (*ACS-NSQIP*), 2011-2014

THESIS

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by

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ABSTRACT OF THE THESIS

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Variations in access to U.S. healthcare have contributed to racial and ethnic disparities in cervical cancer survival and mortality patterns. Evaluation of postoperative complications after cervical cancer surgery in American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) hospitals' remains limited. In this study, we investigate the association between race/ethnicity and 30-day morbidity in women undergoing cervical cancer surgery.

Using ACS-NSQIP database, 1248 patients undergoing surgery in 2011-2014 were identified. In this cohort, 70.6% were non-Hispanic White, 12.8% Black and 16.5% Hispanic. Compared to non-Hispanic White, these minority groups were more likely to have medical comorbidities. In adjusted multivariable models, the odds of any postoperative complication were 50% greater in Black compared to non-Hispanic White ($p<0.05$), including non-surgical complications (OR=1.55, $p<0.05$). Hispanic ethnicity was not a predictor of 30-day morbidity (OR=0.76; $p>0.05$).

While Black patients experienced greater non-surgical adverse outcomes, no disparity was observed for Hispanic patients. Findings suggest that to some extent access to ACS NSQIP hospitals can attenuate disparities in postoperative complications after cervical cancer surgery, but much more work is still required to eliminate racial/ethnic disparities.

INTRODUCTION

The National Cancer Institute estimates that 12,820 new cases of cervical cancer will be diagnosed in the U.S. in 2017 and 4,210 women will die from this disease. Cervical cancer is projected to constitute 0.8% of all cancer deaths in 2017.[1] While screening programs and preventive vaccination have contributed to the decline in cervical cancer rates through early detection and intervention, certain ethnic minorities in the U.S. continue to experience disparities in cervical cancer incidence after diagnosis.[2] In 2008-2012, the number of cervical cancer cases was approximately 7.7 per 100,000. Black and Hispanic women comprised a disproportionate number of the cases.[3] Of this total, incidence of cervical cancer in non-Hispanic White is estimated at 7.7 per 100,000. Comparatively, the incidence of cervical cancer in Black and Hispanic women is approximately 9.2 and 9.9, respectively.[4] [5] [6]

Several studies have pointed to a disparity in cervical cancer incidence, survival and mortality rates in Black and Hispanic women as compared to non-Hispanic White women. The etiology of these disparities is multifactorial and influenced by factors like variability in screening patterns, socioeconomic status, insurance status, treatment access and patients' acumen regarding cervical cancer risk factors.[7] A comprehensive analysis of 1992-2011 cancer data from the Centers for Disease Control and Prevention's National Program of Cancer Registries (NPCR) revealed incidence rates of 10.2 and 10.5 for Black and Hispanic women compared to 7.1 in non-Hispanic White women.[8] Per this analysis, susceptibility to risk factors and limited access to cervical cancer prevention services contributes to differences in cervical cancer rates.[8]

Previous research has also explored disparity in mortality and survival outcomes in Black and Hispanic women after cervical cancer treatment. A retrospective study of 1992-1997 SEER data showed higher mortality rates among minority women with cervical cancer after controlling for stage, lymph node status. Compared to non-Hispanic White, Black women are 36% more likely to

die of cervical cancer. On the other hand, Hispanic patients have a mortality rate of 2.8 versus 2.0 in their White counterparts.[9] Furthermore, a population-base investigation of 1992-1998 SEER data found a lower 5-year survival rate for Blacks but not for Hispanics when compared to non-Hispanic Whites (72, 85 vs. 86.8) after controlling for stage.[10] [11]

Although these studies provide valuable insight on existing disparities in cervical cancer population-base indicators, the majority of this work extrapolates from samples that conglomerate across various types of institutions with and without quality improvement programs—defined as a program which institutes changes that lead to better patient outcomes, system performance and professional development.[12] [13] Emerging evidence indicates that quality improvement interventions can yield better care across racial/ethnic groups and mitigate outcome disparities in minority populations.[14] This movement has engendered programs like ACS NSQIP whose goal is to improve surgical quality across participating members by examining structures, processes of care and short-term outcomes among surgical services and subspecialties.[15] In fact, a prospective study evaluating improvement in ACS NSQIP hospitals', found that 66-82% of participants showed reductions in risk-adjusted mortality and risk-adjusted complication rates.[16]

Despite the numerous research produced using NSQIP databases, there are limited studies assessing post-surgical complications in minority women diagnosed with cervical cancer in NSQIP participating-hospitals. The bulk of these studies have focused on general cancer care or on subtypes of gynecological cancer other than cervical cancer. With inequalities in cervical cancer persisting against the backdrop of declining rates, this thesis explores short-term postoperative outcomes in Black and Hispanic women with cervical cancer by using data from ACS NSQIP. We evaluate short-term outcomes such as complications, prolonged-hospital-stay and reoperations as these influence treatment decisions and interventions which ultimately determine cervical cancer population-base parameters like survival and mortality.[17]

CHAPTER 1: Fundamentals of Cervical Cancer

Overview of Cervical Cancer— Staging, Patterns & Management

Cervical cancer was the number one cause of death for women in U.S. in the 1930s but with the advent of screening, primary prevention and therapeutic improvements, annual rates have declined to ≥ 75%.[18] [19] Unfortunately, cervical cancer remains ever present in underserved populations in the U.S. and continues to rank second only to breast cancer worldwide.[20] [21]

Cervical cancer is a gynecological cancer that affects the cervix. Anatomically, the cervix is the lower third of the uterus located between the internal and external os. The vaginal portion of the cervix, *exocervix,* is lined by squamous epithelium, whereas the *endocervix* is covered by glandular or columnar epithelium.[22] Approximately 80% of cervical cancers are squamous cell and 15% are adenocarcinomas.[23] Risk factors associated with the development of cervical cancer include young age at first sexual encounter, multiple sexual partners, high parity, history of sexually transmitted disease, smoking and as has been widely documented, infection with human papillomavirus (HPV).[22]

The International Federation of Gynecology and Obstetrics (FIGO) staging system is used to evaluate cervical cancer clinically (Table 1).[24] Cancer staging is the process of determining quantity and location of cancer. It describes the severity of disease based on the magnitude and metastases or the extent of primary tumor spread in the body.[25] Staging can be determined by physical exam in combination with screening and diagnostic procedures like Pap smear, colposcopy, cervical or cone biopsy.[22] While the physical exam may reveal macropathologic features in the cervix via direct visualization and palpation, the screening and diagnostic interventions can identify micropathologic features.[24] Other adjunct procedures useful for staging metastatic disease include cystoscopy, proctoscopy, intravenous pyelography and chest radiography.[26] The utility of staging cervical cancer lies in the ability to have reliable evaluation criteria to compare methods of treatment, determine

prognosis and therapeutic and epidemiological statistics. In turn, this data can be used to compare the equity and quality of cervical cancer care across racial and ethnic groups.

Management of Cervical Cancer

The standard management of cervical cancer is based on clinical stage, and generally, early disease is managed surgically whereas more advanced lesions are managed by chemotheraphy and radiotheraphy.[22] While the ladder are important treatment modalities this thesis focuses mainly on the former as the analyses of this study are founded solely on NSQIP surgical data. To better understand the management of cervical cancer, we provide an overview of the surgical approach since its technical aspects can contribute to differential outcomes after treatment.

Briefly, hysterectomy is a surgical intervention employed in the treatment of cervical cancer and other gynecological malignancies and conditions. The standard management for early stage—I through IIA—cervical cancer is by simple or radical hysterectomy with pelvic lymphadenectomy or lymph node removal.[27] Simple hysterectomy removes the uterus and the cervix, while radical hysterectomy resects wider margins like the ovaries, fallopian tubes, cardinal uterosacral ligaments and segments of the vagina.[28] [29] [30]

This standard treatment is non-fertility sparing, but modalities to retain reproductive function are available to patients who desire fertility preservation and meet stage and tumor characteristic criteria. Specifically, FIGO stages IA1-IB1, tumor <2 cm in diameter, minimal stromal invasion or confined to the cervix and no pelvic lymph node involvement with histology negative for small-cell neuroendocrine markers.[31] The treatment repertoire for fertility-sparing therapy consists of cervical conization, loop electrosurgical excision procedure (LEEP) and trachelectomy.[32] These procedures preserve the uterus, while also targeting atypical epithelium for removal at the level of ecto-, endocervix to upper vagina by using cold-knife or standard surgical scalpel excision in cone and trachelectomy or wire loop heated by electrical current in LEEP.[33]

As previously alluded, the basis for treatment of more advanced lesions (greater than IIA) are single or combination therapy with pelvic radiation therapy (RT), brachytherapy and chemotherapy.[31 32 34 35 36] The criteria for selecting treatment plans is beyond the scope of this thesis, but it is well documented in the literature that more advanced disease is more responsive to the aforementioned types of therapy in comparison to just surgery as in early stage disease.[37 38 39 40]

