UNIVERSITY OF CALIFORNIA,
IRVINE

Influence of race/ethnicity and measures of healthcare access on the incidence, stage at diagnosis, and survival of rare gynecologic cancers in California women

THESIS

submitted in partial satisfaction of the requirements
for the degree of

MASTER OF SCIENCE

in Epidemiology

by

Amanda Blithe Hawkins

Thesis Committee:
Associate Adjunct Professor Deborah Goodman, Chair
Professor Hoda Anton-Culver, Department Chair
Assistant Professor Hannah L. Park

2014

DEDICATION

To

My mentor, Deborah
For guiding me along this path, and pushing me forward when I needed it

My mother
For introducing me to the world of Epidemiology

My family and friends
For keeping it all in perspective and keeping me sane

And most of all,
My husband, Sam
For your unconditional love

Thank you all for your unwavering support.

Table of Contents

LIST OF FIGURES

LIST OF TABLES

ACKNOWLEDGMENTS

I would like to express the deepest gratitude to my committee chair, Associate Adjunct Professor Deborah Goodman. Thank you for supporting me, pushing me and guiding me through this project. I am so grateful to have had you as a mentor. I could never have realized my dream of becoming an epidemiologist without you.

I would like to thank my committee members, Professor Hoda Anton-Culver and Assistant Professor Hannah L. Park, for your scientific, biological and epidemiological perspectives. You have shaped me into a better scientist, critical thinker, and scientific writer.

In addition, I would like to show my appreciation to Associate Adjunct Professor Argyrios (Al) Ziogas. Thank you for your continual advice on the best statistical methods, for your troubleshooting support, and for your bio-statistical perspective throughout the creation and fruition of this project.

ABSTRACT OF THE THESIS

Influence of race/ethnicity and measures of healthcare access on the incidence, stage at diagnosis, and survival of rare gynecologic cancers in California women

By

Amanda Blithe Hawkins

Master of Science in Epidemiology

University of California, Irvine, 2014

Associate Adjunct Professor Deborah Goodman, Chair

Rare gynecologic cancers represent 3.4% of all cancers of women in the US and may disproportionately affect specific demographic groups due to access to healthcare. In California, the gynecologic cancers that meet the NCI criteria of rare cancer are ovarian, cervical, vulvar, vaginal, and other gynecologic cancers. The influence of race/ethnicity and measures of healthcare access on incidence, risk of late stage at diagnosis, and 5-year cancer site-specific survival rates for all rare gynecologic cancers were examined in the large and racially diverse population of the California Cancer Registry from 1988-2009. Factors of healthcare access were measured by SES, health insurance status, and US-born status.

We found that the association between healthcare access and rare gynecologic cancer outcomes varied by cancer site, cancer outcome, race/ethnicity and the particular measure of healthcare access. Proportional incidence of HPV-related cancers were increased for women with low SES, especially NH Whites. Private insurance and US birthplace status decreased proportional incidence by race/ethnicity for all rare gynecologic cancer sites. Risk of late stage at diagnosis for HPV-related cancers varied by measures of healthcare access. Race/ethnicity and insurance status were the most important predictors of ovarian cancer late-stage risk while private insurance was associated with lower risk of late stage at diagnosis for other female

genital organ cancers. Cervical and ovarian cancer survival were associated with race/ethnicity, SES and insurance status. The risk of death for all rare gynecologic cancers, except other gynecologic cancers, was reduced for women born outside the US.

CHAPTER 1: Introduction

The importance of understanding rare gynecologic cancers is high because rare gynecologic cancers represent 3.4% of all cancers of women in the United States (US) and may disproportionately affect specific demographic groups due to access to healthcare. According to the National Cancer Institute (NCI), rare cancers are defined by an age-adjusted incidence rate of 15 cases or less per 100,000 per year (1). According to the rates published by Greenlee et al., approximately 26% of gynecologic cancers are rare, because only cancers of the ovary and corpus uteri (uterus) have national incidence rates high enough to be considered common; consequently, cervical, vulvar and vaginal cancers are all gynecologic cancers that meet the criteria of being rare (2). Therefore, cervical cancer makes up 18%, vulvar cancer makes up 5%, and vaginal cancer makes up 1.5% and other female genital organ (other gynecologic) cancers make up 1% of gynecologic cancers in the US (ovary and uterus make up 26% and 48% to total 100% gynecologic). In California, the gynecologic cancers that meet the NCI criteria for rare cancer are ovarian, cervical, vulvar, vaginal, and other female genital organ cancers. In Greenlee's analysis, other gynecologic cancer sites were broken down further and shown to be comprised of 67% fallopian tube cancers.

Etiologies of Rare Gynecologic Cancers

The rare gynecologic cancers can be broken into two groups to help us understand their etiologies: HPV (Human papillomavirus) infection-related cancers and ovarian/fallopian

tube cancers, though it should be recognized that all of these diseases are multi-factorial and therefore one exposure does not necessitate carcinogenesis (3–6). The HPV infection-related cancers, which are cancers of the cervix, vulva, and vagina, are mostly attributed to a chronic exposure to carcinogenic HPV strains (4). Ovarian and fallopian tube cancers are attributed to hormonal exposures, including ovulation, parity, and hormone therapy (7–9).

Cervical cancer is the largest burden worldwide of all gynecologic cancers, which has decreased in incidence and mortality in countries with screening programs (10,11). Cervical cancer screening is currently recommended for all women, not just those with an HPV-positive test. No screening protocol is currently in place for all HPV-related cancers despite available testing. HPV (Human papillomavirus) accounts for 100% of cervical cancer, 40% of squamous vulvar cancer, 65% of vaginal cancer and are mostly attributable to HPV-16 (12). It is well known that infection and persistence of HPV is necessary for the development of cervical cancer (4,13). The quadrivalent HPV vaccine, which targets HPV Types 6, 11, 16, and 18, has been proven to prevent cervical, vaginal and vulvar cancers, but despite potential advantages of HPV testing and self-collection of samples, these practices are currently not recommended (4,14). It is unclear as to whether colposcopy (visual examination of the cervix, vagina and vulva for signs of disease, often combined with the Pap test) is necessary and/or cost-effective for all HPV-positive patients (4).

Due to the introduction of the HPV vaccine, researchers estimated age-specific incidence rates for a baseline of surveillance to help monitor how targeting of the infection will reduce the burden of cervical, vulvar and vaginal cancers and calculated the population attributable fraction to determine the expected effect of the HPV 16/18 vaccine on the incidence of these cancers and their pre-cancerous neoplasias (15). A US population-based study of HPV-associated cancers has reported the estimates of new cancer cases and deaths for cervical, vulvar, and vaginal/other genital organs, and another study of the burden of HPV-related disease has emphasized that although cancer death rates are continuing to decline, some incidence rates are increasing and coverage for vaccination is low in some areas, highlighting a need for additional prevention efforts for these cancers (16,17). Race and socioeconomic status (SES) have been shown with SEER data (Surveillance, Epidemiology End Results program; nationally-based registry data) to be associated with the incidence of HPV-related cancers (18,19). Despite the knowledge that certain HPV types are carcinogenic, screening by colposcopy remains the gold standard for HPV-related disease diagnosis. Many strategies have been examined, such as self-swabs and genotyping, but nothing matches the diagnostic and predictive value of colposcopy (14).

One HPV-associated cancer, vulvar cancer, has seen an unusual trend despite the positive outcome of cervical cancer screening. It has been noted, over the past four decades, that there has been an increase in invasive vulvar cancer incidence in the US of approximately 1% per year, and that rise is “evident in every age category, race, and geographic region” (20). The increase of incident cases could be expected to have a

negative impact on other outcomes, such as mortality. It is expected, however, that the advent of the HPV vaccine implementation should change this trend due to the expectation of the prevention of a percentage of vulvar cancer (21). It has been shown that treatment is a strong predictor of survival (22), and that treatment modality is impacted by race and ethnicity (23). Survival of vulvar cancer has been shown to be strongly affected by age (younger or older than 50 years) even when the researchers controlled for race, stage, grade and treatment (24).

Vaginal cancer is the rarest of all HPV-related gynecologic cancers. It has been previously shown that vaginal cancer is associated with chronic exposure to foreign bodies and history of cervical carcinoma (shared exposure to carcinogenic stimuli). It is a disease of older women with peak incidence in the 60s-70s, and stage is the major prognostic factor (25). Incidence and survival by race, ethnicity and age has been described using SEER data (1998-2003) and found that Black, Asian-Pacific Islander, and Hispanic women, in addition to older women, had a high proportion of late-stage disease and a low 5-year survival rate (26).

Due to their physical proximity and similar risk factors, investigators have examined the potential similarities between ovarian and fallopian tube cancers (9,27–29). Incidence and survival analysis of fallopian tube cancers using SEER data has shown that fallopian tube cancers present with earlier stage, and advanced stage is associated with better overall survival than ovarian cancers (30). It is suspected that the better

prognosis of fallopian tube cancer is due to clinical presentation, but due to the extreme rarity of this cancer (1% of gynecologic malignancies), the causes are unclear (29).

Trends in Rare Gynecologic Cancer Incidence

The California Cancer Registry (CCR) has very recently reported the temporal trends in cervical and ovarian cancer incidence, stating that both have significantly declined between 1988-2010. The 2014 report stated that cervical cancer rates in 2010 were less than half of those in 1988 and that the average annual percent change of ovarian cancer rates were 16-22% lower in each racial/ethnic group except among Latinas (31). Vaginal and vulvar cancers were never common enough to be ranked overall or for any race/ethnicity.

In a 2013 publication of cancer incidence of the most commonly diagnosed cancers in California from 1988-2009, ovary was the 8th most common type of cancer incidence among California females, but the rank of common cancers by race/ethnicity showed a slightly different pattern. Ovary moved to 7th most common newly diagnosed cancer site in Non-Hispanic (NH) Whites, and up to as high as 5th most common in certain Asian/PI groups (South Asian), while it remained 8th most common in NH Blacks and Hispanics (32). Ovarian cancer incidence was consistently higher in Non-Hispanic Whites, but declined from 1988-2005. The incidence rates of ovarian cancer for the other race/ethnicities overlapped over time, but the trend for every group was some degree of decline from 1988-2005 (33).

Cervical cancer is considered the 13th most common cancer of California women; however, incidence has decreased appreciably (33%) from 1988-2007 (34). Although cervix is not common overall, it was ranked 6th for Hispanics and up to 3rd for certain Asian/Pacific Islander (PI) categories (Laotian/Hmong) of diagnosed cancers in California from 1988-2009 (32). In a similar report of the 5-year incidence from 2003-2007, Hispanics were noted to be twice as likely to be diagnosed with cervical cancer than non-Hispanic women (34). According to a report of California cancer incidence from 1988-2005, Latinos had a consistently high cervical cancer incidence, which increased from 1988-1992 before dropping between 1992-2005. Incidence of cervical cancer was consistently lower in Non-Latino Whites, and declined overall from 1988-2005. Cervical incidence was moderate for African Americans and Asian/ Pacific Islanders, which declined overall from 1988-2005, though Asians saw a slight incline from 1988-1994 followed by a steep decline from 1994-2000 (33). The reason for the decrease in cervical cancer incidence by race/ethnicity has been primarily attributed to the increased use of the Pap test, though changes in modifiable risk factors such as cigarette smoking must also be considered (34,35).

Age-adjusted incidence of rare gynecologic cancers reported to SEER from 1975-2011 can be seen in Figure 1.1. Ovarian cancer had the highest incidence, exceeding the maximum rate for rare cancers prior to 1992, but due to a small but steady decline, decreased to a rate of approximately 12 cases/year/100,000 women. Cervical cancer had a precipitous drop in incidence to less than 7 cases/year/100,000 women by the

year 2005. Cancer incidence of the vagina and vulva were considerably lower, less than 1 and 3 cases/year/100,000 women for each cancer site, respectively; no trends in incidence were seen for these cancer sites (36).

The incidence of rare gynecologic cancers in California, stratified by race/ethnicity from 1988-2009, can be seen in Figures 1.2 and 1.3. Ovarian cancer had the highest incidence overall, followed by cervical cancer and cancers of the vagina, vulva, and other female genital organs which had distinctly lower incidence rates. Cervical cancer incidence was highest in Hispanics and declined in all race/ethnicities over time. The incidence of ovarian cancer was highest in NH Whites and a small decline in rates was seen in all race/ethnicities over time. NH Blacks and Hispanics had the highest vaginal cancer incidence rates, and incidence for all race/ethnicities did not change markedly over time. Vulvar cancer incidence was highest for NH Whites and Blacks, and no discernable change in rates over time was seen for any race/ethnicity. NH Whites and Blacks also had the highest rates of other female genital organ cancers; incidence for all race/ethnicities did not change over time.

The Use of Proportional Incidence Rate Ratios

Proportional incidence rate ratios (PIRs) are a useful method that has been used by various studies when risk population data for a specific risk factor of interest are not available for calculating incidence rates. For example, registry data was used to evaluate the risk of cancer between veterans of the Gulf War and non-Gulf War

veterans, and the proportional incidence ratio identified a relative excess of lung cancer for Gulf War veterans (37). In a study examining the efficacy of a new mammography screening program, proportional incidence was determined between interval breast cancer and risk estimated age-specific incidence expected in the absence of screening (38). In addition, a meta-analysis of occupational exposure and the risk of thyroid cancer identified an inconsistent relationship of incidence from 30 separate studies using proportional incidence methods (39).

In the last 10 years, several studies have utilized PIR methods to supplement cancer data. A presumed decline of small cell lung cancer (SCLC) led to a temporal trend analysis of SEER data. Proportional incidence was created relative to non-SCLC by race, sex, and age, and investigators found that the SCLC incidence had only declined slightly over the 3-decade period (40). Middle Eastern population risk of thyroid cancer in California was calculated by estimating the population at risk, and then calculating the age-adjusted rate ratio of incident cancer within the Middle Eastern heritage population (41). In a meta-analysis of the association between venous thromboembolic events (VTE) and cancer, the majority of the reports did not provide risk estimates, so a proportional incidence study was performed on these reports which found an excess of risk for multiple cancer sites for VTE patients (42).

When a cancer registry cannot identify the risk population from which an excess of cancer incidence is suspected, proportional incidence ratio (PIR) approaches are utilized. The Florida Cancer Registry created a special report about cancer in Hispanics

due to the ethnic predominance in the Florida population. Due to the lack of detailed census population data for Hispanic sub-groups, PIR analysis was performed in lieu of incidence rates. Their analysis determined distributions of incidence across the Hispanic population that was informative of potentially disproportionate cancer risk factor burdens and identified a proportional increase of screenable cancers (including cervical cancer) among certain subpopulations for the potential implementation of targeted screening interventions (43).

Access to Healthcare

Disparities by demographic factors such as race, ethnicity, and age exist in all aspects of healthcare (44). Race/ethnicity is strongly associated with healthcare access and therefore must be considered when evaluating other measures of healthcare access. Racial and ethnic minorities tend to receive a lower quality of healthcare than non-minorities, even when access-related factors, such as patients' insurance status and income, are controlled. In 2013, it was shown by Bristow and colleagues that for ovarian cancer patients, receipt of guideline (NCCN-guideline concordant) therapy and survival were related to race, even when controlled for SES indicators, tumor characteristics, and healthcare system factors (45). Chronic disease disparities exist for American Indians and Alaska Native (AI/AN) populations that may be due to access to quality healthcare, but programs that increase access may reduce rates of these diseases (46).

Access to medical care has been tracked in the US to determine which variables impact the quality of care received. Researchers are particularly interested in determining modifiable factors that influence access, in order to meet the goals outlined in the World Health Organization (WHO) agenda for the ethical principle of equity (47). Healthcare access has been defined in many different ways, depending on the healthcare outcome that is being measured and depending on which healthcare disparities are accounted for. In determining risk and burden of cervical cancer, healthcare access is determined by the quality of care rendered, such as the number of colposcopies performed to prevent cervical cancer and cervical cancer deaths (48). Measures related to structure and process (hospital or physician case volumes and diagnostic tests, procedures and adjuvant therapies) influence quality of care outcomes such as stage at diagnosis and overall survival for cancer. Health care delivery is influenced by process and structural factors which vary by socio-demographics at a population level (3). The WHO agenda points out that health is a driver of socioeconomic progress and therefore there is a need for more resources to improve access to life-saving or health-promoting interventions (47).

There are many negative effects blocking minorities' ability to obtain quality care, barriers beyond the conditions in which many clinical encounters take place, such as language, geography, and cultural familiarity that compound the issue of unequal treatment (49). Language barriers, particularly for Hispanics in the US, affect healthcare outcomes, including health insurance coverage, having a personal health care provider, forgoing care because of cost, and having a routine check-up within the past five years,

suggesting that language preference leads to disparities in healthcare access (50). In a study of colon cancer outcomes due to gender and ethnic disparities, researchers found that baseline characteristics, such as metastatic disease or screening diagnosis, were unequally affecting women and minorities, but that adjustment for these characteristics made any disparities by gender and ethnicity on outcomes non-significant (51). Therefore, if minority status such as race/ethnicity influences baseline characteristics which in turn impact outcome, then race/ethnicity is indirectly affecting outcome. Ethnic disparities, particularly for Mexican Americans in California, may be due to language barriers, which decreased access for colorectal screening. Specifically, it was found that Mexican Americans with limited English proficiency cited provider and patient barriers more often than non-Latino Whites (52). Similarly, within a cohort of breast and cervical cancer screening patients, foreign-born Latina immigrants were believed to have limited access to health care (53).

In a study of mammography efficiency, health insurance status was an important predictor of cancer screening, while race was not (in the multivariate model) (54). Analysis of trends in healthcare access and identification of who is disproportionately affected showed that poverty and lack of insurance increased the risk of unmet medical need and delayed care (55). In a study of appendicitis patients, there was an increased rate of adverse events between county and private hospitals, which was driven by healthcare access, and even within the county hospital cohort, there were differences in access to healthcare beyond racial and socioeconomic disparities that led to worse prognosis (56).

There is a concept of upstream versus downstream causes of healthcare disparities; upstream causes of disparities in access include factors of socioeconomic status (education, poverty, insurance coverage) but downstream interventions such as improving the health system, provider-patient interactions, and clinical decision making could also affect health outcomes (57). It could be argued that these downstream interventions could become upstream for chronic diseases such at cancer, especially cancers with pre-cursor lesions such as those associated with HPV infections (cervical, vaginal, and vulvar). It has been shown that increasing access to care in communities of low-income persons (adding more federally-funded health centers) is important for reducing adverse health outcomes in individuals (58). Policies have begun to work at reducing inequitable healthcare access, but have so far fallen short of their goals, treating symptoms but not preventing disease or reducing disease burden (59). In recent years, the question has arisen: will healthcare reform improve health outcomes? Using a population in Massachusetts where reform was implemented, researchers found that in a group of low SES, insurance status had a greater effect in improving outcomes on the absolute but not relative scale, implying that barriers due to SES were continuing to affect healthcare access (60).

Previous research on disparities in rare gynecologic cancer incidence has shown that certain measures can be good proxies for healthcare access. Disparities in ovarian cancer quality of care (such as adherence to National Comprehensive Cancer Network (NCCN) guideline care, which was defined by stage-appropriate surgical procedures

and recommended chemotherapy) and survival have been shown for race, socioeconomic status, and insurance status (45,61–63). Country of origin may play a role in cervical cancer incidence, particularly in the US Hispanic population as compared to non-Hispanic whites (64,65). A review of cancer in US Hispanics has shown that the incidence and mortality of many cancers are higher in Hispanics than in NH Whites, including cervical cancer. Incidence, treatment, mortality and survival of cervical cancer in Hispanics may be due to the effects of country of origin, SES, and health insurance status on screening rates (66). Country of origin has also been shown to affect cancer incidence, though not specifically in rare gynecologic cancers (67). Insurance status plays a vital role in the prevention, detection, treatment of gynecologic cancers because the majority of those covered by Medicare and Medicaid are women, and Medicaid is the primary payer for women's reproductive health services (68). In Greenlee's analysis, the incidence rates of most rare malignancies varied by age, race, and ethnicity, and rare cancers were more common than non-rare cancers among young adults aged 20–29 years, NH Blacks and Hispanics (2).

Although invasive incidence and other outcomes of rare gynecologic cancers have been investigated previously, as seen above, the analysis has been limited by the cancer sites that could be studied due to small sample size, the variables analyzed, particularly measures associated with healthcare access, and the duration of the study period. It is clear that a detailed analysis, utilizing an updated time period of data, is needed to compare these rare gynecologic cancers and to see whether their outcomes are associated with access to healthcare. Population-based cancer registries are a great

resource in the study of rare cancers because of their size and the extensive data collected on all cases which can be used to analyze the demographic, clinical and outcome characteristics of rare cancers at a population level. The results from these studies can then be used to generate hypotheses about etiology, disparities, and possible strategies for optimal prevention, detection and treatment.

Aims of This Study

This is a novel study to investigate the influence of race/ethnicity and measures of healthcare access on the incidence, stage at diagnosis, and survival of all rare gynecologic cancers. Although we were limited by the use of surrogate measures of healthcare access, as measured in the CCR, it has been shown that the factors of healthcare access we used are validated proxies of access to medical care. The majority of rare gynecologic cancers may be prevented or the burden lessened by access to healthcare. A great many of HPV-related cancers, including cervical, vaginal and vulvar cancers could be prevented through the HPV vaccine. Cervical cancers could be prevented or diagnosed early through the use regular colposcopies combined with Pap testing. Ovarian cancers have no screening test, but could be diagnosed earlier when seen by a specialist and could have better survival when receiving guideline-concordant treatment. An advantage of this study is the use of recently released data from the CCR to 2009; thus, we are thereby updating the literature relevant to these cancers.

Preventative medicine combined with optimal care could potentially reduce the burden of rare gynecologic cancers, but barriers related to healthcare access are restricting this potential. It is of great importance to verify that these barriers are associated with our studied outcomes of each rare gynecologic cancer. This study aimed to identify the factors of healthcare access that influence our outcomes of interest in order to determine how the changing of policies could be most effective and where the allocation of resources could be most successful. We hypothesized that invasive incidence, stage at diagnosis, and survival of each rare gynecologic cancer varied by race/ethnicity and measures of healthcare access, as measured by SES (socioeconomic status), health insurance status, and US-born status in California women.

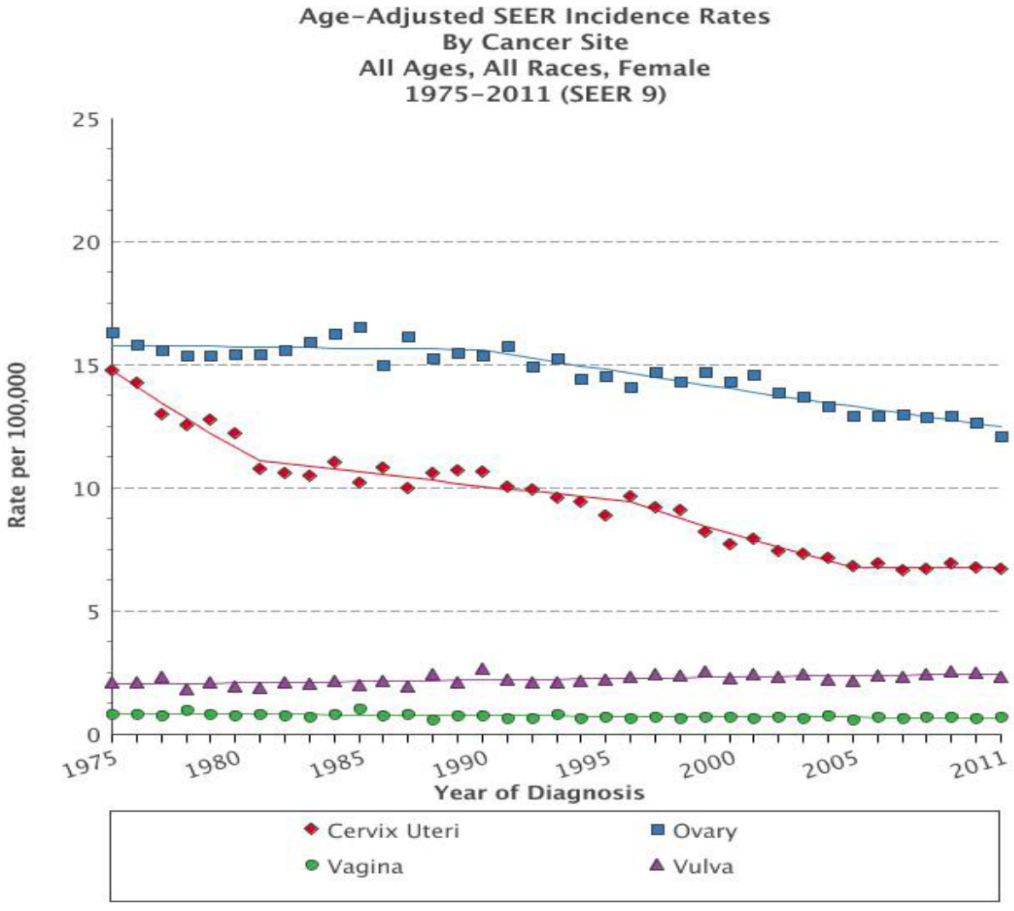
Due to the diversity seen in California, the California Cancer Registry is the optimal resource for studying cancers suspected to have healthcare access differences by race/ethnicity. The California Cancer Registry (CCR) is a powerful resource that has been used to show that late stage at diagnosis for cervical cancer is associated with Medicaid status for women diagnosed in California (69). Incidence of five major cancer sites, including cervical cancer, have been shown to have SES disparities across the racial/ethnic groups in California (70). The CCR has also been used to show that there are disparities by race for the incidence, treatment, and survival of cervical cancer (71). The goal of this study was to determine how the incidence of invasive disease, late stage at diagnosis, and survival of rare gynecologic cancers are associated with race/ethnicity and measures of healthcare access in the racially diverse population of the California Cancer Registry.

The following aims were carried out through the analysis of all women (aged 20 years or above) reported in the California Cancer Registry diagnosed with a first primary invasive tumor between 1988-2009 for a cancer site defined by NCI as a rare gynecologic cancer: cervical, ovarian, vaginal, vulvar, or other gynecologic:

(1) To determine if the incidence rates of each of the rare invasive gynecologic cancers differ by race/ethnicity and measures of healthcare access. Factors of healthcare access were measured by SES (socioeconomic status), health insurance status, and US-born status.
(2) To determine if the proportions of late stage at diagnosis of each of the rare invasive gynecologic cancers differ by race/ethnicity and measures of healthcare access.
(3) To determine if survival rates of each of the rare invasive gynecologic cancers differ by race/ethnicity and measures of healthcare access.

The analysis was restricted to the diagnosis of invasive tumors and therefore excluded women with in-situ and borderline tumor diagnoses. The results of this study may influence policy makers and inform clinicians how these cancers should be approached. In addition, this study may impact the relation of public health policies and how women diagnosed with these diseases are treated, how their disease is managed, and how prognosis is determined. However, because this is a registry-based study, we recommend further detailed investigation of the significant associations identified in this study.

Figure 1.1 SEER Incidence Rates of Gynecologic Cancers, 1975-2011: Data accessed from the publicly-available software tool found on the SEER website of rare gynecologic cancers defined by CCR data. SEER does not collect data on cancers of other female genital organs. Cancer sites included invasive cases only, excluding ovarian borderline cases or those with histologies: 8442, 8451, 8462, 8472, 8473. Rates were per 100,000 women and were age-adjusted to the 2000 US standard population. Regression lines were calculated using the Joinpoint Regression Program Version 4.1.0, April 2014, National Cancer Institute. Incidence source was SEER 9 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, and Atlanta). [Fast Stats: An interactive tool for access to SEER cancer statistics. Surveillance Research Program, National Cancer Institute. http://seer.cancer.gov/faststats. (Accessed on 6-12-2014)] (36)



Cancer sites include invasive cases only unless otherwise noted.
Ovary excludes borderline cases or histologies 8442, 8451, 8462, 8472, and 8473.
Rates are per 100,000 and are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130). Regression lines are calculated using the Joinpoint Regression Program Version 4.1.0, April 2014, National Cancer Institute.
Incidence source: SEER 9 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, and Atlanta).

Figure 1.2 CCR Incidence Rates of Gynecologic Cancers, 1988-2009: Incidence rates of rare gynecologic cancers diagnosed in California since 1988 reported to the CCR. Incidence rates from 1988-2009 in California, by year and race/ethnicity, were age-adjusted from the 2000 census population. Rates were calculated per 100,000 women. No statistical testing between rates was performed.

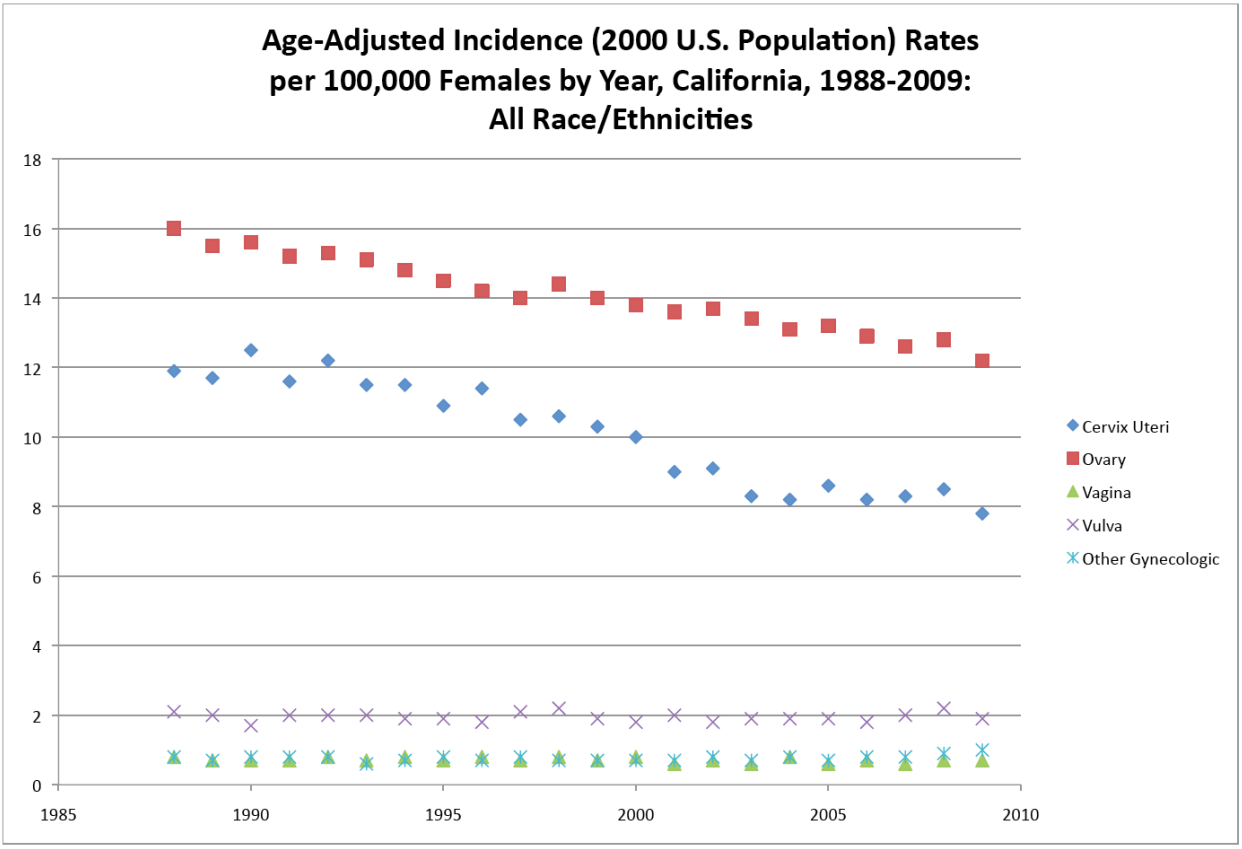
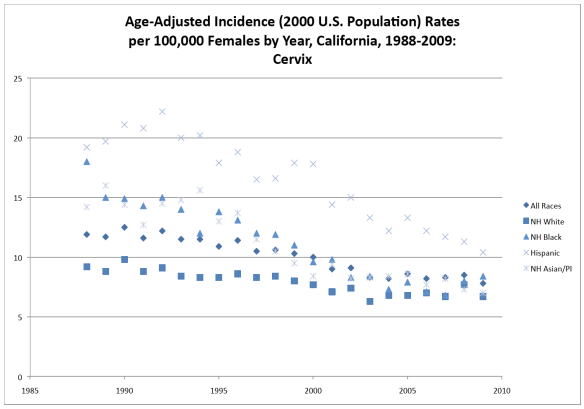
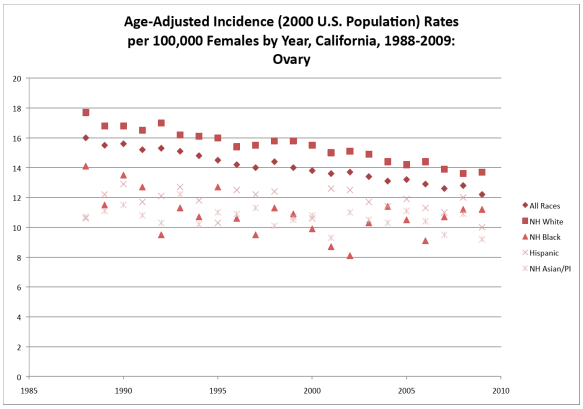


Figure 1.3 (a-e) CCR Incidence Rates, Stratified by Race/Ethnicity: Incidence rates from 1988-2009 by race/ethnicity for each rare gynecologic cancer: cervical (a); ovarian (b); vaginal (c); vulvar (d); and other gynecologic (e).

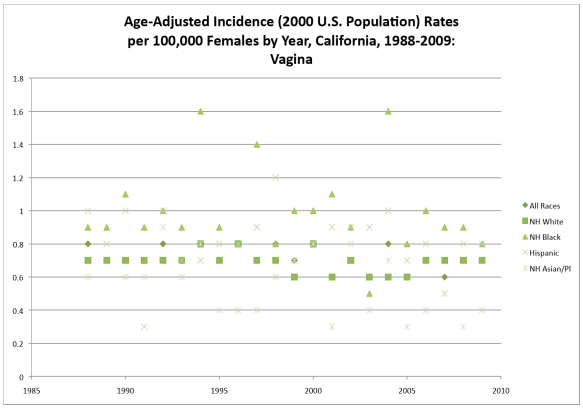
a)



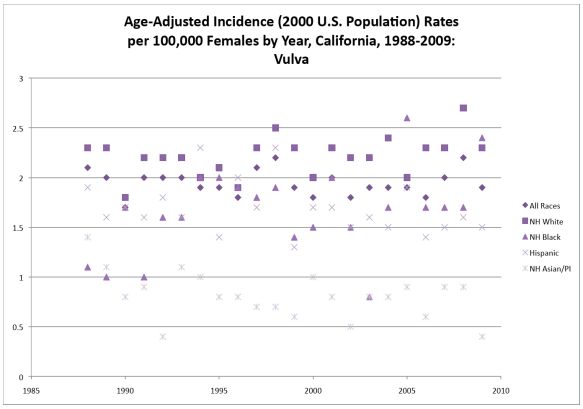
b)



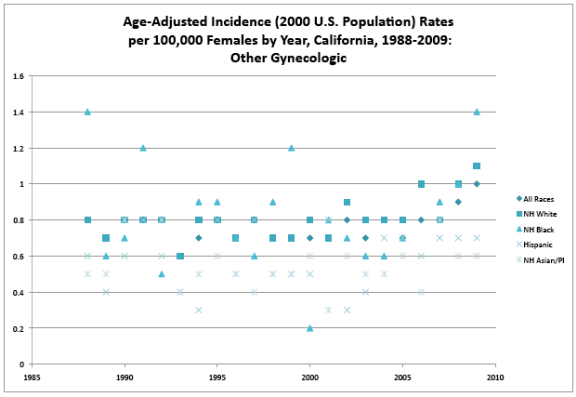
c)



d)



e)



CHAPTER 2: Methods

Study Population

The California Cancer Registry (CCR) is a statewide surveillance system that collects demographic, tumor characteristic, treatment and follow-up data from hospital medical records over time, and has been collecting data on all cancer patients in California since 1988. This study involved analysis of CCR data which had been de-identified, without patient identifiers or contact information. Data from 1988-2009 was used to examine rare gynecologic cancer outcomes. In California, the gynecologic cancers that meet the National Cancer Institute (NCI) criteria of low rates (age-adjusted) are ovarian, cervical, vulvar, vaginal, and other female genital organ cancers (including fallopian tube, ligaments, and parametrium) (72).

In our studied CCR cohort, it is impossible to define the proportion of cancer sites in the other female genital organ cancers category because these cases were not classified by specific tumor type. But due to Greenlee's analysis of all rare cancers it is assumed that trends seen for other gynecologic cancers will represent changes of fallopian tube cancer outcomes (2). In Greenlee's analysis, other gynecologic cancer sites were broken down further and shown to be 67% fallopian tube cancers with a rate of 0.563 cases per 100,000 women per year.

Race/Ethnicity, Healthcare Access Measures, and Tumor Characteristics

Our analysis focused on the four major racial/ethnic groups seen in California: non-Hispanic white (NH White), non-Hispanic black (NH Black), Hispanic, and non-Hispanic Asian/Pacific Islander (NH Asian/PI). The CCR abstracted data on race/ethnicity from medical records. The North American Association of Central Cancer Registries (NAACCR) Hispanic Identification Algorithm (NHIA) was used to enhance Hispanic ethnicity. The NHIA considers surname, maiden name, birthplace, and Hispanic origin to more accurately classify Hispanic ethnicity. Asian/PI patients have been identified using the NAACCR Asian/Pacific Islander Identification Algorithm (NAPIIA) from NAACCR. The NAPIIA uses gender, birthplace, first name, and surname from medical records to assign race status to a more specific Asian Race group. Recently these two algorithms were combined into a single SAS program called NHAPIIA to correct for misclassification.

Age at diagnosis was grouped into four age categories based on menopausal status, insurance eligibility, and age. Menopausal status was defined by the median age of menopause, less than versus greater than or equal to 50 years. Insurance eligibility was defined by Medicare eligibility, less than versus greater than or equal to 65 years. Advanced age was defined by any age equal to or greater than 80 years. Therefore the four age groups were: pre-menopausal (aged 20-49 years), post-menopausal before eligibility for Medicare (aged 50-64 years), post-menopausal after eligibility age for Medicare is met (aged 65-79 years), and advanced age (80+ years).

The CCR's quintile of SES, QUINYOST, which is based on YOSTSCL score (an SES scale from principal components analysis derived from Census variables), was used to analyze area-based socioeconomic status (SES) based on residence at diagnosis (73). This census block group level variable ranges from 1 (low SES) to 5 (high SES) and represents quintiles of the US population. In general, cancer populations do not reflect the even 20% per quintile distribution seen in the US population. The primary source of payment to the hospital variable (PAYER) was used to determine who had private insurance and who did not. US-born status was determined (born in US or foreign-born) from birthplace country of origin, which was either recorded in a patient's medical record, her death certificate, or both.

Histology and stage are tumor characteristics that were used for analysis. Histology is potentially a detailed tumor characteristic that can be deterministic of both treatment and outcome. Histologies were condensed by site to include the two or three most common histology groups and ICD-O-3 (International Classification of Diseases for Oncology) codes for defining the histologies can be seen in the table below for cancers of the cervix, ovary, vagina, and vulva (Table 2.1). Histology was not defined for other female genital organ cancers by the CCR, and so other female genital organ cancers histology was not examined. Stage is another tumor characteristic that helps clinicians determine treatment and predict survival. Stage was characterized by FIGO (International Federation of Gynecology and Obstetrics) definition. Analysis was

constricted to cases with epithelial histology and known stage, cases with non-epithelial histology were excluded.

Table 2.1 Histology Group ICD-O-3 codes by cancer site

Cancer Site	Histology Group	ICD-O-3 Code
Cervix		
	Squamous	8050-8130
	Adenocarcinoma	8140-8147; 8160-8162; 8180-8221; 8250-8506; 8520-8550; 8570-8573; 8940-8941
	Other	any other 8000-9989
Ovary		
	Adenocarcinoma, Endometrioid	8380-8383
	Adenocarcinoma, All other	8050; 8140-8147; 8160-8162; 8180-8221; 8250-8379; 8382-8461; 8462-8506; 8520-8550; 8560; 8570-8575; 8940-8941; 9110
	Other	any other 8000-9989
Vagina		
	Squamous	8050-8130
	Other	any other 8000-9989
Vulva		
	Squamous	8050-8130
	Other	any other 8000-9989

Exclusion Criteria

The following criteria were used for exclusion of certain cases from the CCR dataset to create a well-defined study population. Details of the proportions of cases excluded from analysis within this study can be seen in the table below (Table 2.2). Cancer cases that were identified by death certificate or autopsy were excluded. Primary tumors that were not the first cancer in the sequence of cancer diagnoses were not included in our analysis, such that women with a previous history of a cancer diagnosis were excluded from the study population. Our analysis was restricted to women defined by one of the four major racial/ethnic groups. All others were excluded including Non-Hispanic

American Indians (NH AI) and Other/Unknowns. Women diagnosed prior to age 20 were not considered adult and were therefore excluded from analysis. Tumors with non-invasive behavior (type) were excluded from analysis as well.

Table 2.2 Exclusion criteria proportions: Proportion of cases excluded from study population. NH AI = Non-Hispanic American Indian

Exclusion Criteria Proportions		Cervix		Ovary		Vagina		Vulva		Other Gynecologic	
		%	N	%	N	%	N	%	N	%	N
Total			92789		58788		5127		18503		2790
Type of Abstract Information											
	Autopsy	0.03	27	0.15	91	0.06	3	0.01	2	0.25	7
	Death Certificate	0.19	173	0.82	485	0.31	16	0.14	25	0.65	18
Sequence of Primary Tumor											
	Not-First	3.80	3523	20.09	11811	33.90	1738	20.19	3735	18.85	526
Race/Ethnicity											
	NH AI, Other/Unknown	6.86	6361	0.77	451	4.41	226	5.74	1062	1.15	32
Age											
	Not-Adult	1.84	1706	1.55	913	1.40	72	1.01	186	1.79	50
Type											
	Not-Invasive	61.96	57493	16.46	9677	50.97	2613	62.62	11586	4.05	113

Missing/Unknowns

Data with missing or unknown values including stage, insurance status, and US-born status, could not be excluded from all analyses due to the large proportion of data that would be lost and the bias it would have caused with outcome associations. Details of the proportions of cases defined as unknown stage, missing or unknown insurance status, or unknown US-born status can be seen in the table below (Table 2.3). Since these data are not informative on their own, subsets of data were analyzed for univariate analysis and were adjusted for in multivariate model analysis but estimates were not reported.

Table 2.3 Missing/Unknowns data proportions: Proportion of data defined as missing or unknown for analysis.

Missing/Unknowns Data Proportions		Cervix		Ovary		Vagina		Vulva		Other Gynecologic	
		%	N	%	N	%	N	%	N	%	N
Total			32317		40785		1565		5164		2109
Stage at Diagnosis											
	Unknown	5.11	1652	6.47	2638	12.01	188	5.58	288	11.71	247
Insurance Status											
	Missing	5.07	1640	4.89	1993	3.96	62	4.12	213	4.88	103
	Unknown	36.90	11924	31.30	12766	31.95	500	30.77	1589	28.31	597
US-born Status											
	Unknown	26.61	8601	19.57	7980	20.58	322	26.08	1347	23.85	503

Statistical Analysis

Certain measures had to be taken to account for the small number of cases within stratified groups. Histologies for each cancer site were condensed into two or three categories so that, when stratified by race/ethnicity and outcomes analyzed, the cell counts would not be so small as to obscure statistical test results. Characteristics were summarized using descriptive analysis, but logistic regression and Cox proportional hazards were used for modeling of significant associations with cancer outcomes. Statistical significance was defined by a p-value <0.05 and all statistical computing was performed with SAS software, version 9.3.

Overview: Site-specific frequency of rare gynecologic cancers by demographic, tumor, and healthcare access characteristics

The frequency of characteristics for each rare gynecologic cancer was calculated. Chi-squared analysis was performed by race/ethnicity to determine if the frequency of invasive cervical, ovarian, vaginal, vulvar, and other female genital organ cancers varied by demographic, tumor, and healthcare access factors. The frequency counts and percentages, with chi-squared p-values, were reported in table format.

Aim 1 Analysis

Overall:

Evaluated whether racial/ethnic minorities or those burdened with lower healthcare access are associated with an increased incidence for each rare gynecologic cancer. Incidence rates by race/ethnicity were calculated using standard methods of ascertainment for each rare gynecologic cancer. Population at risk for each racial/ethnic group was determined using 5-year age-specific rates and 2000 census data. Due to issues with sample size, rates were not reported but are described within the discussion section of this paper. Incidence rates by the studied measures of healthcare access could not be calculated directly. Due to the method of ascertainment, there are not equivalent measures of SES (socioeconomic status), insurance status, nor foreign status available for the census population. The closest substitute for a population at risk

was the population of cancer patients that were found within the cancer registry for the same time period. A common practice when using registry data is to use the proportional incidence ratio (PIR) method, which allows for the comparison of data sets where a standard set of age-specific proportions for each cancer type is available within the registry as a whole (74).

Aim 1a Site-specific Incidence Rates by Race/Ethnicity:

Using 5-year age-specific rates and 2000 census data to determine the population at risk, age-adjusted incidence rates by race/ethnicity were calculated for each rare gynecologic cancer. Due to low case counts, the calculated rates were not reported.

Aim 1b Site-specific proportional incidence rate ratios (PIRs) for Measures of Healthcare Access by Race/Ethnicity:

Following the Boyle and Parkin method, PIRs were calculated for the following healthcare access measures and stratified by race/ethnicity: SES, insurance status, and US-born status (75). The proportional incidence ratio method allows for age-specific rates to be summed and compared to determine if the observed frequency of cases for a specific rare gynecologic cancer of a given level of healthcare access differs from the expected frequency if the frequency is independent of the level of healthcare access. Frequency of each rare gynecological cancer was calculated for 5-year age groups from 20-85+ years. To create the reference cancer population used in the ratio analysis to compare the potential differences in age-adjusted incidence, a pool of “all cancers” was restricted to the same “risk population” of adult women aged 20-85+ years with the

same inclusion/exclusion criteria that was used to collect data on the women with rare gynecologic cancers. The following equation comes from “Statistical methods for registries” by Boyle and Parkin (75). The following general equation was used to calculate PIRs for every rare gynecologic cancer stratified by racial/ethnic groups across the levels of each measure of healthcare access: **PIR = O/E * 100** O = observed cases; E = expected cases, calculated from the age-specific sum of cases for all cancers within a subgroup multiplied against the proportion of all cases of the cancer of interest [all subgroups combined] and all cases of all cancers [all subgroups combined] . The interpretation of PIRs were as such: a PIR (relative SIR) greater than 100% (1.00) suggested that the cause-specific incidence in the study population was greater than would have been expected on the basis of incidence rate for all cancers. Therefore a healthcare access measure level with greater than 1.00 had a excess of incident cancer. For each rare gynecologic cancer and stratified by racial/ethnic group, a PIR for every measure of healthcare access was calculated (SES, insurance status, and foreign status).

Boyle and Parkin’s equation for an approximate standard error for the log PIR was used to calculate confidence intervals for the PIR estimates (75). This standard error equation is an acceptable approximation for determining statistical significance for observed differences if the fraction of cases due to the cause of interest is small. PIR estimates with 95% confidence intervals were used to test for statistical significance. PIRs with 95% confidence intervals that excluded one were considered statistically significantly different and were used to determine if the cancer incidence differed across levels of

measures of healthcare access and the distribution varied by race/ethnicity. The distributions considered between cancer sites were such that the distributions of a healthcare access variable were potentially different, whether that variable varied by race/ethnicity for each cancer and therefore the differences in the strength of association by cancer site for each healthcare access variable were then observed. The PIR estimates with 95% Confidence Intervals were presented in both table format and graphical representation. PIR tables and figures for each invasive rare gynecologic cancer site by race/ethnicity and each healthcare access measure were reported.

Aim 2 Analysis

Overall:

Calculated proportion of late stage of diagnosis of each of the rare invasive gynecologic cancers. The outcome late stage at diagnosis was dichotomized to allow for binomial distribution and logistic regression analysis. According to the FIGO definition, late stage is the same for each rare gynecologic cancer site according to clinical significance (see table below, Table 2.4). Essentially, localized disease (Stage 1 and 2) was considered early stage, while regional, distant, or metastatic disease (Stage 3 and 4) were considered late stage. Stage 0 (in situ or intraepithelial neoplasia) is not collected by the CCR. According to the CCR variable SUMStage: 0 – in situ; 1 – local; 2-5 – regional; 7 – remote; 8 – not given; 9 – unknown. Therefore late stage was classified as regional or remote disease (SUMStage 2-7) and early as local disease (SUMStage 1) and reported when stage was not reported or was unknown (SUMStage 8-9).