Lastly, the technical approach (abdominal, vaginal or laparoscopic) to performing hysterectomy is briefly reviewed as it can be associated with less or more morbidity.[41] In short, the abdominal method removes the uterus from a vertical or horizontal incision in the abdominal wall, the vaginal via a small incision at the top of the vagina and the laparoscopic by either the abdomen or vagina through a small incision made with laparoscopic tools.[42 43 44] Importantly, a meta-analysis of randomized control trials comparing morbidity across methods indicates vaginal hysterectomy is associated with better outcomes and less complications.[45 46] Multiple retrospective studies show mix findings for laparoscopic surgery, but relative to abdominal hysterectomy it is associated with better outcomes.[47 48 49]

Patterns of Cervical Cancer Management in Black and Hispanic women

Following diagnosis, an individualized treatment plan is developed and guided by stage of disease, prognostic indicators, comorbidities or contraindications to treatment and, ideally, in concordance with a patient's beliefs and personal preferences. This complex process is also influenced by other factors like variations in receipt of treatment, the approach to surgery, the desire to preserve fertility and race/ethnicity.[10] For instance, a meta-analysis of treatment studies suggest that Black and Hispanic women are less frequently treated or receive non-definitive primary therapy for cervical cancer despite controlling for clinically relevant factors.[10 50] In fact, a single-institution analysis of 1988-1994 SEER data indicates Black women are less likely to be treated with surgery, more likely to be treated with radiation therapy for stage IB cervical cancer in an inner-city

hospital.[11] Similarly, a multi-institution prospective study evaluating guideline-based treatment of cervical cancer found that Hispanic women have lower rates of appropriate therapy after adjusting for stage.[51] The literature shows treatment variations exist across racial/ethnic groups, differences that extend to surgical treatment route.

In short, evolving research of surgical technology and training indicates vaginal or laparoscopic route is associated with better outcomes. Importantly, existing research reveals abdominal approach is performed at higher rates and is associated with minority race.[52] [53] A nationwide study of 2009 SEER data found a positive relationship between minority race, insurance status and undergoing abdominal hysterectomies for oncologic or benign disease.[54] Similarly, adjusted analyses of a retrospective cohort study of 1998-2002 Healthcare Cost and Utilization Project Nationwide Inpatient Sample (NIS) showed abdominal hysterectomy is performed at higher rates than laparoscopic route and suggests Black and Hispanic women are less likely to undergo laparoscopic surgery compared to non-Hispanic White women.[55]

Previous studies have also noted variations in treatment based on the desire to preserve fertility. Literature evaluating the efficacy of fertility-sparing treatment as compared to the standard of care for early stages of cervical cancer demonstrate inconclusive results.[32] [56] [57] [58] [59] Yet, a retrospective study of 1990-1995 SEER data found that Black and Hispanic women are more likely to be treated with fertility-sparing procedures for IA1-IA2 cervical cancer rather than with hysterectomy.[60] [61] In summary, the cause of racial and ethnic differences in receipt of treatment for cervical cancer is affected by a complex set of factors besides clinical staging and the standard of care. These factors include patient preferences, clinical determinants and socioeconomic-demographic patterns. In the setting of existing treatment variations among racial/ethnic groups, the upcoming chapter delves into the effects of these variations on the health outcomes of Black and Hispanic women, which provides a framework for this thesis.

CHAPTER 2: Framework & Significance

General Trends of Cervical Cancer in the U.S

Cervical cancer incidence rates in the U.S. declined from 14.8 in 1975 to 6.7 in 2012, with a prevalence of 248,920 and an average 5-year survival rate of 67.5 percent.[62] These evolving trends have been impacted by the advent of screening, vaccination and treatment advances. Specifically, Pap smear is deemed as the most cost-effective screening modality given that a single lifetime screening with acetic acid or HPV testing can reduce the risk of cervical cancer by 25-36%.[63] Recent predictions also indicate primary prevention efforts with HPV vaccines can yield a 51% reduction in cervical cancer rates over time.[64] [65] Fortunately, treatment advances like cisplatin-based chemotherapy combined with radiation therapy and neoadjuvant chemotherapy have also contributed to reductions in mortality in advanced cervical cancer disease. [66] [67] Currently, newly documented analyses of nationwide SEER data point to a 91.3% 5-year relative survival for localized cervical cancer, versus 57.4% in regional or contiguous spread and 16.8% in metastasis.[3] On average 46% of women are diagnosed at the local stage, 36% at the regional stage and 14% at metastasis.[2] In relation to these averages, we next review the inherent cervical cancer trends documented in the literature for Black and Hispanic women. Ultimately, this review sets the backdrop for the this thesis which seeks to evaluate if differences in complication rates after cervical cancer surgery exist in Black and Hispanic patients treated in ACS NSQIP participating hospitals.

Systematic Review of Cervical Cancer among Black and Hispanic Women

Notwithstanding the aforementioned scientific gains and the overall decline in cervical cancer rates, not all segments of the U.S. population have benefited to the fullest extent from these advances. It has been widely documented that certain ethnic minorities experience higher cervical cancer incidence, survival and mortality rates.[68] Among these, cervical cancer particularly affects

Black and Hispanic women with the former known to experience the highest mortality and the latter the highest incidence.[69] [20] Particularly, 2009-2013 SEER data indicates the proportion of new cases by race/ethnicity to be 7.5 for non-Hispanic White, 8.9 for Black and 9.4 for Hispanic, while the number of deaths are 2.1, 3.9, 2.6 per 100,000 women.[2] Moreover, while a statistical difference in the 5-year relative-survival for Black compared to non-Hispanic White women (59% vs. 69%) was found, no comparative difference was noted for Hispanic women (69% vs. 73%).[70] [71] [72]

The underlying cause of the observed differences in incidence, survival and mortality patterns of cervical cancer is multifactorial, research posits screening, awareness of cervical cancer risks factors, socioeconomic status (SES), access to care as contributors.[68] Research suggests variable receipt of cervical cancer screening and acumen regarding cervical cancer risk factors affect incidence patterns. From the previous section, cervical cancer incidence has declined by more than 75% over the last 50 years due to regular screening with Pap smears. Despite the documented benefits of screening, a study population of Hispanic and Black women in Los Angeles County showed that 51% of Hispanic and 22% of Black women reported no screening within the last year. Of this sample, 29% also stated not receiving any screening recommendations by their provider.[73] Furthermore, an individual's awareness of cervical cancer risk can modulate disparities in cervical cancer incidence. Prior studies suggest that while cervical cancer screening and HPV vaccination are positively viewed by Black and Hispanic women, awareness of cervical cancer prevention and knowledge of the relationship between HPV and cervical cancer risk is relative low.[74] [75]

According to the literature, SES and access to care are also noteworthy components contributing to differences in survival and mortality cervical cancer rates. A 1995-2008 population study in Texas evaluated the link between race/ethnicity and SES and found higher rates of advanced-stage diagnosis among Black and Hispanic which are associated with increased mortality and decreased survival rates.[76] Moreover, racial differences in cervical cancer survival and mortality

outcomes have been linked to barriers to care like insurance status. A study using 1998-2003 datasets from Florida Cancer Data System and Agency for Health Care Administration found a lower survival rate for Black than non-Hispanic White women (28.8 vs 47.1 months) with invasive cervical cancer as a function of insurance status; whereby 20.8% of Black compared to 13% non-Hispanic White patients were uninsured.[77] Similarly, a 2008 multi-institution study examining cervical cancer care revealed Hispanic ethnicity was associated with higher barriers to care (e.g. public/no health insurance) compared to their non-Hispanic White counterparts, 34% and 23%, respectively which directly affects mortality and survival rates.[78]

A thorough review of the literature points to the preceding factors as contributing to differences in cervical cancer incidence, survival and mortality in Black and Hispanic women as compared to non-Hispanic White women. This review was necessary to put into context the purpose of this thesis, which examines whether differences in short-term outcomes following cervical cancer surgery exist in Black and Hispanic women relative to non-Hispanic White women treated in NSQIP hospitals. The next section delves further into objectives, specific goals and significance of this thesis.

Research Objectives, Hypothesis and Relevance

In short, the findings of the preceding literature review suggests that differences in cancer population-base indicators in minority women are influenced by factors like inconsistency in treatment, SES and care access, variability in screening patterns and awareness of risk factors.[79] [80] [81] [82] [83] Whereas a vast number of these studies explore the interlink between race/ethnicity and long-term cervical cancer outcomes, a select few evaluate short-term morbidity outcomes following surgical treatment. The research pool narrows further after adding the quality improvement variable into the equation. In fact, studies that integrate all of these variables are primarily focused on other cancers besides cervical cancer.

Research Objectives & Hypothesis

With this in mind, this thesis seeks to shed light to this missing element by analyzing the relationship between short-term morbidity after cervical cancer surgery and Black and Hispanic race/ethnicity by using ACS NSQIP databases. Thus, aim 1 of this thesis is to explore whether there are any differences among these racial or ethnic groups in 30-day-postoperative complications following surgery. Given this framework, we used nationwide data collected from a multitude of hospitals subscribing to ACS NSQIP. As described in the introduction, we opted for this database to isolate hospitals that champion quality improvement programs—programs with an overarching goal to decrease, even eliminate, patient morbidity and mortality—given their association with better health outcomes across racial/ethnic groups.[13] [14] With this in mind, aim 2 of this thesis is to observe whether using ACS NSQIP datasets yields results congruent with existing literature findings in other cancer types. A succinct review of these studies for other cancer types will follow.

A retrospective study explored postoperative 30-day morbidity and mortality after surgery for endometrial cancer and found that Black women have a significantly higher risk of surgical (17% vs. 10%) and non-surgical (7% vs. 4%) postoperative complications compared to non-Hispanic White women.[84] In a nationwide NIS investigation of post-treatment outcomes after surgical treatment for breast cancer, the odds of experiencing postoperative complications are 35% greater for Black versus non-Hispanic White patients.[85] Similarly, a cross-sectional analysis of NIS datasets showed Hispanic race/ethnicity to be associated with prolonged-length-of-stay, a measure of postop morbidity, as compared to non-Hispanic Whites, $p<0.04$.[86] Prior research indicates that Hispanic patients experience more postoperative complications like surgical site infections and prolonged hospital-stay in comparison to non-Hispanic White patients after numerous surgical procedures.[87] [88]

Whereas these studies allude to existing disparities in cervical cancer post-treatment morbidity for Black and Hispanic women, other studies have found no differences in morbidity by

race in cancer care facilities with quality improvement programs. This research studies suggests that White, Black and Hispanic patients who are managed in these facilities have no differences in short-term outcomes after endometrial and prostate cancer treatment.[89] [12] For example, there is no statistical differences along racial/ethnic lines in morbidity following post-surgical treatment for ovarian cancer or after major general surgery.[90] [91] Similarly, multiple studies show no significant differences in morbidity outcomes by race after treatment of lung, breast and colorectal cancers in NSQIP hospitals.[92] [93] [94] Extrapolating from this evidence, in this thesis, we hypothesize that short-term postoperative morbidity outcomes for Black and Hispanic women are comparable to those of White women in NSQIP participant-hospitals.

Research Significance

Ultimately, there is evidence suggestive of continued disparities in cervical cancer population-base indicator outcomes in Black and Hispanic women. This research also highlights the importance of seeking equitable care for minority populations. Eliminating cancer disparities is critical and necessary to avert the deleterious effect on the health of Black and Hispanic women and their communities. Thus, it is imperative we continue to analyze and monitor temporal trends in racial/ethnic differences via short-term morbidity outcomes, as these are potential predictors of population-base indicators.

This work contributes to this effort by examining short-term postoperative morbidity across racial/ethnic lines only in cervical cancer. To date, few studies have examined race/ethnicity and postoperative morbidity after cervical cancer surgery in ACS NSQIP data. Therefore, this thesis can shed light on whether NSQIP hospitals provide care that mitigates outcome disparities in minority women with cervical cancer. In the following chapters, we delineate the study methods, results and discussion.

CHAPTER 3: Methods

Study Design and Data Source

This is a retrospective study that investigates short-term postoperative complications after hysterectomy surgery for the treatment of cervical cancer in Black, Hispanic and non-Hispanic White patients.

We used 2011-2014 data from American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP), a large, retrospective, multihospital database. To elaborate on this database, cases represent a sample of surgeries from participating institutions with hospitals contributing about 1600 new cases yearly.[95] ACS NSQIP cases include all major cases based on Current Procedural Terminology (CPT) inclusion list and exclude cases of patients under 18 years of age.[96] Furthermore, a surgical clinical reviewer from ACS NSQIP collects data from university, private and other affiliating hospitals in the form of case files, which originate from a patient's medical chart. The database reports demographic information and 30-day morbidity and mortality variables for surgical procedures. Per guide, communication with patients by letter or telephone continues after discharge to assure a 30-day follow-up period.[95] Data collection is in compliance with HIPAA. The dataset does not contain any identifiable information on hospitals, providers or patients.[96]

Study Participants

We identified female patients who were 20 years or older who had a primary diagnosis of cervical cancer by the International Classification of Diseases (ICD-9) in the database. We continue to narrow our sample by including only patients that self-identified as Black, Hispanic and non-Hispanic White. The final sample size for this research is 1248 female patients, of which 238, 245, 377 and 388 were derived from the years 2011, 2012, 2013 and 2014, respectively.

Outcome Definitions

Outcome Variables

The primary outcome was *All-Cause Complications,* a composite variable created from several postoperative complications. Postoperative events were classified as *Surgical Site Complications, Non-Surgical Site Complications* and *All-Cause Adverse Outcomes.* A postoperative complication was defined as a patient experiencing a complication after surgery within 30-days of the procedure per the ACS NSQIP guide. To further unravel the types of complications experienced, the primary outcome was broken down into the aforementioned components and analyzed as outcome variables. The first component, *Surgical Site Complications,* was created by essentially tabulating complication events across different existing variables that pertained to wound-related outcomes. Specifically, *Surgical Site Complications* was defined as sequelae of superficial site infection, deep incision infection, organ/space site infection or wound dehiscence. Similarly, the second component of the primary outcome, *Non-Surgical Site Complications,* was devised by combining major complication events exempting wound-related events. The *Non-Surgical Site Complications* component was constructed from ACS NSQIP variables describing postoperative occurrences of pneumonia, acute renal failure or progressive renal failure, urinary tract infection, deep venous thrombophlebitis, pulmonary embolism, bleeds requiring transfusion, sepsis or septic shock, ventilator use >48 hours, unplanned intubation, cerebrovascular accidents or stroke, myocardial infarction or cardiac arrest.

Essentially, the primary outcome was the total number of events, coded as 0/1, summed across *Surgical Site Complications, Non-Surgical Site Complications and All-Cause Adverse Outcomes.* Lastly, *All-Cause Adverse Outcomes* were generated by combining the variables of prolonged length of stay (LOS) and return to the operating room for any reason relating to the surgery. LOS refers to the number of days from surgery to hospital discharge. As it is customary with NSQIP data, we characterized LOS as a stay beyond the 75th percentile for the entire 1,248 cases.[97] In this project,

75% of the cohort was discharged before postoperative day 3.75. Using 3.75 days as a reference, prolonged LOS was transformed into a dichotomous variable; patient LOS under 3.75 days or beyond 3.75 days.

Independent Variables

The research investigation posit race as the independent variable (IV). Specifically, the IV was race or ethnicity as defined by non-Hispanic White, Black and Hispanic. The independent variable was generated from the *new race* and *ethnicity Hispanic* variables included in the database. Ultimately, the race or ethnicity variable includes only cases noted as *Black, White and Yes Hispanic.* For the purposes of data analysis, the race variable was transformed from string to numeric categories and defined as non-Hispanic White=1, Black=2, Hispanic=3.

Additional Variables

In order to account for covariates, it was necessary to recode and create new variables based on variables in the ACS NSQIP database. Please refer to appendix for complete list of the main variables utilized in these analyses. Variables that were created or recoded to generate patient demographics include; *age, height, weight, current smoker within one year, functional health status prior to surgery, ASA classification, disseminated cancer, >10% loss of body weight in the last 6 months.* Similarly, variables recoded for comorbid conditions are *diabetes on agents or insulin, dyspnea, hypertension requiring medication, history of COPD, congestive heart failure (CHF) 30 days prior to surgery, renal failure preoperative or preop, currently on dialysis (preop).* Other database variables that were transformed to denote pre- and intraoperative variables are: *preop transfusion of ³ 1 unit pRBCs, preop BUN, preop serum creatinine, preop albumin, preop WBC, preop hematocrit, preop platelet count, total operation time, work relative value unit, concurrent relative value unit 1-10 and other work relative value unit 1-10.*

In order to capture any age effects, the variable age was recoded using the age distributions reported in the Surveillance, Epidemiology, and End Results (SEER) program for cervical cancer.[2] Statistics for cervical cancer cases for years 2009-2013 indicate that cervical cancer is most frequently diagnosed in American women ages 35-44. However, since women are also often diagnosed at age of 20-34, 45-54, 55-64 and 65-74, we capture these ranges in the demographic information.[2] To clarify, both the age group and age as a continuous variable are investigated. Additionally, body mass index (BMI) is a new variable that generated from height and weight. BMI was then transformed into four BMI ranges based on the standardized weight category. For the purposes of this study the ranges and standardized weight classifications include; below 18.5, 18.5-24.9, 25.0-29.9, 30.0 and above, each defined as underweight normal weight, overweight and obese, respectively.[98]

Several preoperative clinical indicators were analyzed in this thesis as multiple research studies have confirmed their role in predicting morbidity and mortality after surgery. These laboratory values required re-coding prior to analysis. Preoperative serum creatinine (Cr) was transformed into a dichotomous variable based on Cr levels greater than or equal to 1.0 mg/dL or less than that threshold. This threshold was selected given that at moderate levels and definitely at level of 1.5, Cr was found to serve as a significant predictor of morbidity and mortality after surgery.[99] Similarly, preoperative serum albumin was converted to a dichotomous variable using the threshold less than or equal to 3 g/dL or greater since a decrease in serum albumin was linked to higher rates of morbidity ranging between 10-65% postoperatively.[100]