Table 2.4 Staging classifications – FIGO: Staging classifications of gynecologic cancers according to FIGO report (6).

Stage/Cancer Type	Ovarian	Cervical	Vaginal	Vulvar
Stage 0	borderline or non-invasive	CIS, CIN3	in situ or VAIN	in situ or VIN
Stage 1	within ovary, early	invasive within cervix	within vagina	within vulva
Stage 2	local mets, lymph nodes (LN)	local spread, no LN	local spread to connective tissue	local spread, no LN
Stage 3	spread to abdomen or LN	further local spread, no LN regional	local further spread and/or LN, regional	local further spread, with LN
Stage 4	distant mets	local or distant mets, w/ w/o LN, remote	local further or distant mets, and/or LN, distant	local or distant mets, w/ or w/o LN

Unknown and missing insurance status, and unknown US-born status were removed from univariate analysis, but for multivariate analysis, these were retained to maximize the number of cases for the final model. The model was adjusted for unknown and missing insurance status and unknown US-born, but estimates were not reported. Insurance status was found to be unreliably recorded prior to 1996. In univariate analysis, this had no effect on the overall outcome, but when it was included in the multivariate model, which included year of diagnosis and other time-dependent variables, the outcome was unstable when risk of late stage was assessed for the full time period, 1988-2009. Therefore a truncated time period was used for both univariate and multivariate analysis from 1996-2009 to remove the issues caused by insurance status.

Aim 2a Univariate Stage Analysis:

For each rare gynecological cancer, contingency table analysis was performed between race/ethnicity, healthcare access characteristics and proportions of early versus late stage at diagnosis, using chi-squared tests.

Aim 2b Multivariate Stage Analysis:

Unconditional logistic regression was performed for each rare gynecological cancer, where the outcome late stage at diagnosis, and independent covariates included all characteristics identified in the univariate analysis and all known covariates of stage. Stepwise logistic regression was performed in order to determine the final model that included all characteristics associated with late stage at diagnosis at a p=0.05 significance level. Estimates of model coefficients and odds ratios (ORs) for all stepwise analysis chosen covariates were reported in table format. Graphical representations of ORs with 95% confidence intervals (95% CIs) were presented in figures to allow for a visual comparison between rare gynecologic cancer sites.

Aim 3 Analysis

Overall:

Calculated 5-year site-specific survival of each of the rare invasive gynecologic cancers, using the time from invasive cancer diagnosis to the time of death caused by cancer for each cancer site specifically, or censored for all other causes of death or alive at time at last follow-up.

Unknown and missing insurance status, and unknown US-born status were removed from univariate analysis, but for multivariate analysis, these were retained to maximize the number of cases for the final model. The model was adjusted for unknown and missing insurance status and unknown US-born, but estimates were not reported. Similar to multivariate stage analysis, insurance status was found to be unreliably recorded prior to 1996 and when it was included in the multivariate model, the outcome was unstable when survival time was assessed for the full time period, 1988-2009. Therefore a truncated time period was used for multivariate analysis from 1996-2009 to remove the issues caused by insurance status.

Cancer-specific cause of death was defined by ICD criteria, using ICD-0-10 codes. The codes used for identifying rare gynecological cancer deaths were: cervical cancer [C530-C539 and 1800-1809]; ovarian cancer [C560-C569 and 1830]; vaginal cancer [C520-C529 and 1840]; vulvar cancer [C510-C519 and 1841-1844]; other female genital organ cancers [C570-C589, 1810-1819, 1832-1835, 1838-1839, and 1848-1849]. Deceased patient cases were identified annually by CCR staff review of state death certificates and hospital registrars which contacted cases annually. Therefore the last date of follow-up was the date of death or last date of contact. The number of identified rare gynecologic cancer site-specific deaths which occurred between 1988-2009 were as follows: deaths by cervical cancer were 6,869; deaths by ovarian cancer were 19,565; deaths by vaginal cancer were 346; deaths by vulvar cancer were 864; deaths by other gynecologic cancers were 238.

Aim 3a Univariate 5-year Survival Analysis:

Kaplan-Meier survival curves of 5-year survival rates were generated from survival time by race/ethnicity and healthcare access measures. Survival times were calculated using the period of time from the diagnosis date to the date of death (or censoring). Differences between survival curves were compared using the log rank test. Figures of Kaplan-Meier curves for each cancer site by race/ethnicity and healthcare access measures were presented.

Aim 3b Multivariate 5-year Survival Analysis:

The main interest of this study was in the effects of race/ethnicity and healthcare access measures. Thus for each cancer site, the impact of healthcare access-related factors on survival in the presence of known factors that were associated with survival on the risk of death from site-specific cancer was evaluated. Multivariate Cox proportional hazard ratios (HR) for all variables shown to be significantly associated with survival in the univariate analysis were entered in a stepwise analysis. Hazard ratios were presented for every significantly associated characteristic which either improved survival (or reduced the risk of death) or worsened survival (or increased the risk of death). All variables on the final model were presented in addition to 95% confidence intervals (CI) in table format and in graphical form to allow for a visual comparison between rare gynecologic cancer sites.

CHAPTER 3: Results

Overview: Site-specific frequency of rare gynecologic cancers by demographic, tumor, and healthcare access characteristics

Cervix

As shown in Table 3.1, significant differences were seen for the frequency of characteristics of invasive cervical cancer by race/ethnicity. The majority of invasive cervical cancer cases were either in NH White (N=14,369; 44.46%) or Hispanic women (N=11,739; 36.32%). Cervical cancer was predominantly diagnosed at a younger age (20-49 years) and at an early stage. There were more NH Asian PI in the 65-79 years age group (20.89%) than for the other race/ethnicities and NH Blacks had a slightly higher proportion of cervical cancers with a late stage at diagnosis (23.51%). The majority of cervical cancer cases had a squamous histology (66.37% - 76.58%). The second most common histology was adenocarcinoma, which was more prevalent in NH Whites and Asian PIs (21.87%; 20.17%). Other histologies were seen in much smaller proportions. The majority of NH Whites and Asian PIs had higher quintiles of socioeconomic status (SES = IV or V), while NH Blacks and Hispanics had a reverse distribution of SES quintiles. NH Whites had the largest percentage of private insurance while Hispanics had the highest for non-private insurance. NH Whites and Blacks had relatively high proportions of US-born individuals (58.51%; 70.80%), while Hispanics and NH Asians had much higher proportions who were not US-born (58.40%; 73.71%).

Table 3.1 Cervix Frequency: Frequency of characteristics of invasive cervical cancer, 1988-2009, stratified by race/ethnicity.

Cervix Frequency:	NH White		NH Black		Hispanic		NH Asian/PI		Chi-Sq P value
	%	N	%	N	%	N	%	N	
Total: 32317	44.46	14369	6.84	2212	36.32	11739	12.37	3997	
Age									
20-49 years	56.51	8120	53.75	1189	62.93	7387	43.68	1746	<0.0001
50-64 years	23.54	3383	24.82	549	23.20	2724	31.27	1250	
65-79 years	14.55	2090	15.51	343	11.41	1339	20.89	835	
80+ years	5.40	776	5.92	131	2.46	289	4.15	166	
Stage									
Early	74.08	10645	69.39	1535	74.75	8775	75.66	3024	<0.0001
Late	21.52	3092	23.51	520	19.64	2306	19.21	768	
Unknown	4.40	632	7.10	157	5.61	658	5.13	205	
Histology									
Squamous	66.37	9536	76.58	1694	74.00	8687	68.68	2745	<0.0001
Adenocarcinoma	21.87	3143	11.57	256	15.97	1875	20.17	806	
Other	11.76	1690	11.84	262	10.03	1177	11.16	446	
SES Quintile									
I	13.22	1899	42.04	930	44.49	5223	17.89	715	<0.0001
II	21.04	3023	23.10	511	23.83	2797	18.31	732	
III	22.46	3227	16.82	372	15.27	1793	21.77	870	
IV	22.76	3271	10.44	231	10.53	1236	21.89	875	
V	20.52	2949	7.59	168	5.88	690	20.14	805	
Insurance Status									
Private	32.32	4644	21.70	480	19.55	2295	26.17	1046	<0.0001
Non-private	22.45	3226	34.86	771	41.00	4813	36.98	1478	
Unknown	38.40	5518	40.82	903	35.78	4200	32.60	1303	
Missing	6.83	981	2.62	58	3.67	431	4.25	170	
US-born Status									
Yes	58.51	8407	70.80	1566	19.29	2265	4.95	198	<0.0001
No	9.26	1330	6.69	148	58.40	6856	73.71	2946	
Unknown	32.24	4632	22.51	498	22.30	2618	21.34	853	

Ovary

As shown in Table 3.2, significant differences were seen for the frequency of invasive ovarian cancer characteristics by race/ethnicity. The vast majority of invasive ovarian cancer cases were seen in NH White women (N=28,783; 70.57%) and were considerably more rare in women of racial/ethnic minorities. Although the overall majority of cases were diagnosed at an age between 50-79 years, NH Whites had a higher percentage within the 80+ years age group (15.85%), while the other racial/ethnic groups had a larger percentage with a young age at diagnosis (20-49 years) (NH Black: 26.02%; Hispanic: 33.10%; NH Asian/PI: 35.74%). All of the

racial/ethnic groups had a high proportion of ovarian cancers with a late stage at diagnosis, though NH Asian PIs had the largest percentage of early stage cancers (37.60%). The preponderance of ovarian histologies fell under one of the adenocarcinoma subtypes for all racial/ethnic groups. Adenocarcinoma, all other subtypes was the most prevalent histology for all racial/ethnic groups and was highest in NH Whites (72.92%). Although the proportion of Endometrioid Adenocarcinoma cancer cases was smaller, NH Asian PIs had almost twice the percent (12.33%) as NH Blacks (6.63%). NH Whites had the lowest percentage of other histologies (17.02%). As seen for cervical cancer, the majority of NH Whites and Asian PIs had a higher SES (IV or V), while NH Blacks and Hispanics had a reverse distribution of SES quintiles. NH Asian PIs had the largest proportion for private insurance (39.36%) and Hispanics had the highest for non-private insurance (39.76%). NH Whites and Blacks had high percentages of US-born (68.17%; 76.40%), while NH Asians had much higher percentage of women who were not US-born and Hispanics had a moderate percentage of not US-born women (47.95%; 70.08%).

Table 3.2 Ovary Frequency: Frequency of characteristics of invasive ovarian cancer, 1988-2009, stratified by race/ethnicity.

Ovary Frequency:	NH White		NH Black		Hispanic		NH Asian/PI		Chi-Sq P value
	%	N	%	N	%	N	%	N	
Total: 40785	70.57	28783	4.77	1945	15.57	6350	9.09	3707	
Age									
20-49 years	17.84	5135	26.02	506	33.10	2102	35.74	1325	<0.0001
50-64 years	30.66	8826	30.85	600	32.50	2064	34.91	1294	
65-79 years	35.65	10260	31.77	618	26.58	1688	22.17	822	
80+ years	15.85	4562	11.36	221	7.81	496	7.18	266	
Stage									
Early	23.98	6902	22.37	435	29.23	1856	37.60	1394	<0.0001
Late	69.54	20015	69.72	1356	63.76	4049	57.73	2140	
Unknown	6.48	1866	7.92	154	7.01	445	4.67	173	
Histology									
Adenocarcinoma, All Other	72.92	20989	68.23	1327	68.30	4337	70.38	2609	<0.0001
Adenocarcinoma, Endometrioid	10.06	2895	6.63	129	10.46	664	12.33	457	
Other	17.02	4899	25.14	489	21.24	1349	17.29	641	
SES Quintile									
I	8.90	2562	32.24	627	32.33	2053	12.27	455	<0.0001
II	16.92	4871	26.32	512	25.04	1590	16.91	627	
III	22.09	6357	18.66	363	18.60	1181	19.91	738	
IV	25.07	7216	13.83	269	14.55	924	24.01	890	
V	27.02	7777	8.95	174	9.48	602	26.90	997	
Insurance Status									
Private	32.63	9391	29.51	574	31.24	1984	39.36	1459	<0.0001
Non-private	28.51	8206	36.04	701	39.76	2525	31.99	1186	
Unknown	33.46	9631	32.08	624	25.86	1642	23.44	869	
Missing	5.40	1555	2.37	46	3.13	199	5.21	193	
US-born Status									
Yes	68.17	19622	76.40	1486	33.61	2134	9.82	364	<0.0001
No	11.86	3413	7.35	143	47.95	3045	70.08	2598	
Unknown	19.97	5748	16.25	316	18.44	1171	20.10	745	

Vagina

As shown in Table 3.3, significant differences were seen for the frequency of characteristics of invasive vaginal cancer by race/ethnicity. The greater part of invasive vaginal cancer cases were found in NH White women (N=1004; 64.15%), followed by Hispanic women (N=291; 18.59%) and then women of the other minority racial/ethnic groups. A majority of NH Whites had an older age at diagnosis (65-80+ years: 61.35%) though a different pattern of age was seen for the other racial/ethnic groups. The age of diagnosis for most of the Asian PIs was between 50-79 years (75.88%) and the largest

percentages of cancer cases were diagnosed for NH Blacks and Hispanics within the youngest age group (20-49 years: 23.26%; 21.65%). There was a trend of mostly early stage cancers seen for all racial/ethnic groups (58.91% - 64.60%), but there was not a significant difference in the percentage of cancers with early/late stage by race/ethnicity. The proportions of histologies for vaginal cancer varied considerably by race/ethnicity. Although the majority of cancers had a histology diagnosis of squamous, NH Blacks and Asian PIs had less cancers diagnosed with a squamous histology (52.71%; 51.77%) than the other racial/ethnic groups (NH White: 62.25%; Hispanic: 71.48%) and were therefore more likely to have an histology diagnosis of “other” (47.29%; 48.23%). Again as seen for cervical cancer, the majority of NH Whites and Asian PIs had a higher SES (IV or V), while NH Blacks and Hispanics had a reverse distribution of SES quintiles. Although NH Whites had an even proportion of private and non-private insurance, the proportion of non-private insurance was much higher for NH Blacks, Hispanics, and NH Asian PIs (38.76%; 41.92%; 43.26%). The majority of Hispanics and NH Asian PIs were not US-born (52.23%; 72.34%), while NH Whites and Blacks were primarily US-born (66.73%; 75.19%).

Table 3.3 Vagina Frequency: Frequency of characteristics of invasive vaginal cancer, 1988-2009, stratified by race/ethnicity.

	NH White		NH Black		Hispanic		NH Asian/PI		Chi-Sq
Vagina Frequency:	%	**N**	%	**N**	%	**N**	%	**N**	**P value**
Total: 1377	64.15	1004	8.24	129	18.59	291	9.01	141	
Age									
20-49 years	13.75	138	23.26	30	21.65	63	10.64	15	<0.0001
50-64 years	24.90	250	31.01	40	30.93	90	41.13	58	
65-79 years	34.26	344	30.23	39	31.96	93	34.75	49	
80+ years	27.09	272	15.50	20	15.46	45	13.48	19	
Stage									
Early	62.05	623	58.91	76	64.60	188	62.41	88	0.3636
Late	25.40	255	33.33	43	23.02	67	26.24	37	
Unknown	12.55	126	7.75	10	12.37	36	11.35	16	
Histology									
Squamous	62.25	625	52.71	68	71.48	208	51.77	73	<0.0001
Other	37.75	379	47.29	61	28.52	83	48.23	68	
SES Quintile									
I	11.65	117	34.88	45	33.68	98	13.48	19	<0.0001
II	19.92	200	31.01	40	25.43	74	21.28	30	
III	23.11	232	18.60	24	20.96	61	21.99	31	
IV	23.80	239	9.30	12	11.34	33	17.73	25	
V	21.51	216	6.20	8	8.59	25	25.53	36	
Insurance Status									
Private	29.48	296	31.78	41	24.74	72	28.37	40	0.0276
Non-private	31.97	321	38.76	50	41.92	122	43.26	61	
Unknown	34.26	344	26.36	34	29.21	85	26.24	37	
Missing	4.28	43	3.10	4	4.12	12	2.13	3	
US-born Status									
Yes	66.73	670	75.19	97	31.62	92	9.22	13	<0.0001
No	11.25	113	3.10	4	52.23	152	72.34	102	
Unknown	22.01	221	21.71	28	16.15	47	18.44	26	

Vulva

As shown in Table 3.4, significant differences were seen for the frequency of characteristics by race/ethnicity of invasive vulvar cancer. The preponderance of invasive vulvar cancer cases were identified in NH White women (N=3,951; 76.51%), followed by Hispanic women (N=693; 13.42%) and then women of the other minority racial/ethnic groups. The age distribution of women diagnosed with invasive vulvar cancer was similar to that of vaginal cancer. The majority of NH Whites were diagnosed at an older age than the other racial/ethnic groups (65-80+: 60.74%) and although the

majority of the other groups were diagnosed at an age between 50-79 years (NH Black: 53.15%; Hispanic: 58.01%; NH Asian PI: 63.25%), NH Blacks had the largest percentage of cases diagnosed at the youngest age group (20-49 years: 32.52%). The percentage of women diagnosed at the oldest age group (80+ years) was half as much for NH Asian PIs as that for NH Whites (13.48%; 27.09%). The percentage of women diagnosed with late stage cancers was low for all racial/ethnic groups, though it was slightly higher for Hispanics (26.70%). The vast majority of histology diagnoses fell under squamous for all racial/ethnic groups. The proportion of squamous histology was highest for NH Blacks (84.62%) and was lowest for NH Asian PIs (58.55%), leading to a larger proportion of “other” histology (41.45%). Again as seen for cervical and vaginal cancer, the majority of NH Whites and Asian PIs had a higher SES (IV or V), while NH Blacks and Hispanics had a reverse distribution of SES quintiles. Like vaginal cancer, NH Whites diagnosed with invasive vulvar cancer had an even proportion of women private and non-private insurance, and the proportion of women with non-private insurance was much higher for NH Blacks, Hispanics, and NH Asian PIs (40.91%; 44.16%; 44.44%). And like cervical cancer, NH Whites and Blacks diagnosed with vulvar cancer had relatively high percentages of US-born individuals (62.19%; 66.43%), while Hispanics and NH Asians had much higher proportions of women who were not US-born (41.99%; 67.95%).

Table 3.4 Vulva Frequency: Frequency of characteristics of invasive vulvar cancer, 1988-2009, stratified by race/ethnicity.

Vulva Frequency:	NH White		NH Black		Hispanic		NH Asian/PI		Chi-Sq P value
	%	N	%	N	%	N	%	N	
Total: 5164	76.51	3951	5.54	286	13.42	693	4.53	234	
Age									
20-49 years	15.41	609	32.52	93	19.62	136	17.09	40	<0.0001
50-64 years	23.84	942	30.07	86	23.81	165	24.36	57	
65-79 years	34.07	1346	23.08	66	34.20	237	38.89	91	
80+ years	26.68	1054	14.34	41	22.37	155	19.66	46	
Stage									
Early	73.93	2921	73.43	210	67.10	465	73.93	173	0.0199
Late	20.55	812	21.68	62	26.70	185	20.51	48	
Unknown	5.52	218	4.90	14	6.20	43	5.56	13	
Histology									
Squamous	81.07	3203	84.62	242	79.37	550	58.55	137	<0.0001
Other	18.93	748	15.38	44	20.63	143	41.45	97	
SES Quintile									
I	12.71	502	36.01	103	36.08	250	13.25	31	<0.0001
II	19.21	759	25.87	74	23.38	162	18.38	43	
III	23.39	924	15.38	44	16.88	117	21.37	50	
IV	22.73	898	13.99	40	14.00	97	22.65	53	
V	21.97	868	8.74	25	9.67	67	24.36	57	
Insurance Status									
Private	29.28	1157	31.82	91	26.41	183	26.92	63	<0.0001
Non-private	33.94	1341	40.91	117	44.16	306	44.44	104	
Unknown	32.30	1276	23.78	68	26.70	185	25.64	60	
Missing	4.48	177	3.50	10	2.74	19	2.99	7	
US-born Status									
Yes	62.19	2457	66.43	190	34.78	241	10.26	24	<0.0001
No	11.14	440	5.24	15	41.99	291	67.95	159	
Unknown	26.68	1054	28.32	81	23.23	161	21.79	51	

Other Gynecologic

As shown in Table 3.5, significant differences were seen for the frequency of characteristics by race/ethnicity of invasive cancer cases of other female genital organs. Similar to ovarian cancer, the majority of invasive cancer cases of other female genital organs were diagnosed in NH White women (N=1,395; 66.15%). Unlike ovarian cancer, however, the distribution by age was more profoundly different by race/ethnicity. Although the largest percentage of NH Whites were aged 65-79 years when diagnosed (36.77%), the largest percentage of NH Blacks, Hispanics, and NH Asian PIs were aged

20-49 years when diagnosed with invasive other gynecologic cancers (38.35%; 56.89%; 44.97%). There was not a significant difference in the percentage of early/late stage cancers by race/ethnicity but there was a trend of mostly diagnosed late stage cases for all groups. Cancers placed in the other female genital organ “catch-all” category were not defined by histology. As seen for all other gynecological cancers, the majority of NH Whites and Asian PIs with other gynecologic cancers had a higher SES (IV or V), while NH Blacks and Hispanics had a reverse distribution of SES. NH Asian PIs had the largest percentage of individuals with private insurance (39.15%); NH Blacks and Hispanics had the largest percentage of individuals with non-private insurance (39.85%; 39.80%). Like cervical and vulvar cancer, NH Whites and Blacks identified in this cancer category had relatively high percentages of US-born women (63.44%; 69.17%), while Hispanics and NH Asians had much higher proportions of individuals who were not US-born (46.94%; 68.78%).

Table 3.5 Other Gynecologic Frequency: Frequency of characteristics of invasive other gynecologic cancers, 1988-2009, stratified by race/ethnicity.

Other Gynecologic Frequency:		NH White		NH Black		Hispanic		NH Asian/PI		Chi-Sq P value
		%	N	%	N	%	N	%	N	
Total: 2109		66.15	1395	6.31	133	18.59	392	8.96	189	
Age										
	20-49 years	16.56	231	38.35	51	56.89	223	44.97	85	<0.0001
	50-64 years	31.61	441	24.81	33	22.19	87	34.92	66	
	65-79 years	36.77	513	26.32	35	15.31	60	16.93	32	
	80+ years	15.05	210	10.53	14	5.61	22	3.17	6	
Stage										
	Early	37.49	523	38.35	51	38.27	150	38.10	72	0.1227
	Late	52.04	726	44.36	59	47.45	186	50.26	95	
	Unknown	10.47	146	17.29	23	14.29	56	11.64	22	
SES Quintile										
	I	9.03	126	28.57	38	35.97	141	19.05	36	<0.0001
	II	15.05	210	27.07	36	22.45	88	13.23	25	
	III	22.65	316	18.05	24	18.88	74	15.34	29	
	IV	24.66	344	14.29	19	15.56	61	24.34	46	
	V	28.60	399	12.03	16	7.14	28	28.04	53	
Insurance Status										
	Private	34.77	485	26.32	35	26.53	104	39.15	74	0.0065
	Non-private	31.76	443	39.85	53	39.80	156	31.22	59	
	Unknown	28.32	395	32.33	43	28.57	112	24.87	47	
	Missing	5.16	72	1.50	2	5.10	20	4.76	9	
US-born Status										
	Yes	63.44	885	69.17	92	26.53	104	6.35	12	<0.0001
	No	13.62	190	6.77	9	46.94	184	68.78	130	
	Unknown	22.94	320	24.06	32	26.53	104	24.87	47	

Aim 1 part b: Site-specific proportional incidence rate ratios of healthcare access measures by race/ethnicity

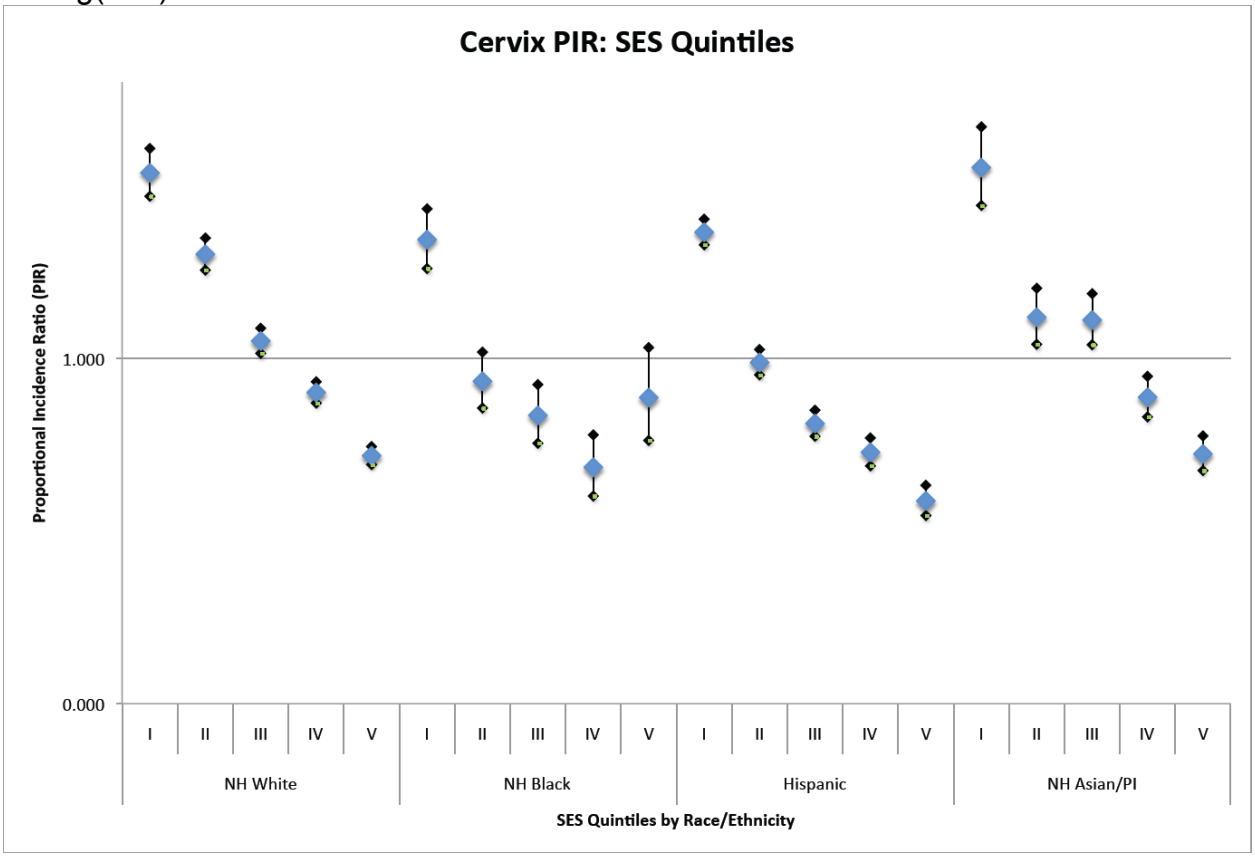
Cervix

SES: Comparisons of cervical cancer proportional incidence rate ratios (PIRs) by quintile of SES (socioeconomic status) are shown in Table 3.6 and Figure 3.1a. For all racial/ethnic groups, PIR decreased with increasing SES, and except for the Non-Hispanic Black group, the greatest cervical cancer PIR was seen in the lowest SES quintile. High SES was most protective for Hispanics [PIR = 0.587; (0.545, 0.633)]. Low SES increased risk for NH Whites by 53.7%, 30.1% and 5.0% while high SES decreased risk by 9.9% and 27.7%.

Table 3.6 Cervix PIR: PIR estimates and 95% confidence intervals (95% CI) for invasive cervical cancer of healthcare access measures by race/ethnicity.

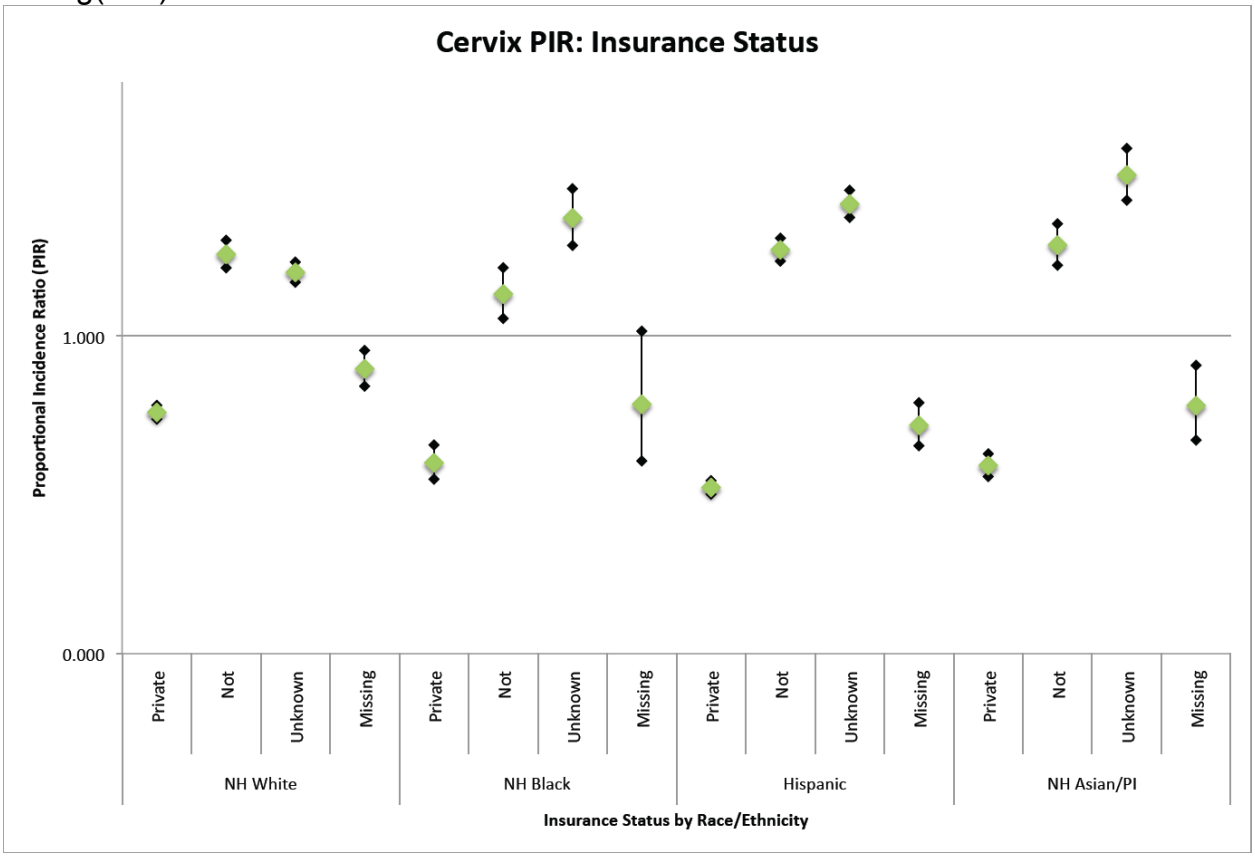
	NH White		NH Black		Hispanic		NH Asian/PI	
Cervix PIR:	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI
SES Quintiles								
I	1.537	(1.469, 1.608)	1.344	(1.260, 1.433)	1.365	(1.329, 1.403)	1.552	(1.443, 1.670)
II	1.301	(1.256, 1.348)	0.934	(0.856, 0.754)	0.988	(0.952, 1.025)	1.119	(1.041, 1.203)
III	1.050	(1.015, 1.087)	0.835	(0.754, 0.924)	0.811	(0.775, 0.850)	1.111	(1.039, 1.187)
IV	0.901	(0.871, 0.932)	0.684	(0.602, 0.779)	0.728	(0.688, 0.770)	0.887	(0.830, 0.948)
V	0.718	(0.693, 0.744)	0.887	(0.762, 1.031)	0.587	(0.545, 0.633)	0.723	(0.675, 0.775)
Insurance Status								
Private	0.760	(0.738, 0.782)	0.601	(0.549, 0.657)	0.523	(0.502, 0.545)	0.592	(0.557, 0.629)
Non-private	1.258	(1.215, 1.302)	1.132	(1.055, 1.215)	1.272	(1.236, 1.308)	1.287	(1.223, 1.354)
Unknown	1.201	(1.169, 1.233)	1.372	(1.285, 1.464	1.416	(1.374, 1.459)	1.507	(1.428, 1.591)
Missing	0.897	(0.842, 0.955)	0.785	(0.607, 1.015)	0.719	(0.654, 0.790)	0.781	(0.672, 0.908)
US-born Status								
Yes	1.020	(0.998, 1.042)	1.007	(0.958, 1.058)	0.646	(0.620, 0.673)	0.507	(0.441, 0.583)
No	1.068	(1.012, 1.127)	1.126	(0.958, 1.323)	1.331	(1.300, 1.363)	1.120	(1.081, 1.162)
Unknown	0.950	(0.923, 0.977)	0.948	(0.868, 1.035)	0.849	(0.817, 0.882)	0.873	(0.816, 0.933)

Figure 3.1a Cervix PIR – SES: PIR estimates and 95% confidence intervals (95% CI) for invasive cervical cancer calculated for socioeconomic status (SES) quintile by race/ethnicity.
Legend: Error Bars = 95% Confidence Intervals (95% CI) of each PIR, calculated from the log(PIR) estimate.



Insurance: The distribution of cervical PIRs varied insurance status for all race/ethnicities as seen in Table 3.6 and Figure 3.1b. Private insurance was associated with a significantly decreased risk of cervical cancer for all racial/ethnic groups, while non-private and unknown insurance status were associated with a significant increased risk. The lowest risk was seen for Hispanics; private insurance reduced risk by 47.7%. The highest risk was observed when insurance status was unknown for NH Asian PIs, which raised risk by 50.7%. Missing insurance status decreased risk for all race/ethnicities, reaching statistical significance for all but NH Blacks.

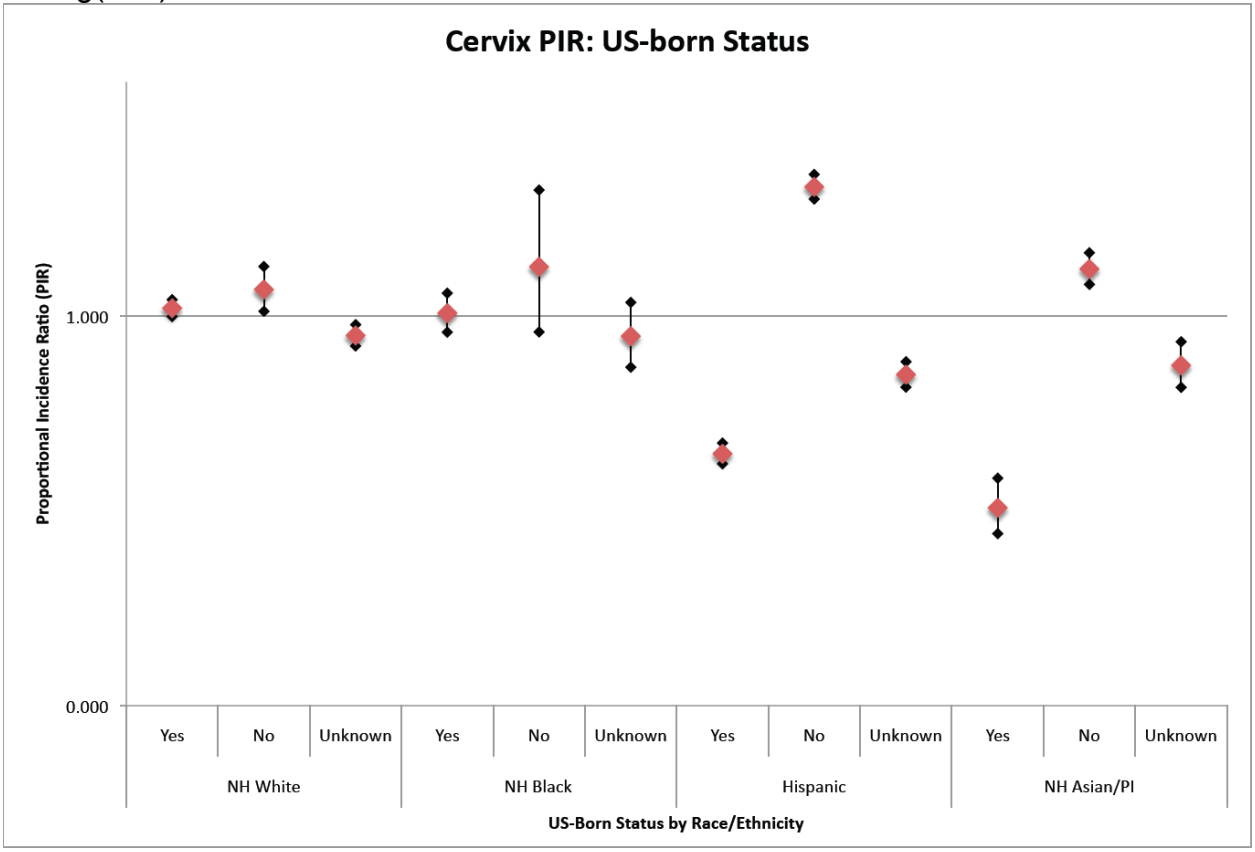
Figure 3.1b Cervix PIR – Insurance Status: PIR estimates and 95% confidence intervals (95% CI) for invasive cervical cancer calculated for insurance status by race/ethnicity.
Legend: Error Bars = 95% Confidence Intervals (95% CI) of each PIR, calculated from the log(PIR) estimate.



US-born: Cervical PIR by US-born status did not show consistent findings across race/ethnicity as seen as Table 3.6 and Figure 3.1c. A birthplace within the US significantly decreased the risk of cervical cancer for Hispanics and NH Asian PIs (PIR = 0.646 and 0.507), and although an increased risk was seen in NH Whites and Blacks, it did not reach statistical significance. The largest reduction in risk was seen for NH Asian PIs, where risk was lowered by 49.3%. The greatest increase in risk was seen in Hispanics, with an increase of 33.1% for those born outside the US. Unknown status of

US-birthplace had a slight protective effect for NH Whites, Hispanics, and NH Asian PIs (PIRs = 0.950, 0.849, and 0.873 respectively).

Figure 3.1c Cervix PIR – US-born Status: PIR estimates and 95% confidence intervals (95% CI) for invasive cervical cancer calculated for US-born status by race/ethnicity. Legend: Error Bars = 95% Confidence Intervals (95% CI) of each PIR, calculated from the log(PIR) estimate.



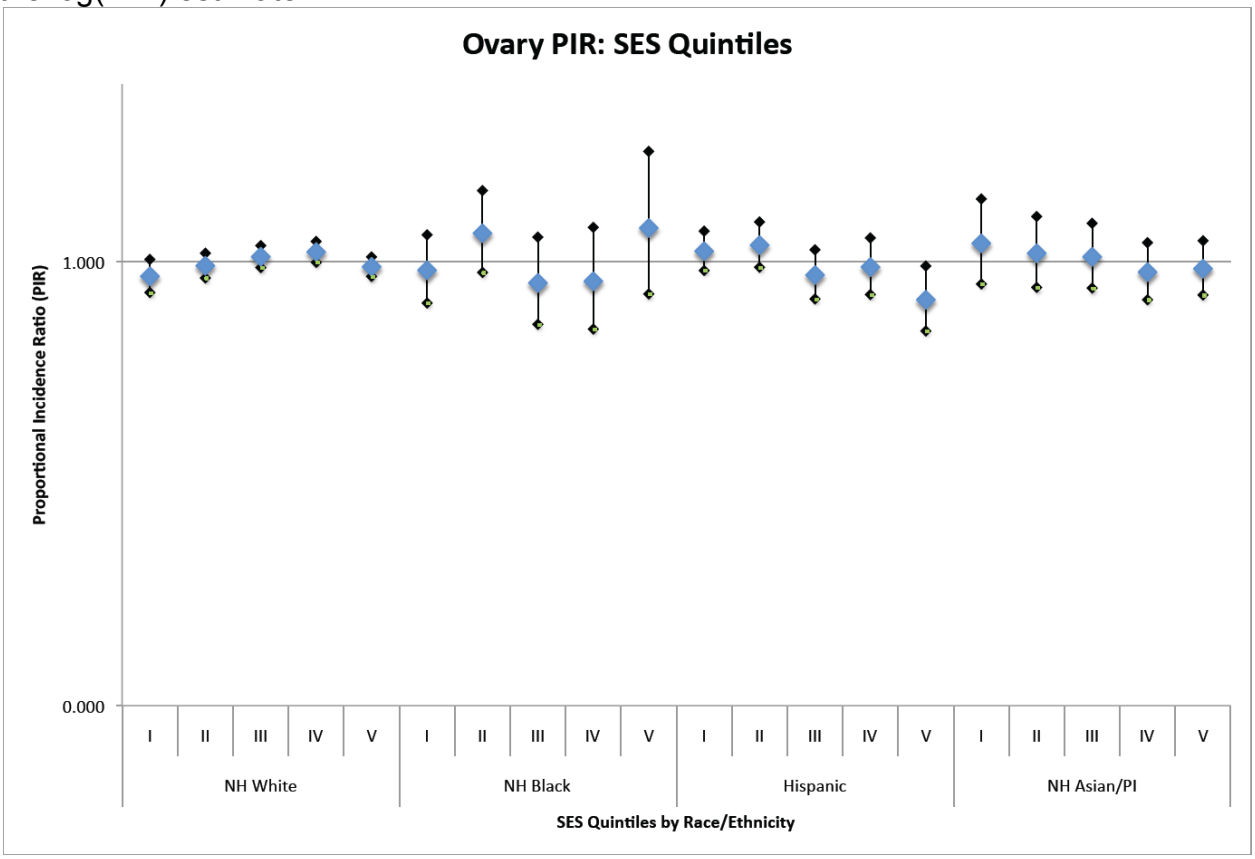
Ovary

SES: The distribution of PIRs of ovarian cancer did not vary for quintiles of SES as seen in Table 3.7 and Figure 3.2a. No single level of SES had a significantly increased or decreased risk for any racial/ethnic group, with one exception: the highest quintile of SES (=5) for Hispanics reduced the risk of ovarian cancer by 8.6%.

Table 3.7 Ovary PIR: PIR estimates and 95% confidence intervals (95% CI) for invasive ovarian cancer of healthcare access measures by race/ethnicity.

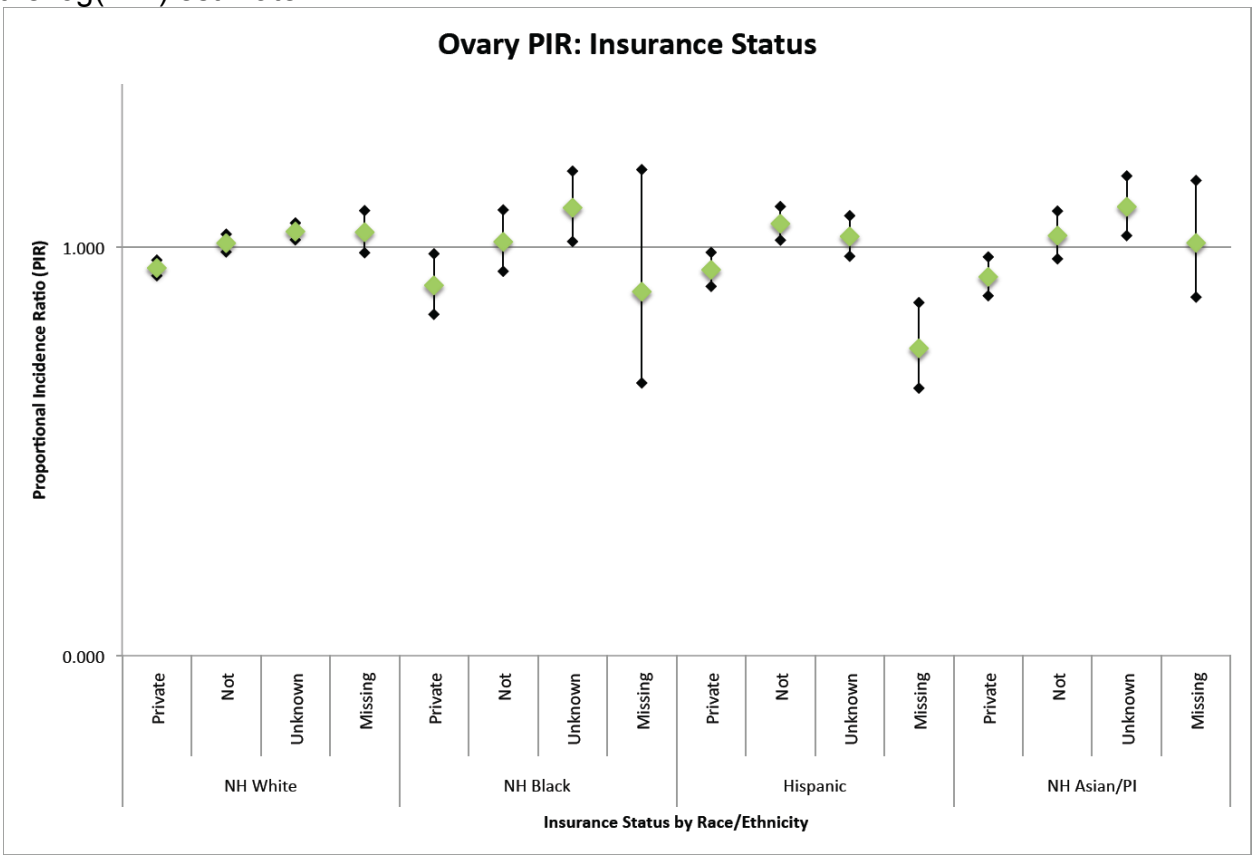
	NH White		NH Black		Hispanic		NH Asian/PI	
Ovary PIR:	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI
SES Quintiles								
I	0.967	(0.930, 1.005)	0.981	(0.907, 1.060)	1.024	(0.980, 1.069)	1.041	(0.950, 1.141)
II	0.991	(0.963, 1.019)	1.064	(0.976, 1.160)	1.037	(0.987, 1.089)	1.019	(0.942, 1.102)
III	1.011	(0.987, 1.036)	0.952	(0.859, 1.055)	0.970	(0.916, 1.027)	1.011	(0.940, 1.086)
IV	1.022	(0.998, 1.046)	0.956	(0.848, 1.077)	0.988	(0.926, 1.054)	0.977	(0.914, 1.043)
V	0.988	(0.967, 1.011)	1.076	(0.927, 1.248)	0.914	(0.844, 0.990)	0.984	(0.925, 1.047)
Insurance Status								
Private	0.950	(0.931, 0.969)	0.907	(0.836, 0.984)	0.945	(0.904, 0.987)	0.928	(0.881, 0.977)
Non-private	1.010	(0.989, 1.032)	1.014	(0.941, 1.091)	1.058	(1.018, 1.100)	1.029	(0.972, 1.089)
Unknown	1.039	(1.018, 1.060)	1.097	(1.014, 1.187)	1.027	(0.978, 1.078)	1.099	(1.029, 1.175)
Missing	1.037	(0.987, 1.090)	0.892	(0.668, 1.190)	0.753	(0.655, 0.865)	1.011	(0.878, 1.164)
US-born Status								
Yes	1.080	(1.065, 1.096)	1.042	(0.990, 1.096)	1.023	(0.980, 1.067)	0.953	(0.860, 1.056)
No	1.108	(1.072, 1.146)	1.243	(1.055, 1.464)	1.089	(1.051, 1.128)	1.062	(1.022, 1.104)
Unknown	0.762	(0.743, 0.782)	0.784	(0.702, 0.875)	0.799	(0.754, 0.846)	0.848	(0.789, 0.911)

Figure 3.2a Ovary PIR – SES: PIR estimates and 95% confidence intervals (95% CI) for invasive ovarian cancer calculated for SES quintile by race/ethnicity.
Legend: Error Bars = 95% Confidence Intervals (95% CI) of each PIR, calculated from the log(PIR) estimate.