Likewise, hematocrit (Hct) was modified to a dichotomous variable defined as either, less than or equal to 38% or greater to account for the odds of increased morbidity postoperatively are 1.24 times as great for levels below this marker than above.[101] [15] White blood cell count (WBC) was reclassified into levels above and below 11 k/uL. Elevated WBC has been shown to be predictive of increased morbidity with odds 1.21 times greater with higher counts compared to lower counts.[100] In

a similar fashion, preoperative platelet count was recoded in terms of levels equal to or below 150k and above. Studies investigating postoperative morbidity have identified platelet count equal to or below 150k as an important predictor of morbidity, OR= 1.29, $p<0.05$.[102] [101] Blood urea nitrogen (BUN) was categorized into either greater than or less than 40 as at this reference level BUN is a predictive variable for postoperative morbidity.[101]

The set of physician work relative value (RVU) variables are combined to generate a *cumulative RVU* variable, which yields the sum of work relative value per case. The recoding of these variables is necessary given work RVU is used as a marker of operative complexity and predictive of operative mortality.[103] Moreover, the variable *surgery treatment* was developed from CPT codes either specifying hysterectomy or fertility sparing procedure whereby non-fertility sparing procedure was coded as 0 and fertility sparing as 1. Furthermore, an independent variable *non-fertility sparing* was created to be able to classify hysterectomies into abdominal=1, vaginal=2, laparoscopic=3 and unknown hysterectomy=4. Similarly, an independent variable *fertility sparing* was created to categorize procedures based on conization/LEEP=0 and trachelectomy=1.

Inclusion & Exclusion Criteria

For this study only women with a cervical cancer diagnosis as specified by the ICD-9 were included in the analysis. Since we were interested in comparing postoperative complication events by race, only women whom identified as non-Hispanic White, Black and Hispanic are included. On the basis of these criteria, no cases were excluded if the race/ethnicity identifier was non-Hispanic White, Black or Hispanic. For this thesis we only used cases with a complete set of data on race, ICD 9 diagnosis and CPT code information.

Furthermore, it is important to note that clinically most patients only have information for a limited range of laboratory values during a hospitalization. Since only relevant and appropriate labs may be ordered patients do not require orders for all preoperative laboratory tests. This in turn,

creates missing values across patients' files. As a result of this, some of these variables in the ACS NSQIP database have a high percentage of missing values, ranging from 15-45%.[95] Since a high percentage of missing data can affect the results of a logistic regression model, we used only variables that have a complete dataset. Ultimately, lab variables with a high percentage of missing values were not included in our analyses but we did include variables known historically and from the literature to influence the results of this research.

Statistical Analysis

Multivariate logistic regression analyses are performed to evaluate models that might predict short-term postoperative complications based on race/ethnicity, the IV, after adjusting for demographic, pre- and postoperative characteristics. In this analysis only predictors of short-term postoperative outcomes without missing values were included, please refer to the inclusion criteria section for more details.

We compared the unadjusted differences in patient short-term postoperative outcomes and surgery received across patient racial/ethnic groups using chi-square tests. Additional confounders are identified via chi-squared analyses in order to explore a possible association between covariates, the IV and other outcome variables. The covariates included in the short-term postoperative outcomes study are race/ethnicity, age, smoking status, ASA classification, BMI, hypertension, diabetes, Hct, WBC and non-fertility sparing surgery. BMI and age variables were included as covariates in the continuous and categorical forms given previous research shows an associated between these and the IV.

All covariates were found to be associated with the primary outcome and IV except for age, smoking status and non-fertility sparing surgery; however, these were included in the regression models given their known association with the primary outcome. For analyses, statistical significance was set at p value <0.05. All statistical analyses were performed using SPSS version 20.

CHAPTER 4: Results

Sample Demographics

Baseline characteristics for the 1,248 female patients are depicted in Tables 2-5**.** The reference group for all analyses is White race. The average age of diagnosis was 47 years. We reviewed five age groups with the approximate average within each group being 30, 39, 49, 58, 71 years, respectively. In this study, 70% of the cohort was non-Hispanic White, 12% Black and 16% Hispanic. On average, 31% of non-Hispanic White women and 35% Black women were current smokers. The average BMI for this cohort was 29.3 or overweight. In particular, 59% of Black and 41% of Hispanic women were obese with BMI >30, compared to only 36% of non-Hispanic White women. In this cohort, Black and Hispanic women have higher percentages of diabetes, 12% and 10%, respectively, relative to their non-Hispanic White counterparts (5%). A greater proportion of Black than White female patients had hypertension (42% vs. 23%), cardiac (9% vs. 2%) and pulmonary conditions (4% vs. 1%) and had ASA scores of 3 or greater (48% vs. 35%). All p values <0.05. In this sample, 90% of patients underwent hysterectomy and only 9% underwent a fertility-sparing procedure. There were no statistically significant differences across race/ethnicity in the proportion of subjects undergoing fertility-sparing procedures or in hysterectomy route.

To summarize these demographic findings, in comparison to non-Hispanic White female patients, Black and Hispanic patients had higher proportions of obesity and diabetes. Also Black female patients, relative to non-Hispanic White patients, had greater proportion of comorbidities like hypertension, cardiac and pulmonary conditions and higher ASA classification—indicative of more systemic disease.

Unadjusted and Multivariate Analyses

Table 6 shows the results of univariable analyses which evaluate the impact of race/ethnicity on 30-day outcomes after surgery in women with cervical cancer. All analyses use non-Hispanic White race as the reference group. Unadjusted analyses showed that Black patients experience statistically significantly higher rates, 48%, of any postoperative complication compared to White patients, 35%, $p<0.01$. Specifically, Black women experienced higher unadjusted rates in all complication subdivisions, including All-Cause Adverse Outcomes (B 36% vs W 27%, $p<0.01$), Non-Surgical Site (B 28% vs W 19%, $p<0.01$) and Surgical Site (B 8% vs W 4%, $p>0.05$). On the other hand, relative to complication rates (35%) in White women, Hispanic patients experienced lower rates (29%) of any type of complication, $p<0.01$.

Moreover, unadjusted logistic regression analyses show Black race to be a predictor of any postoperative complications (OR=1.73, 95% CI 1.23-2.44, $p<0.05$; Table 7) which includes All-Cause Adverse outcomes (OR=1.56; 95% CI 1.10-2.22, $p<0.05$; Table 8), Surgical Site (OR=1.97; 95% CI 1.05-3.70), $p<0.05$; Table 9) and Non-Surgical Site (OR=1.72; 95% CI 1.18-2.53, $p<0.05$; Table 10) complications subcategories. In contrast, Hispanic ethnicity was not found to be a predictor of All-Cause complications or subdivisions excepting All-Cause Adverse outcomes (OR=0.64; 95% CI 0.44-0.93, $p<0.05$; Table 10).

Multivariate Analysis

The results of multivariable analyses examining the effect of race/ethnicity on any short-term postoperative complications after adjusting for age, smoking status, ASA class, BMI, hct, WBC, non-fertility sparing surgery and associated comorbidities are shown on Table 7. The logistic regression model was statistically significant, $c^2(12)=94.54$, $p<0.001$. The model explained 10.1% (Nagelkerke R^2) of the variance in any complication occurrences and correctly classified 68.2% of the cases.

Considering All-Cause Complications, Black race was an independent predictor of any complications, (OR=1.50; 95% CI 1.04-2.16, $p<0.05$). On the other hand, Hispanic ethnicity was not an independent predictor of any postoperative complications (OR 0.76, 95% CI 0.54-1.08, $p>0.05$). In fact, only Black race, ASA class, Htc, WBC and non-fertility sparing surgery were independent predictors of 30-day postoperative morbidity. Patients with ASA class ≥ 3 were 84% (OR=1.84; 95% CI 1.42-2.40) more likely to experience postoperative complications compared to patients with ASA class ≤2. Compared to patients with Hct ≥38%, those with Htc ≤38% were 81% (OR=1.81; 95% CI 1.41-2.32) more likely to have post-surgical morbidity. Women with WBC >11 k/mL, were 63% (OR=1.63; 95% CI 1.15-2.32) more likely to be afflicted with 30-day adverse outcomes than those with WBC<11. Lastly, patients undergoing hysterectomy were 60% (OR=1.60; 95% CI 1.03-2.51) more likely to face postoperative complications relative to those undergoing fertility sparing procedures. Also, there were no differences among the abdominal, vaginal and laparoscopic routes of hysterectomy.

A logistic regression was performed for each of the 3 subcategories of All-Cause Complications to ascertain the effects of Black race, Hispanic ethnicity, demographics, clinical characteristics and associated comorbidities on the likelihood that participants have 30-day All-Cause Adverse Outcomes, Surgical Site Complications and Non-Surgical Site Complications (Tables 8-10). The multivariable model for All-Cause Adverse outcomes was statistically significant $c^2(12)=117.74$, $p<0.001$. The model explained 13.1% (Nagelkerke R^2) of the variance in prolonged LOS and return to OR and correctly classified 74.9% of the cases. Furthermore, the global model for Non-Surgical Site Complications, was statistically significant $c^2(12)=68.54$, $p<0.001$. The model explained 8.5% (Nagelkerke R^2) of the variance in non-surgical related morbidity and correctly classified 80.2% of the cases. Lastly, the overall fit of the logistic regression model for Surgical Site

Complications by race was not statistically significant $c^2(12)=16.73$, $p=0.16$. The model explained 3.9% (Nagelkerke R^2) of the variance in surgically related complications.

Results of the multivariable models for the 3 subdivisions of All-Cause Complications, Black patients have greater odds of experiencing Non-Surgical Site complications after surgery for cervical cancer (OR=1.55; 95% CI 1.03-2.33, $p<0.05$; Table 10) compared to their non-Hispanic White counterparts. While results are indicative of a trend suggestive of Black women having greater odds of developing Surgical Site Complications (OR=1.85; 95% CI 0.94-3.65); Table 9) and All-Cause Adverse Outcomes (OR=1.35; 95% CI 0.92-1.99, Table 8), the differences were not statistically significant. Results for Hispanic women exhibited a reverse pattern to those observed in Black women. Specifically, Hispanic patients had lower odds of experiencing All-Cause Adverse Outcomes (OR=0.65; 95% CI 0.44-0.97, $p<0.05$) and comparable odds of Non-Surgical Site complications (OR=0.85; 95% CI 0.55-1.29) relative to non-Hispanic White patients.

In sum, the adjusted logistic regression model for All-Cause Adverse Outcomes, Hispanic ethnicity, age, ASA class, BMI, Htc and WBC were found to be independent predictors of prolonged LOS and Return to OR (Table 8). Factors associated with Non-Surgical Site complications are Black race, ASA class, diabetes, cardiac/pulmonary comorbidities, Htc, WBC and non-fertility conserving surgery. Results of the logistic regression indicate the model for Surgical Site Complications does not fully capture the data resulting in poor goodness of fit. BMI was the only independent predictor of surgical related complications.

CHAPTER 5: Discussion

In our study of 1248 patients with cervical cancer undergoing surgery in ACS NSQIP hospitals, we examined the relationship between race/ethnicity and postoperative outcomes. We hypothesized that the short-term postoperative outcomes for Black and Hispanic women would be comparable to those of non-Hispanic White women. Interestingly, our findings only partially support the hypothesis. For instance, we found Black and Hispanic patients were more likely to have higher levels of comorbidities, but only Black and not Hispanic, relative to non-Hispanic White patients were more likely to experience adverse outcomes postoperatively. A stepwise analysis of all complications revealed that among All-Cause Complications only non-wound complications were found to be significantly higher among Black compared to White women, even after adjusting for confounders. Although a trend towards increased rates in surgical complications, prolonged LOS and return to OR was also observed for Black patients, these effects dissipated after controlling for covariates. Consequently, these results suggest that complication rates in Black women for these three outcome measures are comparable to non-Hispanic White patients. Conversely, Hispanic women in this cohort were less or comparably likely to have adverse short-term postoperative complications as their White counterparts.

We briefly revisit the objectives of this study and summarize our major findings. Objective 1 was to evaluate 30-day-postoperative complications following surgery among Black, Hispanic and non-Hispanic White women. In sum, our results show that Black women, relative to White women do experience higher rates of short-term non-wound-related complications. But no differences in short-term outcomes exist between Hispanic and White patients. In objective 2, we examined whether our analyses of NSQIP data were consistent with the current literature that suggests that disparities in short-term outcomes are lessened by hospitals with quality improvement programs.

Our analyses of NSQIP data depict existing disparities in cervical cancer in Black patients but not for Hispanic patients. Thus our results are only partially consistent with existing literature.[86 88 85 94 102]

Prior reports on racial disparities of short-term morbidity in cervical cancer are limited. However, several studies have found racial disparities in operative outcomes after cancer surgery for Black patients in similar and in different hospital settings.[86 84 85 104] In corroboration with these studies, our results suggest that Black patients with cervical cancer experience higher rates of non-surgical related adverse postoperative outcomes with diminution in disparities observed for prolonged LOS, reoperation and surgical complications in ACS NSQIP hospitals.

In our study, minority patients were more likely to have preoperative risk factors like active smoking, ASA class 3, higher BMI and chronic conditions, some of which are associated with postoperative morbidity in multivariable analysis. Consequently, this association may only partially explain the observed differences in short-term adverse outcomes between Black and non-Hispanic White patients because this effect persists even after controlling for these covariates. Conjecture regarding other contributing factors include uninsured status, SES, higher likelihood delayed diagnosis, having more aggressive tumor characteristics, differential treatment or clustering in lower-income hospitals.[105 10 106 107 108] These factors likely compound the probability of disparities downstream. Therefore intervening early on in this trajectory may help disrupt negative post-treatment outcomes.

Notwithstanding some of the favorable findings, it must be appreciated that important racial/ethnic differences in care upstream and downstream still exist for Hispanic women. In fact, several studies have highlighted continued disparities in SES, insurance status, preventive screening and treatment for cervical cancer in Hispanic women; all correlates of overall disease patterns for cervical cancer.[73 106 109 110] Important to interpreting these findings is understanding that Hispanic are an extremely diverse group with multiple ancestries and cultural influences, immigration patterns and

health trends.[111] In our optimism we remain cognizant of these differences and are mindful not to amalgamate Hispanic into one homogenous group and assume an equitable improvement in medical care across all subgroups.

Our findings also identified several independent predictors of adverse postoperative complications like ASA class, Htc level, WBC count and Non-fertility sparing surgery. In conjunction with prior studies that evaluated postoperative adverse outcomes following surgical treatment of cervical cancer and other gynecological malignancies; we also found higher ASA class, anemia of Hct less than 38%, leukocyte WBC count greater than 11 k/mL and hysterectomy surgery to be positively associated with postoperative complications.[112] [113] [114] [115] Except for surgical procedure, our results suggest the preceding factors in combination with age and BMI are linked to prolonged LOS and reoperation. Consistent with findings in Procter et al. and Anupama et al., we found ASA III and greater, decreased Htc, elevated WBC count, increasing age and decreased BMI to predict extended hospital stay and reoperations after gynecologic surgery.[116] [117]

Multiple significant correlates of non-surgical site complications like ASA classification, anemia, leukocytosis, hysterectomy surgery, and medical comorbidities—DM, cardiac and pulmonary—were identified. Likewise, retrospective and prospective studies investigating these variables in association with non-wound related adverse outcomes, have found them to increase the risk of complications after surgery for gynecological malignancy.[91] [118] [119] [120] [121] Our finding revealed higher BMI to be the only significant predictor of wound-related complications. This result is consistent with the literature, in which overweight and obesity predict adverse surgical site outcomes after gynecologic oncologic surgeries.[115] [122]

Study Limitations

Notable limitations in these studies should be considered when interpreting results. A limitation in this study is that it does not include critical demographic information like insurance

status, income, education and other measures of socioeconomic (SES) status that can greatly contribute to the interpretation of our results. Thus, this study is unable to adjust for patients' SES and insurance status, which are strongly linked to race and disparities in medical care. Since we lack information on important SES identifiers, we cannot assess whether differences exist in minority patients treated in ACS NSQIP hospitals versus minority patients treated in other hospital settings. Consequently, we are limited in our ability to formulate conclusions and inferences about improvements in care for minority patients treated in NSQIP hospitals relative those treated in other types of hospitals, since these samples may be in fact inherently different. Likewise, using NSQIP data has some inherent limitations like the lack of data collection beyond 30 days postoperatively. This limitation prohibits us from evaluating whether differences in complication rates exist beyond the threshold period of 30-days since this database cannot capture long-term health effects.

Other limitations of this study include the inability to adjust for stage of disease, which is widely known to impact treatment, survival and outcomes. Prior to 2014 ACS NSQIP did not collect information on cancer staging, but even in 2014 data, staging information was reported only for selected cases, as a result we could not incorporate staging as a covariate. Furthermore, not all factors associated with 30-day postoperative complications were adjusted for in the logistic regression model since these were not found to be significantly associated with any of the outcome variables or to the IV. For instance, our models did not account for operative time and cumulative RVU, both measures of operative complexity, which have been demonstrated to predict postoperative morbidity.[105 106 108] These variables were not included in the analyses since this cohort did not exhibit any differences across race/ethnicity for either operation time or cumulative RVU. Moreover, we can assume that operative complexity was accounted by controlling for medical comorbidities and clinically significant preoperative characteristics like ASA class, Htc, WBC and type of surgery performed.