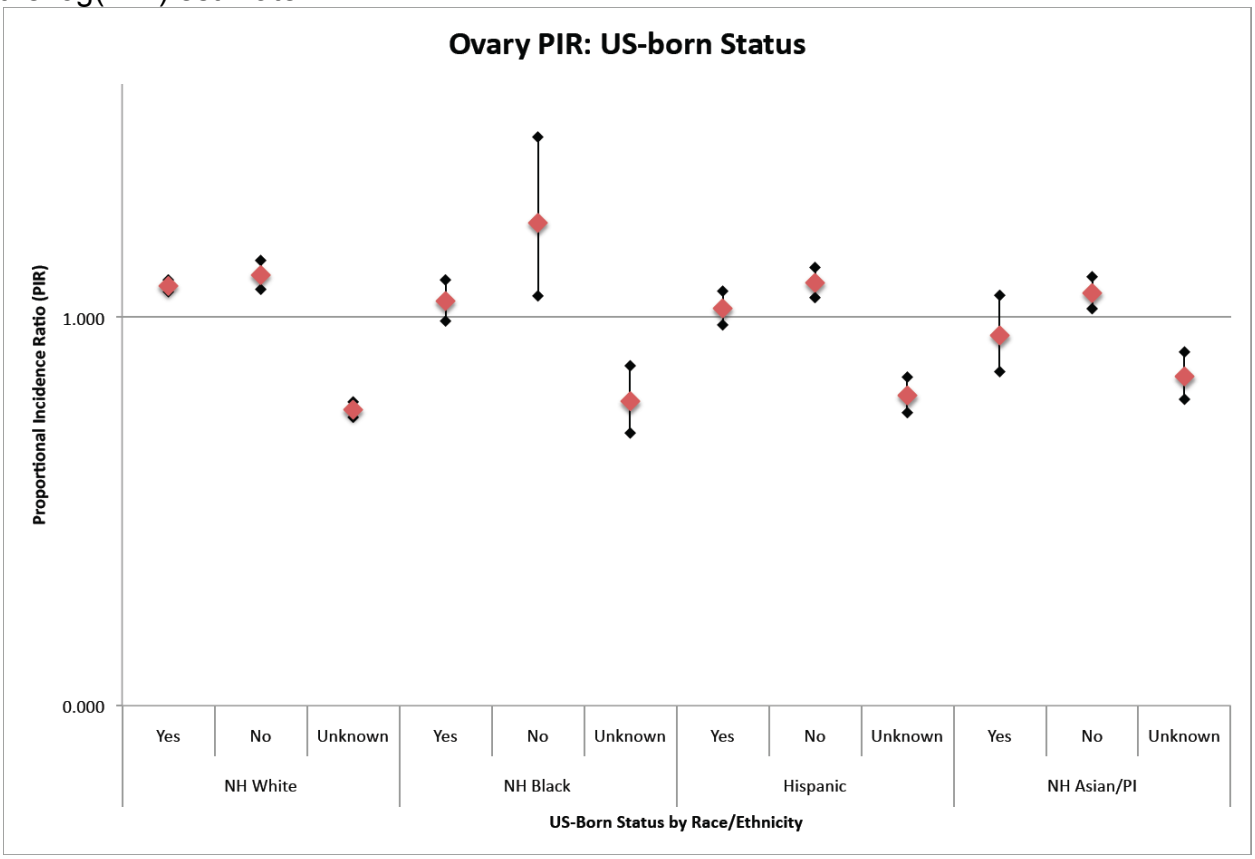
Insurance: The PIR distribution of ovarian cancer varied for insurance status by race/ethnicity as seen in Table 3.7 and Figure 3.2b. There was a small benefit of private insurance for all racial/ethnic groups, ranging a 5.0%-9.3% reduction. Having a non-private insurance status did not affect risk except for a small, but significant 5.8% increase for Hispanics. For the other racial/ethic groups (NH Whites, Blacks and Asian PIs) an unknown insurance status increased risk by 2.7-9.9%. Missing insurance status was beneficial only for Hispanics (PIR = 0.753; (0.655, 0.865)).

Figure 3.2b Ovary PIR – Insurance Status: PIR estimates and 95% confidence intervals (95% CI) for invasive ovarian cancer calculated for insurance status by race/ethnicity. Legend: Error Bars = 95% Confidence Intervals (95% CI) of each PIR, calculated from the log(PIR) estimate.



US-born: The PIR distribution of ovarian cancer for US-born status was considerably different for each racial/ethnic group as seen in Table 3.7 and Figure 3.2c. For NH Whites, a US-born status of yes or no increased risk slightly (PIRs= 1.080 and 1.108, respectively). For the racial/ethnic minorities, a birthplace within US did not significantly affect risk. A birthplace status outside the US raised risk for NH Blacks, Hispanics and NH Asian PIs by 6.2%-24.3%. A significant protective effect was seen for all race/ethnicities among those whose US-born status was unknown.

Figure 3.2c Ovary PIR – US-born Status: PIR estimates and 95% confidence intervals (95% CI) for invasive ovarian cancer calculated for US-born status by race/ethnicity. Legend: Error Bars = 95% Confidence Intervals (95% CI) of each PIR, calculated from the log(PIR) estimate.



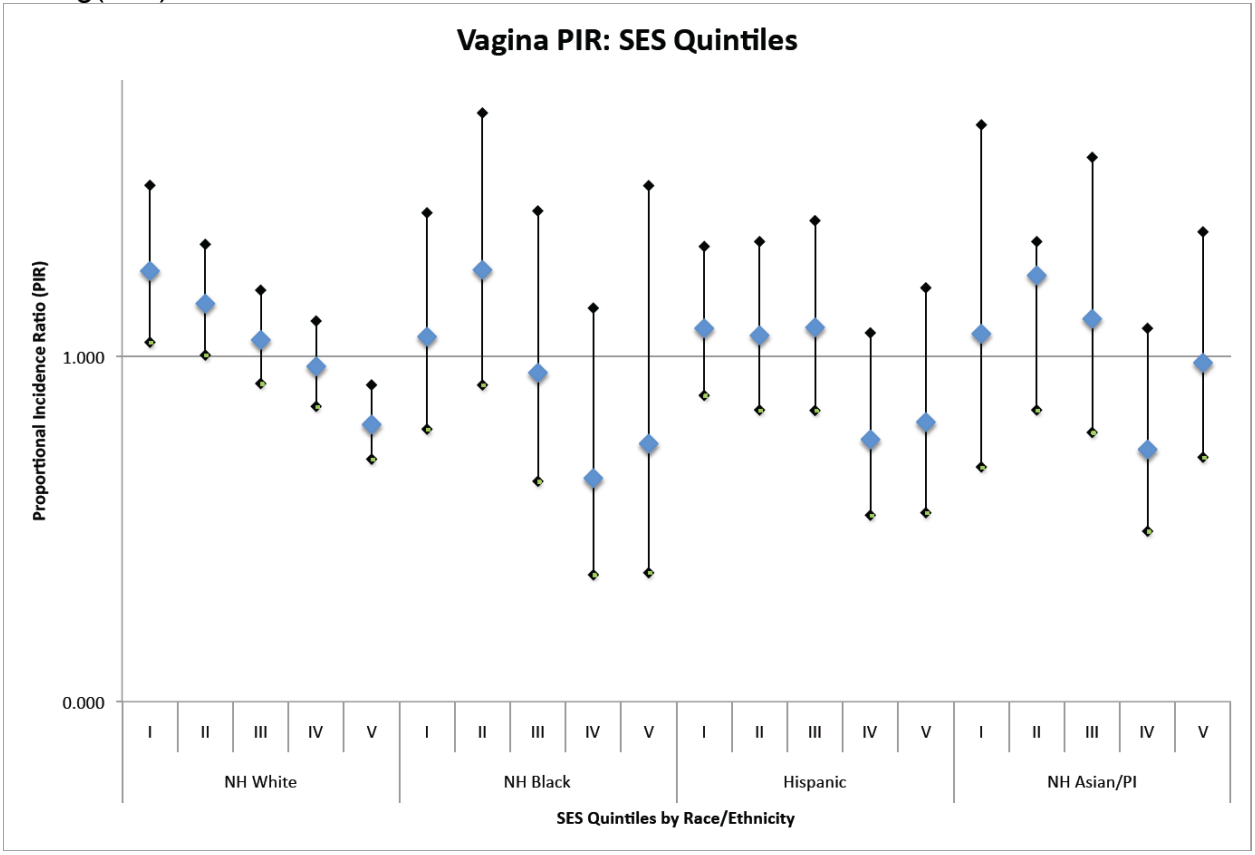
Vagina

SES: The effects SES on PIR for vaginal cancer PIR by race/ethnicity are shown in Table 3.8 and Figure 3.3a. The effects of low SES were seen most clearly for NH Whites, which had high PIRs for low SES (PIRs = 1.247 and 1.153) and decreased risk with high SES, with a 19.7% reduction for the highest SES group. While similar trends of SES on the risk of vaginal cancer were seen for other racial/ethnic groups (low SES increased risk by 5.7%-8.1% and high SES decreased risk by 1.9%-25.3%), none reached statistical significance.

Table 3.8 Vagina PIR: PIR estimates and 95% confidence intervals (95% CI) for invasive vaginal cancer of healthcare access measures by race/ethnicity.

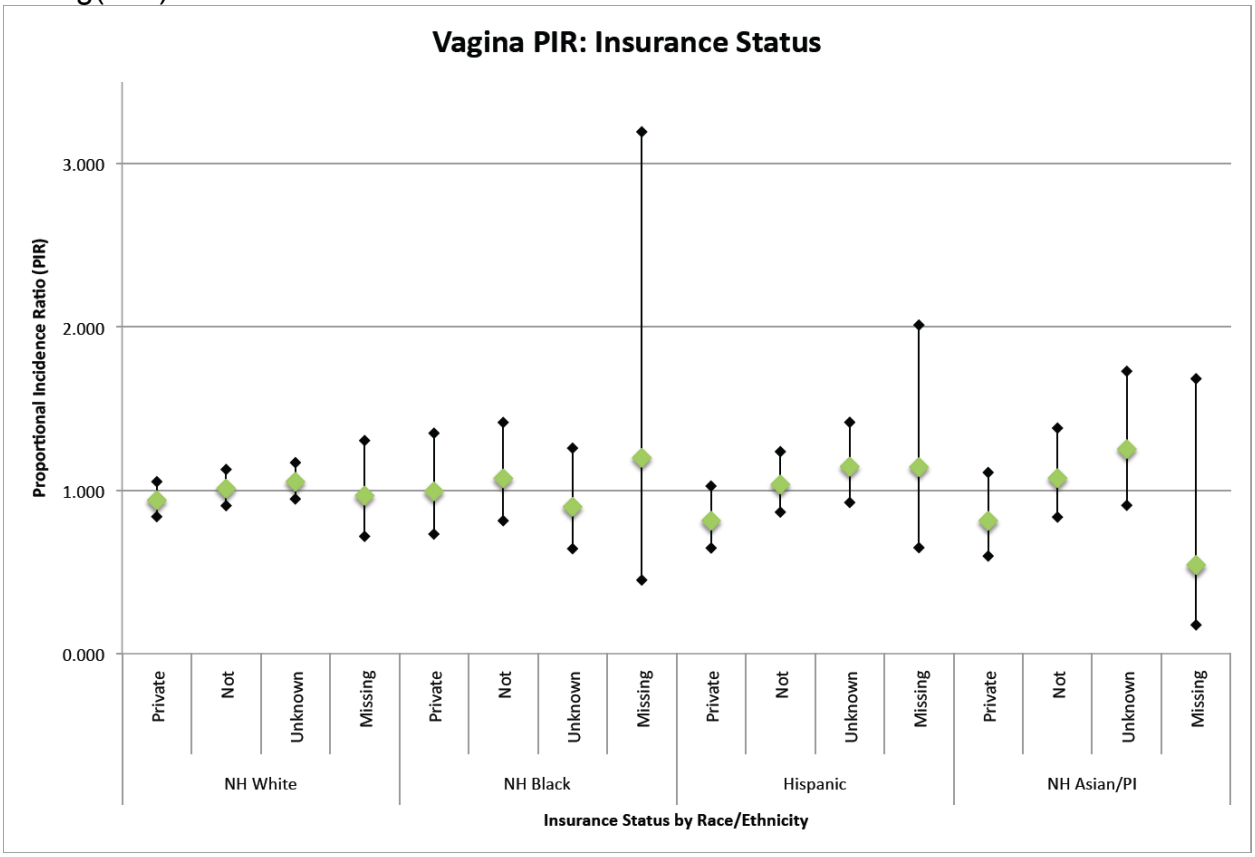
	NH White		NH Black		Hispanic		NH Asian/PI	
Vagina PIR:	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI
SES Quintiles								
I	1.247	(1.041, 1.495)	1.057	(0.789, 1.416)	1.081	(0.887, 1.318)	1.065	(0.680, 1.670)
II	1.153	(1.004, 1.324)	1.251	(0.917, 1.705)	1.061	(0.845, 1.332)	1.235	(0.845, 1.332)
III	1.048	(0.921, 1.192)	0.952	(0.638, 1.421)	1.084	(0.843, 1.393)	1.109	(0.780, 1.576)
IV	0.971	(0.855, 1.102)	0.647	(0.368, 1.140)	0.759	(0.540, 1.068)	0.731	(0.494, 1.081)
V	0.803	(0.702, 0.917)	0.747	(0.374, 1.494)	0.810	(0.547, 1.198)	0.981	(0.708, 1.360)
Insurance Status								
Private	0.939	(0.838, 1.053)	0.994	(0.732, 1.349)	0.814	(0.646, 1.026)	0.814	(0.597, 1.109)
Non-private	1.011	(0.906, 1.127)	1.073	(0.813, 1.416)	1.035	(0.867, 1.236)	1.074	(0.836, 1.381)
Unknown	1.053	(0.947, 1.170)	0.899	(0.643, 1.258)	1.145	(0.926, 1.416)	1.253	(0.908, 1.729)
Missing	0.968	(0.718, 1.305)	1.199	(0.450, 3.195)	1.143	(0.649, 2.012)	0.543	(0.175, 1.683)
US-born Status								
Yes	1.031	(0.956, 1.113)	1.021	(0.837, 1.246)	0.940	(0.766, 1.153)	0.832	(0.483, 1.432)
No	0.986	(0.820, 1.185)	0.523	(0.196, 1.394)	1.158	(0.988, 1.357)	1.060	(0.873, 1.287)
Unknown	0.922	(0.808, 1.052)	1.062	(0.733, 1.537)	0.760	(0.571, 1.011)	0.893	(0.608, 1.312)

Figure 3.3a Vagina PIR – SES: PIR estimates and 95% confidence intervals (95% CI) for invasive vaginal cancer calculated for SES quintiles by race/ethnicity.
Legend: Error Bars = 95% Confidence Intervals (95% CI) of each PIR, calculated from the log(PIR) estimate.



Insurance: For all racial/ethnic groups, a protective effect was seen in the private insurance group and an increase in risk of vaginal cancer was seen in the non-private insurance group (Table 3.8 and Figure 3.3b). Unknown insurance status increased risk for NH Whites, Hispanics and NH Asian PIs (5.3%, 14.5%, and 25.3%) while missing insurance status decreased risk for NH Whites and Hispanics (3.2% and 45.7%). However confidence intervals were quite large, especially for the missing group, and estimates did not reach the level of statistical significance.

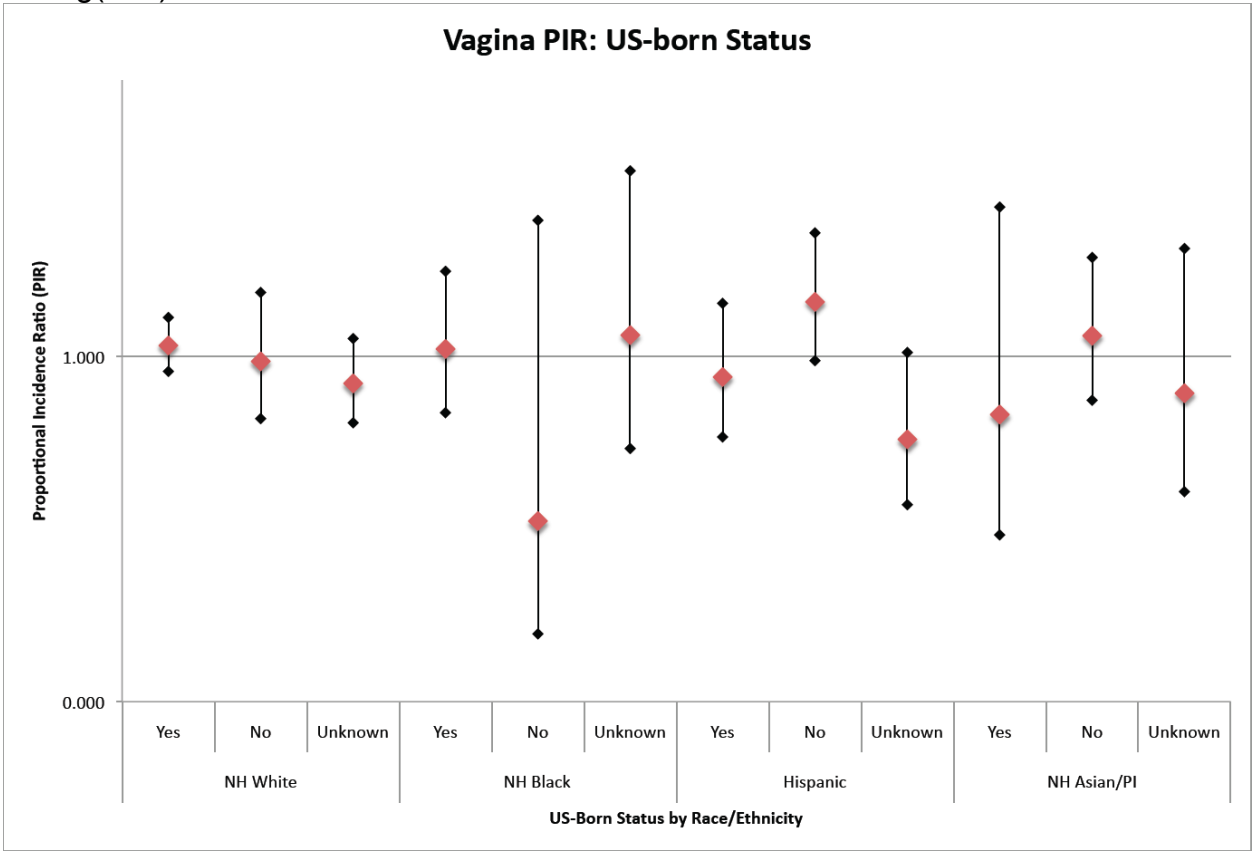
Figure 3.3b Vagina PIR – Insurance Status: PIR estimates and 95% confidence intervals (95% CI) for invasive vaginal cancer calculated for insurance status by race/ethnicity.
Legend: Error Bars = 95% Confidence Intervals (95% CI) of each PIR, calculated from the log(PIR) estimate.



US-born: Opposing patterns of the effects of US-born status were seen for NH Whites and Blacks versus Hispanics and NH Asian/PIs, as seen in Table 3.8 and Figure 3.3c. Although the following trends were seen, none reached statistical significance. A positive US-born status gave a higher PIR for NH Whites and Blacks (1.031, 1.021), but a lower PIR for Hispanics and Asian PIs (0.940, 0.832). A negative US-born status gave a lower PIR for NH Whites and Blacks (0.986, 0.583), but a higher PIR for Hispanics and Asian PIs (1.158, 1.060). Unknown US-born status decreased risk for NH Whites,

Hispanics, and NH Asian PIs (PIR = 0.922, 0.760, 0.893) but increased risk for NH Blacks (PIR = 1.062).

Figure 3.3c Vagina PIR – US-born Status: PIR estimates and 95% confidence intervals (95% CI) for invasive vaginal cancer calculated for US-born status by race/ethnicity. Legend: Error Bars = 95% Confidence Intervals (95% CI) of each PIR, calculated from the log(PIR) estimate.



Vulva

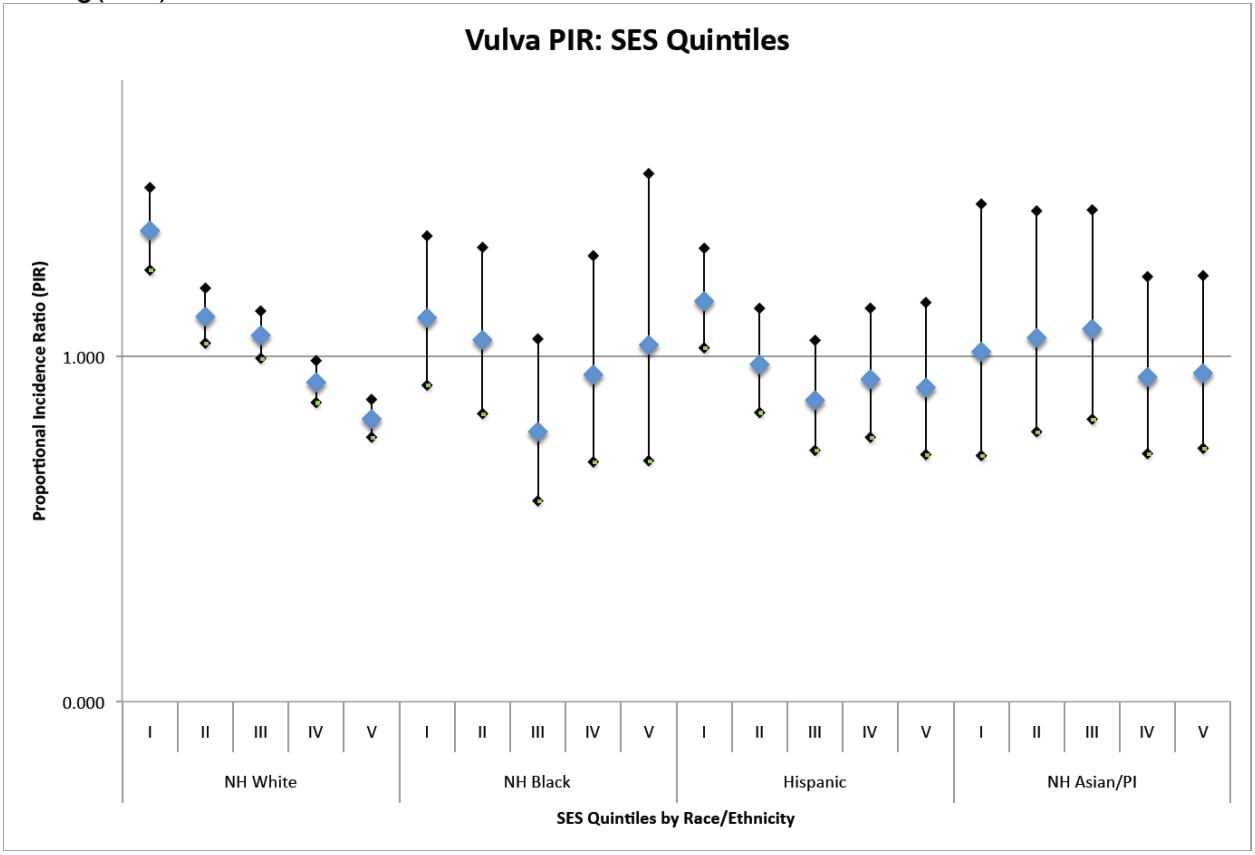
SES: The distribution of PIR by quintile of SES varied by race/ethnicity for vulvar cancer, as seen in Table 3.9 and Figure 3.4a. The strongest effects of SES were seen for NH Whites. Low SES for NH Whites raised risk by 36.4%-11.5% (SES= 1 and 2) while higher SES (= 4 and 5) reduced risk by 7.5%-18.1%. NH Blacks and Hispanics

had the highest PIR for the lowest SES (1.112, 1.160) but the overall trend by SES was not apparent for any racial/ethnic group but NH White.

Table 3.9 Vulva PIR: PIR estimates and 95% confidence intervals (95% CI) for invasive vulvar cancer of healthcare access measures by race/ethnicity.

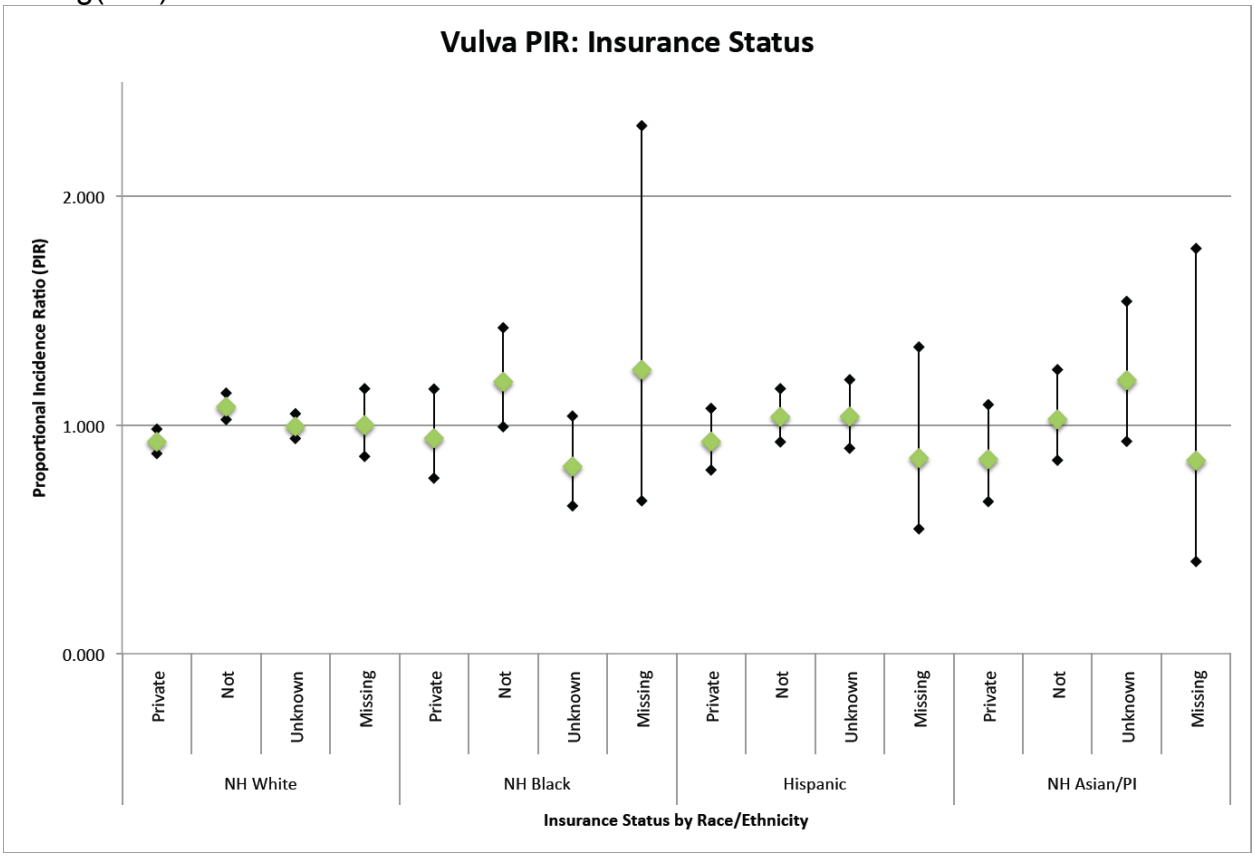
	NH White		NH Black		Hispanic		NH Asian/PI	
Vulva PIR:	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI
SES Quintiles								
I	1.364	(1.250, 1.489)	1.112	(0.916, 1.349)	1.160	(1.025, 1.313)	1.013	(0.713, 1.441)
II	1.115	(1.038, 1.197)	1.048	(0.834, 1.316)	0.977	(0.837, 1.139)	1.054	(0.782, 1.421)
III	1.061	(0.994, 1.131)	0.782	(0.582, 1.051)	0.873	(0.728, 1.046)	1.079	(0.818, 1.424)
IV	0.925	(0.866, 0.987)	0.947	(0.695, 1.291)	0.934	(0.765, 1.140)	0.940	(0.718, 1.231)
V	0.819	(0.766, 0.875)	1.033	(0.698, 1.529)	0.910	(0.716, 1.156)	0.951	(0.734, 1.233)
Insurance Status								
Private	0.927	(0.875, 0.982)	0.942	(0.767, 1.157)	0.928	(0.803, 1.073)	0.851	(0.665, 1.089)
Non-private	1.080	(1.024, 1.140)	1.190	(0.992, 1.426)	1.036	(0.926, 1.159)	1.025	(0.846, 1.242)
Unknown	0.994	(0.941, 1.050)	0.819	(0.646, 1.039)	1.038	(0.898, 1.198)	1.196	(0.929, 1.540)
Missing	1.000	(0.863, 1.158)	1.242	(0.668, 2.309)	0.856	(0.546, 1.341)	0.845	(0.403, 1.772)
US-born Status								
Yes	0.964	(0.926, 1.002)	0.910	(0.789, 1.049)	1.016	(0.895, 1.152)	0.871	(0.584, 1.299)
No	0.980	(0.893, 1.076)	0.882	(0.532, 1.463)	0.920	(0.820, 1.032)	0.998	(0.854, 1.165)
Unknown	1.107	(1.042, 1.176)	1.345	(1.082, 1.673)	1.154	(0.989, 1.347)	1.084	(0.824, 1.426)

Figure 3.4a Vulva PIR – SES: PIR estimates and 95% confidence intervals (95% CI) for invasive vulvar cancer calculated for SES quintiles by race/ethnicity.
Legend: Error Bars = 95% Confidence Intervals (95% CI) of each PIR, calculated from the log(PIR) estimate.



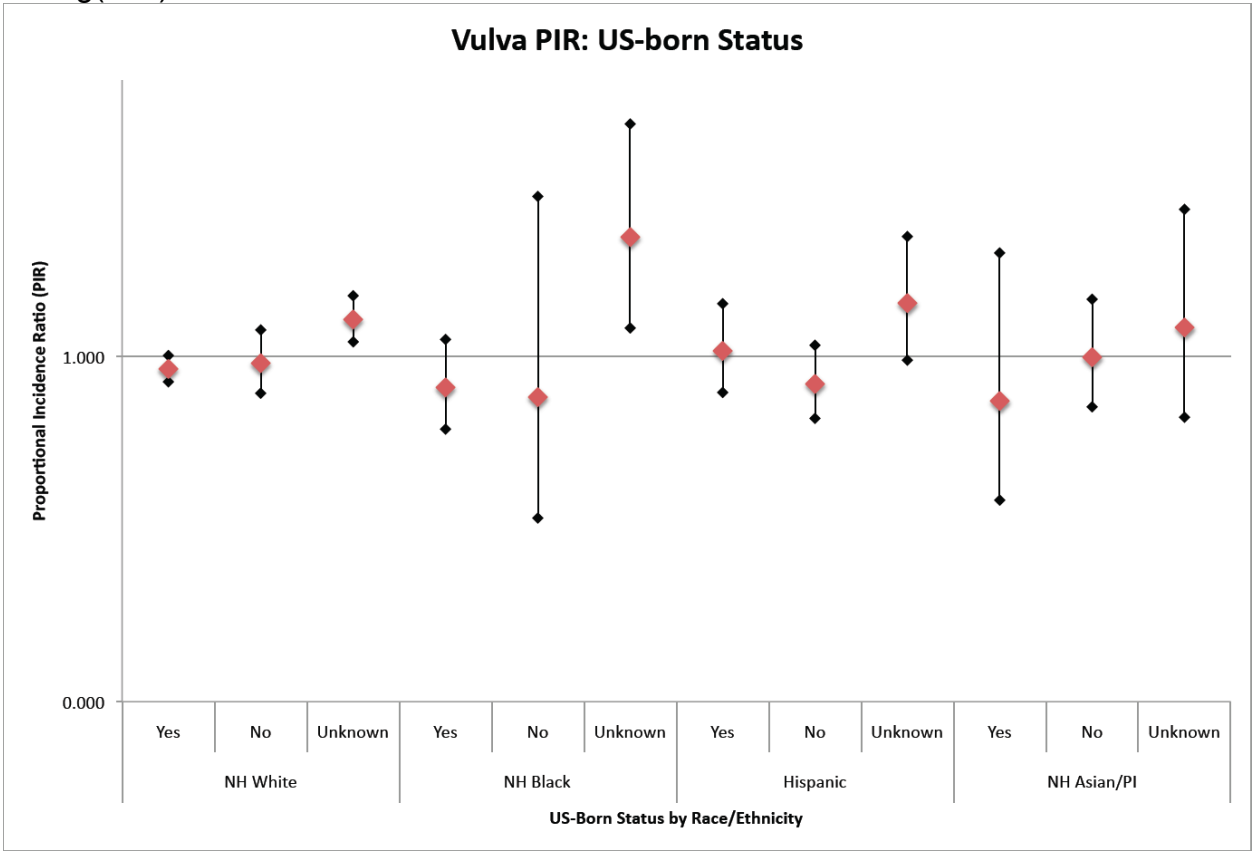
Insurance: The effects of insurance status on PIR of vulvar cancer varied by race/ethnicity as seen in Table 3.9 and Figure 3.4b. Private insurance was protective while a small increased risk was seen in the non-private insurance group. However, only for whites did these estimates reach statistical significance (Private PIR = 0.927, (0.875, 0.982); Non-private PIR = 1.080 (1.024, 1.140)). Unknown and missing status both had opposing effects by race/ethnicity. Unknown status lowered risk for NH Whites and Blacks (0.6% and 18.1%) while it increased risk for Hispanics and NH Asian PIs (3.8% and 19.5%). Missing status had no effect on NH Whites, had a higher PIR for Blacks (1.242) and lower PIRs for Hispanics and Asian PIs (0.856, 0.845).

Figure 3.4b Vulva PIR – Insurance Status: PIR estimates and 95% confidence intervals (95% CI) for invasive vulvar cancer calculated for insurance status by race/ethnicity. Legend: Error Bars = 95% Confidence Intervals (95% CI) of each PIR, calculated from the log(PIR) estimate.



US-born: The PIR distribution for US-born status varied by race/ethnicity as seen in Table 3.9 and Figure 3.4c. US birthplace saw lower PIRs for NH Whites, Blacks and Asian PIs (0.964, 0.910, 0.871) but a higher PIR for Hispanics (1.016) and a non-US birthplace consistently reduced risk, though not significantly so. Although a US-born status of yes or no was not significantly affecting PIR, an unknown status increased risk for NH Whites and Blacks (PIRs = 1.107 and 1.345).

Figure 3.4c Vulva PIR – US-born Status: PIR estimates and 95% confidence intervals (95% CI) for invasive vulvar cancer calculated for US-born status by race/ethnicity. Legend: Error Bars = 95% Confidence Intervals (95% CI) of each PIR, calculated from the log(PIR) estimate.



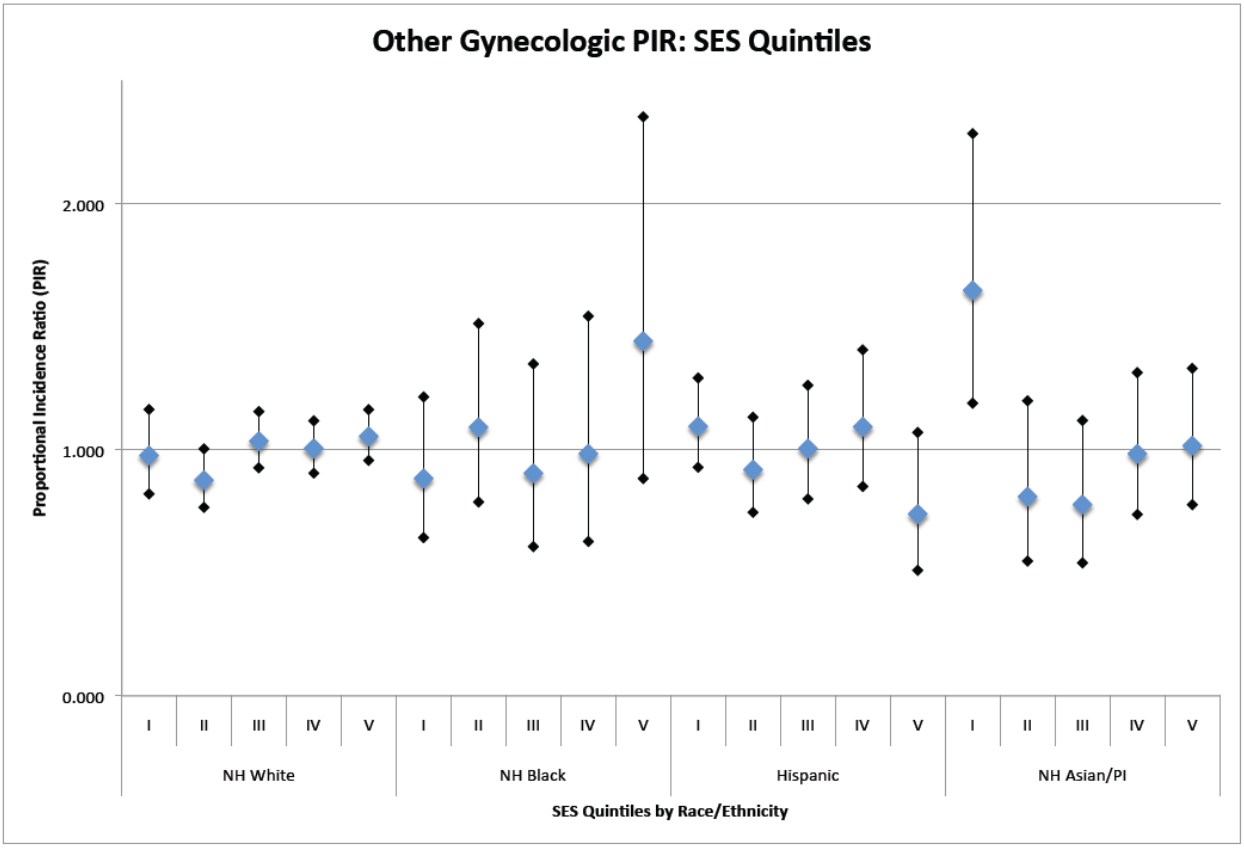
Other Gynecologic

SES: The PIR distribution for quintiles of SES varied by race/ethnicity for all other gynecolgic cancers as seen in Table 3.10 and Figure 3.5a. The lowest quintile of SES for NH Asian PIs affected risk of other female genital organ cancers by increasing risk by 64.7%, but PIRs of no other level of SES or any other racial/ethnic group reached significance. There was a strange pattern of other gynecologic PIRs by SES for NH Whites and Blacks where low SES decreased risk (2.3% and 11.7%) and high SES increased risk (5.4% and 44.1%) but this was not seen for Hispanics.

Table 3.10 Other Gynecologic PIR: PIR estimates and 95% confidence intervals (95% CI) for invasive other gynecologic cancers of healthcare access measures by race/ethnicity.

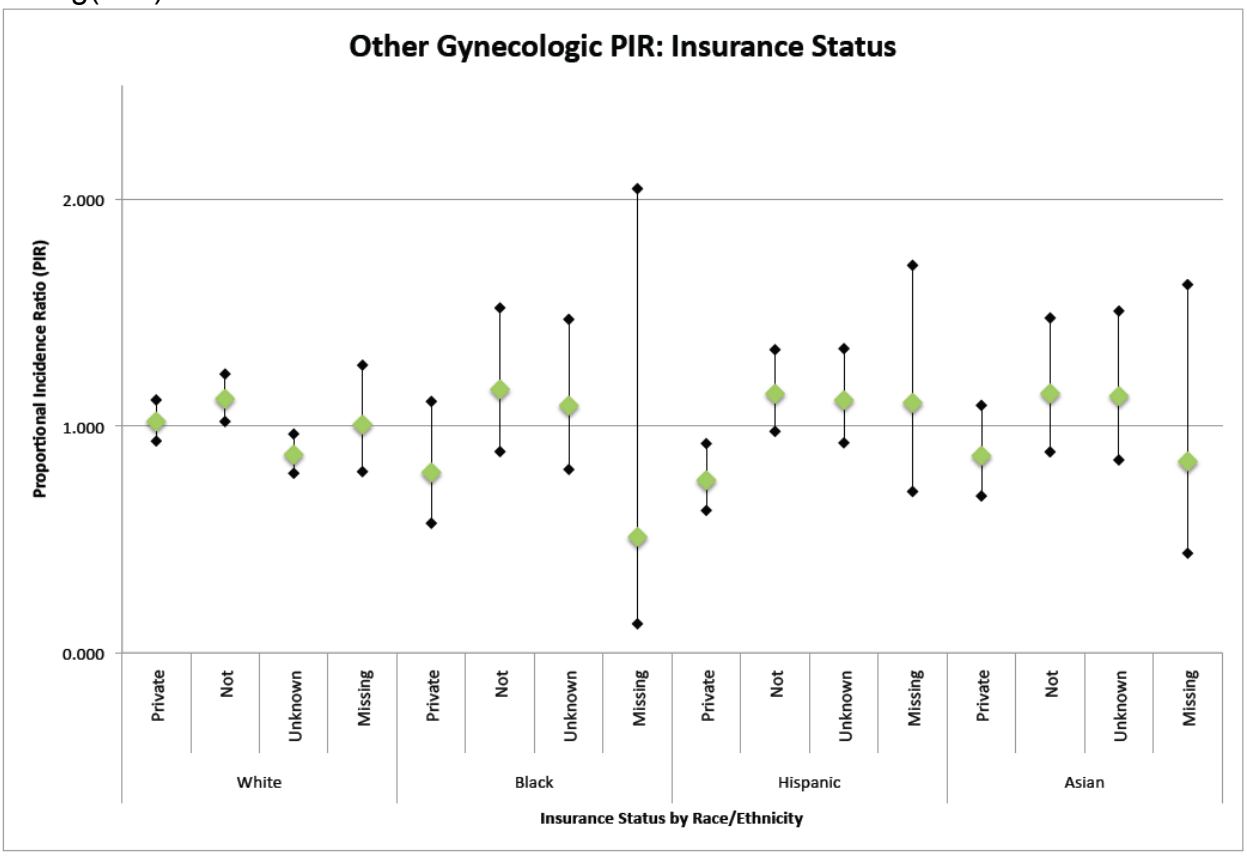
Other Gynecologic PIR:		NH White		NH Black		Hispanic		NH Asian/PI	
		Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI
SES Quintiles									
	I	0.977	(0.820, 1.163)	0.883	(0.643, 1.214)	1.095	(0.928, 1.291)	1.647	(1.188, 2.284)
	II	0.876	(0.765, 1.003)	1.091	(0.787, 1.513)	0.919	(0.745, 1.132)	0.810	(0.547, 1.198)
	III	1.034	(0.926, 1.155)	0.904	(0.606, 1.348)	1.004	(0.800, 1.261)	0.777	(0.540, 1.118)
	IV	1.005	(0.904, 1.117)	0.984	(0.627, 1.542)	1.093	(0.850, 1.405)	0.983	(0.737, 1.313)
	V	1.054	(0.956, 1.163)	1.441	(0.883, 2.352)	0.738	(0.510, 1.069)	1.016	(0.776, 1.330)
Insurance Status									
	Private	1.020	(0.933, 1.115)	0.795	(0.571, 1.108)	0.761	(0.628, 0.922)	0.869	(0.692, 1.091)
	Non-private	1.119	(1.020, 1.229)	1.161	(0.887, 1.520)	1.142	(0.976, 1.336)	1.143	(0.886, 1.476)
	Unknown	0.874	(0.792, 0.964)	1.090	(0.808, 1.470)	1.114	(0.925, 1.340)	1.132	(0.850, 1.506)
	Missing	1.006	(0.799, 1.267)	0.511	(0.128, 2.045)	1.102	(0.711, 1.708)	0.844	(0.439, 1.622)
US-born Status									
	Yes	1.006	(0.942, 1.075)	0.965	(0.786, 1.183)	0.832	(0.687, 1.008)	0.607	(0.345, 1.069)
	No	1.278	(1.109, 1.473)	1.157	(0.602, 2.224)	1.109	(0.960, 1.281)	1.067	(0.898, 1.267)
	Unknown	0.873	(0.782, 0.974)	1.072	(0.758, 1.516)	1.029	(0.849, 1.247)	0.993	(0.746, 1.321)

Figure 3.5a Other Gynecologic PIR – SES: PIR estimates and 95% confidence intervals (95% CI) for invasive other gynecologic cancers calculated for SES quintiles by race/ethnicity.
Legend: Error Bars = 95% Confidence Intervals (95% CI) of each PIR, calculated from the log(PIR) estimate.



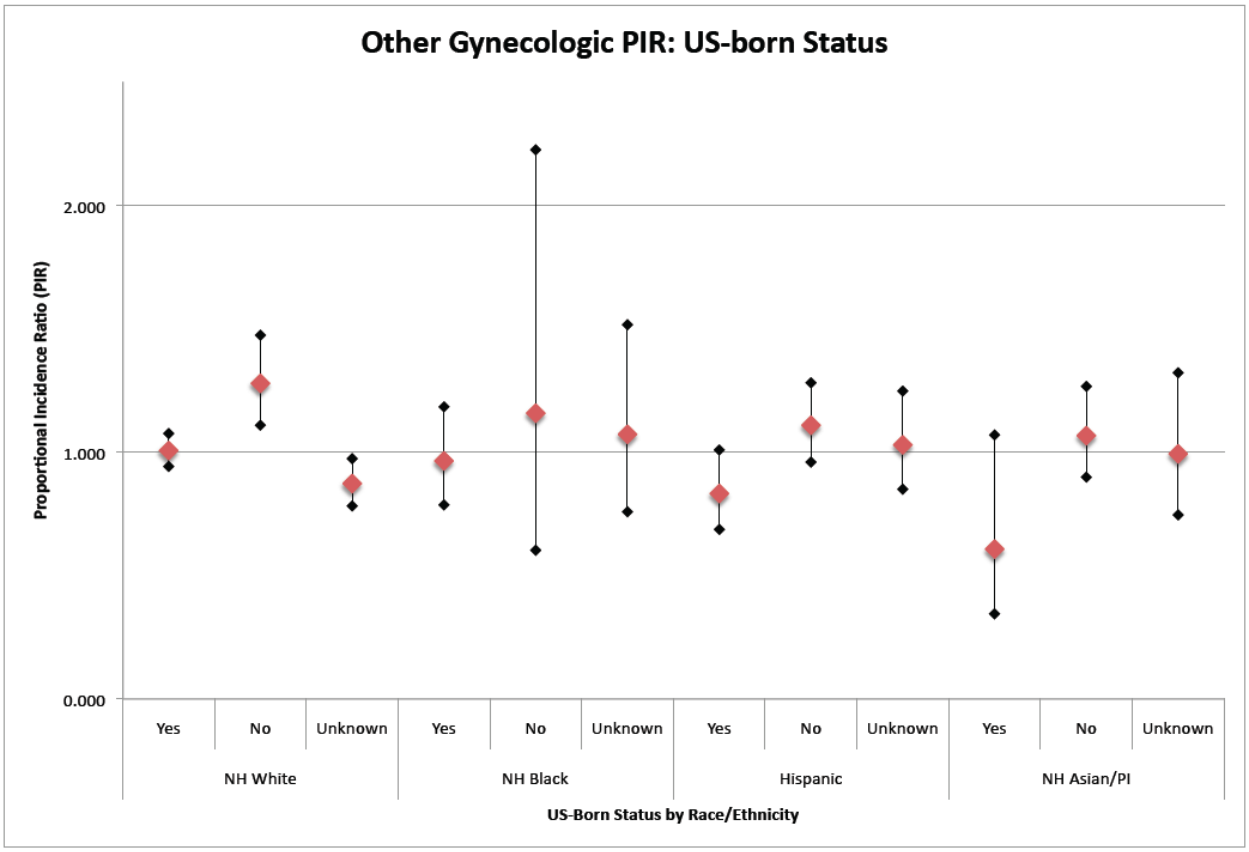
Insurance: The distribution of PIRs of other female genital organ cancers for insurance status varied by race/ethnicity as seen in Table 3.10 and Figure 3.5b. For Hispanics, private insurance status was a significant protective risk factor, reducing risk by 23.9%, though it reduced the risk for the other racial/ethnic groups as well. For NH Whites, not private insurance status was a significant negative risk factor, raising risk by 11.9%, while unknown insurance status was significantly beneficial, reducing risk by 12.6%. Similar effect of non-private and missing insurance status was seen for the others, but none reached statistical significance. Other gynecologic PIR estimates for missing status were different by race/ethnicity, but the confidence intervals were so large that the differences could not be confirmed.

Figure 3.5b Other Gynecologic PIR – Insurance Status: PIR estimates and 95% confidence intervals (95% CI) for invasive other gynecologic cancers calculated for insurance status by race/ethnicity.
Legend: Error Bars = 95% Confidence Intervals (95% CI) of each PIR, calculated from the log(PIR) estimate.