CHAPTER 6: Conclusion

Brief Conclusion

This study contributes important findings that can potentially help assess existing differences in cervical cancer in survival and mortality trends among Black and Hispanic women. Furthermore, our findings also offer a unique outlook from which to view race and ethnic differences in health outcomes in ACS-NSQIP hospitals. This study highlights continued postoperative morbidity after cervical cancer surgery for Black women at a level that differs significantly from non-Hispanic White women. These effects remain significant even after controlling for important covariates and even when studied at hospitals subscribing to ACS-NSQIP. Our study has identified this differential pattern only in non-surgical related morbidity. In accordance with prior studies, there was less disparity in postoperative outcomes for Hispanic patients compared to non-Hispanic White patients. While several of our findings were corroborated by previous reports in the literature, further research is needed to evaluate causal mechanisms contributing to racial and ethnic disparities in postoperative outcomes. Ultimately, several factors contribute to disparities in cervical cancer incidence, survival and mortality, but it remains important to underscore immediate differences in outcomes to formulate interventions that may lessen the effects of the social determinants of health.

TABLES: Cervical Cancer Staging

Table 1. FIGO Staging Classification: Cervical Cancer

Primary Tumor	Pathologic Findings
Stage 0	Carcinoma in situ
Stage IA1	Invasive carcinoma, confined to cervix. Stromal invasion ≤ 3mm in depth and ≤ 7mm in horizontal spread.
Stage IA2	Invasive carcinoma, confined to cervix. Stromal invasion > 3mm and ≤ 5mm in depth and ≤ 7mm in horizontal spread.
Stage IB1	Invasive carcinoma, confined to cervix. Lesion > IA2 or clinically visible lesion ≤ 4cm in greatest dimension.
Stage IB2	Invasive carcinoma, confined to cervix. Clinically visible lesion > 4cm in greatest dimension.
Stage IIA	Tumor extension beyond cervix to vagina but not to lower third of vagina. No parametrical invasion.
Stage IIB	Tumor extension beyond cervix. Parametrical invasion but not to pelvic sidewall and not to lower third of vaginal.
Stage IIIA	Tumor extension to lower third of vagina but not to pelvic sidewall.
Stage IIIB	Tumor extension to pelvic sidewall or causing hydronephrosis or nonfunctioning kidney.
Stage IVA	Tumor invasion into bladder or rectum.
Stage IVB	Distant metastasis.

International Federation of Genecology and Obstetrics (FIGO). Data from Creasman.[24]

TABLES: Patient Demographics

Table 2. Patient Demographic and Preoperative Characteristics (N=1248)

Characteristic	p (%)	μ (s.d.)
Demographics and Preoperative Characteristics		
Age, y		47.2 (13.0)
19—34	208 (16.7)	30.5 (3.2)
35—44	401 (32.1)	39.7 (2.8)
45—54	283 (22.7)	49.2 (2.7)
55—64	213 (17.1)	58.7 (2.8)
65 or older	143 (11.5)	71.9 (5.8)
Race or Ethnicity		
Non-Hispanic White	881 (70.6)	
Black	160 (12.8)	
Hispanic	207 (16.6)	
Current Smoker	348 (27.9)	
Independent Functional Health Status	1235 (99.0)	
ASA Class		
1 + 2	782 (62.7)	
≥ 3	466 (37.3)	
Cardiac Conditions	37 (3.0)	
Pulmonary Conditions	25 (2.0)	
Renal Conditions	6 (0.5)	
Hypertension	327 (26.2)	
Diabetes	93 (7.5)	
BMI		29.3 (8.1)
Underweight	41 (3.3)	
Healthy Weight	381 (30.5)	
Overweight	324 (26.0)	
Obese	496 (39.7)	
Weight loss, >10% loss body weight	27 (2.2)	
Disseminated Primary Neoplasm	56 (4.5)	
Preoperative Laboratory values		
Creatinine ≥1.0 mg/dL, n=1146	1122 (91.8)	
Albumin ≤ 3.0 g/dL, n=686	70 (5.6)	
Hct ≤ 38%	593 (47.5)	
WBC > 11 k/μL, n=1248	165 (13.2)	
Platelet Count ≤ 150s or ≥ 450s, n=1245	86 (6.9)	
BUN> 40 mg/dL, n=1103	8 (0.6)	

P or proportions (%) values are calculated using N=1248 or n for that variable. μ=standard deviation (s.d). ASA, American Society of Anesthesiologists Classification of Physical Status (1=normal 2=mild disease ≥ 3=severe to moribund).

TABLES: Patient Demographics Continued

Table 3. Intraoperative and Surgical Procedure Characteristics (N=1248)

Characteristic	p (%)	μ (s.d.)
Intraoperative Characteristics		
Operative Time, m		205.0 (109.5)
Cumulative RVU		33.4 (17.9)
Blood Transfusion, ≥1 unit pRBCs	16 (1.3)	
Operative Characteristics		
Surgical Procedure		
Fertility Sparing	116 (9.3)	
Conization or LEEP	73 (5.8)	
Trachelectomy	43 (3.4)	
Non-Fertility Sparing	1132 (90.7)	
Abdominal Hysterectomy	495 (39.7)	
Vaginal Hysterectomy	108 (8.7)	
Laparoscopic Hysterectomy	509 (40.8)	
Unknown Hysterectomy	20 (1.6)	

P=proportion (%) values are calculated using N=1248 or n for that variable. μ=standard deviation (s.d). RVU, work relative value unit.

TABLES: Demographics as a function of Race/Ethnicity

Table 4. Patient Demographic and Preoperative Characteristics by Race or Ethnicity (N=1248)

Characteristic	Non-Hispanic White (n=881)	Black (n=160)	Hispanic (n=207)	P Value
Demographics and Preoperative Characteristics				
Age, y	47.5 (13.2)	47.7 (12.8)	45.81 (12.3)	0.216[F] (1.5) 0.266
20—34	150 (17.0)	24 (15.0)	34 (16.4)	
35—44	274 (31.1)	48 (30.0)	79 (38.2)	
45—54	194 (22.0)	41 (25.6)	48 (23.2)	
55—64	153 (17.4)	33 (20.6)	27 (13.0)	
65 or older	110 (12.5)	14 (8.8)	20 (9.5)	
Current Smoker	273 (31.0)	57 (35.6)	18 (8.7)	<0.001
Independent Functional Health Status	874 (99.4)	157 (98.7)	204 (99.9)	0.234[a]
ASA				<0.01
1 + 2	564 (64.1)	82 (51.2)	136 (65.7)	
≥ 3	316 (35.9)	78 (48.8)	71 (34.3)	
Cardiac Conditions	20 (2.3)	15 (9.4)	2 (1.0)	<0.001[a]
Pulmonary Conditions	17 (1.9)	7 (4.4)	1 (0.5)	<0.05[a]
Renal Conditions	2 (0.2)	2 (1.2)	2 (1.0)	0.080[a]
Hypertension	208 (23.6)	68 (42.5)	51 (24.6)	<0.001
Diabetes	51 (5.8)	20 (12.5)	22 (10.6)	<0.01
BMI	28.7 (7.7)	33.2 (10.6)	29.1 (6.3)	<0.001[W] <0.001
Underweight	28 (3.2)	6 (3.8)	7 (3.4)	
Healthy Weight	300 (34.2)	33 (20.6)	48 (23.3)	
Overweight	232 (26.5)	26 (16.2)	66 (32.0)	
Obese	316 (36.1)	95 (59.4)	85 (41.3)	
Weight loss, >10% loss body weight	15 (1.7)	6 (3.8)	6 (2.9)	0.183
Disseminated Primary Neoplasm	36 (4.1)	11 (6.9)	9 (4.3)	0.291
Preoperative Laboratory values				
Creatinine ≥1.0 mg/dL, n=1146	786 (97.9)	148 (97.4)	177 (92.7)	<0.05[a]
Albumin ≤ 3.0 g/dL, n=562	42 (9.0)	13 (13.5)	15 (12.1)	0.305
Hct ≤ 38%	368 (41.8)	110 (68.8)	115 (55.8)	<0.001
WBC > 11 k/μL	129 (14.6)	19 (11.9)	17 (8.2)	<0.05
Platelet Count ≤ 150s	58 (6.6)	17 (10.7)	11 (5.3)	0.108
BUN> 40 mg/dL	4 (0.5)	2 (1.4)	2 (1.1)	0.268[a]

Chi-Square test, p=proportion (%), except where noted; [a]Fisher's Exact Test if expected count less than 5. [F]ANOVA (F), μ=standard deviation (s.d.); Welch [W]p-value if Levene <0.05. ASA, American Society of Anesthesiologists Classification of Physical Status (1=normal 2=mild disease ≥ 3=severe to moribund).