US-born: The PIR distribution of other female genital organ cancers for US-born status was different for each racial/ethnic group as seen in Table 3.10 and Figure 3.5c. Significant effects of birthplace were seen only for NH Whites where US-born had no significant effect, not born in the US raised risk by 27.8%, and unknown birthplace reduced risk by 12.7%. For the minority groups, similar (non-significant) effects of US-born status were seen: US-born had lower other gynecologic PIRs (0.965, 0.832, 0.607) and not-US-born had higher PIRs (1.157, 1.109, 1.067). Unknown had higher PIRs as well, for NH Blacks and Hispanics (1.072, 1.029).

Figure 3.5c Other Gynecologic PIR – US-born Status: PIR estimates and 95% confidence intervals (95% CI) for invasive other gynecologic cancers calculated for US-born status by race/ethnicity.
Legend: Error Bars = 95% Confidence Intervals (95% CI) of each PIR, calculated from the log(PIR) estimate.



Aim 2 part a: Univariate analysis by site of stage by race/ethnicity and measures of healthcare access

Cervix

As shown in Table 3.11, while the majority of cases were diagnosed at an early stage (overall 78.20%), significant differences were seen for the proportion of stage at diagnosis by race/ethnicity and measures of healthcare access. For cervical cancer, NH Blacks had the largest proportion of late stage (25.30%) while NH Asian PIs had the smallest percentage (20.25%; $p<0.0001$). The percent of cases diagnosed at a late stage did not vary significantly by levels of SES. Private insurance status had a lower percentage of late stage (20.22%) than non-private insurance status (24.84%; $p<0.0001$). The proportion of late stage was highest for US-born cases (27.55%; $p<0.0001$).

Table 3.11 Cervix Stage Univariate Analysis: Univariate chi-squared analysis of the frequency of early versus late stage at diagnosis of cervical cancer by race/ethnicity and measures of healthcare access.

Cervix Stage Univariate		Early		Late		Total	Chi-Sq P-Value
		%	N	%	N	N	
Overall:		78.20	23979	21.80	6686	30665	
Race/Ethnicity							
	NH White	77.49	10645	22.51	3092	13737	<0.0001
	NH Black	74.70	1535	25.30	520	2055	
	Hispanic	79.19	8775	20.81	2306	11081	
	NH Asian/PI	79.75	3024	20.25	768	3792	
SES Quintile							
	I	78.40	6436	21.60	1773	8209	0.8272
	II	77.83	5205	22.17	1483	6688	
	III	78.01	4651	21.99	1311	5962	
	IV	78.15	4198	21.85	1174	5372	
	V	78.69	3489	21.31	945	4434	
Insurance Status*							
	Private	79.78	6243	20.22	1582	7825	<0.0001
	Non-private	75.16	6650	24.84	2198	8848	
US-born**							
	Yes	72.45	8579	27.55	3263	11842	<0.0001
	No	77.17	8221	22.83	2432	10653	

* Unknown and missing insurance status were excluded from analysis, which was performed on cases diagnosed from 1996-2009, when insurance data was reliably reported.
** Unknown US-born status was excluded from analysis.

Ovary

Statistically significant differences were seen for the proportion of late stage at diagnosis of ovarian cancer by race/ethnicity and measures of healthcare access (Table 3.12). The proportion of late stage was high for all race/ethnicities (overall 72.25%), though it was highest for NH Blacks and NH Whites (75.71% and 74.36%) and significantly lower for NH Asian PIs (60.55%; $p<0.0001$). SES had no effect on the risk of late stage at diagnosis. The percentage of late stage at diagnosis was lower for private insurance status (66.58%) and was higher for non-private insurance status (77.67%; $p<0.0001$). As seen with cervical cancer, the risk of late stage at diagnosis was highest for a US birthplace (78.68%; $p<0.0001$).

Table 3.12 Ovary Stage Univariate Analysis: Univariate chi-squared analysis of the frequency of early versus late stage at diagnosis of ovarian cancer by race/ethnicity and measures of healthcare access.

Ovary Stage Univariate		Early		Late		Total	Chi-Sq P-Value
		%	N	%	N	N	
Overall:		27.75	10587	72.25	27560	38147	
Race/Ethnicity							
	NH White	25.64	6902	74.36	20015	26917	<0.0001
	NH Black	24.29	435	75.71	1356	1791	
	Hispanic	31.43	1856	68.57	4049	5905	
	NH Asian/PI	39.45	1394	60.55	2140	3534	
SES Quintile							
	I	28.00	1466	72.00	3769	5235	0.3195
	II	27.66	1939	72.34	5071	7010	
	III	27.52	2221	72.48	5850	8071	
	IV	27.12	2369	72.88	6367	8736	
	V	28.50	2592	71.50	6503	9095	
Insurance Status*							
	Private	33.42	4068	66.58	8106	12174	<0.0001
	Non-private	22.33	2326	77.67	8090	10416	
US-born**							
	Yes	21.32	4683	78.68	17284	21967	<0.0001
	No	26.06	2232	73.94	6332	8564	

* Unknown and missing insurance status were excluded from analysis, which was performed on cases diagnosed from 1996-2009, when insurance data was reliably reported.
** Unknown US-born status was excluded from analysis.

Vagina

As seen in Table 3.13, there was no factor that significantly affected the proportion of late stage vaginal cancer, but trends were seen for race/ethnicity and measures of healthcare access. Overall, the proportion of late stage was low (29.19%) for vaginal cancer. As seen with cervical and ovarian cancer, NH Blacks and those with non-private insurance had the greatest proportion of late stage at diagnosis, however, differences did not reach statistical significance for late stage vaginal cancer. Unlike other cancers, NH Asian PIs did not have the lowest risk of late stage of vaginal cancer. Hispanics had the smallest percentage of late stage (26.27%), while NH Blacks had the largest percentage (36.13%). The percentage of late stage decreased with an increase by SES

quintile (from 30.83% to 26.95%). Private insurance status had approximately equal lower proportion of late stage compared to non-private status. A definitive birthplace, in the US or not, had slightly different risk; a US birthplace had slightly more late stage (33.07% versus 30.25%).

Table 3.13 Vagina Stage Univariate Analysis: Univariate chi-squared analysis of the frequency of early versus late stage at diagnosis of vaginal cancer by race/ethnicity and measures of healthcare access.

Vagina Stage Univariate		Early		Late		Total	Chi-Sq P-Value
		%	N	%	N	N	
Overall:		70.81	975	29.19	402	1377	
Race/Ethnicity							
	NH White	70.96	623	29.04	255	878	0.2788
	NH Black	63.87	76	36.13	43	119	
	Hispanic	73.73	188	26.27	67	255	
	NH Asian/PI	70.40	88	29.60	37	125	
SES Quintile							
	I	69.17	166	30.83	74	240	0.8691
	II	69.87	211	30.13	91	302	
	III	71.76	216	28.24	85	301	
	IV	70.14	195	29.86	83	278	
	V	73.05	187	26.95	69	256	
Insurance Status*							
	Private	71.46	288	28.54	115	403	0.6613
	Non-private	70.11	326	29.89	139	465	
US-born**							
	Yes	66.93	512	33.07	253	765	0.3618
	No	69.75	226	30.25	98	324	

* Unknown and missing insurance status were excluded from analysis, which was performed on cases diagnosed from 1996-2009, when insurance data was reliably reported.
** Unknown US-born status was excluded from analysis.

Vulva

Despite an overall high proportion of early stage (77.30%), Table 3.14 shows that the risk of late stage at diagnosis for vulvar cancer varied significantly by race/ethnicity and some measures of healthcare access, except US-born status. Hispanics had the largest percentage of late stage (28.46%) and was lower in NH Whites, Blacks and Asian PIs (21.75%, 22.79%, and 21.72%; p= 0.0025). A significant reduction in late stage

proportion was seen for every increase in SES quintile (from 27.52% to 20.33%; p= 0.0022). The percentage of late stage changed by insurance status, being higher for non-private status than private insurance status (26.46%; p= 0.0029). Unlike other cancers, vulvar cancer cases who reported being born in the US had smaller proportion of late stage (25.63%) compared to non-US-born cases (28.20%), though this difference did not reach statistical significance.

Table 3.14 Vulva Stage Univariate Analysis: Univariate chi-squared analysis of the frequency of early versus late stage of diagnosis of vulvar cancer by race/ethnicity and measures of healthcare access.

Vulva Stage Univariate		Early		Late		Total	Chi-Sq P-Value
		%	N	%	N	N	
Overall:		77.30	3769	22.70	1107	4876	
Race/Ethnicity							
	NH White	78.25	2921	21.75	812	3733	0.0025
	NH Black	77.21	210	22.79	62	272	
	Hispanic	71.54	465	28.46	185	650	
	NH Asian/PI	78.28	173	21.72	48	221	
SES Quintile							
	I	72.48	598	27.52	227	825	0.0022
	II	76.33	745	23.67	231	976	
	III	77.98	832	22.02	235	1067	
	IV	79.11	818	20.89	216	1034	
	V	79.67	776	20.33	198	974	
Insurance Status*							
	Private	78.24	1068	21.76	297	1365	0.0029
	Non-private	73.54	1187	26.46	427	1614	
US-born**							
	Yes	74.37	2040	25.63	703	2743	0.1377
	No	71.80	606	28.20	238	844	

* Unknown and missing insurance status were excluded from analysis, which was performed on cases diagnosed from 1996-2009, when insurance data was reliably reported.
** Unknown US-born status was excluded from analysis.

Other Gynecologic

The proportion of late stage of other gynecologic cancers was moderate overall (57.25%), and differed significantly for insurance status, but not for any other factor (Table 3.15). Although insignificant, NH Blacks had the lowest percentage of late stage

diagnosis (53.64%) while NH Whites had the highest (58.13%). Risk of late stage other gynecologic cancers was slightly higher for low SES than high SES (58.27% and 61.04% versus 55.56% and 56.03%), though not significantly so. Non-private insurance status had significantly higher percentage of late stage (63.19%) compared to private insurance status (52.24%; p=0.0001). A positive US-born status had a higher risk of late stage (63.51%), while a non-US-born status had lower risk (61.26%), but these did not reach statistical significance.

Table 3.15: Other Gynecologic Stage Univariate Analysis: Univariate chi-squared analysis of the frequency of early versus late stage of diagnosis of other gynecologic cancers by race/ethnicity and measures of healthcare access.

Other Gynecologic Stage Univariate		Early		Late		Total	Chi-Sq P-Value
		%	N	%	N	N	
Overall:		42.75	796	57.25	1066	1862	
Race/Ethnicity							
	NH White	41.87	523	58.13	726	1249	0.6869
	NH Black	46.36	51	53.64	59	110	
	Hispanic	44.64	150	55.36	186	336	
	NH Asian/PI	43.11	72	56.89	95	167	
SES Quintile							
	I	41.73	116	58.27	162	278	0.6036
	II	38.96	120	61.04	188	308	
	III	43.19	168	56.81	221	389	
	IV	44.44	188	55.56	235	423	
	V	43.97	204	56.03	260	464	
Insurance Status*							
	Private	47.76	298	52.24	326	624	0.0001
	Non-private	36.81	208	63.19	357	565	
US-born**							
	Yes	36.49	354	63.51	616	970	0.4178
	No	38.74	172	61.26	272	444	

* Unknown and missing insurance status were excluded from analysis, which was performed on cases diagnosed from 1996-2009, when insurance data was reliably reported.
** Unknown US-born status was excluded from analysis.

Aim 2 part b: Multivariate analysis by site of proportion at late stage by measures of healthcare access, race/ethnicity, and other known covariates

Cervix

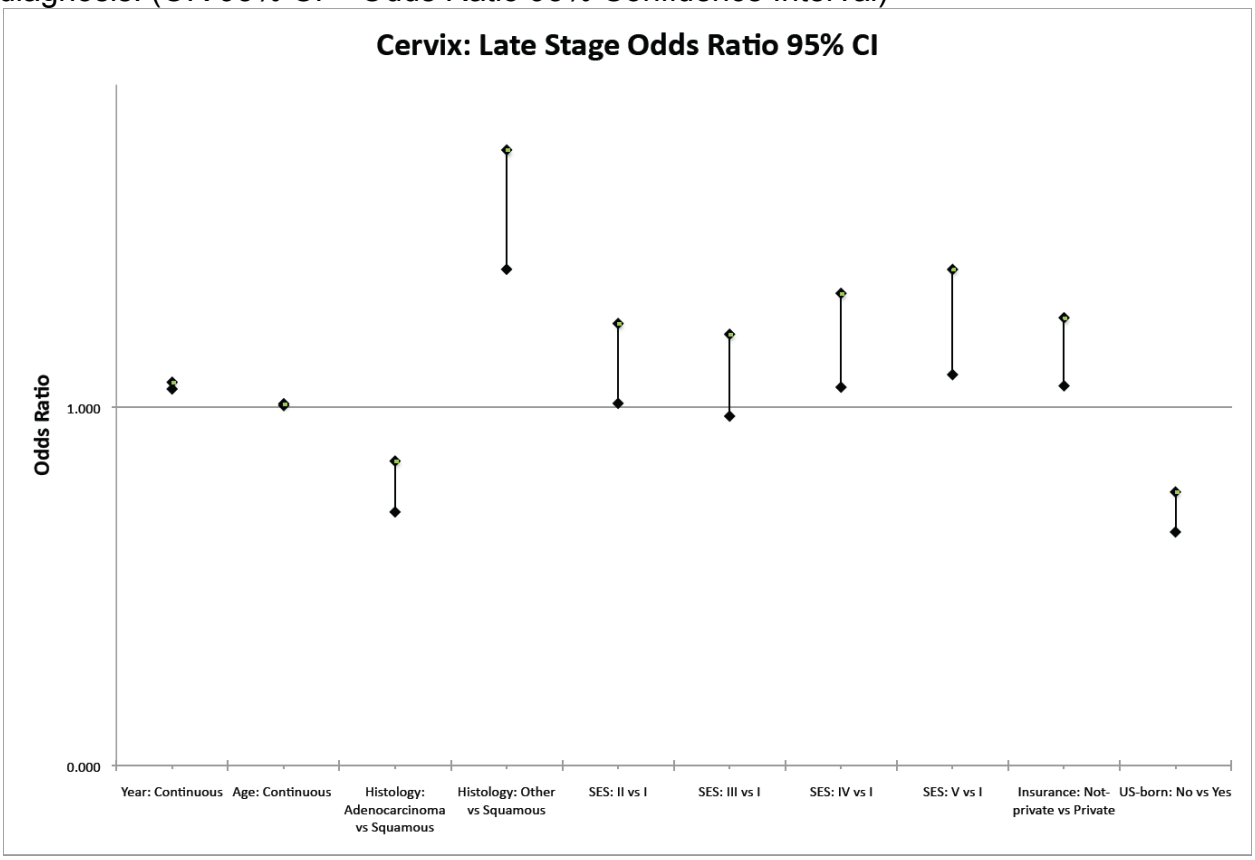
When all variables were analyzed concurrently, as seen in Table 3.16 and Figure 3.6, measures of healthcare access and known covariates, except for race/ethnicity, were significantly associated with late stage at diagnosis for cervical cancer. The chosen significant covariates following multivariate analysis stepwise selection of late stage cervical cancer are presented. For every year increase of year at diagnosis, risk of late stage increased by 6.10% (95% CI: 1.051, 1.070; p<0.0001). Age increased risk of late stage at diagnosis with advancing years, increasing risk 0.80% by year (95%CI: 1.005, 1.010; p < 0.0001). Histology was also a significant factor, with 22.40% decreased odds of late stage for adenocarcinoma (95% CI: 0.708, 0.850; p<0.0001) and 54.20% increased odds for other histology (95% CI: 1.385, 1.718; p<0.0001) compared to squamous histology. Compared to the lowest quintile of SES, higher levels of SES increased the risk of late stage at diagnosis from SES II (OR = 1.117 (1.011, 1.234; p= 0.0297)) to SES V (OR = 1.230 (1.091, 1.385; p= 0.0007)). Non-private insurance status was associated with an increase in risk of 15.10% compared to private insurance (95% CI: 1.063, 1.254; p= 0.0008). US-born status also affected risk of late stage, 29.40% lower risk for not US-born women compared to US-born women (95% CI: 0.674, 0.816; p<0.0001). Unknown and missing insurance status and US-born status were adjusted for in the model but odds ratios were not reported.

Table 3.16 Cervix Stage Regression: Multivariate logistic stepwise regression analysis of cervical cancer proportion of late stage at diagnosis, modeled* by healthcare access measures, race/ethnicity, and other known covariates. (OR 95% CI = Odds Ratio 95% Confidence Interval)

Cervix	Coefficient		Wald Chi-Squared		Odds Ratio	OR 95% CI	
Multivariate Analysis of Stage	**Estimate**	**SE**	**Statistic**	**P-value**	**Estimate**	**Lower**	**Upper**
Intercept	-119.2000	8.9356	177.9966	<0.0001	.	.	.
Year: Continuous	0.0588	0.0045	173.8312	<0.0001	1.061	1.051	1.070
Age: Continuous	0.0075	0.0012	38.5014	<0.0001	1.008	1.005	1.010
Histology: Adenocarcinoma vs Squamous	-0.2539	0.0468	29.3831	<0.0001	0.776	0.708	0.850
Histology: Other vs Squamous	0.4333	0.0549	62.1967	<0.0001	1.542	1.385	1.718
SES: II vs I	0.1105	0.0508	4.7267	0.0297	1.117	1.011	1.234
SES: III vs I	0.0799	0.0539	2.1963	0.1383	1.083	0.975	1.204
SES: IV vs I	0.1653	0.0564	8.5835	0.0034	1.180	1.056	1.318
SES: V vs I	0.2066	0.0609	11.5058	0.0007	1.230	1.091	1.385
Insurance: Not-private vs Private	0.1406	0.0420	11.2325	0.0008	1.151	1.060	1.250
US-born: No vs Yes	-0.3483	0.0403	74.6708	<0.0001	0.706	0.652	0.764

* Model was adjusted for unknown and missing insurance status, and unknown US-born status.

Figure 3.6 Cervix Stage Regression OR: Odds Ratio 95% CI calculated from multivariate logistic stepwise regression analysis of cervical cancer odds of late stage at diagnosis. (OR 95% CI = Odds Ratio 95% Confidence Interval)



Ovary

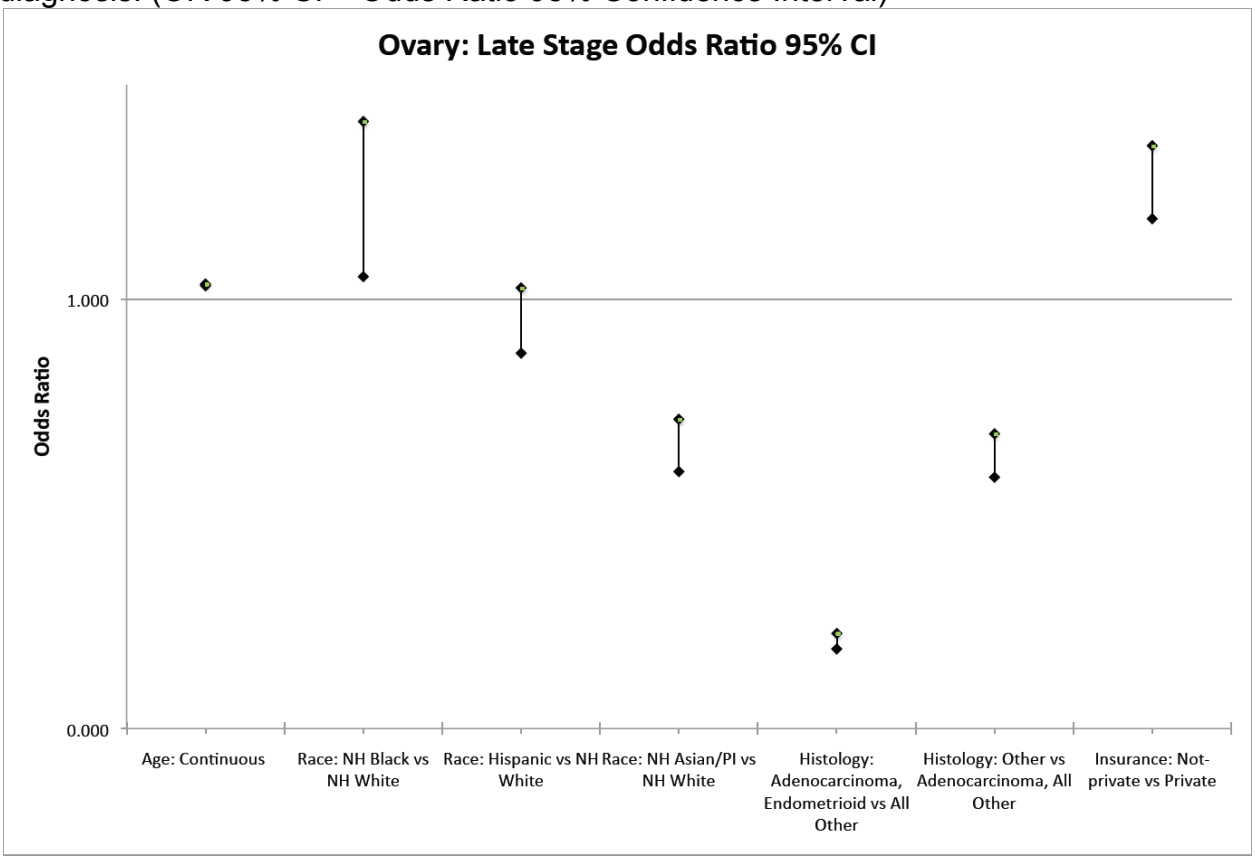
As seen in Table 3.17 and Figure 3.7, race/ethnicity, other known covariates, and measures of healthcare access, except SES, were significantly associated with late stage at diagnosis for ovarian cancer when all variables were analyzed concurrently. The chosen significant covariates following multivariate analysis stepwise selection of late stage ovarian cancer are presented. Multivariate analysis found a change in risk by age at diagnosis for late stage at diagnosis, increasing risk by 3.40% with each year increase in age (95% CI: 1.032, 1.036; p<0.0001). Compared to NH Whites, NH Blacks had 22.10% higher odds of late stage ovarian cancer (95%CI: 1.053, 1.415; p=0.0081) but NH Asian PIs had a 34.30% lower odds of late stage (95% CI: 0.599, 0.721; p <0.0001). The odds were the lowest for histology adenocarcinoma, endometrioid subtype (OR = 0.203 (0.186, 0.222; p<0.0001) but other histology also had lower odds for late stage (OR = 0.635 (0.586, 0.687; p<0.0001)) than adenocarcinoma histology, all other subtypes. Non-private insurance status was significantly associated with late stage at diagnosis, with a 27.00% increase in risk compared with private insurance (95%CI: 1.188, 1.358; p<0.0001). Unknown and missing insurance status and US-born status were adjusted for in the model but odds ratios were not reported.

Table 3.7 Ovary Stage Regression: Multivariate logistic stepwise regression analysis of ovarian cancer proportion of late stage at diagnosis, modeled* by healthcare access measures, race/ethnicity, and other known covariates. (OR 95% CI = Odds Ratio 95% Confidence Interval)

Ovary	Coefficient		Wald Chi-Squared		Odds Ratio	OR 95% CI	
Multivariate Analysis of Stage	**Estimate**	**SE**	**Statistic**	**P-value**	**Estimate**	**Lower**	**Upper**
Intercept	-0.8642	0.0681	161.0367	<0.0001	.	.	.
Age: Continuous	0.0336	0.0011	932.8733	<0.0001	1.034	1.032	1.036
Race: NH Black vs NH White	0.1994	0.0753	7.0095	0.0081	1.221	1.053	1.415
Race: Hispanic vs NH White	-0.0535	0.0409	1.7136	0.1905	0.948	0.875	1.027
Race: NH Asian/PI vs NH White	-0.4194	0.0472	78.9180	<0.0001	0.657	0.599	0.721
Histology: Adenocarcinoma, Endometrioid vs All Other	-1.5945	0.0454	1234.2602	<0.0001	0.203	0.186	0.222
Histology: Other vs Adenocarcinoma, All Other	-0.4544	0.0406	125.2395	<0.0001	0.635	0.586	0.687
Insurance: Not-private vs Private	0.2391	0.0340	49.5146	<0.0001	1.270	1.188	1.358

* Model was adjusted for unknown and missing insurance status, and unknown US-born status.

Figure 3.17 Ovary Stage Regression OR: Odds Ratio 95% CI calculated from multivariate logistic stepwise regression analysis of ovarian cancer odds of late stage at diagnosis. (OR 95% CI = Odds Ratio 95% Confidence Interval)



Vagina

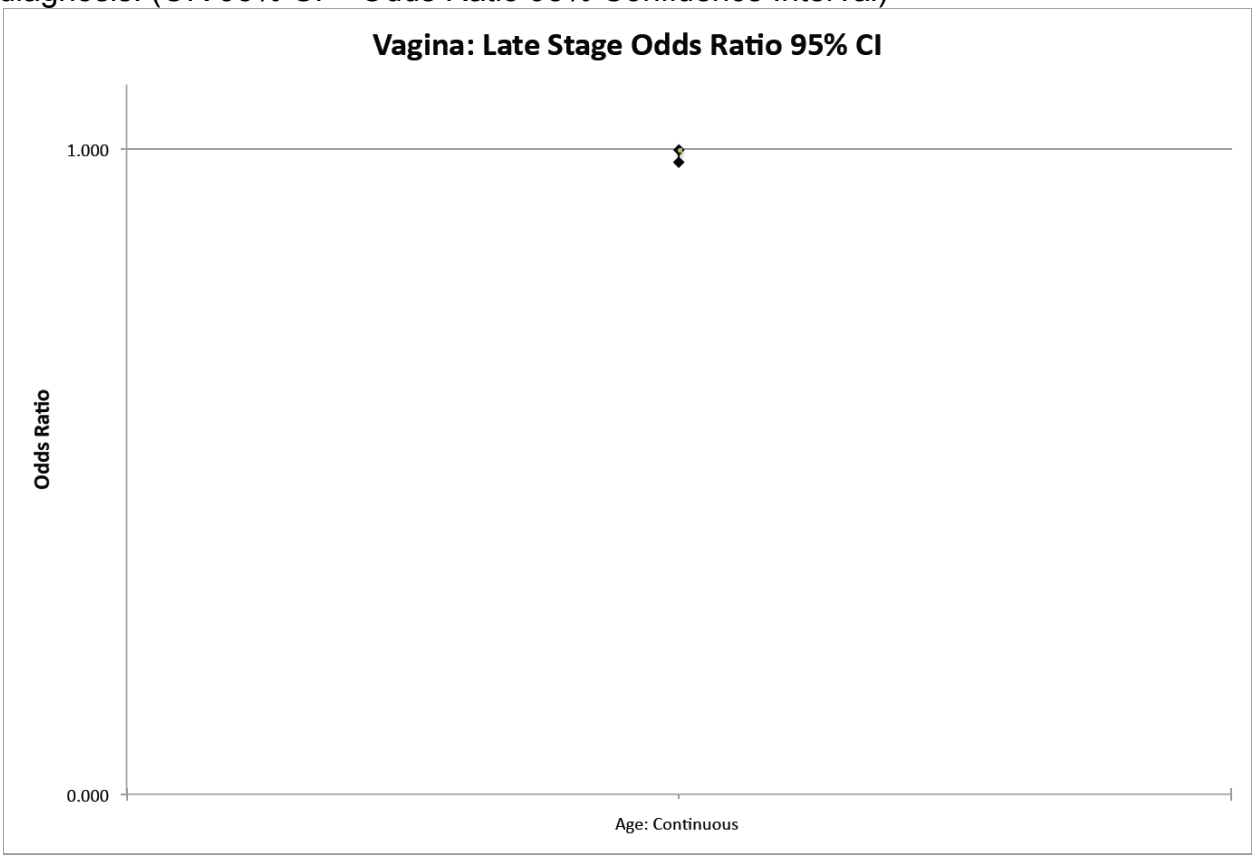
In multivariate analysis, as seen in Table 3.18 and Figure 3.8, the proportion of late stage at diagnosis for vaginal cancer was significantly affected by age only. The chosen significant covariates following multivariate analysis stepwise selection of late stage vaginal cancer are presented. The odds of late stage diagnosis was associated with age at diagnosis, with every year increase in age decreasing risk by 1.10% (95% CI: 0.980, 0.999; p= 0.0288). Unknown and missing insurance status and US-born status were adjusted for in the model but odds ratios were not reported.

Table 3.18 Vagina Stage Regression: Multivariate logistic stepwise regression analysis of vaginal cancer proportion of late stage at diagnosis, modeled* by healthcare access measures, race/ethnicity, and other known covariates. (OR 95% CI = Odds Ratio 95% Confidence Interval)

Vagina	Coefficient		Wald Chi-Squared		Odds Ratio	OR 95% CI	
Multivariate Analysis of Stage	Estimate	SE	Statistic	P-value	Estimate	Lower	Upper
Intercept	0.0149	0.3315	0.0020	0.9642	.	.	.
Age: Continuous	-0.0107	0.0049	4.7792	0.0288	0.989	0.980	0.999

* Model was adjusted for unknown and missing insurance status, and unknown US-born status.

Figure 3.8 Vagina Stage Regression OR: Odds Ratio 95% CI calculated from multivariate logistic stepwise regression analysis of vaginal cancer odds of late stage at diagnosis. (OR 95% CI = Odds Ratio 95% Confidence Interval)



Vulva

When all variables were analyzed concurrently, only age, histology and SES were significantly associated with late stage at diagnosis for vulvar cancer (Table 3.19, Figure 3.9). The chosen significant covariates following multivariate analysis stepwise selection of late stage vulvar cancer are presented. Age at diagnosis increased risk of late stage by 0.90% for every year increase (95% CI: 1.004, 1.015; p= 0.0004). Compared to a squamous histology, risk of late stage was 23.50% lower for the other histology group (95% CI: 0.614, 0.952; p = 0.0164)). Risk of late stage at diagnosis varied by SES, with 32.70%-37.40% lower risk of vulvar cancer for the three highest quintiles (95% CI:

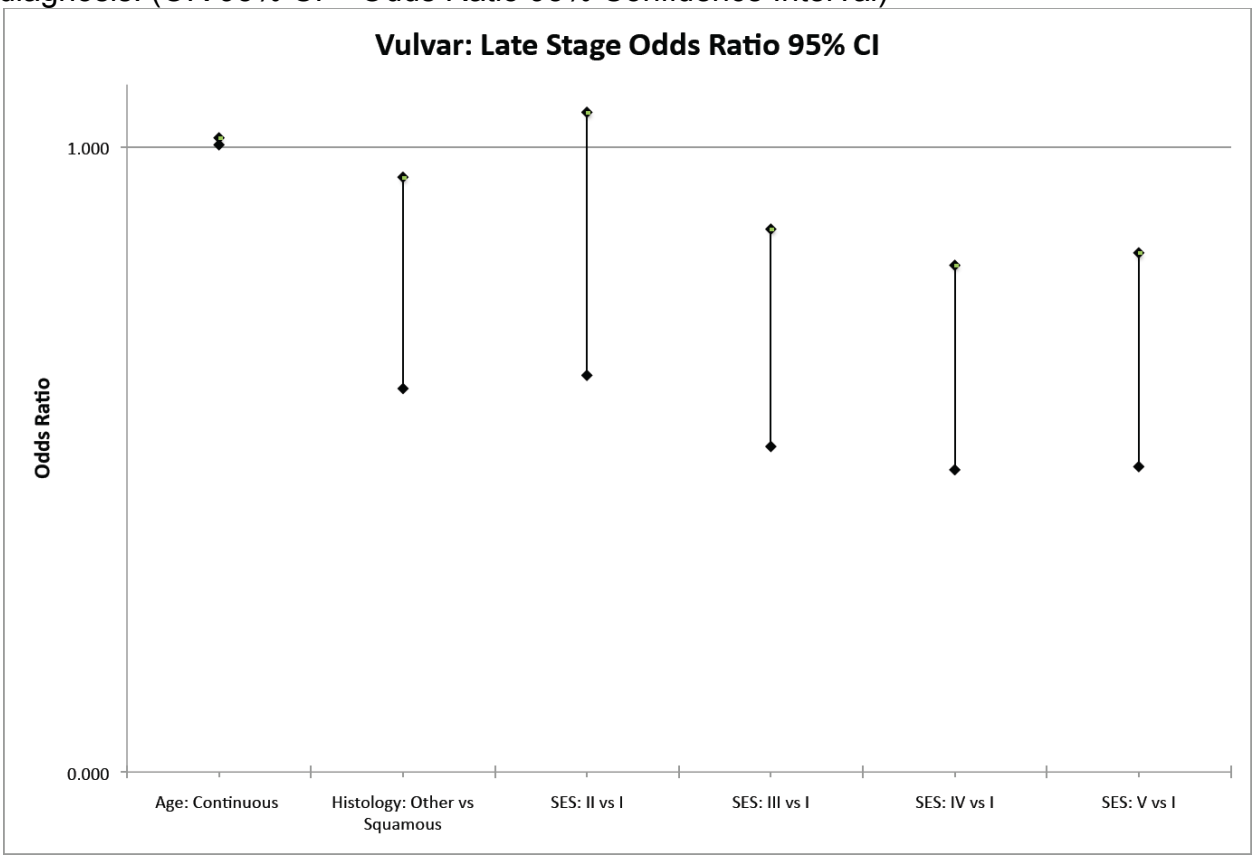
0.521, 0.869; p= 0.0024; 95% CI: 0.484, 0.811; p= 0.0004; and 95% CI: 0.489, 0.831; p = 0.0009 for SES = III, IV, and V, respectively) compared to the lowest level of SES. Unknown and missing insurance status and US-born status were adjusted for in the model but odds ratios were not reported.

Table 3.19 Vulva Stage Regression: Multivariate logistic stepwise regression analysis of vulvar cancer proportion of late stage at diagnosis, modeled* by healthcare access measures, race/ethnicity, and other known covariates. (OR 95% CI = Odds Ratio 95% Confidence Interval)

Vulva	Coefficient		Wald Chi-Squared		Odds Ratio	OR 95% CI	
Multivariate Analysis of Stage	Estimate	SE	Statistic	P-value	Estimate	Lower	Upper
Intercept	-1.4093	0.1956	51.9328	<0.0001	.	.	.
Age: Continuous	0.0093	0.0026	12.5875	0.0004	1.009	1.004	1.015
Histology: Other vs Squamous	-0.2681	0.1117	5.7596	0.0164	0.765	0.614	0.952
SES: II vs I	-0.1999	0.1295	2.3807	0.1228	0.819	0.635	1.056
SES: III vs I	-0.3960	0.1303	9.2423	0.0024	0.673	0.521	0.869
SES: IV vs I	-0.4677	0.1320	12.5449	0.0004	0.626	0.484	0.811
SES: V vs I	-0.4502	0.1351	11.1032	0.0009	0.638	0.489	0.831

* Model was adjusted for unknown and missing insurance status, and unknown US-born status.

Figure 3.9 Vulva Stage Regression OR: Odds Ratio 95% CI calculated from multivariate logistic stepwise regression analysis of vulvar cancer odds of late stage at diagnosis. (OR 95% CI = Odds Ratio 95% Confidence Interval)



Other Gynecologic

In multivariate analysis, seen in Table 3.20, Figure 3.10, age and insurance status were significantly associated with the odds of late stage at diagnosis for other gynecologic cancers. The chosen significant covariates following multivariate analysis stepwise selection of late stage other gynecologic cancers are presented. There was an increase in odds of late stage other gynecologic cancers with increasing age by 1.60% for every year increase (95% CI: 1.009, 1.023); $p<0.0001$) Compared to private insurance, not-private insurance was associated with a 39.50% increase in late stage risk (95% CI:

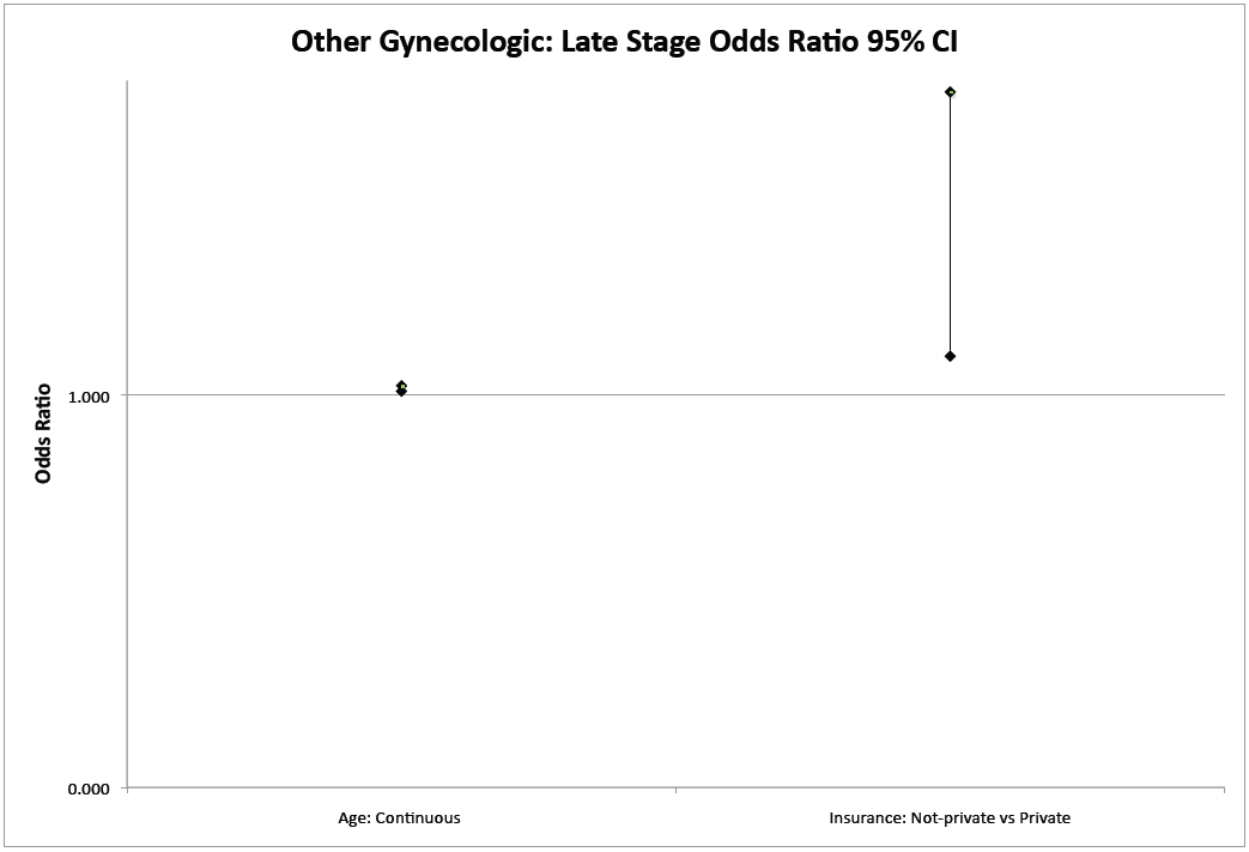
1.098, 1.771; p= 0.0064). Unknown and missing insurance status and US-born status were adjusted for in the model but odds ratios were not reported.

Table 3.20 Other Gynecologic Stage Multivariate: Multivariate logistic regression analysis of other gynecologic cancers proportion of late stage at diagnosis, modeled* by healthcare access measures, race/ethnicity, and other known covariates. (OR 95% CI = Odds Ratio 95% Confidence Interval)

Other Gynecologic	Coefficient		Wald Chi-Squared		Odds Ratio	OR 95% CI	
Multivariate Analysis of Stage	Estimate	SE	Statistic	P-value	Estimate	Lower	Upper
Intercept	-0.8033	0.2110	14.4893	0.0001	.	.	.
Age: Continuous	0.0161	0.0035	20.9308	<0.0001	1.016	1.009	1.023
Insurance: Not-private vs Private	0.3326	0.1219	7.4451	0.0064	1.395	1.098	1.771

* Model was adjusted for unknown and missing insurance status, and unknown US-born status.

Figure 3.10 Other Gynecologic Stage Multivariate OR: Odds Ratio 95% CI calculated from multivariate logistic stepwise regression analysis of other gynecologic cancers odds of late stage at diagnosis. (OR 95% CI = Odds Ratio 95% Confidence Interval)



Aim 3 part a: Kaplan-Meier curve site-specific 5-year survival analysis by race/ethnicity and measures of healthcare access

Cervix

As shown in Figure 3.11, significant differences in 5-year survival rates of cervical cancer were seen by race/ethnicity and measures of healthcare access. The majority of cervical cancer cases survived beyond 5 years, so no median survival time was calculated. NH Blacks had the lowest survival while Hispanics, NH Asian PIs, and NH Whites had significantly higher survival rates ($p<0.0001$; Figure 3.11a). Survival rates increased with increasing quintile of SES ($p<0.0001$; Figure 3.11b). The insurance status associated with the highest survival rate was private and survival was significantly lower for non-private ($p<0.0001$; Figure 3.11c). A positive US-born status was associated with a lower survival rate than a negative US-born status ($p<0.0001$; Figure 3.11d).

Figure 3.11a Cervix Kaplan-Meier Curves – Race/Ethnicity: Cervical cancer survival Kaplan-Meier curves by race/ethnicity for 5-year survival.

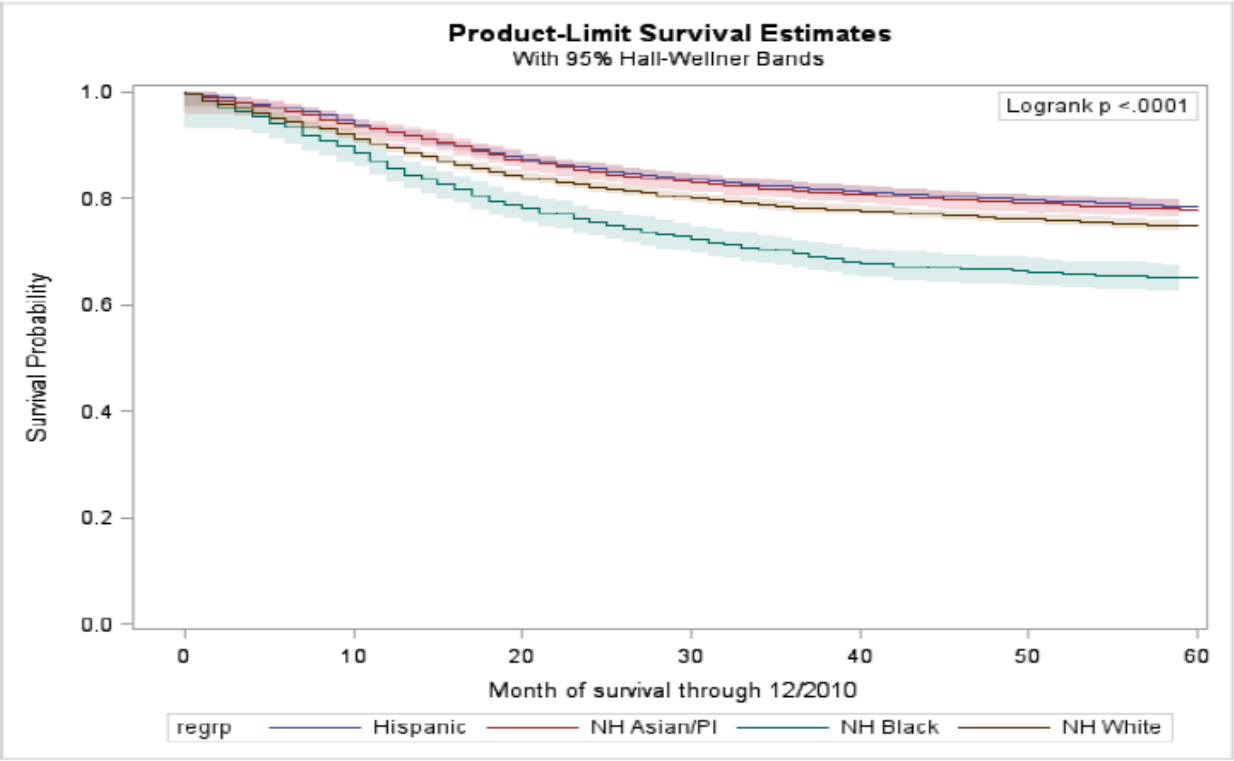


Figure 3.11b Cervix Kaplan-Meier Curves – SES: Cervical cancer survival Kaplan-Meier curves by SES for 5-year survival.

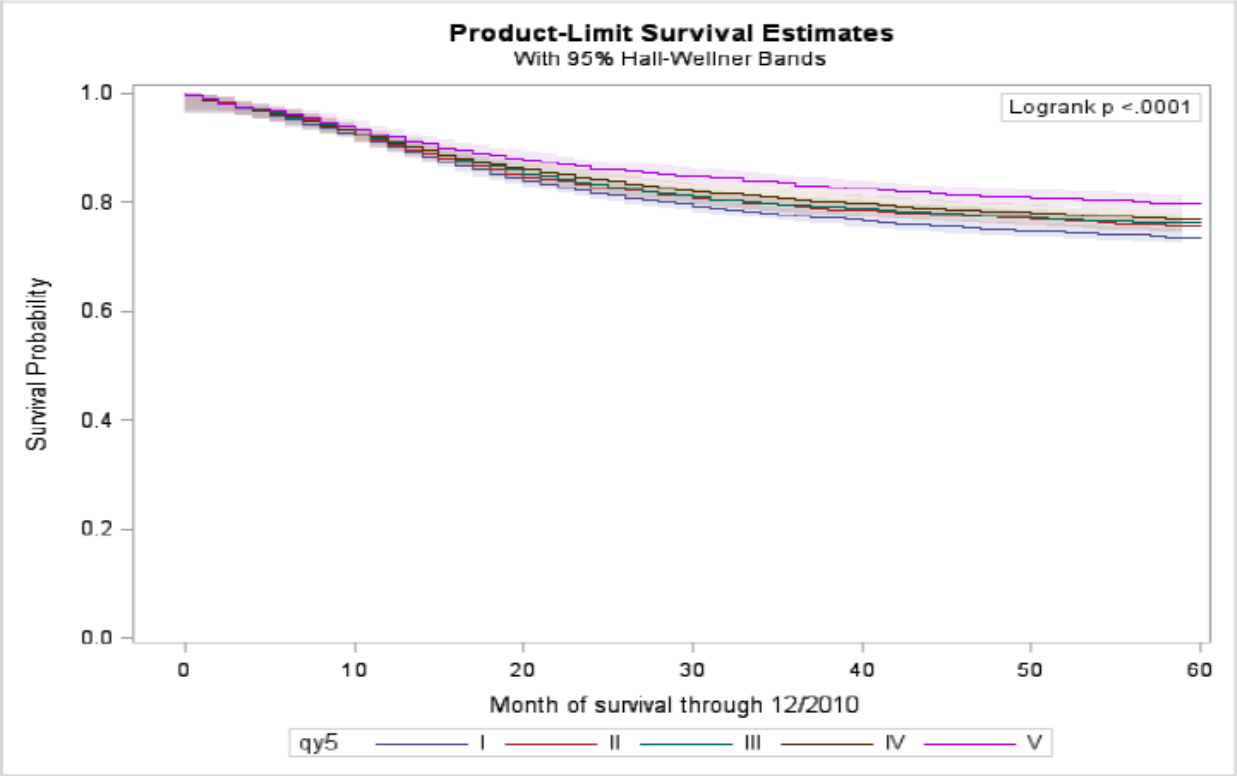


Figure 3.11c Cervix Kaplan-Meier Curves – Insurance Status: Cervical cancer survival Kaplan-Meier curves by insurance status for 5-year survival.