TABLES: Demographics as a function of Race/Ethnicity Continued

Table 5. Intraoperative and Surgical Procedure Characteristics by Race or Ethnicity (N=1248)

Characteristic	Non-Hispanic White (n=881)	Black (n=160)	Hispanic (n=207)	P Value
Intraoperative Characteristics				
Operative Time, m	205.4 (109.4)	207.8 (108.6)	201.2 (111.1)	0.831[F] (0.19)
Cumulative RVU	33.3 (17.8)	34.1 (20.3)	33.1 (16.4)	0.881[F] (0.13)
Blood Transfusion, ≥1 unit pRBCs	10 (1.1)	4 (2.5)	2 (1.0)	0.370[a]
Operative Characteristics				
Surgical Procedure				0.542
Fertility Sparing	77 (8.7)	18 (11.2)	21 (10.1)	
Non-Fertility Sparing	804 (91.3)	142 (88.8)	186 (89.9)	
Fertility Sparing Procedures				<0.05
Conization or LEEP	45 (58.4)	16 (88.9)	12 (57.1)	
Trachelectomy	32 (41.6)	2 (11.1)	9 (42.9)	
Non-Fertility Sparing Procedures				0.228[a]
Abdominal Hysterectomy	339 (42.2)	71 (50.0)	85 (45.7)	
Vaginal Hysterectomy	76 (9.5)	14 (9.9)	18 (9.7)	
Laparoscopic Hysterectomy	378 (47.0)	53 (37.3)	78 (41.9)	
Unknown Hysterectomy	11 (1.4)	4 (2.8)	5 (2.7)	

Chi-Square test, p= proportions (%), except where noted; [a]Fisher's Exact Test if expected count less than 5. [F]ANOVA (F), μ=standard deviation (s.d.). RVU, work relative value unit.

TABLES: Univariate Results

Table 6. Short-Term Postoperative Outcomes by Race/Ethnicity (N=1248)

Outcome Variable	Non-Hispanic White (n=881)	Black (n=160)	Hispanic (n=207)	P Value
All-Cause Complications	314 (35.6)	78 (48.8)	61 (29.5)	<0.01
All-Cause Adverse Outcomes	240 (27.2)	59 (36.9)	40 (19.3)	<0.01
Surgical Site Complications	41 (4.7)	14 (8.8)	12 (5.8)	0.102
Non-Surgical Site Complications	168 (19.1)	46 (28.7)	35 (16.9)	<0.01

Chi-Square test, p=proportions (%). All-Cause Complications= All-Cause Adverse Outcomes + Surgical Site Complications + Non-Surgical Site Complications.

TABLES: Multivariate Results

Table 7. All-Cause Complications by Race or Ethnicity (N=1248)

Characteristic	Unadjusted	Model 1: Race/Ethnicity + Demographics	Model 2: Model 1 + Comorbid Conditions	Model 3: Model 2 + Clinical Characteristics
Race or Ethnicity				
Non-Hispanic White	Ref.	Ref.	Ref.	Ref.
Black	1.73 (1.23-2.44)*	1.67 (1.17-2.3)*	1.64 (1.15-2.34)*	1.50 (1.04-2.16)*
Hispanic	0.75 (0.54-1.05)	0.80 (0.57-1.13)	0.80 (0.57-1.12)	0.76 (0.54-1.08)
Age, y	NA	1.01 (1.002-1.02)*	1.01 (1.00-1.02)	1.01 (1.00-1.02)
Current Smoker	NA	1.13 (0.86-1.48)	1.10 (0.84-1.45)	1.11 (0.84-1.48)
ASA Classification	NA			
1+2	NA	Ref.	Ref.	Ref.
≥ 3	NA	1.99 (1.55-2.57)*	1.94 (1.50-2.52)*	1.84 (1.42-2.40)*
BMI	NA	0.99 (0.98-1.01)	0.99 (0.98-1.01)	0.98 (0.97-1.00)
HTN	NA	NA	1.15 (0.83-1.59)	1.07 (0.77-1.49)
DM	NA	NA	0.98 (0.61-1.58)	1.07 (0.66-1.73)
Cardiac/Pulmonary Cond.	NA	NA	2.3 (0.53-9.6)	2.3 (0.55-10.0)
Hct ≤ 38%	NA	NA	NA	1.81 (1.41-2.32)*
WBC > 11 k/μL	NA	NA	NA	1.63 (1.15-2.32)*
Non-fertility Sparing Surgery	NA	NA	NA	1.60 (1.03-2.51)*
[a]P Value	<0.01	<0.001	<0.001	<0.001

[a]Logistic Regression Models, p-value. Odds ratio (95% confidence interval). *Odds ratio shows statistically significant effect, p<0.05. NA, variable not applied in Model. All-Cause Complications= All-Cause Complications= All-Cause Adverse Outcomes + Surgical Site Complications + Non-Surgical Site Complications.

Table 8. All-Cause Adverse Outcomes by Race or Ethnicity (N=1248)

Characteristic	Unadjusted	Model 1: Race/Ethnicity + Demographics	Model 2: Model 1 + Comorbid Conditions	Model 3: Model 2 + Clinical Characteristics
Race or Ethnicity				
Non-Hispanic White	Ref.	Ref.	Ref.	Ref.
Black	1.56 (1.10-2.22)*	1.52 (1.05-2.21)*	1.48 (1.01-2.16)*	1.35 (0.92-1.99)
Hispanic	0.64 (0.44-0.93)*	0.68 (0.46-1.01)	0.68 (0.46-1.01)	0.65 (0.44-0.97)*
Age, y	NA	1.02 (1.006-1.03)*	1.01 (1.001-1.02)*	1.01 (1.002-1.03)*
Current Smoker	NA	1.09 (0.81-1.46)	1.05 (0.77-1.41)	1.06 (0.78-1.44)
ASA Classification	NA			
1+2	NA	Ref.	Ref.	Ref.
≥ 3	NA	2.51 (1.91-3.31)*	2.42 (1.83-3.21)*	2.29 (1.72-3.04)*
BMI	NA	0.98 (0.97-1.00)	0.98 (0.97-0.999)*	0.98 (0.96-0.99)*
HTN	NA	NA	1.24 (0.88-1.74)	1.15 (0.81-1.63)
DM	NA	NA	0.99 (0.60-1.64)	1.07 (0.64-1.80)
Cardiac/Pulmonary Cond.	NA	NA	3.30 (0.76-14.2)	3.38 (0.77-14.8)
Hct ≤ 38%	NA	NA	NA	1.86 (1.42-2.44)*
WBC > 11 k/μL	NA	NA	NA	1.68 (1.16-2.43)*
Non-fertility Sparing Surgery	NA	NA	NA	1.53 (0.93-2.52)
[a]P Value	<0.01	<0.001	<0.001	<0.001

[a]Logistic Regression Models; p-value. Odds ratio (95% confidence interval). *Odds ratio shows statistically significant effect, p<0.05. NA=variable not applied in Model. All-Cause Adverse Outcomes= Prolonged LOS + Return to OR.

TABLES: Multivariate Results Continued

Table 9. Surgical Site Complications by Race or Ethnicity (N=1248)

Characteristic	Unadjusted	Model 1: Race/Ethnicity + Demographics	Model 2: Model 1 + Comorbid Conditions	Model 3: Model 2 + Clinical Characteristics
Race or Ethnicity				
Non-Hispanic White	Ref.	Ref.	Ref.	Ref.
Black	1.97 (1.05-3.70)*	1.71 (0.89-3.28)	1.81 (0.94-3.51)	1.85 (0.94-3.65)
Hispanic	1.26 (0.65-2.44)	1.26 (0.63-2.53)	1.34 (0.66-2.71)	1.34 (0.66-2.73)
Age, y	NA	1.01 (1.00-1.03)	1.02 (0.99-1.04)	1.01 (0.99-1.04)
Current Smoker	NA	1.39 (0.80-2.42)	1.32 (0.74-2.33)	1.30 (0.73-2.32)
ASA Classification	NA			
1+2	NA	Ref.	Ref.	Ref.
≥ 3	NA	1.03 (0.60-1.75)	1.11 (0.64-1.91)	1.13 (0.65-1.96)
BMI	NA	1.02 (1.00-1.05)	1.03 (1.004-1.06)*	1.03 (1.003-1.06)*
HTN	NA	NA	0.71 (0.36-1.40)	0.71 (0.36-1.41)
DM	NA	NA	0.43 (0.12-1.48)	0.45 (0.13-1.58)
Cardiac/Pulmonary Cond.	NA	NA	4.83 (0.91-25.7)	5.21 (0.97-27.9)
Hct ≤ 38%	NA	NA	NA	0.91 (0.54-1.53)
WBC > 11 k/μL	NA	NA	NA	0.81 (0.36-1.80)
Non-fertility sparing surgery	NA	NA	NA	2.01 (0.61-6.61)
[a]P Value	0.143	0.226	0.102	0.160

[a]Logistic Regression Models; p-value. Odds ratio (95% confidence interval). *Odds ratio shows statistically significant effect, p<0.05. NA=variable not applied in Model. Surgical Site Complications= superficial infection + deep infection + organ/space infection + wound dehiscence.