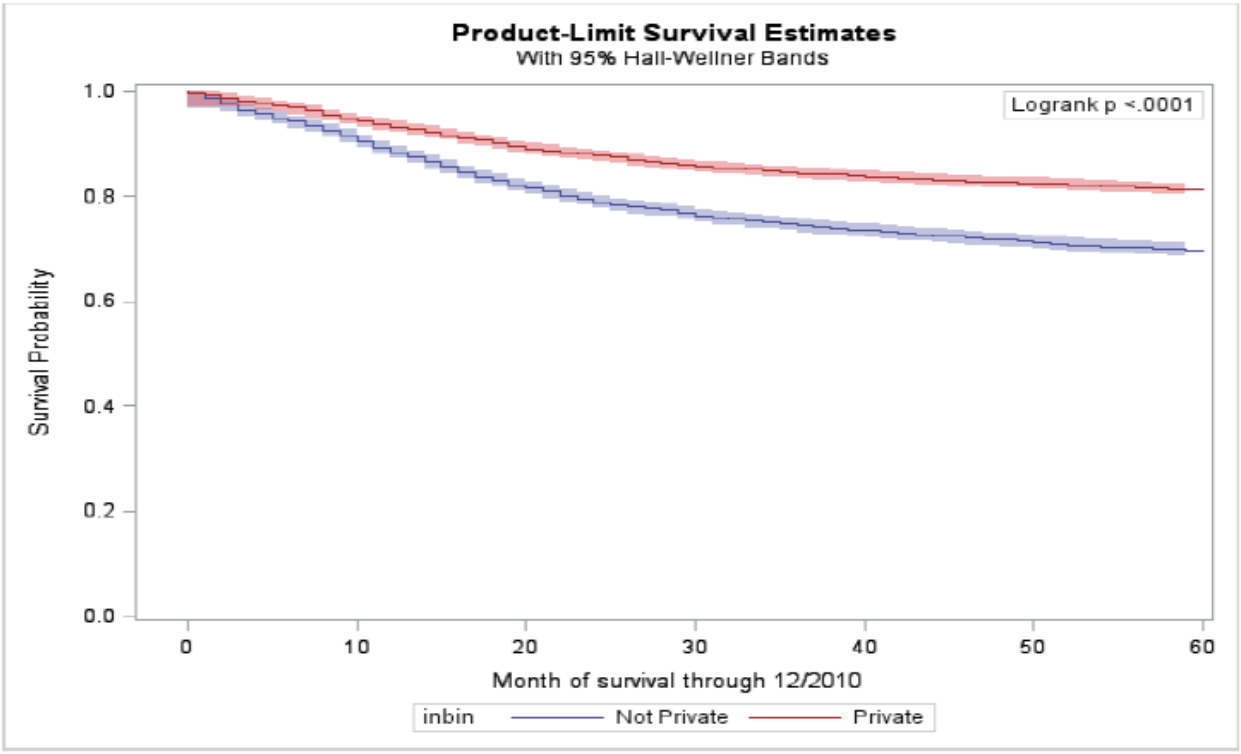
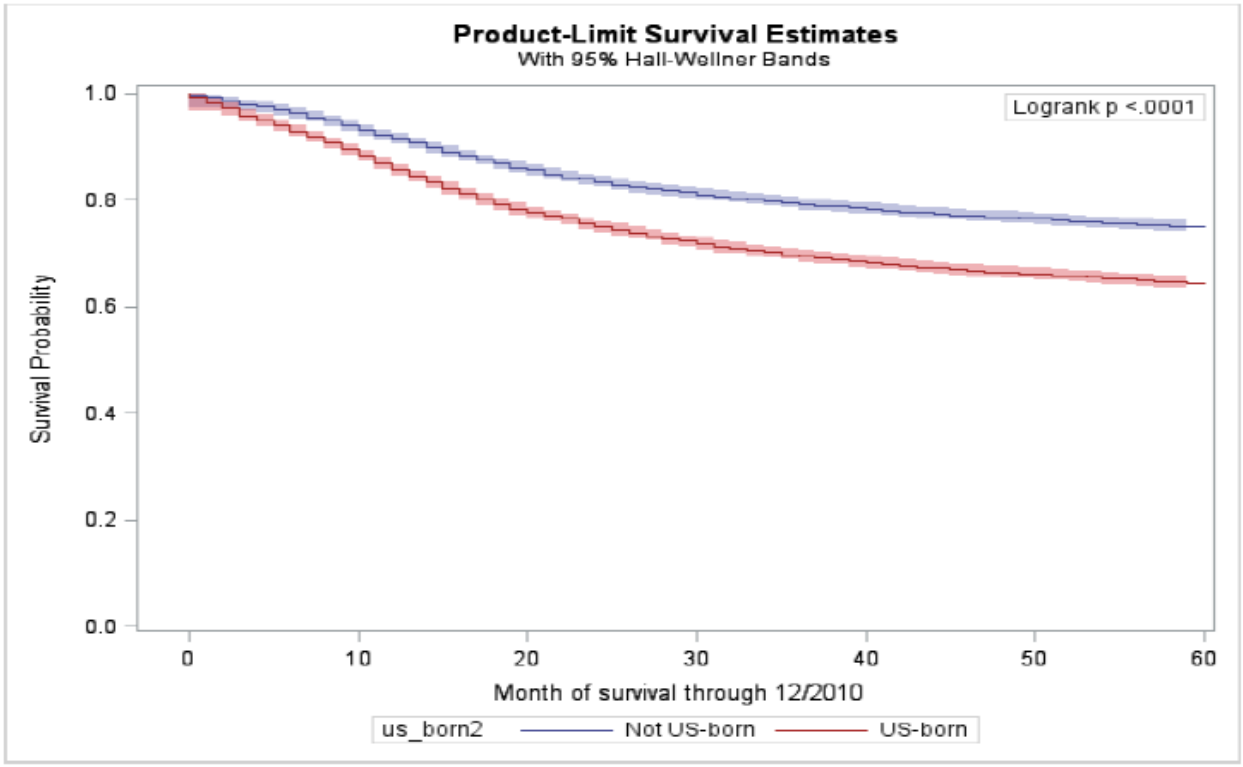


Figure 3.11d Cervix Kaplan-Meier Curves – US-born Status: Cervical cancer survival Kaplan-Meier curves by US-born status for 5-year survival.



Ovary

Ovarian cancer 5-year survival rates, as seen in Figure 3.12, were associated with race/ethnicity and measures of healthcare access. The majority of all ovarian cancer cases did not survive beyond 5 years, and the median survival time was 47 months (95% CI: 46, 48). Survival rates were significantly lower for NH Whites and NH Blacks than for Hispanics or NH Asian PIs ($p<0.0001$; Figure 3.12a). The highest quintile of SES had a significantly better survival rate compared to other levels of SES ($p<0.0001$), but no linear trend of survival rates by SES was seen (Figure 3.12b). Private insurance status was associated with a significantly higher survival rate compared to non-private insurance ($p<0.0001$; Figure 3.12c). A significant association with survival was seen for birthplace; lower survival rates for US-born than not US-born birthplace ($p<0.0001$; Figure 3.12d).

Figure 3.12a Ovary Kaplan-Meier Curves – Race/Ethnicity: Ovarian cancer survival Kaplan-Meier curves by race/ethnicity for 5-year survival.

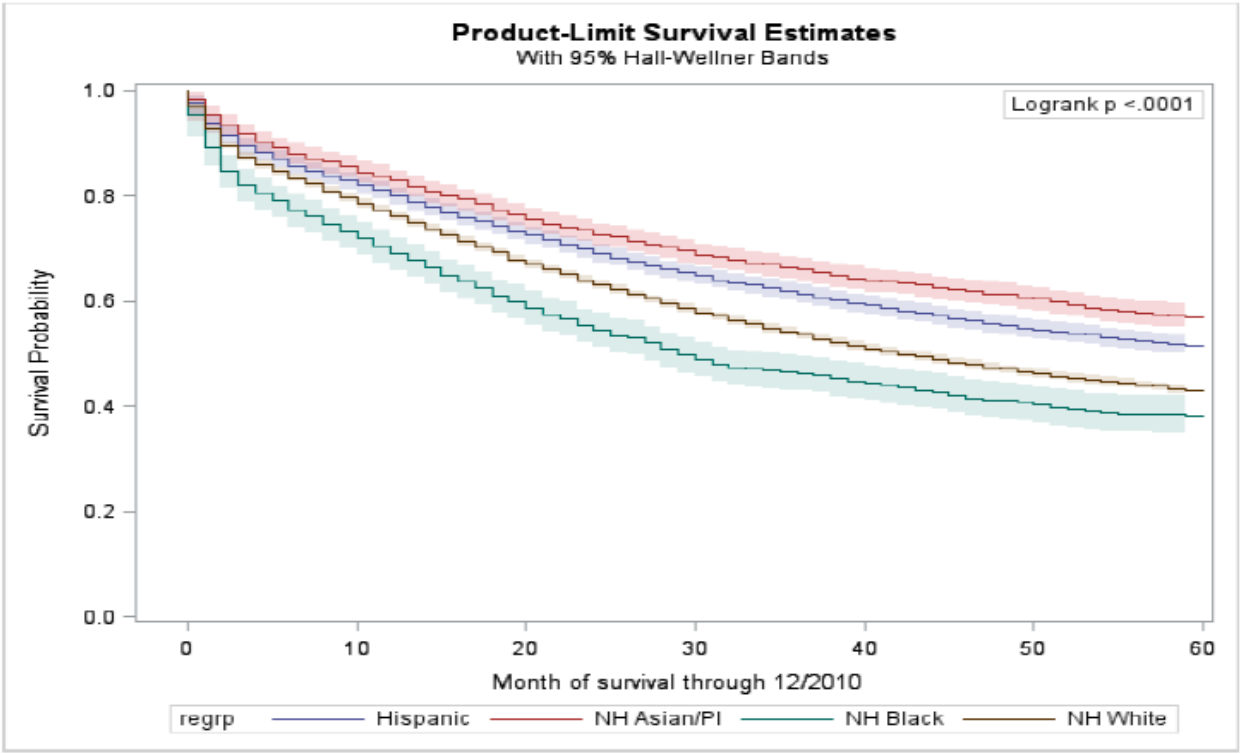


Figure 3.12b Ovary Kaplan-Meier Curves – SES: Ovarian cancer survival Kaplan-Meier curves by SES for 5-year survival.

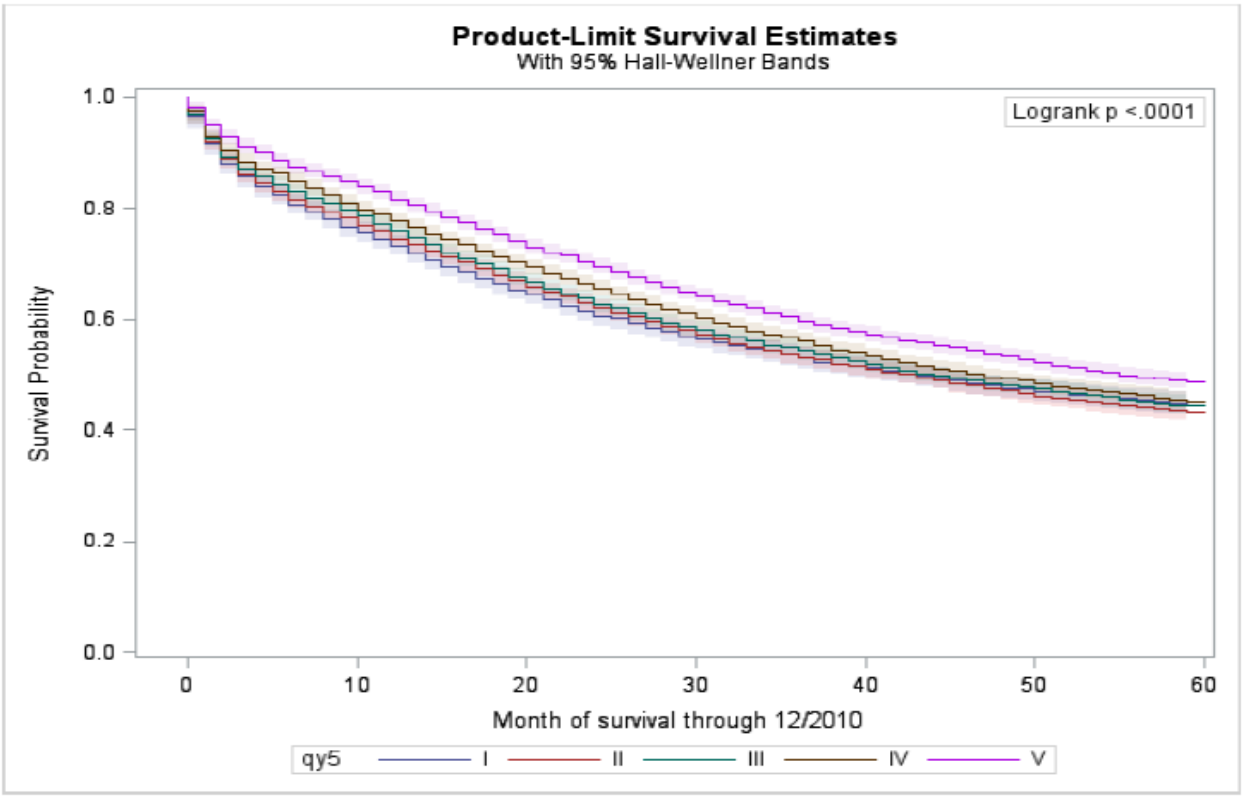


Figure 3.12c Ovary Kaplan-Meier Curves – Insurance Status: Ovarian cancer survival Kaplan-Meier curves by insurance status for 5-year survival.

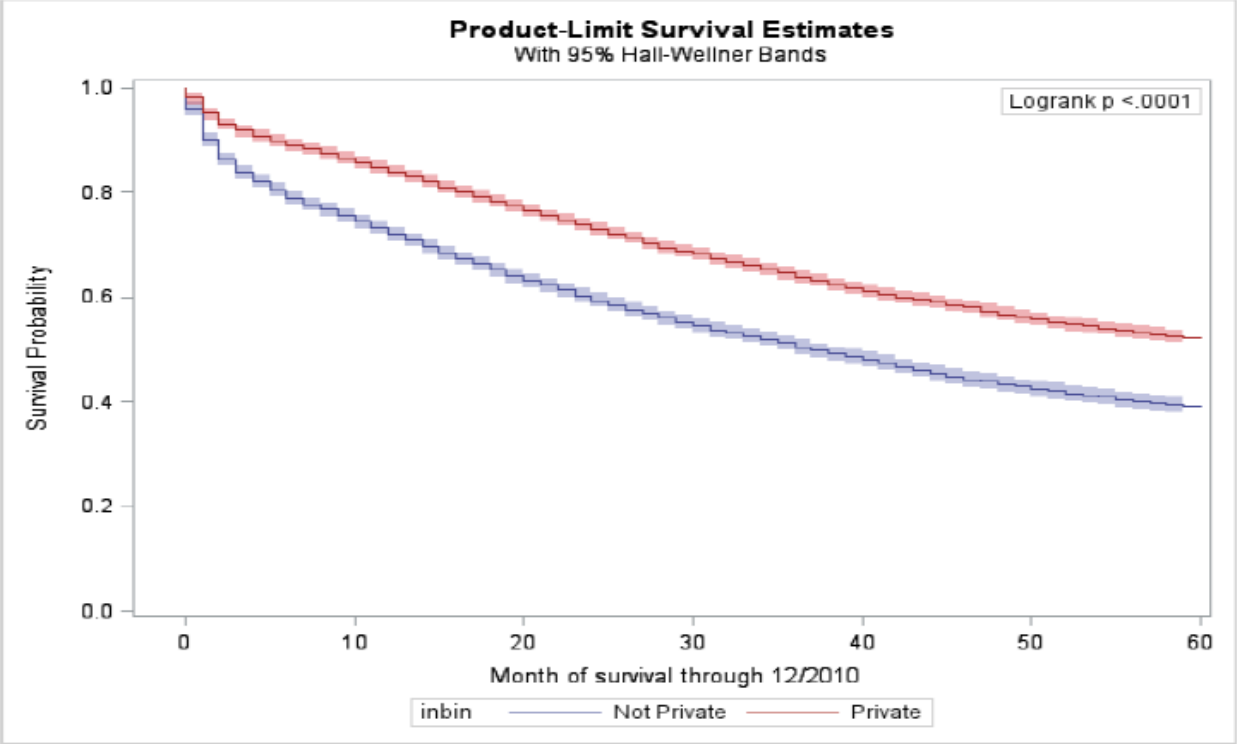
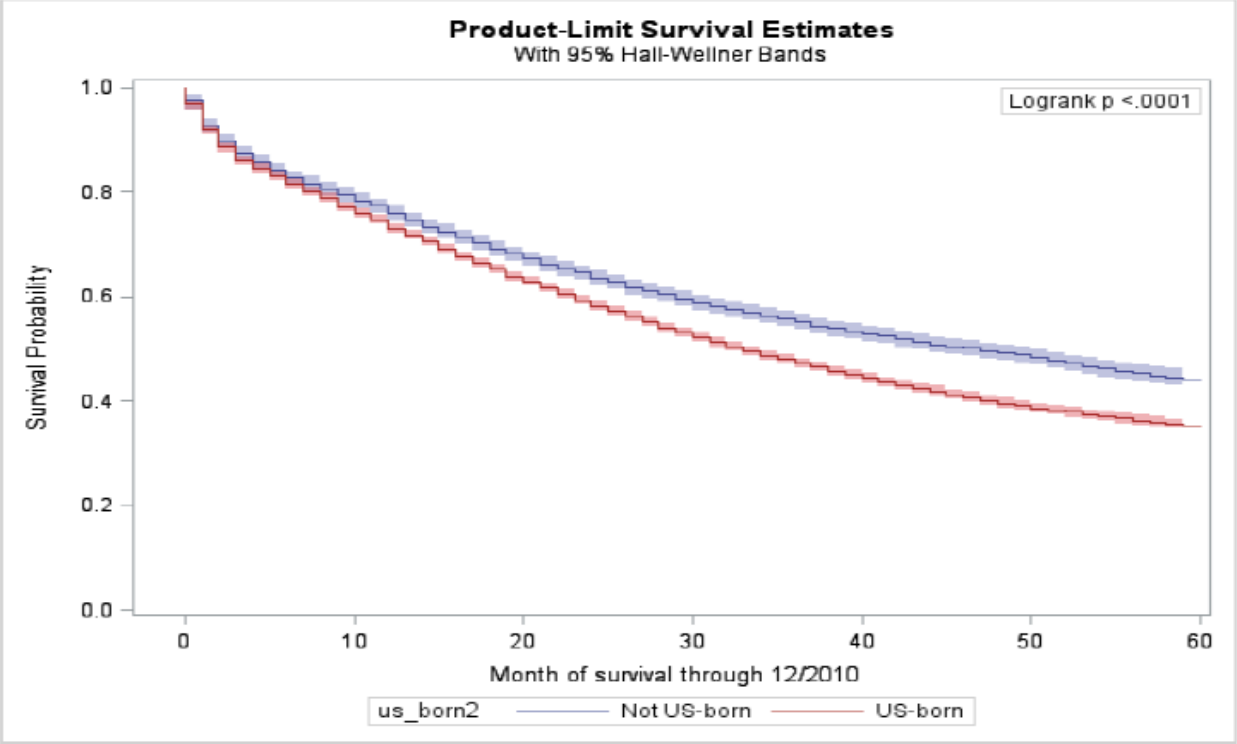


Figure 3.12d Ovary Kaplan-Meier Curves – US-born Status: Ovarian cancer survival Kaplan-Meier curves by US-born for 5-year survival.



Vagina

Vaginal cancer 5-year survival rates, as seen Figure 3.13, were not significantly associated with race/ethnicity and most measures of healthcare access, except for US-born status. Median survival time for 5-year survival was not calculated, due to the overall high survival. A birthplace within the US was associated with lower survival rates compared to a birthplace outside the US (p=0.0129; Figure 3.13d). Vaginal cancer survival was high for all race/ethnicities, and while survival rates were highest for NH Asian/PIs, these did not reach statistical significance when compared to other race/ethnicities (Figure 3.13a). No significant difference in survival was seen between quintiles of SES, though the highest level of SES was associated with slightly higher survival than any other level (Figure 3.13b). Insurance status was not significantly associated with survival, though the survival rates were slightly higher for private insurance (Figure 3.13c).

Figure 3.13a Vagina Kaplan-Meier Curves – Race/Ethnicity: Vaginal cancer survival Kaplan-Meier curves by race/ethnicity for 5-year survival.

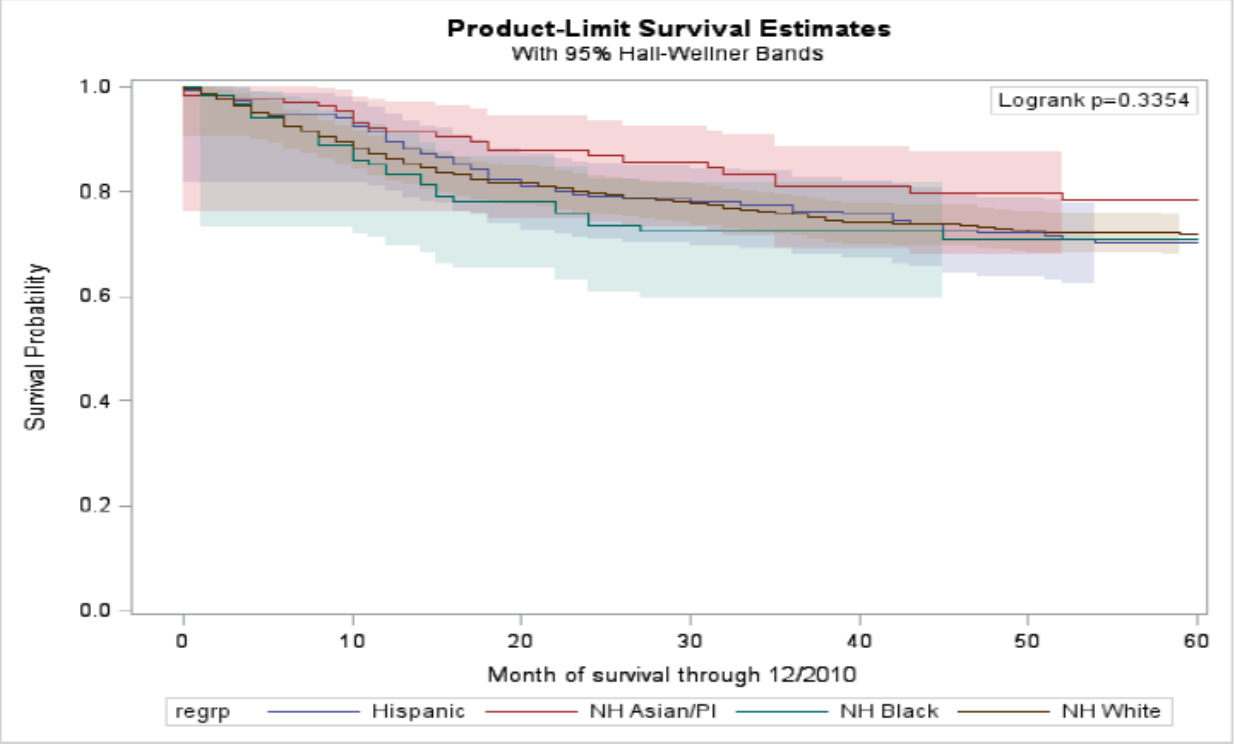


Figure 3.13b Vagina Kaplan-Meier Curves – SES: Vaginal cancer survival Kaplan-Meier curves by SES for 5-year survival.

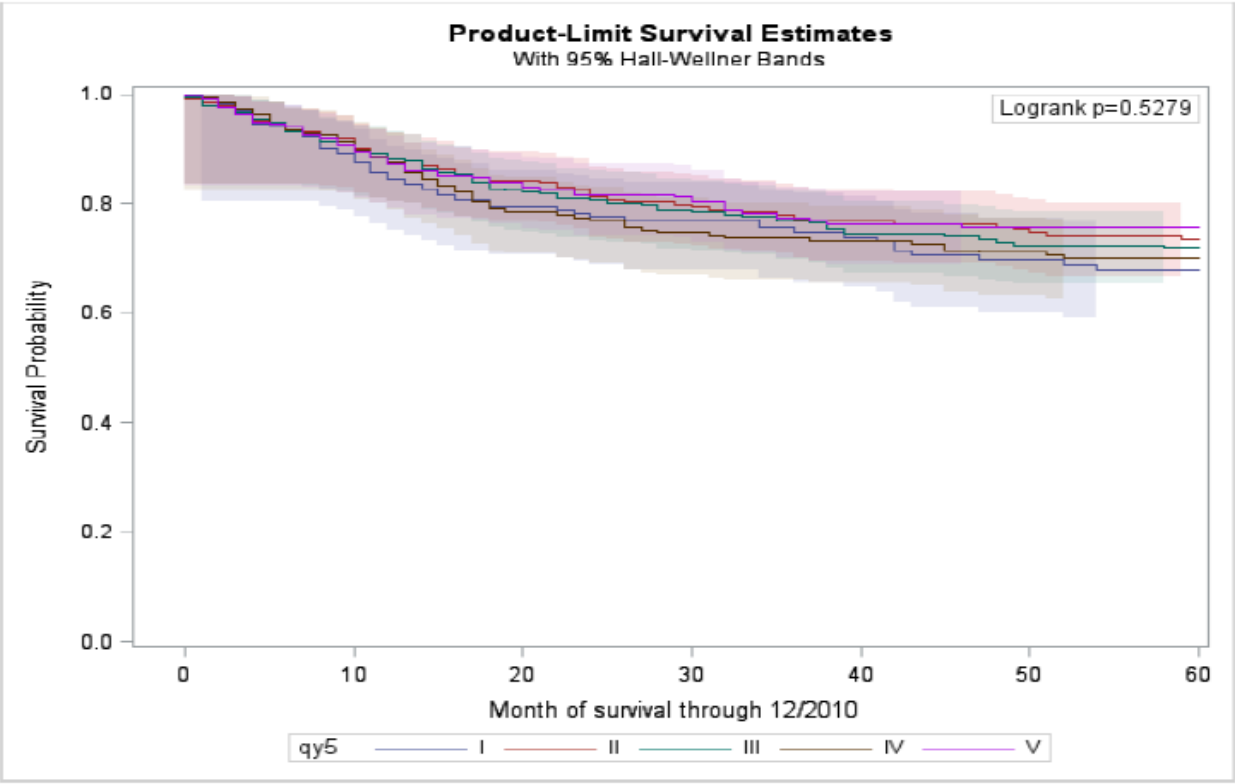


Figure 3.13c Vagina Kaplan-Meier Curves – Insurance Status: Vaginal cancer survival Kaplan-Meier curves by insurance status for 5-year survival.

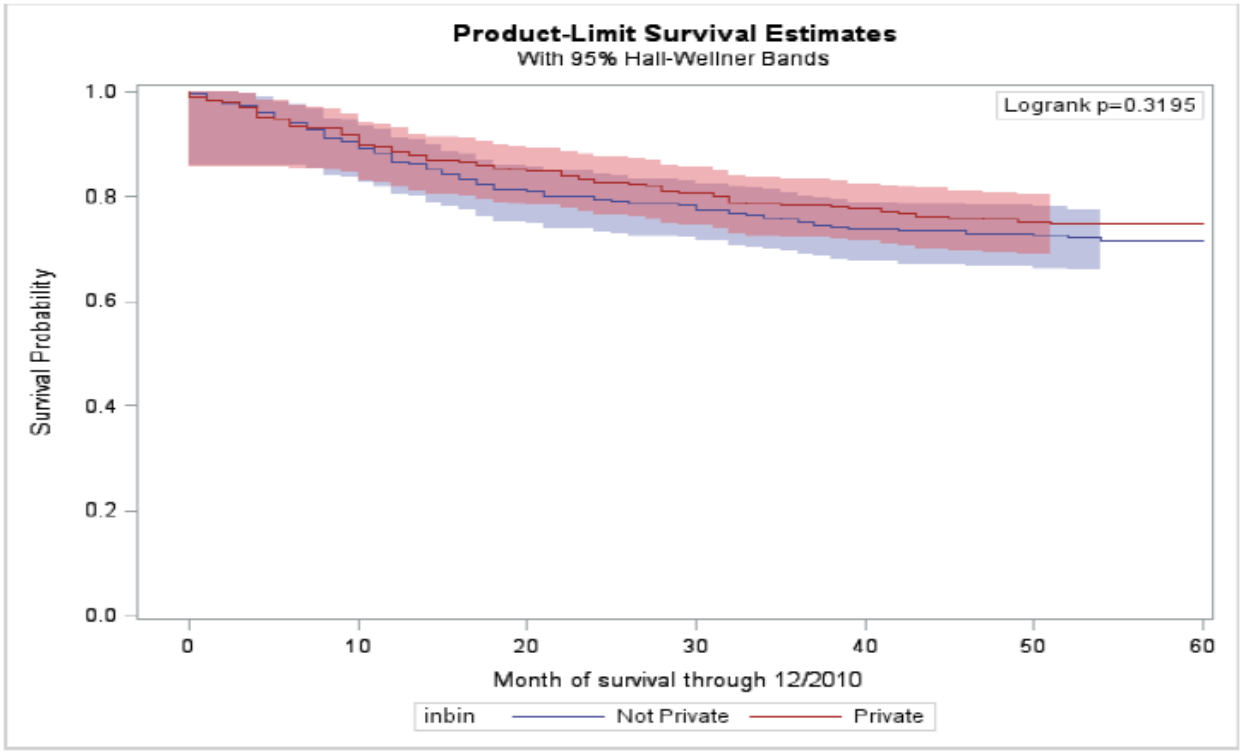
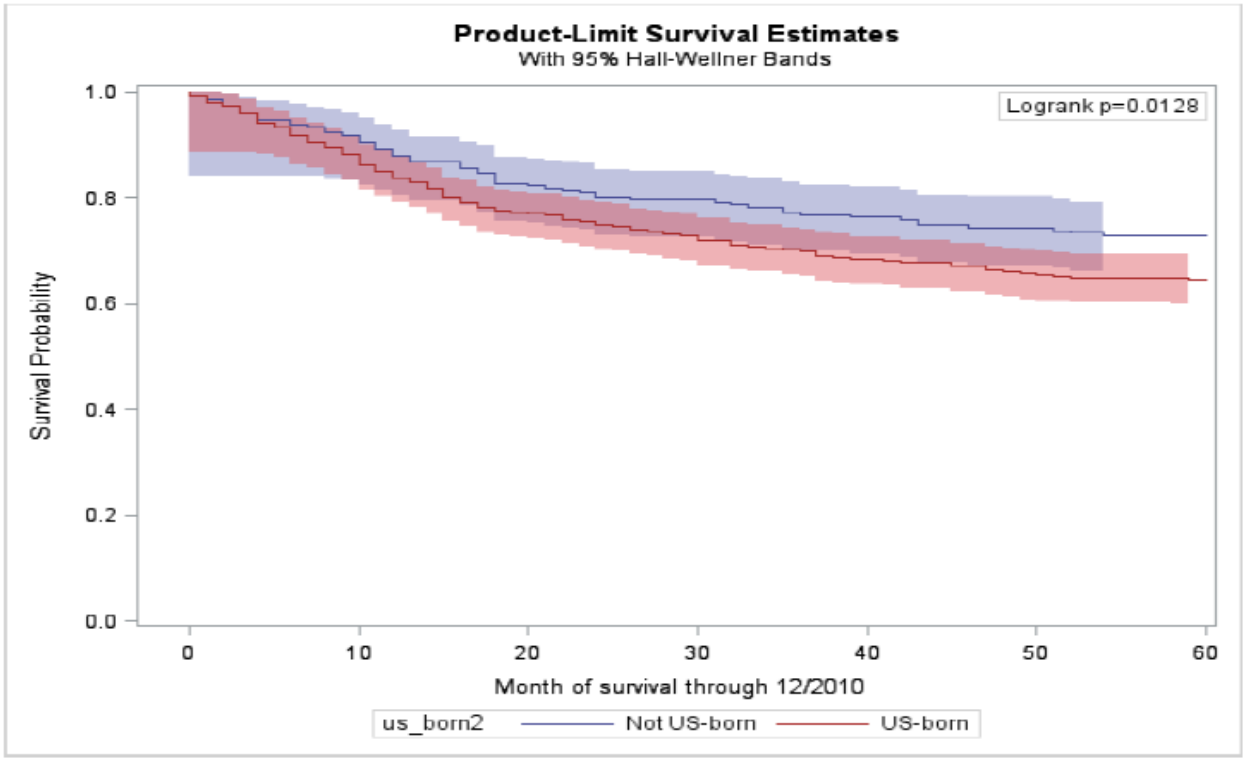


Figure 3.13d Vagina Kaplan-Meier Curves – US-born Status: Vaginal cancer survival Kaplan-Meier curves by US-born status for 5-year survival.



Vulva

As observed in Figure 3.14, significant differences in vulvar cancer 5-year survival rates were seen by race/ethnicity and measures of healthcare access, except US-born status. Due to the overall high survival beyond 5 years, median survival time was not calculated. NH Whites and Hispanics had significantly lower survival than NH Blacks and Asian PIs ($p=0.0363$; Figure 3.14a). Survival rates increased with an increase in quintiles of SES with the highest survival rates for the highest SES ($p=0.0004$; Figure 3.14b). Private insurance was associated with higher survival than non-private insurance ($p<0.0001$; Figure 3.14c). The difference between known birthplace status survival rates was not remarkable (Figure 3.14d).

Figure 3.14a Vulva Kaplan-Meier Curves – Race/Ethnicity: Vulvar cancer survival Kaplan-Meier curves by race/ethnicity for 5-year survival.

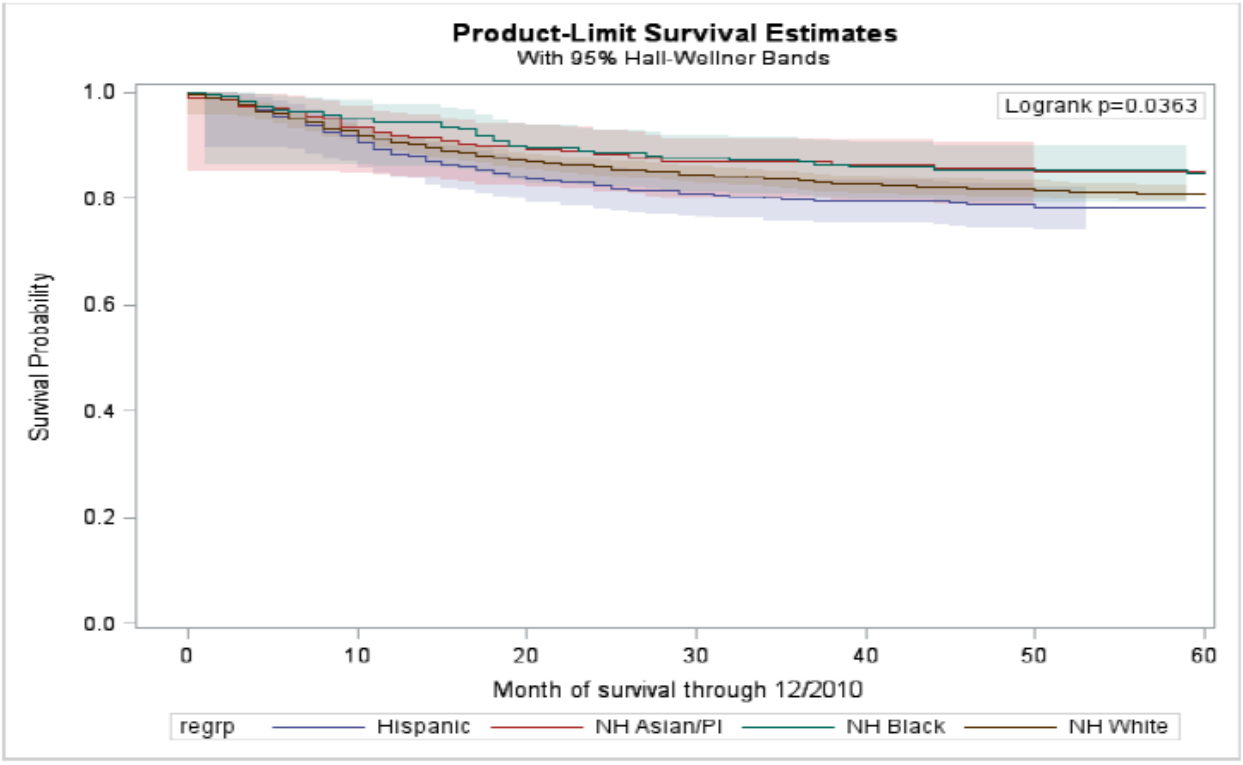


Figure 3.14b Vulva Kaplan-Meier Curves – SES: Vulvar cancer survival Kaplan-Meier curves by SES for 5-year survival.

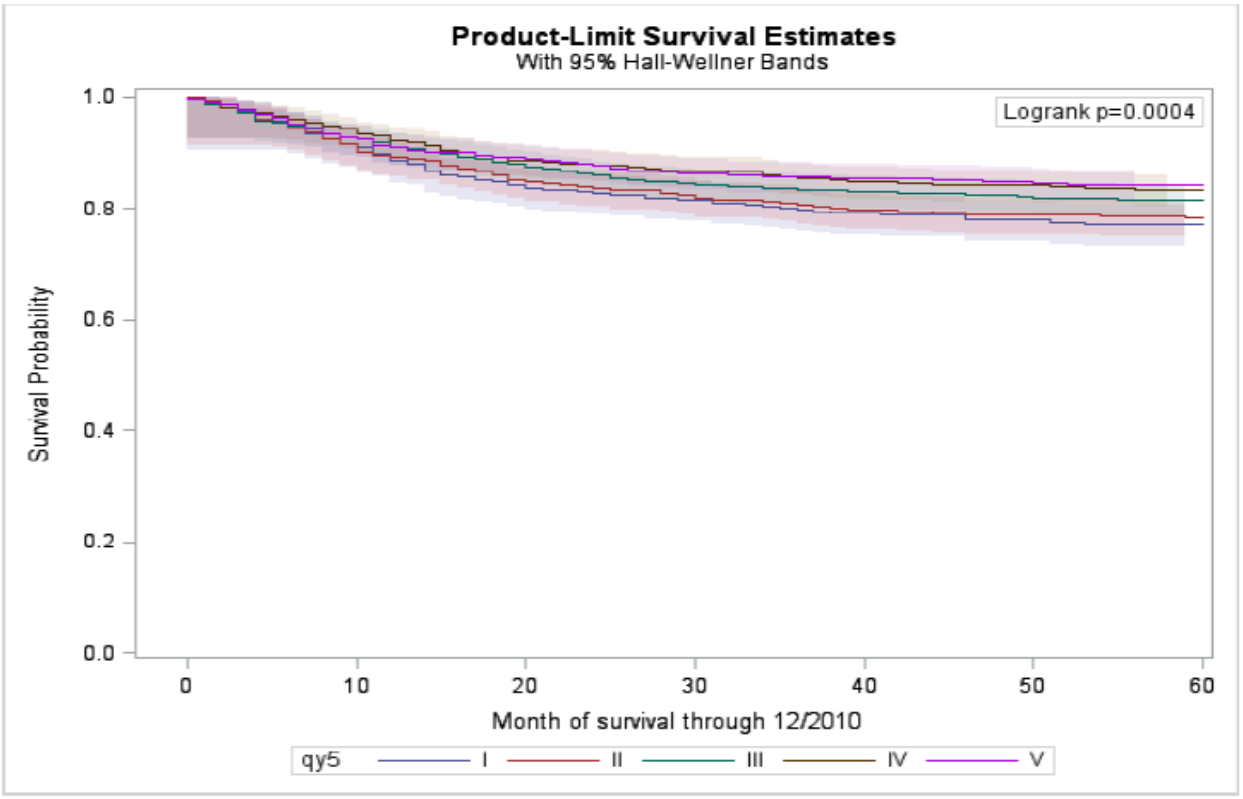


Figure 3.14c Vulva Kaplan-Meier Curves – Insurance Status: Vulvar cancer survival Kaplan-Meier curves by insurance status for 5-year survival.

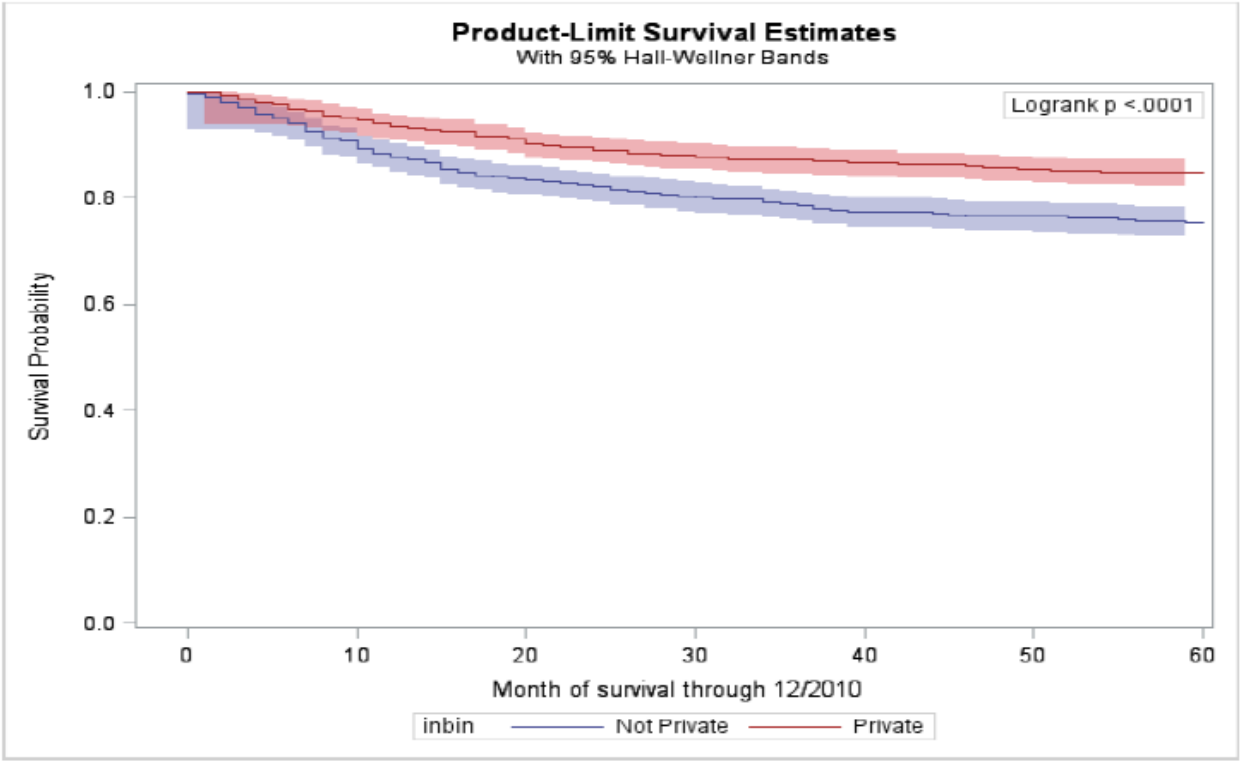
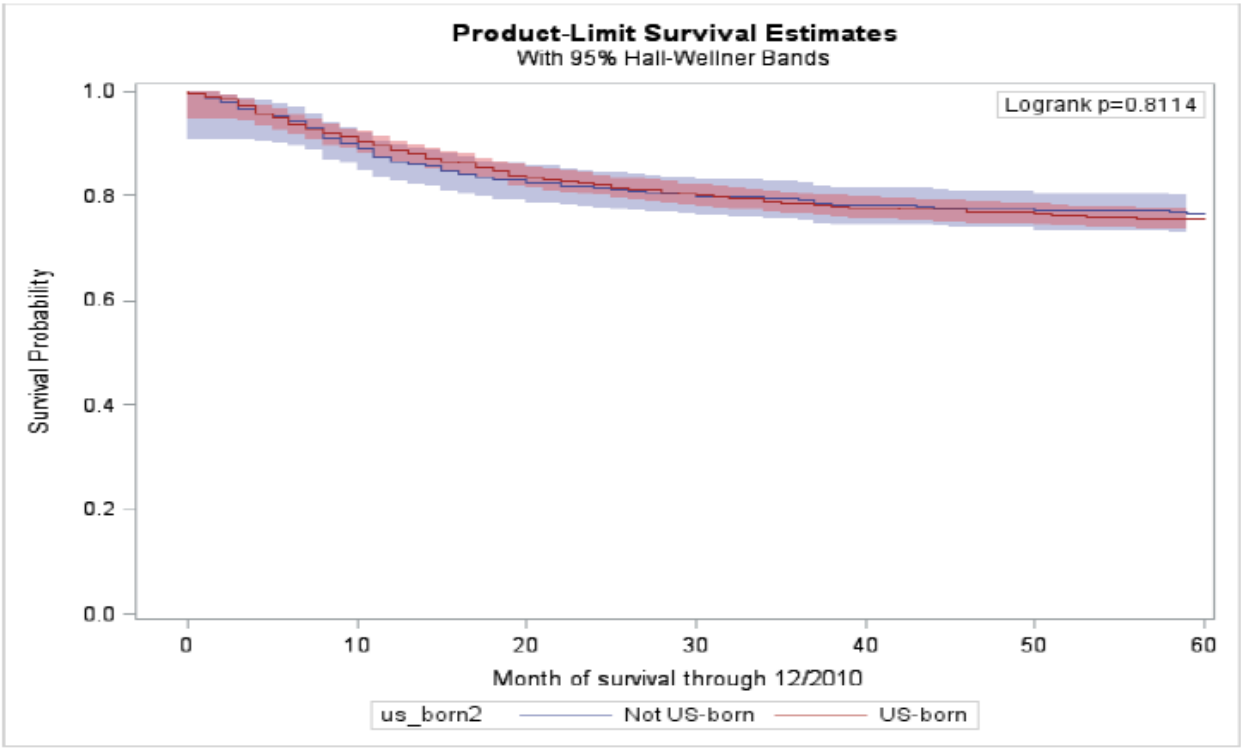


Figure 3.14d Vulva Kaplan-Meier Curves – US-born Status: Vulvar cancer survival Kaplan-Meier curves by US-born status for 5-year survival.



Other Gynecologic

Other gynecologic cancers 5-year survival rates, as seen in Figure 3.15, were associated with SES, but not with race/ethnicity or other measures of healthcare access. A large majority of other gynecologic cancer cases survived beyond 5 years, and so no median survival time was calculated. A trend of survival rates was seen for SES, survival decreasing as SES increased, to the lowest survival for the highest SES ($p=0.0288$; Figure 3.15b). Although survival rates were not significantly different by race/ethnicity, Hispanics had a slightly higher other gynecologic cancer survival than the other racial/ethnic groups (Figure 3.15a). Insurance status was not associated with other female genital organ survival rates (Figure 3.15c). A non-significant association with survival was seen for birthplace; slightly lower survival seen for US-born than not US-born (Figure 3.15d).

Figure 3.15a Other Gynecologic Kaplan-Meier Curves – Race/Ethnicity: Other gynecologic cancers survival Kaplan-Meier curves by race/ethnicity for 5-year survival.

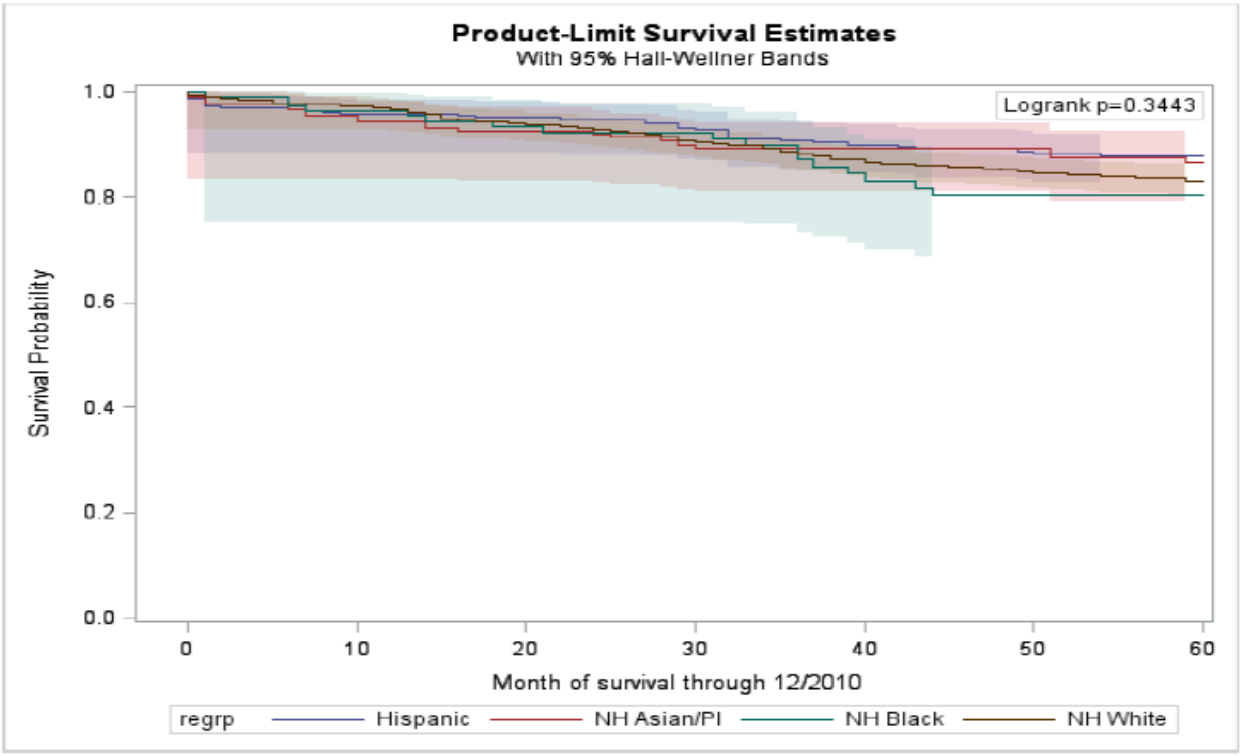


Figure 3.15b Other Gynecologic Kaplan-Meier Curves – SES: Other gynecologic cancers survival Kaplan-Meier curves by SES for 5-year survival.

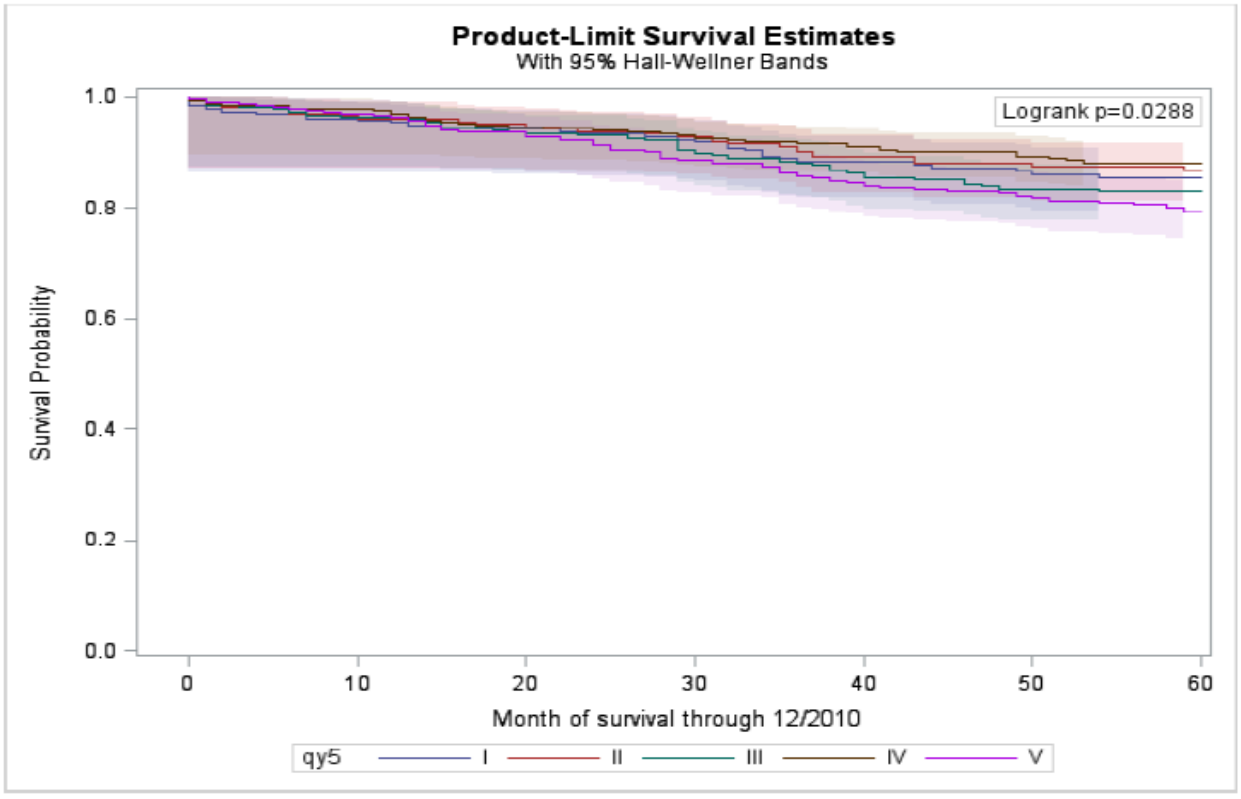


Figure 3.15c Other Gynecologic Kaplan-Meier Curves– Insurance Status: Other gynecologic cancers survival Kaplan-Meier curves by insurance status for 5-year survival.

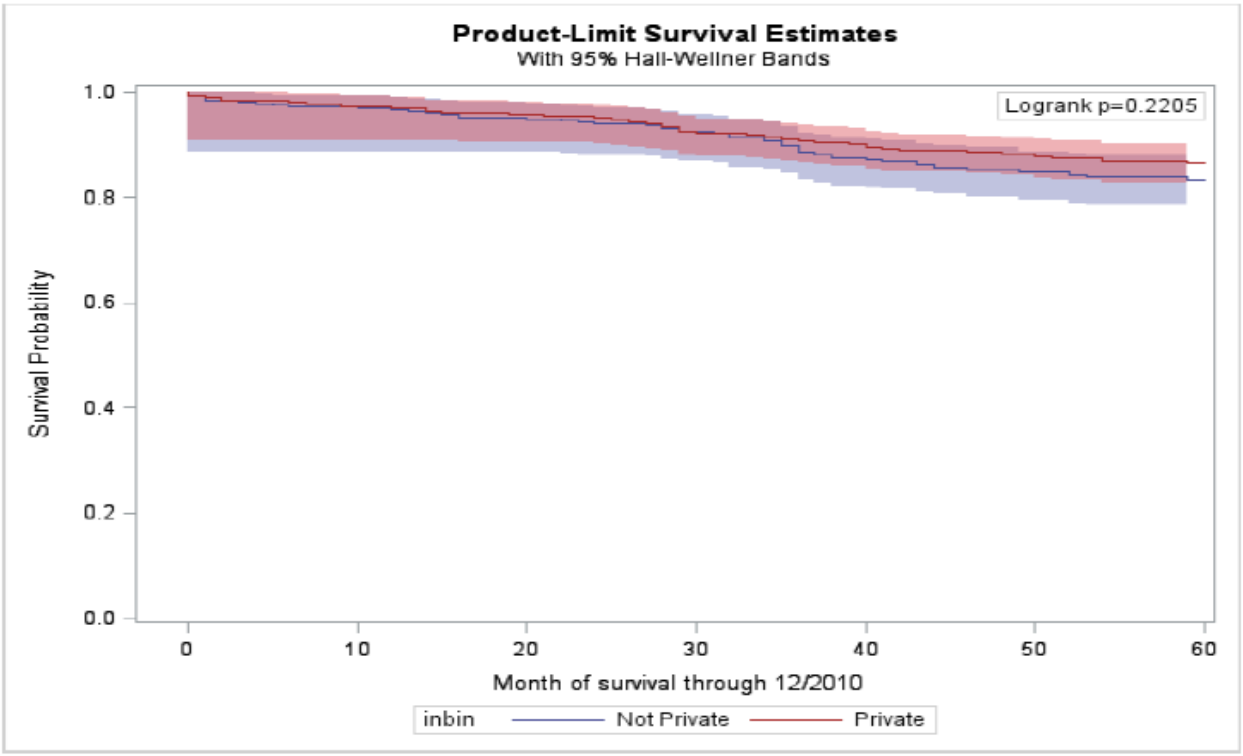
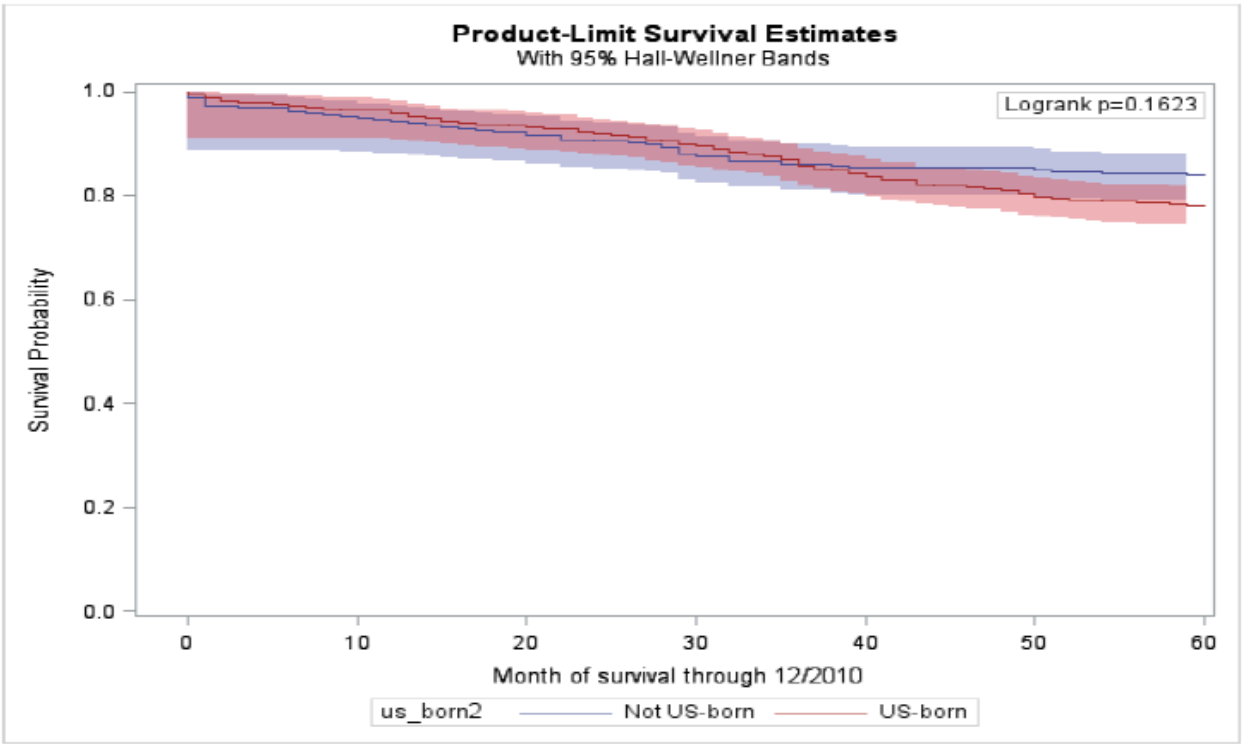


Figure 3.15d Other Gynecologic Kaplan-Meier Curves – US-born Status: Other gynecologic cancers survival Kaplan-Meier curves by US-born status for 5-year survival.



Aim 3 part b: Cox Regression site-specific 5-year survival analysis by race/ethnicity and measures of healthcare access

Cervix

When all variables were analyzed concurrently, known covariates, race/ethnicity and measures of healthcare access were significantly associated with cervical cancer survival. The significant covariates following Cox regression analysis stepwise selection of cervical cancer survival can be seen in Table 3.21 and Figure 3.16. Year at diagnosis increased risk of death by year 5-year survival by 1.90% (95% CI: 1.011, 1.028; p<0.0001). Age at diagnosis increased risk by year for cervical cancer death by 1.90% (95% CI: 1.017, 1.021; p<0.0001).

NH Blacks had a greater risk of cervical cancer death for 5-year survival compared to NH Whites, 13.50% increased risk (95% CI: 1.012, 1.272; p=0.0301). Hispanics had a lower risk compared to NH Whites by 15.60% (95% CI: 0.773, 0.922; p=0.0002). NH Asian PIs had an approximate 10% risk reduction of cervical cancer death compared to NH Whites, but this difference did not reach statistical significance.

Adenocarcinoma, compared to squamous histology, was associated with the lowest risk of cervical cancer death, 21.80% lower for 5-year survival (95% CI: 0.717, 0.853; p<0.0001). Other histology had the highest risk of mortality, 38.40% higher compared to squamous histology (95% CI: 1.269, 1.510; p<0.0001). Late stage had over four times the risk of death compared to early stage for 5-year survival (HR = 4.089 (3.836, 4.358;

p<0.0001)). Unknown stage was adjusted for in the Cox regression model, but a hazard ratio was not reported.

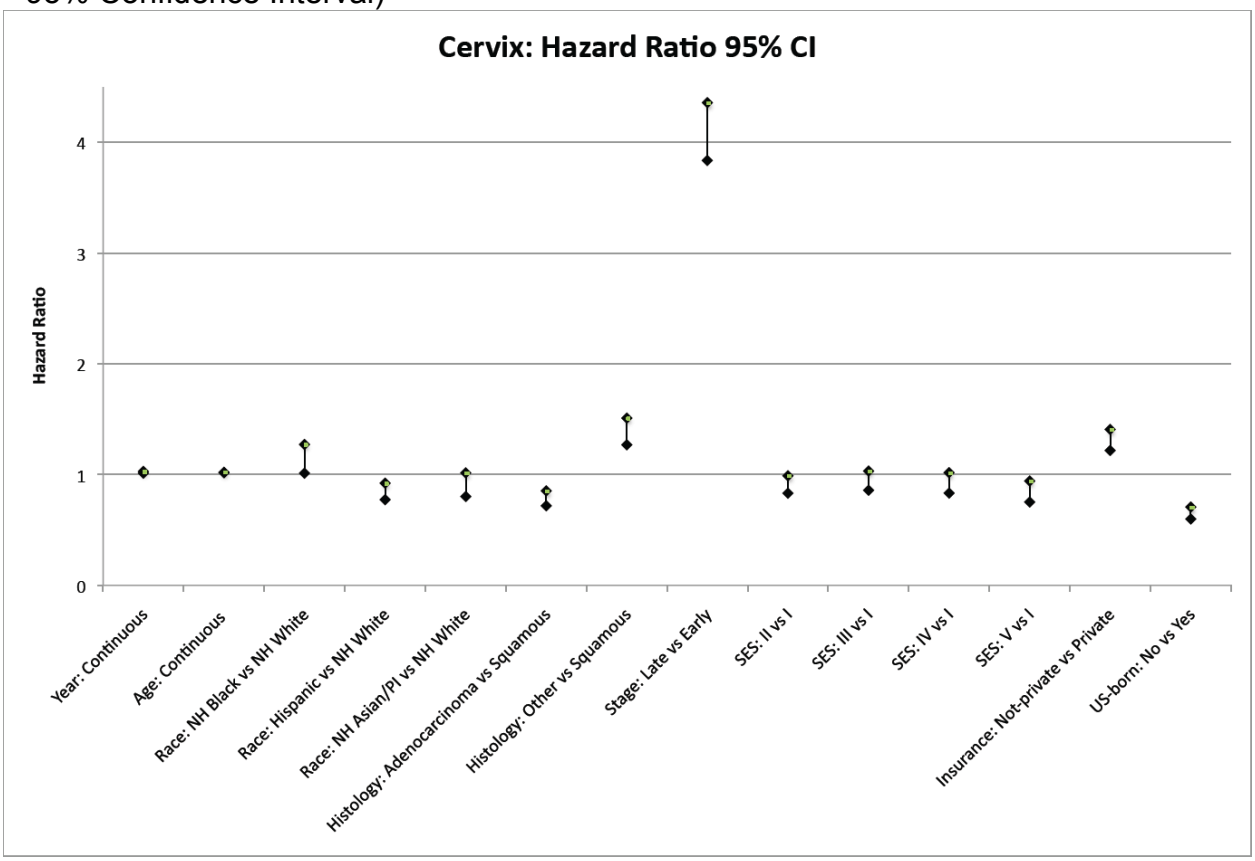
In the presence of all other variables, SES was moderately associated with survival. Although a trend of decreasing risk compared to the lowest level of SES was seen for increasing SES, the only quintile of SES to reach statistically lower risk of cervical cancer death was the highest level of SES, which had 15.80% reduction for 5-year survival (95% CI: 0.752, 0.942; p=0.0027). Women with not-private insurance had significantly higher risk of death 30.90% higher than those with private insurance (95% CI: 1.269, 1.510; p<0.0001). Missing and unknown insurance status were adjusted for in the Cox regression model, but hazard ratios were not reported. A birthplace outside of the US was associated with a higher survival than a birthplace within the US; risk of death was reduced by 35.10% for 5-year cervical survival (95% CI: 0.597, 0.706; p<0.0001). Unknown US-born status was adjusted for in the Cox regression model, but the hazard ratio was not reported.

Table 3.21 Cervix Survival Regression: Stepwise Cox regression analysis of cervical cancer survival, modeled* by healthcare access measures, race/ethnicity, and other known covariates. (95% CI = 95% Confidence Interval)

Cervix 5-year Survival	Coefficient		Wald Chi-Squared		Hazard Ratio		
Cox Regression						95% CI	
Stepwise Selected Covariates	Estimate	SE	Statistic	P-value	Estimate	Lower	Upper
Year: Continuous	0.0193	0.0041	22.4862	<0.0001	1.019	1.011	1.028
Age: Continuous	0.0185	0.0011	304.1084	<0.0001	1.019	1.017	1.021
Race: NH Black vs NH White	0.1264	0.0583	4.7009	0.0301	1.135	1.012	1.272
Race: Hispanic vs NH White	-0.1693	0.0448	14.2914	0.0002	0.844	0.773	0.922
Race: NH Asian/PI vs NH White	-0.1024	0.0603	2.8836	0.0895	0.903	0.802	1.016
Histology: Adenocarcinoma vs Squamous	-0.2458	0.0444	30.7118	<0.0001	0.782	0.717	0.853
Histology: Other vs Squamous	0.3249	0.0444	53.6049	<0.0001	1.384	1.269	1.510
Stage: Late vs Early	1.4082	0.0325	1873.6347	<0.0001	4.089	3.836	4.358
SES: II vs I	-0.0982	0.0443	4.9186	0.0266	0.906	0.831	0.989
SES: III vs I	-0.0619	0.0473	1.7133	0.1906	0.940	0.857	1.031
SES: IV vs I	-0.0833	0.0511	2.6631	0.1027	0.920	0.832	1.017
SES: V vs I	-0.1721	0.0574	8.9999	0.0027	0.842	0.752	0.942
Insurance: Not-private vs Private	0.2694	0.0373	52.2009	<0.0001	1.309	1.217	1.408
US-born: No vs Yes	-0.4321	0.0430	100.9712	<0.0001	0.649	0.597	0.706

* Model was adjusted for unknown stage, unknown and missing insurance status, and unknown US-born status.

Figure 3.16 Cervix Survival Cox Regression HR: Hazard Ratio 95% CI calculated from Cox regression stepwise regression analysis of cervical cancer 5-year survival. (95% CI = 95% Confidence Interval)



Ovary

Cox regression survival analysis found that race/ethnicity and healthcare access measures, in addition to known covariates, were associated with ovarian cancer survival. The chosen significant covariates following stepwise selection of ovarian cancer survival can be seen in Table 3.22 and Figure 3.17. Risk of death increased by year for year at diagnosis by 2.40% (95% CI: 1.019, 1.029; p<0.0001). Ovarian cancer death risk was increased by year for age at diagnosis by 3.20% for 5-year survival (95% CI: 1.031, 1.034; p<0.0001).

Compared to NH Whites, NH Blacks had a significant excess of risk of mortality, increased by 29.90% for 5-year survival (95% CI: 1.198, 1.408; p<0.0001). Hispanics and NH Asian PIs had an approximately equivalent ovarian cancer survival prognosis compared to NH Whites.

Among women with ovarian adenocarcinoma, those with the endometrioid subtype had a significantly lower risk of death compared to those with all other subtypes by 35.30% (95% CI: 0.593, 0.706; p<0.0001). The Hazard Ratio for endometrioid adenocarcinoma was half that of other histologies, showing that women with other histologies had twice the risk of ovarian cancer death as those with endometrioid adenocarcinoma histology (95% CI: 1.330, 1.468; p<0.0001). Late stage had over four times the risk of ovarian cancer death compared to early stage for 5-year survival (HR = 4.448 (4.151, 4.766; p<0.0001)). Unknown stage was adjusted for in the Cox regression model, but a hazard ratio was not reported.

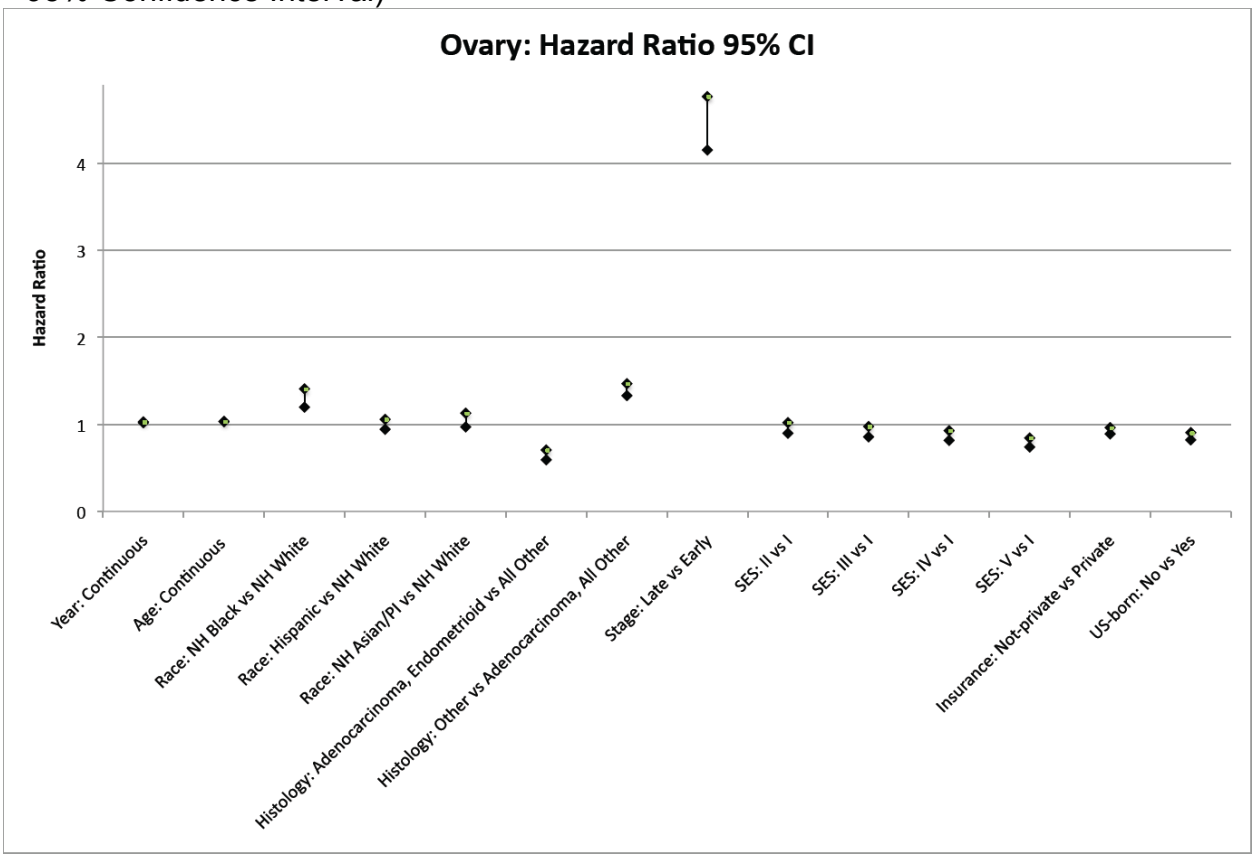
Compared to the lowest quintile of SES, a linear trend of risk reduction was seen for increasing levels of SES. The risk of ovarian cancer death was lowest for the highest SES, lower by 21.00% for 5-year survival (95% CI: 0.740, 0.844; p<0.0001). Not-private insurance was associated with a slightly lower risk of ovarian cancer death than private insurance, statistically significantly lower by 7.40% (95% CI: 0.890, 0.964; p=0.0002). Missing and unknown insurance status were adjusted for in the Cox regression model, but hazard ratios were not reported. Individuals with not US-born status had higher survival rates than those with a US-born status; risk of death was reduced by 13.80% for 5-year survival (95% CI: 0.822, 0.905; p<0.0001). Unknown US-born status was adjusted for in the Cox regression model, but the hazard ratio was not reported.

Table 3.22 Ovary Survival Regression: Stepwise Cox Regression analysis of ovarian cancer survival, modeled* by healthcare access measures, race/ethnicity, and other known covariates. (95% CI = 95% Confidence Interval)

Ovary 5-year Survival	Coefficient		Wald Chi-Squared		Hazard Ratio		
Cox Regression						95% CI	
Stepwise Selected Covariates	Estimate	SE	Statistic	P-value	Estimate	Lower	Upper
Year: Continuous	0.0241	0.0025	96.3803	<0.0001	1.024	1.019	1.029
Age: Continuous	0.0318	0.0008	1749.2059	<0.0001	1.032	1.031	1.034
Race: NH Black vs NH White	0.2618	0.0412	40.3765	<0.0001	1.299	1.198	1.408
Race: Hispanic vs NH White	0.0001	0.0293	0.0000	0.9969	1.000	0.944	1.059
Race: NH Asian/PI vs NH White	0.0466	0.0381	1.4938	0.2216	1.048	0.972	1.129
Histology: Adenocarcinoma, Endometrioid vs All Other	-0.4350	0.0444	95.8574	<0.0001	0.647	0.593	0.706
Histology: Other vs Adenocarcinoma, All Other	0.3346	0.0252	176.9692	<0.0001	1.397	1.330	1.468
Stage: Late vs Early	1.4925	0.0353	1791.8055	<0.0001	4.448	4.151	4.766
SES: II vs I	-0.0430	0.0328	1.7229	0.1893	0.958	0.898	1.021
SES: III vs I	-0.0889	0.0329	7.3204	0.0068	0.915	0.858	0.976
SES: IV vs I	-0.1395	0.0329	17.9691	<0.0001	0.870	0.816	0.928
SES: V vs I	-0.2353	0.0334	49.4796	<0.0001	0.790	0.740	0.844
Insurance: Not-private vs Private	-0.0764	0.0205	13.9133	0.0002	0.926	0.890	0.964
US-born: No vs Yes	-0.1484	0.0245	36.5679	<0.0001	0.862	0.822	0.905

* Model was adjusted for unknown stage, unknown and missing insurance status, and unknown US-born status.

Figure 3.17 Ovary Survival Cox Regression HR: Hazard Ratio 95% CI calculated from Cox regression stepwise regression analysis of ovarian cancer 5-year survival. (95% CI = 95% Confidence Interval)



Vagina

In the presence of known covariates, vaginal cancer survival was not associated with healthcare access measures or race/ethnicity, except US-born status. The chosen significant covariates following stepwise selection of vaginal cancer survival can be seen in Table 3.23 and Figure 3.18. Vaginal cancer death risk for year at diagnosis increased by year, by 3.70% for 5-year vaginal cancer survival (95% CI: 1.002, 1.073; p=0.0372). Risk of death increased by year for age at diagnosis, by 2.70% for 5-year survival (95% CI: 1.017, 1.037; p<0.0001).

Vaginal cancer survival was associated with histologic type, with 37.00% lower risk of death for women with squamous compared to all other histologies (95% CI: 1.054, 1.781; p=0.0185). Late stage at diagnosis had almost three times the risk of vaginal cancer death compared to early stage for 5-year survival (HR = 2.931 (2.224, 3.862; p<0.0001)). Unknown stage was adjusted for in the Cox regression model, but a hazard ratio was not reported.

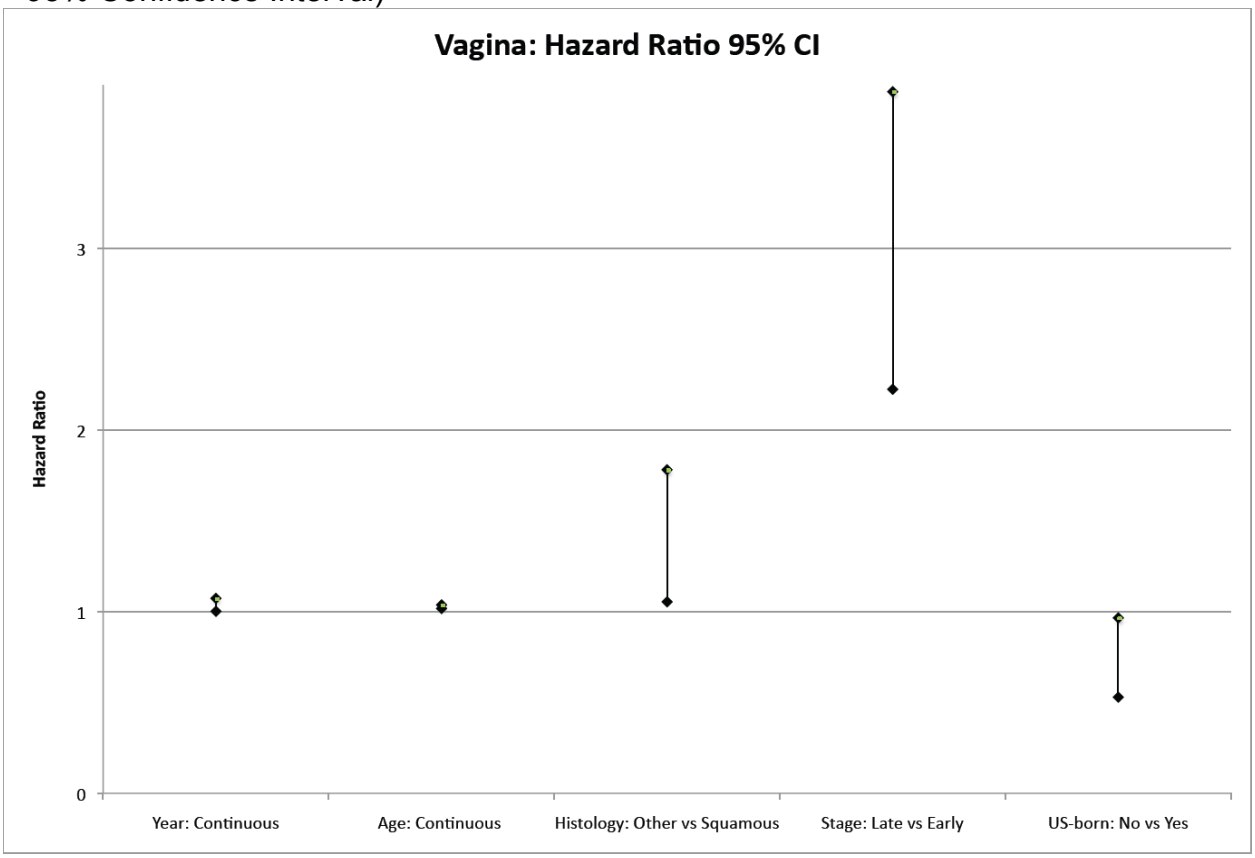
US birthplace was associated with a 28.50% higher risk of vaginal cancer death compared to birthplace outside of the US (95% CI: 0.529, 0.966; p=0.0290). Unknown US-born status was adjusted for in the Cox regression model, but the hazard ratio was not reported. Vaginal cancer risk of death was not associated with race/ethnicity, SES, insurance status in the Cox regression model. Missing and unknown insurance status were adjusted for in the Cox regression model, but hazard ratios were not reported.

Table 3.23 Vagina Survival Regression: Stepwise Cox Regression analysis of vaginal cancer survival, modeled* by healthcare access measures, race/ethnicity, and other known covariates. (95% CI = 95% Confidence Interval)

Vagina 5-year Survival	Coefficient		Wald Chi-Squared		Hazard Ratio		
Cox Regression						95% CI	
Stepwise Selected Covariates	Estimate	SE	Statistic	P-value	Estimate	Lower	Upper
Year: Continuous	0.0365	0.0175	4.3409	0.0372	1.037	1.002	1.073
Age: Continuous	0.0269	0.0049	29.9840	<0.0001	1.027	1.017	1.037
Histology: Other vs Squamous	0.3151	0.1338	5.5499	0.0185	1.370	1.054	1.781
Stage: Late vs Early	1.0753	0.1408	58.2909	<0.0001	2.931	2.224	3.862
US-born: No vs Yes	-0.3358	0.1538	4.7658	0.0290	0.715	0.529	0.966

* Model was adjusted for unknown stage, unknown and missing insurance status, and unknown US-born status.

Figure 3.18 Vagina Survival Cox Regression HR: Hazard Ratio 95% CI calculated from Cox regression stepwise regression analysis of vaginal cancer 5-year survival. (95% CI = 95% Confidence Interval)



Vulva

Vulvar cancer survival was not associated with most healthcare access measures or race/ethnicity, except US-born status, in the presence of known covariates. The chosen significant covariates following stepwise selection of vulvar cancer survival can be seen in Table 3.24 and Figure 3.19. Year at diagnosis increased risk of death by year for survival by 6.60% (95% CI: 1.044, 1.090; p<0.0001). Age at diagnosis increased risk by year for vulvar cancer death for survival by 2.90% (95% CI: 1.023, 1.035; p<0.0001).

Squamous histology was associated with a lower mortality than other histologies, which had a risk reduction of vulvar cancer death of 30.60% for 5-year survival (95% CI: 0.550, 0.875; p=0.0020). Late stage at diagnosis was associated with an almost six times higher risk of death compared to early stage (HR = 5.874 (4.928, 7.002; p<0.0001)). Unknown stage was adjusted for in the Cox regression model, but a hazard ratio was not reported.

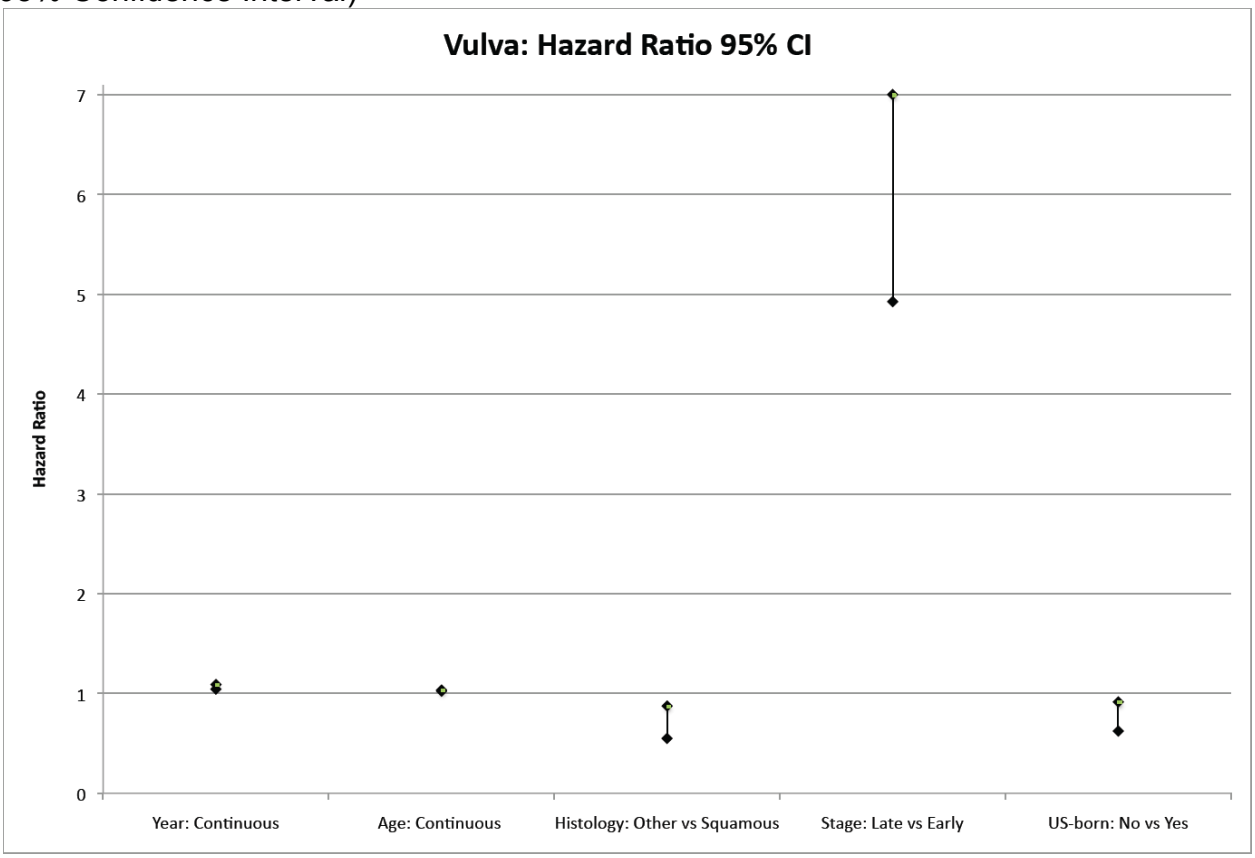
US-born status was associated with risk of vulvar cancer death. Survival for women not US-born was higher than the 5-year survival rate of US-born women; not-US born status was associated with a risk reduction of 24.40% (95% CI: 0.623, 0.917; p=0.0046). Unknown US-born status was adjusted for in the Cox regression model, but hazard ratios were not reported. Vulvar cancer risk of death was not associated with race/ethnicity, SES, or insurance status in the Cox regression model. Missing and unknown insurance status were adjusted for in the Cox regression model, but the hazard ratio was not reported.

Table 3.24 Vulva Survival Regression: Stepwise Cox Regression analysis of vulvar cancer survival, modeled* by healthcare access measures, race/ethnicity, and other known covariates. (95% CI = 95% Confidence Interval)

Vulva 5-year Survival	Coefficient		Wald Chi-Squared		Hazard Ratio		
Cox Regression						95% CI	
Stepwise Selective Covariates	Estimate	SE	Statistic	P-value	Estimate	Lower	Upper
Year: Continuous	0.0643	0.0110	34.1286	<0.0001	1.066	1.044	1.090
Age: Continuous	0.0287	0.0029	95.8896	<0.0001	1.029	1.023	1.035
Histology: Other vs Squamous	-0.3653	0.1184	9.5171	0.0020	0.694	0.550	0.875
Stage: Late vs Early	1.7705	0.0896	390.3505	<0.0001	5.874	4.928	7.002
US-born: No vs Yes	-0.2795	0.0987	8.0229	0.0046	0.756	0.623	0.917

* Model was adjusted for unknown stage, unknown and missing insurance status, and unknown US-born status.

Figure 3.19 Vulva Survival Cox Regression HR: Hazard Ratio 95% CI calculated from Cox regression stepwise regression analysis of vulvar cancer 5-year survival. (95% CI = 95% Confidence Interval)



Other Gynecologic

When all variables were analyzed concurrently, cancer survival for other female genital organs was not associated with healthcare access measures or race/ethnicity. The chosen significant covariates following stepwise selection of other gynecologic cancer survival can be seen in Table 3.25 and Figure 3.20. Risk of death by other gynecologic cancers was associated with year and age at diagnosis. Year at diagnosis increased risk by year, by 5.90% for 5-year other female genital organ cancer survival (95% CI: 1.012, 1.108; p=0.0140). Age at diagnosis increased risk by year, by 2.30% for 5-year survival (95% CI: 1.012, 1.034; p<0.0001). Late stage had over three times the risk of

other female genital organ cancer death compared to early stage for 5-year survival (HR = 3.127 (2.104, 4.648; p<0.0001)). Unknown stage was adjusted for in the Cox regression model, but a hazard ratio was not reported.

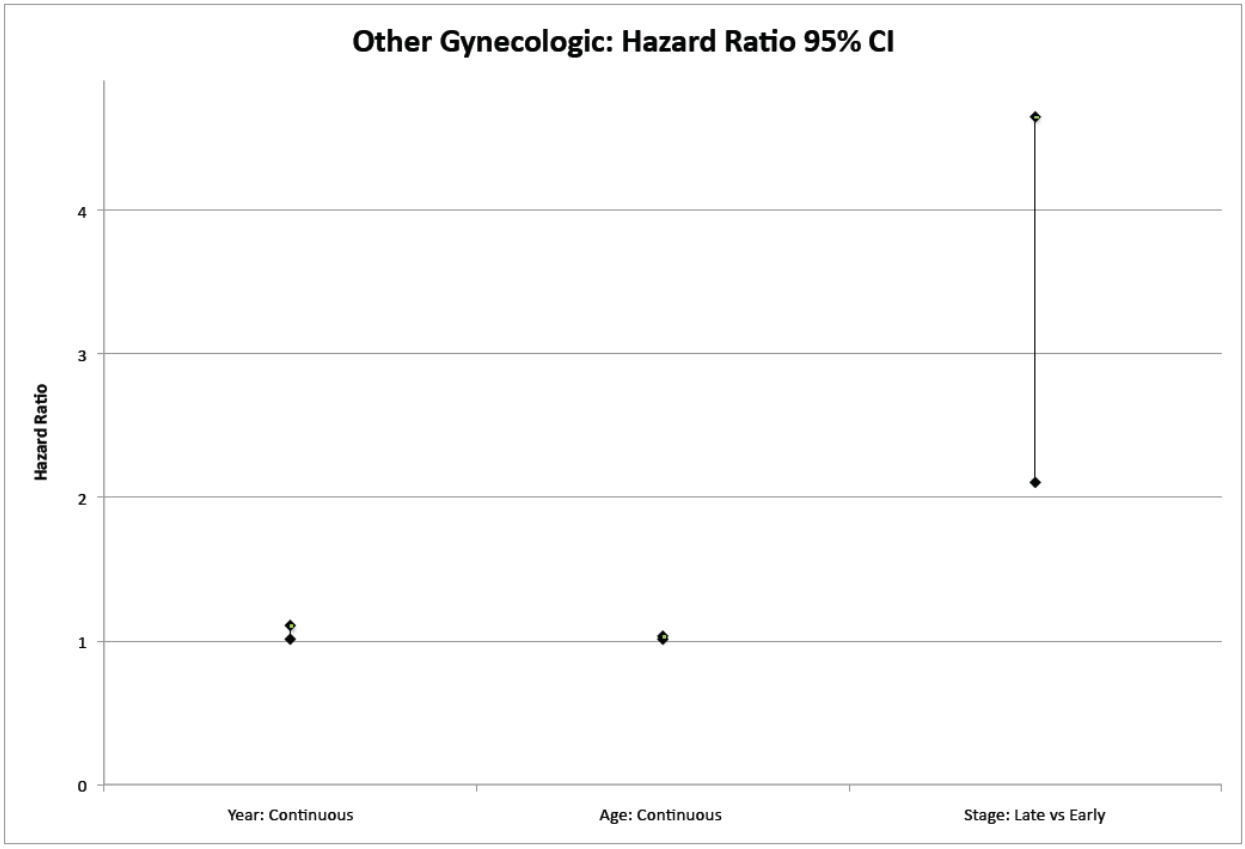
Risk of death by other gynecologic cancers was not associated with race/ethnicity, SES, insurance status or US-born status in the Cox regression model. Missing and unknown insurance status and unknown US-born status were adjusted for in the Cox regression model, but hazard ratios were not reported.

Table 3.25 Other Gynecologic Survival Regression: Stepwise Cox Regression analysis of other gynecologic cancers survival, modeled* by healthcare access measures, race/ethnicity, and other known covariates. (95% CI = 95% Confidence Interval)

Other Gynecologic 5-year Survival	Coefficient		Wald Chi-Squared		Hazard Ratio		
Cox Regression						95% CI	
Stepwise Selected Covariates	Estimate	SE	Statistic	P-value	Estimate	Lower	Upper
Year: Continuous	0.0572	0.0233	6.0382	0.0140	1.059	1.012	1.108
Age: Continuous	0.0227	0.0055	17.3526	<0.0001	1.023	1.012	1.034
Stage: Late vs Early	1.1401	0.2023	31.7753	<0.0001	3.127	2.104	4.648

* Model was adjusted for unknown stage, unknown and missing insurance status, and unknown US-born status.

Figure 3.20 Other Gynecologic Survival Cox Regression HR: Hazard Ratio 95% CI calculated from Cox regression stepwise regression analysis of other gynecologic cancers 5-year survival. (95% CI = 95% Confidence Interval)



CHAPTER 4: Discussion

Summary of Major Findings

This study has investigated the impact of healthcare access on rare gynecologic cancer outcomes, as measured by SES, insurance status, and US-born status. Our findings show that the association between healthcare access and rare gynecologic cancer outcomes varied by cancer site, cancer outcome, race/ethnicity and the particular measure of healthcare access. A summary of the major findings of this study can be seen below:

- Proportional incidence of cervical, vaginal and vulvar cancers was increased for women with low SES, especially in NH Whites.
- Private insurance decreased proportional incidence for all rare gynecologic cancer sites, particularly cervical and ovarian cancers in all racial/ethnic groups, and vulvar cancer in NH Whites.
- Non-US birthplace status increased proportional incidence by race/ethnicity for all rare gynecologic cancer sites:
    - Highest PIRs in Hispanics with cervical cancer.
    - Highest PIRs in NH Blacks with ovarian, vaginal and vulvar cancers.
    - Highest PIRs in NH Whites with other gynecologic cancers.
- Risk of late stage at diagnosis for HPV-related cancers varied by measures of healthcare access:
    - SES was a predictor of late stage for cervical and vulvar cancer.

    - Women with US-born status and non-private insurance were at significantly higher risk of late stage at diagnosis for cervical cancer.
- Race/ethnicity and insurance status were the most important predictors of ovarian cancer late-stage risk.
- Private insurance was associated with lower risk of late stage at diagnosis for other gynecologic cancers.
- Cervical and ovarian cancer survival were associated with race/ethnicity, SES and insurance status.
- Non-US birthplace reduced the risk of death for all rare gynecologic cancers, except other gynecologic cancers.

Proportional Incidence Rate Ratios

Low SES, a potential barrier to healthcare access, was associated with excess rare gynecologic cancer incidence in this study. Of the five rare gynecologic cancer sites studied, socioeconomic status (SES) most profoundly affected the proportional incidence of cervical cancer. The majority of the women diagnosed with invasive cervical cancer in this study were NH White or Hispanic. NH White women predominantly had high SES while the majority of Hispanic women had low SES. While there was an excess of cervical cancer for women of all racial/ethnic groups with low SES, there was a strong opposite effect for women with high SES. Our findings are in agreement with a CCR report describing incidence in California from 1988-2004 by age

and race/ethnicity (35). The most striking observation from this report concerned an observation of the relationship between cervical cancer incidence and SES: "Socioeconomic Status (SES): California women who live in poor (low SES) neighborhoods are nearly three times more likely than women who live in wealthy (high SES) neighborhoods to be diagnosed with cervical cancer. This is probably because women living in poor neighborhoods cannot afford health care including cervical cancer screening."

Cervical cancer incidence seems to be related to all factors related to screening rates: race, ethnicity, geographical region, developing countries without screening programs (11,76). Worldwide, cervical cancer accounts for about half of the infection-related burden of cancer in women (10). Screening of cervical cancer reduces the incidence and mortality of cervical cancer in the population, and 80% of these cancers are seen in economically disadvantaged women (6). It has been shown previously that incidence of cervical cancer is dependent on race and SES, though other risk factors (such as smoking) are potential confounders (19). Independent cervical cancer risk factors include high parity (number of childbirths), high number of lifetime sexual partners, long-term use of oral contraceptives, and cigarette smoking (11). Most cervical pre-cancers develop slowly, and so invasive cancer can possibly be prevented with regular screening (77). Early diagnosis leads to a survival of nearly 100%, but cancer with distant stage is expected to have an approximate 19% 5-year survival, an unfortunate statistic considering that with proper medical care (prevention and early detection), deaths from cervical cancer could be reduced to zero (78). In California, Pap test rates

have significantly increased since 1990, though screening rates differ by race/ethnicity, age and poverty status, and rates are lowest for Hispanics (compared to NH Whites) (35).

Screening, in the context of gynecologic cancer, is considered the examination of women without symptoms to identify cancer in either early stages or pre-malignant form and is meant to reduce the burden of cancer death (79). For a screening test to be recommended, it must be shown to have sufficient sensitivity and specificity to be effective, and be justified in cost on the healthcare system to alleviate public health burdens associated with late-stage cancer diagnoses. To this end, the Pap smear test is a confirmed and recommended screening test for the detection of cervical cancer and guidelines are regularly updated to present the appropriate strategies for screening, including test type, frequency, and age spectrum of women to be tested (14).

No regular screening test is currently implemented for the detection of vaginal or vulvar cancer, though these cancers may be detected during routine colposcopic examinations, performed simultaneously with cervical cancer screening Pap tests (6). Pelvic exams and colposcopies are routinely performed by physicians to identify a spectrum of ailments, including cancer, but as yet there is no evidence to show that these procedures are effective as screening tests for detecting cancer early and reducing the burdens of gynecologic cancers. Special screening conditions are often set for women considered at high-risk, such as women with a medical history of cervical neoplasias or who are immune-compromised (14). It has been suggested that pelvic

exams may lead to early diagnosis and therefore physicians should be sensitive of women with high-risk profiles for HPV-related cancers and encourage examination of ano-genital tissues (including the vagina and vulva) during routine examinations, but the potential benefit of screening women for cancers such as vaginal and vulvar cancers is limited by the discrepancy between age-specific guidelines of gynecologic examination and the prevalence of these diseases in elderly women (3,26,80).