Table 10. Non-Surgical Site Complications by Race or Ethnicity (N=1248)

Characteristic	Unadjusted	Model 1: Race/Ethnicity + Demographics	Model 2: Model 1 + Comorbid Conditions	Model 3: Model 2 + Clinical Characteristics
Race or Ethnicity				
Non-Hispanic White	Ref.	Ref.	Ref.	Ref.
Black	1.72 (1.18-2.53)*	1.70 (1.14-2.52)*	1.69 (1.13-2.51)*	1.55 (1.03-2.33)*
Hispanic	0.88 (0.59-1.31)	0.91 (0.60-1.37)	0.89 (0.59-1.34)	0.85 (0.55-1.29)
Age, y	NA	1.01 (1.00-1.02)	1.01 (0.99-1.02)	1.01 (1.00-1.02)
Current Smoker	NA	1.00 (0.72-1.38)	0.94 (0.67-1.31)	0.95 (0.67-1.33)
ASA Classification	NA			
1+2	NA	Ref.	Ref.	Ref.
≥ 3	NA	1.75 (1.30-2.37)*	1.72 (1.26-2.34)*	1.61 (1.17-2.20)*
BMI	NA	0.99 (0.97-1.007)	0.99 (0.97-1.01)	0.98 (0.96-1.00)
HTN	NA	NA	0.97 (0.66-1.42)	0.87 (0.59-1.29)
DM	NA	NA	1.55 (0.92-2.61)	1.77 (1.04-3.03)*
Cardiac/Pulmonary Cond.	NA	NA	4.01 (1.02-15.7)*	4.33 (1.09-17.3)*
Hct ≤ 38%	NA	NA	NA	1.98 (1.47-2.68)*
WBC > 11 k/μL	NA	NA	NA	1.74 (1.18-2.58)*
Non-fertility Sparing Surgery	NA	NA	NA	2.14 (1.19-3.85)*
[a]P Value	<0.05	<0.001	<0.001	<0.001

[a]Logistic Regression Models; p-value. Odds ratio (95% confidence interval). *Odds ratio shows statistically significant effect, p<0.05. NA=variable not applied in Model. Non-Surgical Site Complications=all adverse events except wound-related complications.

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APPENDIX A: Table of Coding Variables

List of Coding Variables

Variable Name	Coding	Variable Description
All-Cause Complications	0: No complications 1: Yes Complications	Composite Variable of All-Cause Adverse outcomes, Surgical Site Complications, Non-Surgical Site Complications
Surgical Site Complications	0: No complications 1: Yes Complications	Composite Variable of Superficial Surgical Site infection, deep incisional infection, organ/space site infection, wound-dehiscence. *Excluded cases suspicious of preop/intraop surgical-related complications. *Note: Every measure outcome was dichotomized prior to aggregation into composite variable
Non-Surgical Site Complications	0: No complications 1: Yes Complications	Composite variable of: PNA, UTI, ARF, PRF, DVT, PE, Ventilator >48hrs, Unplanned Intubation, Bleeding & Transfusions, Sepsis, Septic shock, CVA/Stroke, MI, Cardiac arrest *Excluded cases where any of these complications existed preop/intraop *Note: Every measure outcome was dichotomized prior to aggregation into composite variable
All-Cause Adverse Outcomes	0: No complications 1: Yes Complications	Composite Variable of prolonged LOS and Return to OR within 30 days
Prolonged LOS	0: No 1: Yes	Variable created from length of hospital stay (TOTHLOS) & based on 75 percentile for entire cohort (3.75d)
Return to OR	0: No 1: Yes	Variable dichotomized from Return to OR (RETURNOR) within 30 days
Race	1: White American 2: Black/AA 3: Hispanic/L	Race classifications based on RACE_NEW & ETHNICITY_HISPANIC variables
Surgical Procedure	0: hysterectomy 1: fertility sparing	Variable created from CPT codes & text classifying hysterectomy and fertility sparing modalities *Note: Variables used to create final variable include: PRNCPTX, CPT, OTHERCPT1-10, CONPCPT1-10
Fertility Sparing Procedure	1: conization/LEEP 2: trachelectomy	Variable created based on Surgical Procedure variable which was originally created from CPT codes.
Non-Fertility Sparing Procedure	1: abdominal hyster. 2: vaginal hyster. 3: laparoscopic hyster. 4: Unknown hyster.	Variable created based on Surgical Procedure variable which was originally created from CPT codes.
ageStrata	1: 19-34 2: 35-44 3: 45-54 4: 55-64 5: >65	Variable stratified from Age (continuous variable), based on age groups used in Surveillance, Epidemiology, and End Results Program data for cervical cancer
Current smoker	0: No 1: Yes	Variable dichotomized from SMOKE variable. Smoking described as current smoker within the past year
Functional health status	0: No 1: Yes	Variable dichotomized from FNSTATUS2 variable. Variable describes functional health status prior to surgery based on ability to perform activities of daily living

ASA classification	0: 1-2 1: ≥ 3	Variable dichotomized from ASACLAS variable. ASA references the American Society of Anesthesiology Physical Status Classification; 1=No disturb, 2=mild disturb, 3=severe disturb, 4=Life Threat, 5=moribund
Disseminated Primary Neoplasm	0: No 1: Yes	Variable dichotomized from DISCANCR variable indicating primary cancer that has metastasized to a major organ & satisfying 1 of several ACS NSQIP criteria
Weight loss	0: No 1: Yes	Variable dichotomized from WTLOSS variable, where patient experienced >10% loss of body weight in last 6 months
Diabetes	0: No 1: Yes	Variable dichotomized from DIABETES variable. Variable refers to diabetes on treatment with oral agents or insulin for >2 wks.
Hypertension	0: No 1: Yes	Variable dichotomized from HYPERMED variable. Variable refers to HTN requiring medication within 30 days prior to principal operative procedure
BMI	1: < 18.5 2: 18.5-24.9 3: 25.0-29.9 4: > 30	Variable created based on nBMI and stratified based on CDC classes 1=underweight, 2=normal/healthy weight 3=overweight, 4=obese
nBMI	Continuous	Variable created based on HEIGHT and WEIGHT variables. Original data were converted to kg and meters then formula used to calculate BMI. *Formula: [BMI=WEIGHT * 0.453592 / (HEIGHT * 0.0254) ** 2]
Cardiac Conditions	0: No 1: Yes	Composite variable of HXCHF and DYSPNEA variables which were first dichotomized based on presence or absence of disease within 30 days prior to surgery. Variables describe congestive heart failure and dyspnea on exertion/rest
Pulmonary Conditions	0: No 1: Yes	Variable based on HXCOPD variable which describes history of COPD by chart/PFT's within 30 days prior to principal operative procedure
Renal Conditions	0: No 1: Yes	Composite variable of RENAFAIL and DIALYSIS variables. Renal failure based on clinical condition with rapid decline of kidney fx 24hrs prior to surgery and dialysis based on whether patient was on dialysis 2 wks prior to surgery.
Creatinine ≥1.0 mg/dL	0: No 1: Yes	Variable dichotomized based on PRCREAT variable. Variable describes preoperative serum creatinine level if ordered. For information regarding threshold see main text.
Albumin ≤ 3.0 g/dL	0: No 1: Yes	Variable dichotomized based on PRALBUM variable. Variable describes preoperative serum albumin level if ordered. For information regarding threshold see main text.
Hct ≤ 38%	0: No 1: Yes	Variable dichotomized based on PRHCT variable. Variable describes preoperative hematocrit if ordered. For information regarding threshold see main text.
WBC > 11 k/μL	0: No 1: Yes	Variable dichotomized based on PRWBC variable. Variable describes preoperative WBC if ordered. For information regarding threshold see main text.
Platelet Count ≤ 150s	0: No 1: Yes	Variable dichotomized based on PRPLATE variable. Variable describes preoperative platelet count if ordered. For information regarding threshold see main text.
BUN> 40 mg/dL	0: No 1: Yes	Variable dichotomized based on PRBUN variable. Variable describes preoperative BUN if ordered. For information regarding threshold see main text.
Blood Transfusion, ≥1 unit	0: No	Variable dichotomized based on TRANSFUS variable.

pRBCs	1: Yes	Variable refers to preoperative transfusion of ≥1pRBCs in 72 hrs prior to surgery
Total Operative time	Continuous	Variable is continuous mainly transformed from string to numeric. Variable OPTIME describes total operation time in minutes
Cumulative RVU	Continuous	Composite variable of WORKRVU, OTHERWRVU1-10, CONWRVU1-10. Variables refer to work relative value unit for all procedures perform during hospitalization including principal surgical procedure.
Age Bracket by Birth Rates	0: 35 and older 1: 20-34	Variable based on Age continuous variable. Variable was dichotomized by group with birth rates > or < 50% in the U.S. For more information, refer to main text.
ParityStrata	0: Parity 0 1: Parity 1-2 2: ≥ 3	Variable was created from HYST_Parity, a continuous variable. Variable was then stratified.
Gross abdominal disease	0: No 1: Yes	Variable dichotomized from HYST_GROSSABDDISEASE variable. Based on presence of gross disease if data was available
Size of Visible Tumor Strata	0: <1 cm 1: 1-2 cm 2: >2 cm 3: Unknown	Variable created from HYST_TUMORSIZE variable. Variable originally was ordinal, which was stratified only if data was available.
Lymph node involvement	0: No 1: Yes	Variable created from HYST_ABDLYMPH variable. Variable refers to gross lymph node involvement. Variable dichotomized if data was available.
Tumor Clinical Staging Category	0: 0,I-IB1 1: IB2-IVB	Variable was dichotomized based on HYST_CERCANCERSTAGE variable. Variable denotes Cervical Cancer FIGO Stage. The categories were based on recommended treatment guidelines, please see main text for more detail.