The proportion vaginal and vulvar cancer incidence rates were affected by SES most clearly for NH Whites, which represent the majority of both invasive vaginal and vulvar cancer cases. Highest SES was associated with a lower risk while low SES had a proportionally higher risk for NH Whites. Similar but non-significant trends were seen for the other racial/ethnic groups. The lowest quintile of SES increased risk of vulvar cancer for NH Whites and Hispanics. This is suggestive that while high SES is only a moderate protective characteristic, women with low SES are at considerably higher risk of an invasive vulvar cancer diagnosis. Our study showed an association of SES with vaginal and vulvar cancer incidence, which has been shown in research previously, particularly for educational level and poverty by race (19). High incidence rates have also been seen with HPV-related cancers and low socioeconomic geographic regions, such as the Appalachia, the Southern US and the Midwest (76,81).

HPV-infection related cancers are dependent on chronic exposure to carcinogenic strains of HPV (4). According to worldwide estimates and based on the presence of high-risk HPV DNA in the tumor tissue, 100% of cervical, 70% of vaginal, and 43% of

vulvar cancers are related to HPV infection (10). In the US, it has been collectively determined that the burden of HPV infection is such: the percent attributable fraction (PAF) of cancer due to HPV is 100% in cervix, 40% in vagina, 40% in vulva, and of HPV-positive confirmed cancers, the vaccine-sensitive strains HPV-16/18 are attributable to 70% cervix, 80% vagina, 80% vulva (76). HPV infections are acquired from sexual exposure, and risk is associated with the number of sexual partners. The cervix is the most common site of transmission, though it should be noted that HPV has been detected in multiple genital skin areas. HPV is the most common of sexually transmitted infections (STIs) and has a spectrum of oncogenic potential; according to HPV-blood tests, the prevalence of high-risk HPV infection is as high as 29% among women in the US (4).

It has been hypothesized that increased HPV infection risk is due to sexual behavior of individuals with lower SES. Since sexual behaviors are relevant risk factors for cervical, vulvar and vaginal cancers, it is possible that individuals with lower SES, including lower levels of education and low income, may be more likely to engage in higher risk sexual activity or have delayed access to medical screening services, leading to higher exposure and infection rates. The data to support this is minimal, but it has been shown that there is a relationship between poverty and high STD infection rates, and that poverty may impact STI rates by shaping an individual's sexual network structure (affecting the probability of a monogamous relationship versus the risk of multiple partners) (82–84). Though it should be noted that, while STD infection rates and SES are significantly related, the relationship between race and STD infection rate is even

stronger, African Americans with the highest poverty category having six times the rate for Whites of the same category (82,84).

Distribution of race/ethnicity-specific cervical cancer incidence varied by health insurance status. NH Whites had the largest percentage of private insurance while Hispanics had the highest for non-private insurance. The deficit of proportional cervical cancer incidence for women with private insurance was compared to women with non-private health insurance: private insurance was associated with a significantly lower cervical cancer PIR for all race/ethnicities while non-private insurance had a significantly higher cervical cancer PIR for all race/ethnicities. This is consistent with findings about insurance and screening rates which showed that women using non-private, government health insurance had lower screening rates (85). This, in turn, may decrease the chances of diagnosing a pre-cancerous lesion before it becomes invasive cancer. Even supplemental private insurance improves the likelihood of early stage cancer (CRC) for Medicare patients, compared to solely government-based insurance options (86). This may be attributable to which preventive screening measures are included in their health plan.

Risk of vaginal and vulvar cancer varied by insurance status. Private insurance was associated with a deficit of vaginal cancer incidence for every racial/ethnic group, while non-private insurance was associated with an excess risk, but these proportional changes in risk did not vary considerably by race/ethnicity as demonstrated by the large PIR confidence intervals. Compared to NH White women with vaginal cancer, the

racial/ethnic minorities had much larger proportions of non-private insurance status. Private insurance was protective for vulvar cancer incidence while non-insurance slightly increased risk; however, only for NH Whites did these estimates reach statistical significance. To our knowledge, insurance status has never been looked at for these cancers before.

The associations seen with vaginal and vulvar cancer PIRs and insurance status may be more of a result of the age distribution of cancer incidence than the effects of insurance on vulvar cancer. Because of the potential confounding of age on the association of insurance status on incidence, the method of assessing incident risk in this study population must be considered. In this study, PIRs were calculated using 5-year age-specific frequencies, to compare the distribution of incidence for a particular cancer (ie vulvar) versus all cancers by one level of one measure at a time (ie private insurance status). The resultant rate ratio calculated from the sums of the observed and expected frequencies was controlled for age using age-specific stratification. Using PIR methods, we could distinguish whether the distribution of incidence was unique to the cancer of interest or a characteristic of all cancers. However, it is impossible to extricate the true cause of the distribution cancer incidence from the PIR data calculated. The unique relationship determined by PIR analysis may be due to the age distribution of the specific cancer population.

Later age is a risk factor for both vaginal and vulvar cancers, so it is possible that age is correlated with insurance status and therefore causes an association between

insurance status and incidence. Age has been examined as a risk factor for these cancers previously. The median age at diagnosis for vaginal cancer is 68 years, and for vulvar cancer is 79 years, while the median age for cervical cancer incidence is 47 years (26,76,87). Insurance status is also correlated with usual source of health care (ie: receipt of physician visit within past 12 months) (58,59); thus, although there is no effective screening test for these cancers (6), the risk of catching clinical symptoms of precancerous lesions (before the development of malignancy) may be related to general medical care access.

Birthplace had a strong effect on cervical cancer risk for all racial/ethnic groups, especially Hispanics and NH Asian/PIs who also had the largest proportions of women not born in the US. US-born status had the same effect on risk for all race/ethnicities among women diagnosed with cervical cancer; NH Asian/PIs born in the US had the lowest proportion of cervical cancer while Hispanics born outside the US had the highest proportion of cervical cancer. Hispanics have an unusually high risk, 1.5 times higher than NH Whites, in developing cervical cancer. Especially for cervical cancer, incidence is related to poverty and foreign-born status according to the California Cancer Registry (78). Both poverty and foreign-born status determine healthcare access and therefore an avenue for early stage at diagnosis and improved survival. Poverty and foreign-born status are associated with inadequate access to health care services, including Pap tests which are used to identify cancer and pre-cancerous lesions. It has been shown that Pap test rates in minorities are significantly and inversely associated with acculturation and poverty. Acculturation and poverty affected

access to a Pap test, access to a doctor's office, health insurance status, and fear of a cervical cancer diagnosis (88).

Acculturation and healthcare access are intertwined, both preventing regular healthcare and cancer screening as immigrants attempt to navigate the US health care system (89). Disproportionately high incidence is related to low rates of cancer screening, for those cancer sites that have screening tests for women in the US (colorectal, breast, and cervical cancers). Screening rates are directly related to higher acculturation levels, which have been seen for migrants from Mexico, Central and South America, Asia, Europe, former Soviet Union, and Africa. Acculturation levels are correlated with receipt of provider/physician recommendation, regular healthcare visits, and having health insurance, even in the presence of socio-demographic characteristics (90,91). Acculturation varies by country of origin, race/ethnicity and subgroup, and depends on both the age of the migrant or the generation within the family, and the number of years spent living in the US, which leads to differential screening rates (92–99). Lower acculturation is associated with low screening rates due to multiple barriers to proper healthcare, including language, culture, poverty and insurance (77,100–102).

A cervical cancer community intervention study found a strong association between knowledge and receipt of Pap smears, underscoring the importance of educating vulnerable populations of the diseases for which they are disproportionately affected (103). Linguistic acculturation is an important factor of comprehension for immigrants, though culture-related factors may further compound this issue (104). The

implementation of HPV vaccines may be cancer preventative for Hispanic women, who are disproportionately burdened with cervical cancer, but acceptability of the vaccine is unknown. HPV awareness and knowledge (that it causes cervical cancer and is a prevalent STI) is heterogeneous among Hispanic women in the US due to acculturation and poverty (105). Previous cervical cancer screening behavior in Filipina women is related to optimism and screening frequency, a proxy of access (106).

Different patterns of the effects of US-born status on vaginal and vulvar cancer incidence were seen by race/ethnicity. US-born status was associated with a higher vaginal cancer PIR for NH Whites and Blacks and a non-US-born status with a lower PIR. But not surprisingly, a US-born status was associated with a lower PIR for Hispanics and Asian PIs and a higher PIR for non-US-born status. US-born status (yes or no) was not associated with vulvar cancer incidence. For NH Whites, Blacks and Asian PIs, a US birthplace was associated with lower PIRs, but a US birthplace was associated with a higher PIR for Hispanics. The proportions of women with a non-US birthplace diagnosed with vulvar cancer were much smaller for NH Whites and Blacks than for Hispanics and NH Asian/PIs. US-born status has not been investigated in these rare cancers previously, but US-born status has been shown to be associated with risky behavior and healthcare access.

Risk factors for vaginal and vulvar cancers include sexual history. Sexual behavior such as early onset of sexual activity, frequency of intercourse, and number of partners increases the risk of HPV infection and chronic inflammatory exposures, leading to risk

of HPV-related cancers (4,25). Acculturation is the influence of the host country's cultural beliefs on an immigrant over time, and can affect sexual behavior and risk of STI infection, particularly for immigrant adolescent Hispanics, by changing the age of onset for sexual intercourse, through altered beliefs regarding behaviors that oppose traditional values (ie monogamous relationships and pre-marital sex) (107,108). Birthplace is a strong indicator of cancer risk for Hispanic women, but despite higher screening rates, more acculturated Mexican American women have higher risk of carcinogenic HPV (and other STIs) than less acculturated women due to sexual behaviors (109). Compared to longer-term immigrants and US-born individuals, the healthy immigrant effect on cancer risk was seen for late-life immigrants (110).

The healthy immigrant effect is seen in all aspects of healthcare; differential health outcomes are impacted by nativity and acculturation. When SES and demographics are kept constant, foreign-born Blacks, Hispanics, Asians/Pacific Islanders and Whites have lower mortality risk than US-born Whites (111). Immigrants have longer life expectancy and lower risk of infant mortality compared to US-born counterparts (by race), but increased acculturation increases risk of disability and chronic disease morbidity (112). A puzzling trend, called the "Hispanic Paradox," has shown that immigrant Hispanics have overcome the obstacles of low income, poor education, discrimination and inadequate access to health care, resulting in equal or better health outcomes including chronic disease, compared to US-born non-Hispanic Whites, through culturally-based resiliency including familial resources and religiosity (113). First versus second generation Middle Eastern immigrants had differential risk of death overall and by

specific cancer site compared to NH Whites, though time since immigration was associated with a convergence of odds towards that of the native California population (114). On the other hand, Arab Americans with high acculturation had better medical adherence and lower lifestyle risk (physical activity and BMI) and better blood pressure control compared to those with lower acculturation (115).

The US Preventive Services Task Force (USPSTF) recommends against screening of ovarian cancer in women (116). The USPSTF is charged with making recommendations to clinicians on preventive services based on explicit criteria after the conduction of systematic review of evidence to determine if a preventive service has net benefit after estimating the benefits and harms. There must be a balance between validity, reliability and predictive power against cost, acceptance and need for follow-up. An effective screening method for the detection of early-stage ovarian cancer requires sufficiently high sensitivity and specificity to account for the low prevalence of ovarian cancer (117). There has been extensive research to improve medical practices to catch ovarian cancer early (118), but none have yet met the requirements of an effective screening tool, such as screening with transvaginal ultrasounds plus CA-125 tests (119). Thus, despite a desire to alleviate the burden of this deadly disease, there is no standard or routine test for screening ovarian cancer (120). Despite this, ovarian cancer groups are advocating that tests should be offered to women, especially those at high risk of ovarian cancer, including bimanual rectovaginal pelvic exam, transvaginal sonography and repeated CA-125 tests (121).

The distribution of ovarian cancer PIRs was not affected by SES, except that Hispanics in the highest quintile for SES had a slightly reduced risk of ovarian cancer. The majority of ovarian cancer cases were NH White and had high SES. The distribution of SES was opposite for Hispanics with ovarian cancer, who mostly had low SES. It may be that SES is a stronger predictor of invasive ovarian cancer incidence for Hispanics than NH Whites, or it may be that the very small percentage of Hispanics with ovarian cancer who had the highest level of SES had lower risk because of another factor related to SES which differentiated these women. Although ovarian cancer has no routine screening test, there are definitive risk factors, including race, which affect incidence and to this end, our results confirm previous study data. In the US, there has been an increase in the proportion of minorities diagnosed with ovarian cancer over the last four decades, hypothesized to be due to improved access to care for these women (122). However, minority women are affected disproportionately by ovarian cancer, from presentation and treatment to mortality/survival, which is likely due to unequal access to care caused by low SES and lack of private insurance (123). Other ovarian cancer risk factors that may influence to possible association of SES with ovarian cancer PIR are smoking, diet, and reproductive factors such as oral contraceptive use (8).

Similar to ovarian cancer, the majority of other gynecologic cancer cases were NH White who predominantly had high SES. The number of gynecologic cancer cases by race/ethnicity was low for certain quintiles of SES, particularly SES=V for NH Blacks and SES=I for NH Asian/PIs, which led to very large PIR confidence intervals. SES was not strongly associated with the proportional incidence of invasive other gynecologic

cancers. However, despite the small proportion of NH Asian/PI other gynecologic cancer cases with the lowest quintile of SES, this level was significantly associated with a proportionally higher risk of cancer incidence. An unusual trend was seen by SES for NH Whites and Blacks, but these PIRs did not reach statistical significance. It is possible that low versus high SES is related to another factor that affects risk of an invasive diagnosis of other female genital organ cancers, which is not related to healthcare access but reverses the risk through either biological, environmental, or other pathways. The unusual pattern was not seen for Hispanics, which had higher PIR for the lowest quintile of SES than highest, though these estimates did not reach the level of statistical significance.

Fallopian tube cancers share many characteristics with ovarian cancer, including hormonal and reproductive risk factors such as parity (7,9,29). Risk of fallopian tube cancers is highest in non-Hispanic Whites, same as ovarian cancer (28). Incidence seems to be related to socioeconomic status as well, as fallopian tube cancer rates are increasing for women with higher social class (9). The management of ovarian cancer is also the same for fallopian tube cancer, though they present differently, suggesting a separate path for etiology. It should be noted that the majority of fallopian tube cancer research is focused on getting as much medical knowledge to clinicians as possible to standardize therapy and improve the prognosis of individual patients, but little is focused on the general epidemiology or etiology and progression of the disease.

For all racial/ethnic groups, ovarian cancer PIRs were slightly but statistically significantly lower for private insurance. Non-private insurance status includes Medicare which provides healthcare coverage for women diagnosed after age 65. Since the median age for ovarian cancer diagnosis is 63 (124) it follows that a larger percentage of ovarian cancer patients were covered by Medicare, which provides a potentially lower quality of care (45), but this would affect survival and other outcomes more than incidence, since no effective screening test for ovarian cancer currently exists. Incidental findings from pelvic exams are not sensitive to the majority of ovarian cancers. NH Asian PIs had the largest proportion for private insurance and Hispanics had the highest for non-private insurance but the proportions did not vary greatly by race/ethnicity.

The PIRs of other gynecologic cancers belied higher risk of incidence for non-private than private insurance. For NH Whites, non-private insurance status was a significant negative risk factor, although NH Whites had larger proportions of women with private insurance than non-private. On the other hand, Hispanics had much lower proportions of women with private insurance than non-private, and for Hispanics, private insurance status was a significant protective risk factor. Similar effects of insurance status were seen for the other race/ethnicities, but none reached statistical significance. The reason for higher incidence of other gynecologic cancers for women with non-private insurance is not clear. The incidence of fallopian tube cancer peaks between ages 60-64 years (125). Age may have an effect on incidence and insurance status, but the importance of

healthcare access, insurance, and compliance with standard of care has not yet been investigated.

The proportion of women born in the US diagnosed with ovarian and other gynecologic cancers varied by race/ethnicity. For all race/ethnicities, there was an increased ovarian cancer incidence for women with a birthplace outside of the US. For NH Whites, Blacks and Hispanics, both women born in the US and born outside the US had excess risk of ovarian cancer (unknown US-born status risk was lower), though women born in the US had lower risk than those born outside the US. For Asian/PI women, US-born status was associated with a relative deficit of ovarian cancer incidence and a non-US status was associated with a relative excess. Women born in the US had consistently lower PIRs for other gynecologic cancers than women born outside the US. The lowest other gynecologic cancer PIR was seen for NH Asian/PIs, though they also had the smallest proportion of women with US birthplace than any other race/ethnicity diagnosed with other gynecologic cancers. NH Whites with non-US birthplace status had significantly higher risk of other female genital organ cancers.

Ovarian cancer risk is associated with many reproductive factors, including early age at menarche, late menopause, and duration of breastfeeding. It has been shown with other cancers that reproductive risk factors are associated with birthplace and acculturation. Among women of Mexican descent with breast cancer, country of residence and language acculturation affected their reproductive and hormonal risk profile (age of menarche, age at first birth, breastfeeding) (126). Breast cancer literature of Eastern

Europeans suggest effects of pre- and post-migration exposures and behaviors that modify risk, which do not necessarily lie between those in the native and host countries, suggesting yet unmeasured protective factors (127).

The immigrant paradox refers to the apparently opposing observations that immigrants tend to experience similar or better health outcomes compared to native-born individuals, despite barriers to health care and a higher risk of low socioeconomic status. In terms of reproductive health, evidence of the immigrant paradox is ethnicity-dependent and the strength of association lessens with length of residence in the host country (128). Despite the cancer risk benefits of breastfeeding, highly acculturated Hispanic women are less likely to breastfeed than those who are less acculturated (129). Breast density is another risk factor that is associated with acculturation, due in part to a change in reproductive and dietary behaviors in Chinese Americans (130).

Ovarian cancer risk is also associated with obesity, alcohol, and dietary factors. In fact obesity, physical inactivity, and poor nutrition are major risk factors for cancer in general and yet 60.3% of adults are overweight or obese in California (78).It may be that early life exposures with diet and obesity-related factors influence risk of ovarian cancer risk for immigrants. In evaluating potential prostate cancer risk, migrant Africans versus indigenous men have different dietary and lifestyle factors (increased fruit intake and physical activity but greater intake of meats, oils and alcohol) with clashing risk factors making it difficult to ascertain the overall proportion of risk (131). The extent of dietary change following immigration into the US increased the risk of poor health (self-

reported) for African immigrants due to a decrease in fruit and vegetable consumption and an increase in fast food consumption (132). South Asian immigrants reported an increase in the consumption of convenience foods, sugar-sweetened beverages, red meat and in dining out (133). On the other hand, food insecurity is a large risk factor for Latinos with low acculturation, exacerbating the effects of nutritional deprivation, poverty, and poor health outcomes (134). Risk of obesity for Hispanic women is associated with a western dietary pattern (135). Recent Polish women had the least dietary change and therefore the smallest cancer risk compared to US-born women or more acculturated migrants (136).

Risk of Late Stage at Diagnosis

Racial/Ethnic disparities of stage at diagnosis differed by HPV-related cancer site. NH Blacks had the largest proportion of late stage for cancers of the cervix and vagina. Hispanics had the smallest percentage of late stage vaginal cancer but the largest percentage of late stage vulvar cancer. NH Asian/PIs had the smallest proportion of late stage for cancers of the cervix but not for other cancers. In the California Facts and Figures 2014 report, the percent of early stage at diagnosis was broken down by race/ethnicity for cervix, which showed that Whites, African-Americans and Hispanics had larger percentages of early diagnosis than Asians (78). The percent of cancer cases for cervical cancer by age group (20-44, 45-64, 65+) and race/ethnicity (NH White, AA, Hispanic, A/PI) were shown to vary significantly by stage (1,2,3,4,unknown)

(137). In California from 1988-2007, five-year relative survival of cervical cancer was reported to be significantly higher for localized disease than regional or distant disease (92% versus 56% or 17%), though less than half of women were diagnosed at early stage (34). Racial/ethnic minorities are at a higher risk of late-stage disease for vaginal cancer (26). Older women are at higher risk of advanced stage, and Whites are more affected by age for vulvar cancer risk than other race/ethnicities (21,138). In a SEER-based study of invasive vaginal cancer racial disparity, Black women presented at an earlier age but a more advanced stage and received different treatment than Whites (139).

The effects of race/ethnicity were not kept in the stepwise regression model of late stage analysis for any of the HPV-related rare gynecologic cancers. Race/ethnicity may not be an independent risk factor of stage at diagnosis; rather, the associations with race/ethnicity may be dependent on either biologic factors or healthcare access. For cervical cancer, the association between race/ethnicity and stage of disease is complicated, and encompasses factors such as acculturation, access to care, screening beliefs, and SES (98,140)(98). Previous studies have shown that the increased odds of late-stage cervical cancer among minorities (Blacks, Vietnamese) were eliminated when factors such as Medicaid status and SES were included in the analysis (69). For vaginal and vulvar cancers, screening tests do not exist and stage is dependent on extent of disease determined at diagnosis. Vaginal cancer diagnosis is based on colposcopy while vulvar cancer from visual examination of external genitalia (141–143). Despite the increase in pre-invasive neoplasias for HPV-related disease, the proportion of late stage

for invasive disease has not changed, and the majority of vulvar cancer have been diagnosed as either in-situ or early stage disease (22,80,144). The risk of late stage vulvar cancer is strongly associated with age, but when age is controlled for, advanced stage is associated with smoking status, HPV infection, history of neoplasia, and immuno-compromised status (145).

For most of the rare HPV-related gynecologic cancers, the distribution of stage at diagnosis by quintile of SES was not significant, but trends were seen. A reduction in late stage vulvar and vaginal cancers was seen with increasing SES and risk of late stage was significantly lower for higher levels of SES. To our knowledge, we are the first to report this finding. Although a screening test does not exist for vulvar or vaginal cancer, precursor lesions can often be identified during general physical examinations by health care providers, which may be limited for women with reduced healthcare access due to low SES. In univariate analysis SES was not significantly associated with late stage cervical cancer. However, for multivariate analysis of cervical cancer, adjusted for other factors including race/ethnicity and healthcare access measures, higher levels of SES were associated with an increased risk of late stage at diagnosis. This finding is in contrast with an earlier study; low SES has been previously shown to be associated with late stage cervical cancer (146). It is not clear why our results do not agree with previous data on the association of SES with risk of late stage cervical cancer, but may be related to the differences in study population and methods of assessing SES. Firstly, our study examined cancer in California, not the entire US, and our exclusion criteria removed a proportion of cervical cancer cases, including 62% of

cancer cases which had non-invasive diagnoses, which is related with stage at diagnosis due to cervical cancer screening. Non-invasive tumor behavior may be associated with a women's SES, and removal of these cases would have then biased the relationship between SES and stage at diagnosis. Secondly, we utilized quintiles of SES calculated from Yost scores rather than individual indicators of SES such as poverty and education levels. The definition of our study population and these study characteristics may have led to an unusual association between SES and late-stage cervical cancer.

Private insurance was associated with lower risk of late stage at diagnosis for every rare HPV-related gynecologic cancer, except vaginal cancer. Women with non-private insurance had significantly higher proportions of late stage for cervical and vulvar cancers. In multivariate analysis, women with private insurance were significantly less likely to have cervical cancer late stage at diagnosis. Our data suggests that additional resources are needed for women at risk to improve access to screening services. This is in agreement with a cervical cancer study of Medicaid status, which showed women were at greatest risk of late-stage diagnosis when enrolled in Medicaid or had no insurance prior to diagnosis (69).

Women with US-born status were at higher risk of late stage at diagnosis for all HPV-related rare gynecologic cancers, except vulvar cancer. Although the difference did not reach statistical significance, vulvar cancer cases who reported being born in the US had smaller proportion of late stage compared to non-US born cases. In the multivariate

model for late stage, US-born status remained a risk factor for cervical cancer stage at diagnosis, but not the others. Foreign-born status is expected to be related to reduced healthcare access and screening programs, increasing risk of late stage and lower survival (78). However, similar to breast cancer screening, risk of late stage cervical cancer may be related to low acculturation rather than reduced access to screening programs for migrant women (147).

In the absence of an acculturation explanation, the proportion of unknown birthplace may inadvertently affect risk of late stage due to issues related to missing-not-at-random data. If one group, for instance US-born women, are differentially categorized as unknown (birthplace) then these women are underrepresented in the data and the relationship between US-born status and late-stage risk is affected. In our study, 27% of cervical cancer cases, 21% of vaginal cancer cases, and 26% of vulvar cancer cases had unknown US-born status, and if these cases would be US-born in the true population, then the increased risk of late stage for US-born women does not accurately represent the true risk of the population. The proportion of unknown US-born status was similar for ovarian and other gynecologic cancers (27% and 24%). The potential benefit of immigrants seen in this study may be attributed to the proportion of unknown birthplace and the potential bias this may have played on all cancer outcomes.

Racial/Ethnic disparities of stage at diagnosis were shown for ovarian and other gynecologic cancers. NH Blacks had the largest proportion of late stage of ovarian cancer diagnosis and the lowest proportion of late stage at diagnosis for other

gynecologic cancers. NH Asian/PIs had the smallest proportion of late stage for ovarian cancer). The effects of race/ethnicity were only kept in the stepwise regression model for ovarian cancer late stage analysis. The model for other female genital organ cancers did not include race/ethnicity. For ovarian cancer, NH Blacks had higher odds of late stage compared to NH Whites, but NH Asian/PIs had lower odds of late stage. These factors are in agreement with previous studies, which also found that African-American women had lower odds of early stage at diagnosis (123,148). This suggests that the effects of race/ethnicity on the etiology of ovarian cancer must be more than tumor biology, as histology group (a known significant factor of tumor aggressiveness and therefore predictor of late stage risk) was also retained in the model. Other studies have offered explanation that race/ethnicity affects the quality of care, delaying definitive cancer diagnosis, which can only be confirmed during surgical removal of the tumor followed by histological confirmation (123,149).

The importance of early stage at diagnosis for ovarian cancer cannot be overstated, which is most likely due to biology, not healthcare access. Women with early stage disease benefit from removal of an intact mass, whereas exposure to an opened mass results in advanced stage and poor prognosis (150). Ovarian cancer stage is dependent on extent of disease and the aggressiveness of the tumor, which determines treatment and prognosis (6). Staging and treatment for fallopian tube cancers are very similar to ovarian cancer. This may be due to a differential presentation, as it is suspected that the relative location of the fallopian tubes increases early clinical suspicion and therefore has higher odds of early diagnosis (28,29). It has been shown previously that rapidly

fatal and aggressive disease is associated with age, OC-use and parity (but not with family history, height, BMI, age at first birth, age at menarche or menopause, breastfeeding, tubal ligation, hysterectomy, IUD use, or smoking status) and thus a prognostic association of OC-use and parity suggest that ovulation drives the carcinogenic pathway toward a more aggressive phenotype (7).

Stage at diagnosis is an important factor in the survival of ovarian cancer. Ovarian cancer is observed to be the most deadly disease of all gynecologic cancers, and in 2012, over half the number expected to be diagnosed were expected to die of the disease. The extent, more than the size of ovarian tumors, is the determining factor for stage, which is a strong prognostic factor (5-year survival: Stage 1 = 87%; Stage 4 = 18%) (137). The percent of ovarian cancer cases by age group (20-44, 45-64, 65+) and race/ethnicity (NH White, AA, Hispanic, A/PI) have been shown to vary significantly by stage (1,2,3,4,unknown) (34). In a SEER study of early diagnosis for ovarian cancer, symptoms established as significant predictors of ovarian carcinoma were examined in relation to patient and tumor characteristics, and it was determined that tumor histological type affected the probability of early diagnosis of ovarian cancer, which was determined by the probability of ovarian cancer-related symptoms (distended abdomen, abnormal bleeding, bowel issues) (151).

No association was seen between SES and stage of diagnosis of ovarian cancer or other gynecologic cancers. This is consistent with previous literature (148). This result is

not unexpected, given the late presentation and diagnosis for most ovarian and fallopian tube cancer cases (137,150).

Private insurance status was associated with lower risk of late stage for these ovarian or other gynecologic cancers. Women with non-private insurance had consistently higher proportions of late stage for ovarian and other gynecologic cancers, even in the presence of known risk factors, which is consistent with previous studies. For ovarian cancer, odds of early stage are not only influenced by race, but also insurance status (148). For other cancers where risk of late stage was associated with race, individuals either lacking health insurance or using Medicaid were more likely to be diagnosed with late-stage disease, but racial differences in stage at diagnosis were not explained by insurance status, suggesting that these factors are not mutually exclusive and both influence disparities to access (152).

Women with US-born status were at higher risk of late stage at diagnosis for ovarian and other gynecologic cancers, however this did not remain significant after adjustment for confounders. Migrants may have lower risk profiles due to reproductive, hormonal, and dietary risk factors. But the protective influence of migrant status was not stronger than the effects of age, race, histology and insurance status on the risk of late stage for ovarian and other gynecologic cancers.

5-year Cancer Site-specific Survival

Disparities of survival of all rare gynecologic cancer sites related to HPV-infection differed by race/ethnicity. Kaplan-Meier curves showed that NH Blacks significantly had the lowest survival rate for cervical cancer and also had low survival for vaginal and other gynecologic cancers, though not significantly so. Kaplan-Meier curves also showed that Hispanics significantly had the lowest rates for vulvar cancer survival. NH Asian/PIs had comparable survival rates to NH Whites for cervical cancer Kaplan-Meier curves, but had somewhat higher survival for vaginal cancer, compared to other race/ethnicities. When other prognostic factors were considered, we found that NH Blacks had a greater risk of cervical cancer death while Hispanics had a lower risk compared to NH Whites. No differences in vaginal and vulvar cancer survival were seen by race/ethnicity. California Facts and Figures, 2014 reported the 5-year relative survival from 2002-2011 by cancer site, including cancer of the cervix (78). Cervical cancer 5-year relative survival was dependent on stage: 71% overall; 93% localized, 60% regional, 19% distant. It has been shown previously that vaginal cancer survival is poorer for Blacks (HR = 1.2), even when controlling for demographic and tumor characteristics (139). Cox proportional hazards modeling of 5-year disease-specific survival of primary vaginal cancer determined that stage alone dramatically affected survival, from 84% for stage 1 to 57% for stage 3/4 (153). In the same study, it was also shown that, besides known prognostic factors, treatment modality significantly affected the risk of vaginal cancer mortality. Treatment modality is dependent on quality of care, which disproportionately affects certain minorities.

The lack of a screening test affects the prognosis of vaginal and vulvar cancers. Vaginal and vulvar cancers are diseases of elderly women with poor prognosis, and treatment changes have lessened morbidity and psychosexual impairment without sacrificing efficacy (154,155). Treatment is individualized, and while it is dependent of histology and stage, it depends on retrospective data rather than clinical trial/evidence-based medicine (6,25,141,155–157). Treatment modality is a prognostic factor for vulvar cancer, and though there are racial/ethnic disparities by treatment, race/ethnicity is not an independent risk factor for poor prognosis (22,23). Despite these findings, age remains the strongest prognostic factor for vulvar cancer (24,87). Vaginal cancer survival is associated with stage, histology, age, race, comorbidities, treatment, recurrence, as well as smoking status or history of abnormal Pap test (139,153,158–160).

A trend of survival rates of all HPV-related cancers was seen for SES. For cancers of the cervix and vulva, survival rates increased with increasing quintiles of SES. Vaginal cancer survival was best for the highest quintile of SES, though not significantly so. When analyzed concurrently with known prognostic factors, SES was moderately associated with cervical cancer survival, but not vaginal or vulvar cancer survival. Risk of cervical cancer death was moderately associated with SES as the highest quintile of SES was associated with statistically significant lower risk of cervical cancer death. Both race/ethnicity and SES caused outcome inequities in an HPV-related cancer (rectal

cancer), and both of which are implicated as potential barriers to access to care, either directly or indirectly to cause worse outcomes (161).

Private insurance status was associated with higher survival than non-private insurance for cervical and vulvar cancers, but not for vaginal cancer. Only cervical cancer survival was associated with insurance status when other prognostic factors were considered; women with non-private insurance had significantly higher risk of cervical cancer death than those with private insurance. As seen in other studies, insurance status affects cancer outcomes through access to quality of care. Racial and ethnic minority populations tend not to use National Cancer Institute (NCI) cancer centers, despite providing high-quality care and better outcomes. It was found that insurance statuses and neighborhood-level education was found to be a more powerful predictor of NCI cancer center use than poverty or unemployment (162). It should also be considered that treatment is often driven by insurance (affordable care) and a statistically significant survival advantage found for another rare cancer (bladder cancer) among those who received at least half of the recommended care, suggesting that observance of recommended treatment by physicians dramatically affects outcome (163). In agreement with our study, evidence of health insurance mediation of cancer care and survival (particularly Medicare) was seen for women with colon cancer in California, eliminating the effects of poverty (164).

A significant association with survival was seen for birthplace; lower survival rates for US-born than not US-born birthplace for cancers of the cervix, and vagina, but US-born

status did not have any effect on vulvar cancer survival. When other prognostic factors were considered, birthplace outside of the US was consistently associated with lower cancer death risk for all cancer sites, including vulvar cancer. Cervical cancer incidence was high in Hispanics, which had a large proportion of women with birthplace outside the US. Cancer mortality of Mexican-American immigrants is lower than US-born Mexican Americans or Mexicans due to community norms and behavioral risk factors, but health promoting behavior reduces with the time spent in the US (165).

However, the relationship between cancer outcome and acculturation is not straight-forward; depending on the cancer site and the racial/ethnic group being studied, the magnitude and directionality of the association between cancer outcome and acculturation is affected. For Asian Americans, lower acculturation was not associated with better breast cancer survival, despite the expectation of protective dietary and reproductive risk factors (166). Migrants to the Netherlands benefit from lower incidence rates of breast cancer due to early life exposures (pregnancy, diet) but remain to have higher mortality due to inadequate healthcare access (167).

NH Asian/PIs had the highest survival for ovarian cancer and Hispanics had somewhat higher survival for other gynecologic cancers. NH Blacks had the lowest survival rates for ovarian cancer and also for other gynecologic cancers, though not significantly so. It may be that the relatively small number of NH Blacks with ovarian and other gynecologic cancers made the associations non-significant. When other prognostic factors were also considered, NH Blacks had a significantly greater risk of ovarian

cancer death for 5-year survival compared to NH Whites but NH Asian PIs had an approximately equivalent prognosis compared to NH Whites. Other gynecologic cancer survival was not statistically significantly associated with any race/ethnicity, which is consistent with previous data (30). Similar to our study, Black race was significantly associated with ovarian cancer survival, which may be related to risk of not receiving NCCN guideline-adherent care (45). However in another ovarian cancer study, although recommended treatment modality was shown to differ by race, the racial effects on survival were not significant when other prognostic factors were considered (168). It has been shown previously that survival of other cancers are affected by race/ethnicity, and the reasons point to biology more than access to treatment (169,170).

Prompt medical evaluation may improve ovarian and fallopian tube cancer prognosis due to detection at the earliest possible stage of disease. Stage is well-established as a strong prognostic factor, affecting 5-year survival of ovarian cancer: 48% overall, 92% localized, 76% regional, 30% distant, in a recent CCR report (78). It should also be noted that this study has previously shown that risk of ovarian cancer late stage at diagnosis was also associated with race/ethnicity. Compared to ovarian cancer survival, fallopian tube cancer has better prognosis perhaps because it presents at an earlier stage and fallopian tube cancer survival is dependent on stage (30). We found other gynecologic cancers to have a slightly lower proportion of late stage, compared to ovarian cancer. We also determined that late stage dramatically increased risk of death of both ovarian and other gynecologic cancers, suggesting that the worse prognosis of

ovarian cancer, compared to other gynecologic cancers, was due to the higher proportion of late stage at diagnosis.

Ovarian and fallopian tube cancers have no screening tests, but are associated with specific symptoms that should encourage rapid evaluation and treatment. These symptoms caused by either a large mass, ascites, or both include: palpation of a chronic lower abdominal mass or bloating, trouble breathing, constipation and nausea (150). Women with persistent symptoms are encouraged to see their doctor and preferably a gynecologist. However, depending on the symptoms and the woman's access to healthcare, the initial evaluation could be delayed. When ovarian cancer is highly suspected, a woman should be referred to a gynecologic oncologist, as diagnosis can be confirmed more quickly and treatment can be most up-to-date, however this is not always the case. Many studies have been performed to show the benefit of treatment by a gynecologic oncologist (171). However, the percentage of women utilizing gynecologic oncologists is only 51.4% at initial phase, and decreases to 28.8% by the final phase of care (149). Also, because of its rarity, the correct preoperative diagnosis of fallopian tube cancer is rarely made, but rather is usually an incidental diagnosis following an exploratory laparotomy procedure (9,125).

Hospital/physician factors and treatment modality strongly affect ovarian cancer outcomes. The proportion of women receiving surgery has increased, and so has the relative survival of ovarian cancer; stage remains the biggest prognostic factor (122). Gynecologic oncologist use, both initially and for follow-up care, continues to be low

among ovarian cancer patients despite the benefits, but use is not different across racial/ethnic groups (149). However, hospital/physician volume, another indicator of prognosis, varies by race, ethnicity, insurance status and socioeconomic status and affects treatment modality by race/ethnicity (172,173). It has also been shown that treatment provided by specialized high-volume physicians at specialized high-volume centers has been shown to improve survival for ovarian cancer (3).

Ovarian and fallopian tube cancers are both cancers that are primarily driven by hormonal risk factors and outcomes are dependent on biological factors, where stage is the most important prognostic factor (122). In a small study of women with ovarian cancer, Black women had a significantly higher HR, but race was also found to be associated with risk factors such as marital status and tubal ligation, and with risk to access to resources such nSES (neighborhood SES), suggesting broader social causes for racial disparities (174). Heterogeneity in ovarian cancer survival may be better explained by BRCA variants than race, which had better prognosis than non-hereditary disease, though in a pool of Caucasians, Hispanics, and Jews, non-Jewish Caucasians had the largest proportion of mutation carriers (175). It is well understood that ovarian cancer prognosis is associated with age at diagnosis, stage, grade and histological type of tumor (122). Age, hormonal and reproductive risk factors are also associated with tumor aggressiveness, suggesting that developmental pathways may play a role in prevention of aggressive tumors and alleviate the burden of high mortality (7). No standard or routine screening test exists for ovarian cancer, but biomarkers such as CA-

125 are used for prediction of treatment responsiveness and prognosis (6). CA-125 is also a prognostic factor for fallopian tube cancers (27).

A trend of survival rates of ovarian and other gynecologic cancers was seen for SES. The effects of SES were quite strong on ovarian cancer survival, which was associated with a linear trend of risk reduction leading to the lowest risk of ovarian cancer death for the highest level of SES. Risk of ovarian cancer death was lowest for the highest quintile of SES. Our results are in agreement with other studies measuring the impact of SES on ovarian cancer survival. Education, a measure of SES, was negatively associated with ovarian cancer mortality (176). However, the effects of SES became non-significant when smoking status, stage, and other prognostic factors were included in analysis. In Ontario, access to surgery was associated with measures of individual SES, which is a treatment modality strongly associated with survival (177). Conversely, a trend of survival rates was seen for other gynecologic cancers, survival decreasing as SES increased, to the lowest survival for the highest SES. Low SES has never been shown previously in the literature to be associated with better outcomes. SES was not retained in the other gynecologic cancer survival model and so it is expected that the effects of SES was an artifact of other prognostic factors.

Survival was associated insurance status with for ovarian cancer but not for other gynecologic cancers. The Kaplan-Meier curve for private insurance was higher for ovarian cancer survival than non-private insurance. Insurance status was retained in the model of ovarian cancer survival and showed that not-private insurance was statistically

significantly associated with a slightly lower risk of ovarian cancer death than private insurance. The Cox regression estimate for insurance is in contrast with the Kaplan-Meier curve survival rates. It is also in contrast with previous studies, which have shown that ovarian cancer quality of care (NCCN guideline concordant treatment) and survival were both associated with insurance status and income (45). Again, US veterans have been shown to be a vulnerable population with high cancer rates; treatment modality for veterans with colon cancer differ by treatment site (VA and non-VA facilities), which may be affecting quality of cancer care (178). It is possible that our study population does not accurately reflect insurance status distribution of the ovarian cancer population of California due to our exclusion criteria. Tumors that were either not first primary or non-invasive were excluded (20% and 16% of ovarian cancer cases), which may cause the biased removal of women with non-private insurance and therefore influence the relationship between insurance status and ovarian cancer survival. Regression analysis of survival was also limited to a truncated population due to the time-dependency of insurance status data completion, which partially explains the 31% of the ovarian cancer study population with unknown insurance status. Additionally, the regression estimate for non-private insurance status may be affected by the definition of non-private insurance. Inadequate healthcare access may not be accurately defined by non-private insurance status, as this includes government-issued insurance, military insurance, or no health insurance coverage. Detailed analyses of these types of non-private health insurance may illuminate the source for the relationship between ovarian cancer survival and non-private insurance status.

A significant association with ovarian cancer survival was seen for birthplace; lower survival rates for US-born than not US-born birthplace for ovarian cancer. After Cox regression analysis, US birthplace remained a significant prognostic factor for ovarian cancer. US-born status did not have any effect on other gynecologic cancer survival. Cancer outcomes may be better for migrants due to societal benefits and lower risk profiles. For gastric cancer, another aggressive and advanced disease, individuals with foreign-born status had a low hazard ratio, and living in impoverished and high immigration communities had better prognosis than those who did not (179). The role of tumor biology may be stronger than access to care.

Strengths, Limitations and Incidence by Race/Ethnicity

Strengths

This research has provided new insights into rare gynecologic cancers. We have identified new prognostic factors and new theories of etiology, progression, and predicted outcomes. Our data also confirm the existence of disparities that not only affect rare gynecologic cancer outcomes, but may also point to the way to moderating these differences through modification of policy. This study has provided insights into the importance of healthcare access and race/ethnicity and implemented innovative methods (PIR analysis) for comparing measures of healthcare access that are not recorded in the general population. According to the CDC, “population-based cancer registries are important surveillance tools to measure the impact on cancer rates of

public health interventions such as vaccination and screening" (180). The reduction of cervical cancer burden depends on effective screening and vaccination programs, but also improved surveillance (181).

A major strength of this study is the relatively large number of cases of rare cancers. The current inadequacy of most rare cancer research is the small number of cases and therefore the limited conclusions that can be drawn because of the potential lack of ability to find statistically significant differences. Due to the long period of time used (1988-2009) and the large and diverse population of California, we were able to examine many aspects of rare gynecologic cancers simultaneously and with minimal bias. The tremendous diversity of California allowed for the examination of certain aspects that couldn't be seen in smaller studies. Since healthcare access in general is highly correlated with race/ethnicity (44), many studies concerning rare gynecologic cancers are not equipped to make observations about healthcare access due to a lack of racial/ethnic representation. As seen previously, invasive cancer disparity by SES has also been shown to vary by race/ethnicity, thanks to the diverse population of California (70). Numerous studies from California have also successfully investigated cancer trends in immigrant sub-populations, due to the large proportion of foreign-born Californians (41,67,114,147,182). Due to the retrospective nature of this study, we were able to examine multiple cancer outcomes across a woman's lifetime, from invasive cancer incidence to survival. Much of the work performed in this study could not be performed with another dataset.

Despite limitations, the current study contributes to our knowledge about rare invasive gynecologic cancers. There is a need to increase the use of evidence-based medicine and reduce the dependency on empirical medicine for gynecologic cancers. It also provides additional baseline data for rare gynecologic cancer epidemiology to the currently small amount of literature concerning the potential efficacy of the HPV vaccine to alleviate cancer burdens. Since little research has been done for extremely rare cancers, such as fallopian tube cancer, any data covering the general epidemiology of the disease can be considered important insight. Examining specific cancer sites with low incidence can be instrumental in improving rare cancer outcomes in the population. Studies of rare forms of breast cancer have provided important insights into how rare forms usually present, what treatments improve survival, as well as potential outcome disparities by race (183–185).

Particularly because of the implementation of HPV vaccinations, there is a big question of how much the vaccine will help to alleviate the burden of HPV-related cancers. In 2009, 21,342 women in the US were diagnosed with an HPV-associated cancer, which represent 3.3% of all cancers reported nationally, and of those, 53.4% was cervix (11,388 cases), 15.2% was vulva (3,242 cases), and 3.4% was vagina (734 cases) (17). In the US, it is expected that HPV is responsible for 26,000 new cancer cases every year, 18,000 for women and 8,000 for men, and according to recent SEER data, the annual incidence of HPV related cancers is 10.8 (per 100,000 population); 8.1 (per 100,000) for males and 13.2 (per 100,000) for females (180). While HPV types 16 and 18 are responsible for 70% of cervical cancers, approximately 60% of vaginal cancer

and 40% of vulvar cancer are expected to be prevented by prophylactic vaccines against HPV 16/18 (180,186). In terms of national HPV vaccination coverage, in 2010 less than half of girls aged 13-17 had received at least 1 of the 3 doses of the vaccine, and coverage levels varied widely by state, age, race/ethnicity, and insurance status (17).

Limitations

The current study is retrospective in nature and shares limitations of other population-based studies. A study of this kind was susceptible to many sources of bias and misclassification that could lead to misinterpretation (187), but these were attenuated by considerations in the study design. The CDC has set many standards for completeness, timeliness and quality of data for state-based cancer registries and the North American Association of Central Cancer Registries (NAACCR) has provided much needed guidance, training, technical assistance and quality audits to states to enhance registries. Due to California legislation, CDC, NAACCR, and SEER standards are met by the CCR, ensuring high-quality registry data (78).

Many pitfalls of cancer registry data exist, but most have been addressed by this study. The exclusion criteria for the definition of the study population removed the threat of potential inaccuracies. Our use of first primary cancer data eliminates the inaccurate estimates due to counts of cases, not people with cancer, or duplicated reports due to multiple reporting locations. The potential limitation of or exclusion criteria such as excluding not-first cancers, not-invasive tumors, or cases abstracted from autopsy and

death certificate was analyzed prior to analysis and found to have minimal effects. It was determined that accurate cancer outcome estimates were more crucial than inclusion of these potentially confounding data. Since the dataset used was prepared by the CCR and de-identified through 2009, this minimizes the issues of reporting delays from registry administrators for quality assurance. To some extent, the use of PIR methods reduces inaccuracies of rates due to numerators, denominators or methods of estimation, since the same data pool was used for numerators and denominators of rate ratios. In our analysis, we discovered an issue with time-dependent analysis and removed all data prior to 1996 in specific instances, which removed the issue of "the 1994 Gap" (187), when the rapid difference in standards for data collection and processing pre- and post-1995 caused a gap in registry data collected from 1994.

However, other issues with cancer registry data persisted, including the conflicting priorities of research and privacy, the potential misclassification of race/ethnicity, and lack of *in situ* published data. A balance between the importance of patient privacy and the needs of research has not yet been found. The difference between census data collection of race by self-report cannot be reconciled with the drastically different protocol of medical record information collection. It is unfortunate that *in situ* data is not recorded by the CCR (including cervix), because it could potentially provide information about disease progression, early risk factors, and other retrospective data susceptible to recall bias or medical record access. However the benefits of this data must be weighed against the burden of collecting, processing, running quality assurance, and analysis.

One major limitation of cancer registry data that has been addressed is the role of SES on cancer outcomes. Neighborhood SES was analyzed as individual-level measures of SES were not collected. However this has been done previously with high accuracy (19). Krieger has described extensively the importance of SES in epidemiologic studies, and how they can be best recorded and analyzed within the context of cancer registry data. SES has been shown by Krieger to be a vital factor for assessing cancer in the population, particularly to be measured by cancer registries (188). Krieger and colleagues have been investigating SES measures for decades, and have identified that census-level SES is more strongly associated with outcomes related to social class than individual-level SES, and is strongly correlated with economic level (189). The protocol of utilizing SES assigned at the neighborhood level when individual-level SES is not available has been well-established in epidemiologic research (190). Krieger continues to show her fellow epidemiologists that SES cannot be ignored (191). Disparities of SES by race/ethnicity for cancer incidence have also been strongly characterized using area-based socioeconomic measures, and without SES, estimates by race/ethnicity are inflated (192,193). Almost 15 years ago, a method was developed to create an SES index using census data, that ranked composite SES scores into quintiles (73). This area-based SES measure (otherwise known as the Yost scale) has since been used by many CCR studies to examine cancer outcomes with high accuracy (69,70,148,169,194–197).

Another issue with epidemiologic data that must be considered here is missingness. In general, missing data is defined as: not all variables are recorded for all individuals or at

all time points. In this study, data was not complete for every cancer case for every studied characteristic. The proportion of unknown stage for each rare gynecologic cancer site was relatively small. The missing insurance status proportion was also small, and the proportion of unknown status was dependent on year at diagnosis, specifically the issue of “the 1994 Gap” which was resolved when data prior to 1996 was removed from time-dependent analysis. There was a large proportion of unknown US-born status (missing birthplace) that may have influenced our estimates. The data in the CCR was abstracted from medical records and there may be many reasons why data is absent from a cancer patient’s medical record. Missing data is a complicated topic when dealing with rare cancers, where the number of cases is already very low. To remove all cases with incomplete data hurts the power of the study to detect any differences in outcomes for the remaining cases and it is also possible that the removal of incomplete data will lead to bias. How to handle missing data in population-based cancer registries and therefore improving the accuracy of cancer registry databases has long been desired, and so the methods and approaches have been investigated (198,199). Multiple imputation with polytomous regression has worked well using cancer registry data to impute missing date, but if missingness for US-born status is analyzed in future studies of rare gynecologic cancers, the mechanism of missingness must be addressed (200).

The characteristics of these cancers may be misinterpreted, and cancer rates underestimated, due to several factors. Our study population only included women diagnosed with primary invasive cancers, so secondary cancers are not represented,

despite the fact that the biggest risk factor for vaginal and vulvar cancers is previous malignant diagnoses (ie: cervical, breast). Cancer cases that were identified by death certificate or autopsy were excluded. *In situ* cancers (CIS, VIS, and VAIS) and neoplasias (CIN, VIN and VAIN) are not recorded by the CCR, and so could not be included in our analysis. We also limited our analyses to epithelial cancers with microscopic confirmation, so that other cancer types and unconfirmed diagnosed cases could not add to the pool of data. It is possible that some of the variables of interest in this study, notably those related to quality of care, would affect the probability of a woman receiving a definitive diagnosis. Other limitations include our use of surrogates of healthcare access, because more direct measures of healthcare access were not collected by the California Cancer Registry. Insurance status is also not 100% accurate in the cancer registry (33). The biggest lingering concern of our measures of healthcare access is the possibility that these do not reflect the women's lifetime risk, but rather her status at the time of diagnosis. However, misclassification of healthcare access in this way would be expected to bias the data toward the null. Therefore, this study's findings are not explained by potential misclassification of healthcare access.

Other limitations specific to our data should be acknowledged. Treatment modality is a strong prognostic factor for all of the cancers studied here, but treatment measures were not reliably recorded for this population because of the multiple treatment locations for surgery, chemotherapy, and radiation therapy. Therefore treatment was not included in the analyses of rare gynecologic cancer survival. We had no information about the potential presence of HPV DNA in tumor tissue, and therefore cannot confirm the

attributable fraction within this population. Even so, when considering the impact of infection-associated cancer research, we must consider the difference between what is theoretically preventable (from PAF calculations) and what is preventable in practice (10). Other risk factors based on individual-level data such as smoking, parity, or use of Pap test screening are not recorded in cancer registries.

Due to the inherent definition of rare cancers, our data was limited by the number of cases for each cancer site, particularly when stratified by race/ethnicity or controlled for other factors related to outcome. Due to the instability of estimates in models based on small numbers, we were limited in our analysis, particularly with trends in incidence rates.

Incidence by Race/Ethnicity

Incidence rates of each rare gynecologic cancer by race/ethnicity were calculated with the data of this study, but none were reported due to protocols of patient security and limitations of statistical testing. The number of cases for each rare gynecologic cancer for the time period covered was quite small, and according to CCR protocol, rates should not be reported if the minimum case number requirements for the health and safety code are not met (201). When stratified by race/ethnicity, the incidence rates of each rare gynecologic cancer threatened to expose the identity of individual cases and therefore could not be reported. Additionally, the rates were then based on such small numbers that they were very unstable, and statistically testing differences between rates would be uninformative. Therefore, no further analysis was performed in this study for

incidence rates. However, we noted that incidence rates of the same cancer sites have been reported by SEER and CCR for national and California populations, respectively.

The CCR recently reported an expected number of new cases and deaths for California in 2014 by cancer site, including cervix, ovary, vagina, and vulva. The estimated incident case number expected in 2014 for each rare gynecologic cancer site is: 1,405 cervix; 2,310 ovary; 145 vagina, 405 vulva. The expected number of associated deaths are: 430 cervix; 1,530 ovary; 50 vagina; 75 vulva. In an attempt to explain these numbers, the CCR referenced key aspects of the diverse population of California. California is not only known for its racial/ethnic diversity, but also the huge number of immigrants. In particular, the diversity is further enhanced due to the fact that the Asian/ Pacific Islander and Hispanic populations are composed of numerous nationalities, many of whom are recent immigrants and research indicates that cancer rates in populations immigrating to the US tend to increase over time. Not surprisingly, Hispanic women are also more likely to develop and die from cervical cancer. The expectation is that the race/ethnicity differences in cancer risk and mortality are due to a complex combination of dietary, lifestyle, environmental, occupational, and genetic factors and healthcare access, such as poverty and insurance status (78).

SEER provides a national view of cancer statistics, that while is not as detailed for certain demographic factors nor as diverse for race/ethnicity as the CCR, can provide more stability of the estimates of cancer incidence and mortality due to the larger numbers afforded to US-wide population data. The SEER website includes a data

analyzing tool called Fast Stats that can give customized views of cancer statistics, including age-adjusted incidence, by cancer site of race (White, Black, All Races) and by race of multiple cancer sites (36). This online resource allows for the comparison of cancer sites by race over time from 1975-2011. Of the rare gynecologic cancers studies here, ovarian cancer had the highest incidence, followed by cervical cancer; both saw a trend in rate reduction which differed by race. Vaginal and vulvar cancer rates were considerably lower and no temporal trends could be evaluated with accuracy. SEER data has also been published in scientific articles, and the incidence of some of these rare gynecologic cancers has been investigated with the use of SEER previously (18,181).

Special precaution must be taken when analyzing the incidence data of rare cancers. Small numbers can lead to erroneous predictions, so incidence reporting methods in Europe require minimum number of cases (per year and per 5-year period) for adjusted models of prognostic prediction to be recorded (202). Also, there is no international definition for a rare cancer, which makes comparisons between Europe and the USA difficult (203). Nonetheless, rare cancers account for more than 20% of all cancer diagnoses worldwide, and tend to have worse outcomes than common cancers. So there is a clear need to report what can be determined with accuracy. The International Rare Cancer Initiative was created in 2011 to address the issues of limited resources and research and there are currently 9 rare cancer projects being headed by this group (204). The project Surveillance of Rare Cancers in Europe (RARECARE) provides estimates of the incidence, prevalence and survival of rare cancers in Europe

(definition: incidence <6/100,000/year). They have estimated that the estimated annual incidence rate of all rare cancers accounts for 22% of all cancer diagnoses and 5-year relative survival was on average worse for rare cancers than common cancers (205).

CHAPTER 5: Conclusions

We found that the invasive incidence, stage at diagnosis, and survival varied by race/ethnicity and measures of healthcare access in rare gynecologic cancers. The results of this study may influence policy makers and inform clinicians how these cancers should be approached. In addition, this study may impact the relation of public health policies and how women diagnosed with these diseases are treated, how their disease is managed, and how prognosis is determined. However, because this is a registry-based study, we recommend further detailed investigation of the significant associations identified in this study. This is the first study to show the influence of healthcare access for certain rare gynecologic cancers, and we report the importance of reducing disparities for at-risk minorities to improve cancer outcomes. There is a further need for research of this kind. There is a need to confirm our findings, and if possible, expand to a larger population and look more in depth at certain factors. Since the survival of cervical, vaginal and vulvar cancers is relatively high, a potential direction would be to follow-up with cancer patients to learn more about their background, their individual access to healthcare via questionnaire.

The implications of this study are far-reaching, from the importance of modifiable risk factors for both HPV-related cancers and ovarian/fallopian tube cancers to the identification of public health areas requiring increased awareness and potential intervention to reduce disparities. The HPV vaccine holds new promise for eliminating the burden of cervical cancer and other HPV-related cancers, but the high cost of the

vaccine will continue to be a barrier for economically-developing countries (11). There is also the importance of time in reporting cancer data, as cancers take decades to develop and therefore intervention programs including HPV vaccination will take decades to take effect (10). In an attempt to stem the cancer-related issues related to healthcare access for women, and answer the question “What can be done?” a program has been organized in California called Every Woman Counts (EWC). This program provides cancer screening, such as mammograms and Pap tests, to California’s underserved women. They aim to save lives by preventing and reducing the devastating effects of cancer through education, early detection and more (78,206,207). The aim of this study was to improve the understanding of rare gynecologic cancers to influence policy makers and inform clinicians how these cancers should be approached and potentially reduce the disparities seen due to healthcare access. It is our goal to provide data to help reduce the inequalities of access to healthcare so that it can be ensured that all women have access to evidence-based care.

References

1. National Cancer Institute. Synergizing Epidemiologic Research on Rare Cancers. *Workshop*. 2013;:1–2.
2. Greenlee RT, Goodman MT, Lynch CF, et al. The occurrence of rare cancers in U.S. adults, 1995-2004. *Public Health Rep.* 2010;125(1):28–43.
3. Reade C, Elit L. Trends in gynecologic cancer care in North America. *Obstet. Gynecol. Clin. North Am.* 2012;39(2):107–29.
4. Erickson BK, Alvarez RD, Huh WK. Human papillomavirus: what every provider should know. *Am. J. Obstet. Gynecol.* 2012;:1–7.
5. Kehoe S. Treatments for gynaecological cancers. *Best Pract. Res. Clin. Obstet. Gynaecol.* 2006;20(6):985–1000.
6. Bender H, Kavanagh J, Kitchener H, et al. Staging classifications and clinical practice guidelines of gynaecologic cancers. *FIGO Report, Elsevier*. 2000;
7. Poole EM, Merritt M a, Jordan SJ, et al. Hormonal and reproductive risk factors for epithelial ovarian cancer by tumor aggressiveness. *Cancer Epidemiol. Biomarkers Prev.* 2013;
8. Faber M. Ph.D. Thesis: Modifiable risk factors for ovarian cancer. University of Copenhagen, Danish Cancer Society Research Center; 2013.
9. Riska A, Leminen A. Updating on primary fallopian tube carcinoma. *Acta Obstet. Gynecol. Scand.* 2007;86(12):1419–26.
10. De Martel C, Ferlay J, Franceschi S, et al. Global burden of cancers attributable to infections in 2008: a review and synthetic analysis. *Lancet Oncol.* 2012;13(6):607–15.
11. American Cancer Society. American Cancer Society. Global Cancer Facts and Figures Second Edition. Atlanta: 2011.
12. Smith JS, Backes DM, Hoots BE, et al. Human papillomavirus type-distribution in vulvar and vaginal cancers and their associated precursors. *Obstet. Gynecol.* 2009;113(4):917–24.
13. Schiffman M, Wentzensen N. Human papillomavirus infection and the multistage carcinogenesis of cervical cancer. *Cancer Epidemiol. Biomarkers Prev.* 2013;22(4):553–60.
14. Saslow D, Solomon D, Lawson HW, et al. American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology screening guidelines for the prevention and early detection of cervical cancer. *Am. J. Clin. Pathol.* 2012;137(4):516–42.
15. Nygård M, Hansen BT, Dillner J, et al. Targeting human papillomavirus to reduce the burden of cervical, vulvar and vaginal cancer and pre-invasive neoplasia: establishing the baseline for surveillance. *PLoS One*. 2014;9(2):e88323.
16. SEER. SEER Cancer Statistics Review 1975-2009 National Cancer Institute, 2012 Estimates of new cases and deaths. 2012;:2012.
17. Jemal A, Simard EP, Dorell C, et al. Annual Report to the Nation on the Status of Cancer, 1975-2009, Featuring the Burden and Trends in Human Papillomavirus (HPV)-Associated Cancers and HPV Vaccination Coverage Levels. *J. Natl. Cancer Inst.* 2013;105(3):175–201.

18. Watson M, Saraiya M, Wu X. Update of HPV-associated female genital cancers in the United States, 1999-2004. *J. Womens. Health (Larchmt).* 2009;18(11):1731–8.
19. Benard VB, Johnson CJ, Thompson TD, et al. Examining the association between socioeconomic status and potential human papillomavirus-associated cancers. *Cancer*. 2008;113(10 Suppl):2910–8.
20. Bodelon C, Madeleine M. Is the incidence of invasive vulvar cancer increasing in the United States? *Cancer Causes Control*. 2009;20(9):1779–1782.
21. Saraiya M, Watson M, Wu X, et al. Incidence of in situ and invasive vulvar cancer in the US, 1998-2003. *Cancer*. 2008;113(10 Suppl):2865–72.
22. Ramanah R, Lesieur B, Ballester M, et al. Trends in of late-stage squamous cell vulvar carcinomas: analysis of the surveillance, epidemiology, and end results (SEER) database. *Int. J. Gynecol. Cancer*. 2012;22(5):854–9.
23. Tergas AI, Tseng JH, Bristow RE. Impact of race and ethnicity on treatment and survival of women with vulvar cancer in the United States. *Gynecol. Oncol.* 2013;129(1):154–8.
24. Kumar S, Shah JP, Bryant CS, et al. A comparison of younger vs older women with vulvar cancer in the United States. *Am. J. Obstet. Gynecol.* 2009;200(5):e52–5.
25. Di Donato V, Bellati F, Fischetti M, et al. Vaginal cancer. *Crit. Rev. Oncol. Hematol.* 2012;81(3):286–95.
26. Wu X, Matanoski G, Chen VW, et al. Descriptive epidemiology of vaginal cancer incidence and survival by race, ethnicity, and age in the United States. *Cancer*. 2008;113(10 Suppl):2873–82.
27. Shamshirsaz AA, Buekers T, Degeest K, et al. A single-institution evaluation of factors important in fallopian tube carcinoma recurrence and survival. *Int. J. Gynecol. Cancer*. 2011;21(7):1232–40.
28. Stewart SL, Wike JM, Foster SL, et al. The incidence of primary fallopian tube cancer in the United States. *Gynecol. Oncol.* 2007;107(3):392–7.
29. Ajithkumar T V, Minimole AL, John MM, et al. Primary fallopian tube carcinoma. *Obstet. Gynecol. Surv.* 2005;60(4):247–52.
30. Wethington SL, Herzog TJ, Seshan VE, et al. Improved survival for fallopian tube cancer: a comparison of clinical characteristics and outcome for primary fallopian tube and ovarian cancer. *Cancer*. 2008;113(12):3298–306.
31. Morris C, Angel E, Martinsen R, et al. Trends in Cancer Incidence and Mortality in California, 1988–2010. Sacramento, CA: 2014.
32. Cook SN, Giddings BM, Parikh-Patel A, Kizer KW, Kwong SL, Bates JH SK. Cancer in California, 1988-2009; An Overview of California's Recent Cancer Incidence and Mortality Statistics. Sacramento, CA: 2013.
33. Morris CR, Epstein J, Nassere K, Hofer BM, Rico J, Bates JH SK. Trends in Cancer Incidence, Mortality, Risk Factors, Health Behaviors in California. Sacramento, CA: 2010.
34. Hofer BM, Kwong SL, Allen M, Bates JH SK. Cancer in California, 1988-2007. Sacramento, CA: 2010.
35. Hofer BM, Bates JH, Mccusker ME, et al. Cervical Cancer in California, 2008. Sacramento, CA: 2008.

36. Surveillance Research Program: National Cancer Institute. Fast Stats: An interactive tool for access to SEER cancer statistics. (http://seer.cancer.gov/faststats). (Accessed June 12, 2014)
37. Young HA, Maillard JD, Levine PH, et al. Investigating the risk of cancer in 1990-1991 US Gulf War veterans with the use of state cancer registry data. *Ann. Epidemiol.* 2010;20(4):265–272.e1.
38. Pellegrini M, Bernardi D, Di Michele S, et al. Analysis of proportional incidence and review of interval cancer cases observed within the mammography screening programme in Trento province, Italy. *Radiol. Med.* 2011;116(8):1217–25.
39. Aschebrook-Kilfoy B, Ward MH, Della Valle CT, et al. Occupation and thyroid cancer. *Occup. Environ. Med.* 2014;71(5):366–80.
40. S. Navada, P. Lai AGS and GPK. Temporal trends in small cell lung cancer: Analysis of the national Surveillance, Epidemiology, and End-Results (SEER) database. In: *ASCO Meeting Abstracts*. 2006
41. Nasseri K. Thyroid cancer in the Middle Eastern population of California. *Cancer Causes Control*. 2008;19(10):1183–91.
42. Iodice S, Gandini S, Löhr M, et al. Venous thromboembolic events and organ-specific occult cancers: a review and meta-analysis. *J. Thromb. Haemost.* 2008;6(5):781–8.
43. Hernandez M, Fleming L, MacKinnon J, et al. Cancer in Florida Hispanics 1989-2006. Miami, Florida: 2010.
44. Kelley E, Moy E, Stryer D, et al. The National Healthcare Quality and Disparities Reports CONCEPTS AND DEFINITIONS IN QUALITY. 2005;43(3):3–8.
45. Bristow RE, Powell MA, Al-Hammadi N, et al. Disparities in ovarian cancer care quality and survival according to race and socioeconomic status. *J. Natl. Cancer Inst.* 2013;105(11):823–32.
46. Hutchinson RN, Shin S. Systematic review of health disparities for cardiovascular diseases and associated factors among American Indian and Alaska Native populations. *PLoS One*. 2014;9(1):e80973.
47. The World Health Organiziation. The WHO Agenda. (http://www.who.int/about/agenda/en/). (Accessed May 3, 2014)
48. Kulasingam S, Havrilesky L, Ghebre R, et al. Screening for cervical cancer: a decision analysis for the US Preventive Services Task Force. 2011;(11).
49. Committee on Understanding and Eliminating Racial and Ethnic Disparities in Health Care, Board on Health Sciences Policy I of M. Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care (with CD). National Academies Press; 2009.
50. Pearson WS, Ahluwalia IB, Ford ES, et al. Language preference as a predictor of access to and use of healthcare services among Hispanics in the United States. *Ethn. Dis.* 2008;18(1):93–7.
51. Amri R, Stronks K, Bordeianou LG, et al. Gender and ethnic disparities in colon cancer presentation and outcomes in a US universal health care setting. *J. Surg. Oncol.* 2014;109(7):645–51.
52. Johnson-Kozlow M, Roussos S, Rovniak L, et al. Colorectal cancer test use among Californians of Mexican origin: influence of language barriers. *Ethn. Dis.* 2009;19(3):315–22.

53. White KL, Schildkraut JM, Palmieri RT, et al. Ovarian cancer risk associated with inherited inflammation-related variants. *Cancer Res.* 2012;72(5):1064–9.
54. Akinyemiju TF, Soliman AS, Yassine M, et al. Healthcare access and mammography screening in Michigan: a multilevel cross-sectional study. *Int. J. Equity Health*. 2012;11:16.
55. Boukus E, Cunningham P. Mixed signals: trends in Americans' access to medical care, 2007-2010. *Track. Rep*. 2011;
56. Lee SL, Yaghoubian A, Kaji A. County versus private hospitals: access of care, management and outcomes for patients with appendicitis. *JSLS*. 2012;16(2):283–6.
57. Franks P, Fiscella K. Reducing disparities downstream: prospects and challenges. *J. Gen. Intern. Med.* 2008;23(5):672–7.
58. Andersen RM, Yu H, Wyn R, et al. Access to medical care for low-income persons: how do communities make a difference? *Med. Care Res. Rev.* 2002;59(4):384–411.
59. Litaker D, Koroukian SM, Love TE. Context and healthcare access: looking beyond the individual. *Med. Care*. 2005;43(6):531–40.
60. Pande AH, Ross-Degnan D, Zaslavsky AM, et al. Effects of healthcare reforms on coverage, access, and disparities: quasi-experimental analysis of evidence from Massachusetts. *Am. J. Prev. Med.* 2011;41(1):1–8.
61. Bristow RE, Ueda S, Gerardi MA, et al. Analysis of racial disparities in stage IIIC epithelial ovarian cancer care and outcomes in a tertiary gynecologic oncology referral center. *Gynecol. Oncol.* 2011;122(2):319–323.
62. Bristow RE, Zahurak ML, Ibeanu O a. Racial disparities in ovarian cancer surgical care: a population-based analysis. *Gynecol. Oncol.* 2011;121(2):364–8.
63. Terplan M, Temkin S, Tergas A, et al. Does equal treatment yield equal outcomes? The impact of race on survival in epithelial ovarian cancer. *Gynecol. Oncol.* 2008;111(2):173–178.
64. Montealegre JR, Follen M, Scheurer ME. Nativity Differences in Behaviors Associated with High-Risk HPV Infection Among Hispanic Women in Houston, Texas, USA. *J. Immigr. Minor. Health*. 2013;
65. Coughlin SS, Richards TB, Nasseri K, et al. Cervical cancer incidence in the United States in the US-Mexico border region, 1998-2003. *Cancer*. 2008;113(10 Suppl):2964–73.
66. Haile RW, John EM, Levine AJ, et al. A review of cancer in U.S. Hispanic populations. *Cancer Prev. Res. (Phila).* 2012;5(2):150–63.
67. Horn-Ross PL, McClure LA, Chang ET, et al. Papillary thyroid cancer incidence rates vary significantly by birthplace in Asian American women. *Cancer Causes Control*. 2011;22(3):479–85.
68. Ranji U, Salganicoff A, Beamesderfer A, et al. The Role of Medicaid and Medicare in Women's Health Care. *JAMA*. 2013;309(19):1984.
69. O'Malley CD, Shema SJ, Clarke LS, et al. Medicaid status and stage at diagnosis of cervical cancer. *Am. J. Public Health*. 2006;96(12):2179–85.
70. Yin D, Morris C, Allen M, et al. Does socioeconomic disparity in cancer incidence vary across racial/ethnic groups? *Cancer Causes Control*. 2010;21(10):1721–30.

71. Abidi A, Xing G, Nasseri K, et al. Age and race disparity in incidence, treatment and survival of cervical cancer in California. *Gynecol. Oncol.* 2008;111(2).
72. The California Cancer Registry. Numbers taken from CCR inquiry system. *Q. Extr.* 2011;
73. Yost K, Perkins C, Cohen R, et al. Socioeconomic status and breast cancer incidence in California for different race/ethnic groups. *Cancer Causes Control*. 2001;12(8):703–11.
74. Quach T, Doan-Billing PA, Layefsky M, et al. Cancer incidence in female cosmetologists and manicurists in California, 1988-2005. *Am. J. Epidemiol.* 2010;172(6):691–9.
75. Boyle P, Parkin DM. Statistical methods for registries. In: Jensen O, Parkin D, MacLennan R, eds. *Cancer Registration: Principles and Methods.* Lyon, France: International Agency for Research on Cancer; IARC Scientific Publication 95.; 1991:126–158.
76. Watson M, Saraiya M, Ahmed F, et al. Using population-based cancer registry data to assess the burden of human papillomavirus-associated cancers in the United States: overview of methods. *Cancer*. 2008;113(10 Suppl):2841–54.
77. Limmer K, LoBiondo-Wood G, Dains J. Predictors of cervical cancer screening adherence in the United States: a systematic review. *J. Adv. Pract. Oncol.* 2014;5(1):31–41.
78. American Cancer Society, California Department of Public Health, California Cancer Registry. California Cancer Facts and Figures 2014. 2014.
79. National Cancer Institute. Cancer Screening Overview (PDQ®). (http://www.cancer.gov/cancertopics/pdq/screening/overview/patient). (Accessed August 19, 2014)
80. Stroup A, Harlan L, Trimble E. Demographic, Clinical, and Treatment Trends Among Women Diagnosed with Vulvar Cancer in the U.S. *Gynecol. Oncol.* 2008;108(3):577–583.
81. Reiter PL, Fisher JL, Hudson AG, et al. Assessing the burden of HPV-related cancers in Appalachia. *Hum. Vaccin. Immunother.* 2013;9(1):90–6.
82. Springer YP, Samuel MC, Bolan G. Socioeconomic gradients in sexually transmitted diseases: a geographic information system-based analysis of poverty, race/ethnicity, and gonorrhea rates in California, 2004-2006. *Am. J. Public Health*. 2010;100(6):1060–7.
83. Fichtenberg CM, Jennings JM, Glass TA, et al. Neighborhood socioeconomic environment and sexual network position. *J. Urban Health*. 2010;87(2):225–35.
84. Harling G, Subramanian S, Bärnighausen T, et al. Socioeconomic disparities in sexually transmitted infections among young adults in the United States: examining the interaction between income and race/ethnicity. *Sex. Transm. Dis.* 2013;40(7):575–81.
85. Perkins CI, Allen ME, Wright WE, et al. Breast Cancer in California: Stage at Diagnosis and Medi-Cal Status. Sacramento, CA: 2000.
86. Lee-Feldstein A, Feldstein PJ, Buchmueller T. Health care factors related to stage at diagnosis and survival among Medicare patients with colorectal cancer. *Med. Care*. 2002;40(5):362–74.

87. Ghebre RG, Posthuma R, Vogel RI, et al. Effect of age and comorbidity on the treatment and survival of older patients with vulvar cancer. *Gynecol. Oncol.* 2011;121(3):595–9.
88. Moreland S, Engelman K, Greiner KA, et al. Papanicolaou testing among Native American and Hispanic populations. *Ethn. Dis.* 2006;16(1):223–7.
89. Pourat N. Access versus acculturation: Identifying modifiable factors to promote cancer screening among Asian American women. *Med. Care*. 2010;48(12):1088–1096.
90. Savas LS, Vernon SW, Atkinson JS, et al. Effect of Acculturation and Access to Care on Colorectal Cancer Screening in Low-Income Latinos. *J. Immigr. Minor. Health*. 2014;
91. Ma GX, Fang CY, Feng Z, et al. Correlates of cervical cancer screening among Vietnamese American women. *Infect. Dis. Obstet. Gynecol.* 2012;2012:617234.
92. Nguyen AB, Clark TT, Belgrave FZ. Gender roles and acculturation: relationships with cancer screening among Vietnamese American women. *Cultur. Divers. Ethnic Minor. Psychol.* 2014;20(1):87–97.
93. Rosales M, Gonzalez P. Mammography screening among Mexican, Central-American, and South-American women. *J. Immigr. Minor. Health*. 2013;15(2):225–33.
94. Ma GX, Shive SE, Wang MQ, et al. Cancer screening behaviors and barriers in Asian Americans. *Am. J. Health Behav.* 2009;33(6):650–60.
95. Jibara G, Jandorf L, Fodera MB, et al. Adherence to physician recommendation to colorectal cancer screening colonoscopy among Hispanics. *J. Gen. Intern. Med.* 2011;26(10):1124–30.
96. Lawsin C, Erwin D, Bursac Z, et al. Heterogeneity in breast and cervical cancer screening practices among female Hispanic immigrants in the United States. *J. Immigr. Minor. Health*. 2011;13(5):834–41.
97. Ivanov LL, Hu J, Leak A. Immigrant women's cancer screening behaviors. *J. Community Health Nurs.* 2010;27(1):32–45.
98. Watts L, Joseph N, Velazquez A, et al. Understanding barriers to cervical cancer screening among Hispanic women. *Am. J. Obstet. Gynecol.* 2009;201(2):199.e1–8.
99. Afable-Munsuz A, Liang S-Y, Ponce NA, et al. Acculturation and colorectal cancer screening among older Latino adults: differential associations by national origin. *J. Gen. Intern. Med.* 2009;24(8):963–70.
100. Hurtado-de-Mendoza A, Song M, Kigen O, et al. Addressing cancer control needs of African-born immigrants in the US: A systematic literature review. *Prev. Med. (Baltim).* 2014;67C:89–99.
101. Lee S, Chen L, Jung MY, et al. Acculturation and cancer screening among asian americans: role of health insurance and having a regular physician. *J. Community Health*. 2014;39(2):201–12.
102. Ryu SY, Crespi CM, Maxwell AE. What factors explain disparities in mammography rates among Asian-American immigrant women? A population-based study in California. *Womens. Health Issues*. 2013;23(6):e403–10.

103. O'Brien MJ, Halbert CH, Bixby R, et al. Community health worker intervention to decrease cervical cancer disparities in Hispanic women. *J. Gen. Intern. Med.* 2010;25(11):1186–92.
104. Thomson MD, Hoffman-Goetz L. Cancer information comprehension by English-as-a-second-language immigrant women. *J. Health Commun.* 2011;16(1):17–33.
105. Kobetz E, Kornfeld J, Vanderpool RC, et al. Knowledge of HPV among United States Hispanic women: opportunities and challenges for cancer prevention. *J. Health Commun.* 2010;15 Suppl 3:22–9.
106. Ayres CG, Atkins R, Lee JH. Factors related to health practices: cervical cancer screening among Filipino women. *Res. Theory Nurs. Pract.* 2010;24(3):197–208.
107. Adam MB, McGuire JK, Walsh M, et al. Acculturation as a predictor of the onset of sexual intercourse among Hispanic and white teens. *Arch. Pediatr. Adolesc. Med.* 2005;159(3):261–5.
108. Coonrod D V, Bay RC, Balcazar H. Ethnicity, acculturation and obstetric outcomes. Different risk factor profiles in low- and high-acculturation Hispanics and in white non-Hispanics. *J. Reprod. Med.* 2004;49(1):17–22.
109. Kepka D, Coronado G, Rodriguez H, et al. Acculturation and HPV infection among Latinas in the United States. *Prev. Med. (Baltim).* 2010;51(2):182–4.
110. Choi SH. Testing healthy immigrant effects among late life immigrants in the United States: using multiple indicators. *J. Aging Health*. 2012;24(3):475–506.
111. Singh GK, Siahpush M. Ethnic-immigrant differentials in health behaviors, morbidity, and cause-specific mortality in the United States: an analysis of two national data bases. *Hum. Biol.* 2002;74(1):83–109.
112. Singh GK, Miller BA. Health, life expectancy, and mortality patterns among immigrant populations in the United States. *Can. J. Public Health*. 2004;95(3):I14–21.
113. Gallo LC, Penedo FJ, Espinosa de los Monteros K, et al. Resiliency in the face of disadvantage: do Hispanic cultural characteristics protect health outcomes? *J. Pers.* 2009;77(6):1707–46.
114. Nasseri K, Moulton LH. Patterns of death in the first and second generation immigrants from selected Middle Eastern countries in California. *J. Immigr. Minor. Health*. 2011;13(2):361–70.
115. Tailakh AK, Evangelista LS, Morisky DE, et al. Acculturation, Medication Adherence, Lifestyle Behaviors, and Blood Pressure Control Among Arab Americans. *J. Transcult. Nurs.* 2014;
116. US Preventive Services Task Force. 9-11-12 Final Recommendation Statement: Screening for Ovarian Cancer. (http://www.uspreventiveservicestaskforce.org/uspstf/uspsovar.htm). (Accessed August 19, 2014)
117. Clarke-Pearson DL. Clinical practice. Screening for ovarian cancer. *N. Engl. J. Med.* 2009;361(2):170–7.
118. Nguyen L, Cardenas-Goicoechea SJ, Gordon P, et al. Biomarkers for early detection of ovarian cancer. *Womens. Health (Lond. Engl).* 2013;9(2):171–85; quiz 186–7.

119. Buys SS, Partridge E, Black A, et al. Effect of screening on ovarian cancer mortality: the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Randomized Controlled Trial. *JAMA*. 2011;305(22):2295–303.
120. National Cancer Institute. Ovarian Cancer Screening (PDQ®). (http://www.cancer.gov/cancertopics/pdq/screening/ovarian/Patient/page3). (Accessed August 19, 2014)
121. National Ovarian Cancer Coalition. National Ovarian Cancer Coalition: How is Ovarian Cancer Diagnosed.
122. Barnholtz-Sloan J. Ovarian cancer: changes in patterns at diagnosis and relative survival over the last three decades. *Am. J. Obstet. Gynecol.* 2003;189(4):1120–1127.
123. Chornokur G, Amankwah EK, Schildkraut JM, et al. Global ovarian cancer health disparities. *Gynecol. Oncol.* 2013;129(1):258–64.
124. Howlader N, Noone A, Krapcho M, et al. SEER Cancer Statistics Review, 1975-2011. Bethesda, MD: 2014.
125. Shetty, PK Balaiah, K Bafna, UD Gnana Prakash S. Primary Fallopian Tube Carcinoma. *Online J. Heal. Allied Sci.* 2010;9(4):6–8.
126. Nodora JN, Gallo L, Cooper R, et al. Reproductive and hormonal risk profile according to language acculturation and country of residence in the Ella Binational Breast Cancer Study. *J. Womens. Health (Larchmt).* 2014;23(6):532–40.
127. Andreeva V a, Unger JB, Pentz MA. Breast cancer among immigrants: a systematic review and new research directions. *J. Immigr. Minor. Health*. 2007;9(4):307–22.
128. Urquia ML, O'Campo PJ, Heaman MI. Revisiting the immigrant paradox in reproductive health: the roles of duration of residence and ethnicity. *Soc. Sci. Med.* 2012;74(10):1610–21.
129. Ahluwalia IB, D'Angelo D, Morrow B, et al. Association between acculturation and breastfeeding among Hispanic women: data from the Pregnancy Risk Assessment and Monitoring System. *J. Hum. Lact.* 2012;28(2):167–73.
130. Tseng M, Byrne C, Evers KA, et al. Acculturation and breast density in foreign-born, U.S. Chinese women. *Cancer Epidemiol. Biomarkers Prev.* 2006;15(7):1301–5.
131. Kumar NB, Yu D, Akinremi TO, et al. Comparing dietary and other lifestyle factors among immigrant Nigerian men living in the US and indigenous men from Nigeria: potential implications for prostate cancer risk reduction. *J. Immigr. Minor. Health*. 2009;11(5):391–9.
132. Okafor M-TC, Carter-Pokras OD, Zhan M. Greater dietary acculturation (dietary change) is associated with poorer current self-rated health among african immigrant adults. *J. Nutr. Educ. Behav.* 2014;46(4):226–35.
133. Lesser IA, Gasevic D, Lear SA. The association between acculturation and dietary patterns of South Asian immigrants. *PLoS One*. 2014;9(2):e88495.
134. Iglesias-Rios L, Bromberg JE, Moser RP, et al. Food Insecurity, Cigarette Smoking, and Acculturation Among Latinos: Data From NHANES 1999-2008. *J. Immigr. Minor. Health*. 2013;

135. Murtaugh MA, Herrick JS, Sweeney C, et al. Diet composition and risk of overweight and obesity in women living in the southwestern United States. *J. Am. Diet. Assoc.* 2007;107(8):1311–21.
136. Dunham DP, Czysczon A, Chávez N, et al. Dietary differences among women of Polish descent by country of birth and duration of residency in the United States. *Ethn. Dis.* 2004;14(2):219–26.
137. Morris CR, Ramirez CN, Cook SN, Parikh-Patel A, Kizer KW, Bates JH SK. Cancer Stage at Diagnosis, 2013. Sacramento, CA: 2013.
138. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA*. 2000;283(15):2008–12.
139. Mahdi H, Kumar S, Hanna RK, et al. Disparities in treatment and survival between African American and White women with vaginal cancer. *Gynecol. Oncol.* 2011;122(1):38–41.
140. Lee EE, Eun Y, Lee S-Y, et al. Age-related differences in health beliefs regarding cervical cancer screening among Korean American women. *J. Transcult. Nurs.* 2012;23(3):237–45.
141. Kondi-Pafiti a, Grigoriadis C, Kalampokas T, et al. Clinicopathological study of 112 cases of benign, pre-invasive and invasive lesions of the vagina: a 15-year review. *Eur. J. Gynaecol. Oncol.* 2012;33(5):463–6.
142. Chhabra S, Bhavani M, Deshpande A. Trends of vulvar cancer. *J. Obstet. Gynaecol.* 2014;34(2):165–8.
143. Canavan TP, Cohen DMD. Vulvar Cancer. *Am. Fam. Physician*. 2002;66(7):1269–1274.
144. Kurdgelashvili G, Dores GM, Srour SA, et al. Incidence of potentially human papillomavirus-related neoplasms in the United States, 1978 to 2007. *Cancer*. 2013;119(12):2291–9.
145. Lanneau GS, Argenta PA, Lanneau MS, et al. Vulvar cancer in young women: demographic features and outcome evaluation. *Am. J. Obstet. Gynecol.* 2009;200(6):645.e1–5.
146. Singh GK, Miller B a, Hankey BF, et al. Persistent area socioeconomic disparities in U.S. incidence of cervical cancer, mortality, stage, and survival, 1975-2000. *Cancer*. 2004;101(5):1051–7.
147. Castañeda SF, Malcarne VL, Foster-Fishman PG, et al. Health care access and breast cancer screening among latinas along the california-mexican border. *J. Immigr. Minor. Health*. 2014;16(4):670–81.
148. Morris CR, Sands MT, Smith LH. Ovarian cancer: predictors of early-stage diagnosis. *Cancer Causes Control*. 2010;21(8):1203–11.
149. Austin S, Martin MY, Kim Y, et al. Disparities in use of gynecologic oncologists for women with ovarian cancer in the United States. *Health Serv. Res.* 2013;48(3):1135–53.
150. Chen L, Berek JS. UpToDate: Epithelial carcinoma of the ovary, fallopian tube, and peritoneum: Clinical features and diagnosis. *UpToDate*. 2014;:1–31. (www.uptodate.com). (Accessed January 8, 2014)

151. Lurie G, Wilkens LR, Thompson PJ, et al. Symptom presentation in invasive ovarian carcinoma by tumor histological type and grade in a multiethnic population: a case analysis. *Gynecol. Oncol.* 2010;119(2):278–84.
152. Roetzheim RG, Pal N, Tennant C, et al. Effects of health insurance and race on early detection of cancer. *J. Natl. Cancer Inst.* 1999;91(16):1409–15.
153. Shah CA, Goff BA, Lowe K, et al. Factors affecting risk of mortality in women with vaginal cancer. *Obstet. Gynecol.* 2009;113(5):1038–45.
154. Carter JS, Downs LS. Vulvar and vaginal cancer. *Obstet. Gynecol. Clin. North Am.* 2012;39(2):213–31.
155. Woelber L, Kock L, Gieseking F, et al. Clinical management of primary vulvar cancer. *Eur. J. Cancer*. 2011;47(15):2315–21.
156. Woelber L, Trillsch F, Kock L, et al. Management of patients with vulvar cancer: a perspective review according to tumour stage. *Ther. Adv. Med. Oncol.* 2013;5(3):183–92.
157. Sharma DN and. Radiation in vulvar cancer. *Curr. Opin. Obstet. Gynecol.* 2012;24(1):24–30.
158. Ghia AJ, Gonzalez VJ, Tward JD, et al. Primary vaginal cancer and chemoradiotherapy: a patterns-of-care analysis. *Int. J. Gynecol. Cancer*. 2011;21(2):378–84.
159. Gunderson CC, Nugent EK, Yunker AC, et al. Vaginal Cancer: The Experience From 2 Large Academic Centers During a 15-Year Period. *J. Low. Genit. Tract Dis.* 2013;
160. Lilic V, Lilic G, Filipovic S, et al. Primary carcinoma of the vagina. *J. BUON.* 2010;15(2):241–7.
161. Kim J, Artinyan A, Mailey B, et al. An interaction of race and ethnicity with socioeconomic status in rectal cancer outcomes. *Ann. Surg.* 2011;253(4):647–54.
162. Huang LC, Ma Y, Ngo J V, et al. What factors influence minority use of National Cancer Institute-designated cancer centers? *Cancer*. 2014;120(3):399–407.
163. Chamie K, Saigal CS, Lai J, et al. Quality of care in patients with bladder cancer: a case report? *Cancer*. 2012;118(5):1412–21.
164. Gorey KM, Luginaah IN, Holowaty EJ, et al. Effects of being uninsured or underinsured and living in extremely poor neighborhoods on colon cancer care and survival in California: historical cohort analysis, 1996-2011. *BMC Public Health*. 2012;12:897.
165. Carter-Pokras O, Zambrana RE, Yankelvich G, et al. Health status of Mexican-origin persons: do proxy measures of acculturation advance our understanding of health disparities? *J. Immigr. Minor. Health*. 2008;10(6):475–88.
166. Pineda MD, White E, Kristal AR, et al. Asian breast cancer survival in the US: a comparison between Asian immigrants, US-born Asian Americans and Caucasians. *Int. J. Epidemiol.* 2001;30(5):976–82.
167. Arnold M, Aarts MJ, Siesling S, et al. Diverging breast and stomach cancer incidence and survival in migrants in The Netherlands, 1996-2009. *Acta Oncol.* 2013;52(6):1195–201.
168. Du XL, Sun CC, Milam MR, et al. Ethnic differences in socioeconomic status, diagnosis, treatment, and survival among older women with epithelial ovarian cancer. *Int. J. Gynecol. Cancer*. 2008;18(4):660–9.

169. Le H, Ziogas A, Taylor TH, et al. Survival of distinct Asian groups among colorectal cancer cases in California. *Cancer*. 2009;115(2):259–70.
170. Li B, Brown M, Lau D, et al. Improved Survival With Chemoradiation Therapy Compared to Radiation Therapy Alone for Asian-Americans: Results From the California Cancer Registry. *Int. J. Radiat. Oncol.* 2012;84(3):S490–S491.
171. Stewart SL, Rim SH, Richards TB. Gynecologic oncologists and ovarian cancer treatment: avenues for improved survival. *J. womens Heal. 2002*. 2011;20(9):1257–1260.
172. Bristow RE, Chang J, Ziogas A, et al. High-volume ovarian cancer care: survival impact and disparities in access for advanced-stage disease. *Gynecol. Oncol.* 2014;132(2):403–10.
173. Liu FW, Randall LM, Tewari KS, et al. Racial disparities and patterns of ovarian cancer surgical care in California. *Gynecol. Oncol.* 2014;132(1):221–6.
174. Kim S, Dolecek TA, Davis FG. Racial differences in stage at diagnosis and survival from epithelial ovarian cancer: a fundamental cause of disease approach. *Soc. Sci. Med.* 2010;71(2):274–81.
175. Safra T, Lai WC, Borgato L, et al. BRCA mutations and outcome in epithelial ovarian cancer (EOC): experience in ethnically diverse groups. *Ann. Oncol.* 2013;24 Suppl 8:viii63–viii68.
176. Braaten T, Weiderpass E, Lund E. Socioeconomic differences in cancer survival: the Norwegian Women and Cancer Study. *BMC Public Health*. 2009;9:178.
177. Elit L, Schultz S, Prysbysz R, et al. Patterns of care in the initial management of women with ovarian cancer in Ontario. *Eur. J. Gynaecol. Oncol.* 2009;30(4):361–4.
178. Hynes DM, Tarlov E, Durazo-Arvizu R, et al. Surgery and adjuvant chemotherapy use among veterans with colon cancer: insights from a California study. *J. Clin. Oncol.* 2010;28(15):2571–6.
179. Nguyen DK, Maggard-Gibbons M. Age, poverty, acculturation, and gastric cancer. *Surgery*. 2013;154(3):444–52.
180. Centers for Disease Control and Prevention (CDC). Human papillomavirus-associated cancers - United States, 2004-2008. *MMWR. Morb. Mortal. Wkly. Rep.* 2012;61:258–61.
181. Watson M, Saraiya M, Benard V, et al. Burden of cervical cancer in the United States, 1998-2003. *Cancer*. 2008;113(10 Suppl):2855–64.
182. Nasseri K. Mortality in first generation white immigrants in California, 1989-1999. *J. Immigr. Minor. Health*. 2008;10(3):197–205.
183. Khanfir K, Kallel A, Villette S, et al. Management of adenoid cystic carcinoma of the breast: a Rare Cancer Network study. *Int. J. Radiat. Oncol. Biol. Phys.* 2012;82(5):2118–24.
184. Thompson K, Grabowski J, Saltzstein SL, et al. Adenoid cystic breast carcinoma: is axillary staging necessary in all cases? Results from the California Cancer Registry. *Breast J.* 2011;17(5):485–9.
185. Chavez-MacGregor M, Clarke C, Lichtensztajn D, et al. P4-19-01: Male Breast Cancer According to Tumor Subtype and Race: A California Cancer Registry (CCR)-Population Based Study. *Cancer Res.* 2012;71(24 Supplement):P4–19–01–P4–19–01.

186. De Vuyst H, Clifford GM, Nascimento MC, et al. Prevalence and type distribution of human papillomavirus in carcinoma and intraepithelial neoplasia of the vulva, vagina and anus: a meta-analysis. *Int. J. Cancer*. 2009;124(7):1626–36.
187. Izquierdo JN, Schoenbach VJ. The potential and limitations of data from population-based state cancer registries. *Am. J. Public Health*. 2000;90(5):695–8.
188. Krieger N. Socioeconomic Data in Cancer Registries. *Am. J. Public Health*. 2001;91(1):156–7.
189. Krieger N. Women and social class: a methodological study comparing individual, household, and census measures as predictors of black/white differences in reproductive history. *J. Epidemiol. Community Health*. 1991;45(1):35–42.
190. Krieger N, Chen JT, Waterman PD, et al. Geocoding and monitoring of US socioeconomic inequalities in mortality and cancer incidence: does the choice of area-based measure and geographic level matter?: the Public Health Disparities Geocoding Project. *Am. J. Epidemiol.* 2002;156(5):471–82.
191. Krieger N. Why epidemiologists cannot afford to ignore poverty. *Epidemiology*. 2007;18(6):658–63.
192. Krieger N, Chen JT, Waterman PD, et al. Race/ethnicity and changing US socioeconomic gradients in breast cancer incidence: California and Massachusetts, 1978-2002 (United States). *Cancer Causes Control*. 2006;17(2):217–26.
193. Krieger N, Chen JT, Ware JH, et al. Race/ethnicity and breast cancer estrogen receptor status: impact of class, missing data, and modeling assumptions. *Cancer Causes Control*. 2008;19(10):1305–18.
194. Kent EE, Morris R a, Largent J a, et al. Socioeconomic Impacts on Survival Differ by Race/Ethnicity among Adolescents and Young Adults with Non-Hodgkin's Lymphoma. *J. Cancer Epidemiol.* 2010;2010(2):824691.
195. Parikh-Patel A, Bates JH, Campleman S. Colorectal cancer stage at diagnosis by socioeconomic and urban/rural status in California, 1988-2000. *Cancer*. 2006;107(5 Suppl):1189–95.
196. Parise CA, Caggiano V. Breast Cancer Survival Defined by the ER/PR/HER2 Subtypes and a Surrogate Classification according to Tumor Grade and Immunohistochemical Biomarkers. *J. Cancer Epidemiol.* 2014;2014:469251.
197. Gomez SL, Clarke CA, Shema SJ, et al. Disparities in breast cancer survival among Asian women by ethnicity and immigrant status: a population-based study. *Am. J. Public Health*. 2010;100(5):861–9.
198. Koru-Sengul T, Tannenbaum S, Miao F, et al. 141st APHA Annual Meeting and Exposition, Think Global Act Local: Best Practices Around the World. In: *Handling missing values in population-based cancer registries: Application to female breast cancer with missing hormonal status*. 2013
199. He Y, Yucel R, Zaslavsky A. Here's to Your Health: Misreporting, Missing Data, and Multiple Imputation: Improving Accuracy of Cancer Registry Databases. *Chance*. 2008;21(3):55–58.
200. Eisemann N, Waldmann A, Katalinic A. Imputation of missing values of tumour stage in population-based cancer registration. *BMC Med. Res. Methodol.* 2011;11(1):129.

201. California Cancer Registry, Chronic Disease Surveillance and Research Branch. Policies and Procedures for Access to and Disclosure of Confidential Data From the California Cancer Registry January 2014. Sacramento, CA: 2014.
202. Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J, et al. Cancer incidence and mortality patterns in Europe: estimates for 40 countries in 2012. *Eur. J. Cancer*. 2013;49(6):1374–403.
203. Keat N, Law K, Seymour M, et al. International rare cancers initiative. *Lancet Oncol.* 2013;14(2):109–10.
204. International Rare Cancer Initiative. IRCI: International Rare Cancer Initiative. 2011;(http://www.irci.info/). (Accessed July 28, 2014)
205. Gatta G, van der Zwan JM, Casali PG, et al. Rare cancers are not so rare: the rare cancer burden in Europe. *Eur. J. Cancer*. 2011;47(17):2493–511.
206. Every Woman Counts. Cancer Detection Programs: Every Woman Counts February 2012 Report to the Legislature: Breast Cancer & Cervical Cancer Screening and Diagnotic Services. 2012.
207. California Department of Health Care Services. Every Woman Counts. (http://www.dhcs.ca.gov/services/Cancer/ewc/Pages/default.aspx). (Accessed August 5, 2014)