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THE IMPACT OF SOCIOECONOMIC STATUS ON OVARIAN CANCER SURVIVAL AMONG GEORGIA WOMEN DIAGNOSED FROM 2001-2005

By

Lisa Melissa Matz

Master of Science in Public Health

Epidemiology

Dr. Kevin C. Ward

Faculty Thesis Advisor

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An abstract of

A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University

in partial fulfillment of the requirements for the degree of
Master of Science in Public Health
in
Epidemiology

2013

Abstract

THE IMPACT OF SOCIOECONOMIC STATUS ON OVARIAN CANCER SURVIVAL AMONG GEORGIA WOMEN DIAGNOSED FROM 2001-2005

By Lisa Melissa Matz

Objectives: The goal of this study was to examine the impact of socioeconomic status (SES) on ovarian cancer survival among women in Georgia who were diagnosed with malignant ovarian cancer from 2001-2005 with follow-up until 2008. Low SES has been previously shown to negatively impact health outcomes, though the impact on ovarian cancer survival is relatively unknown. Knowing the impact of SES will help to more fully understand disparities in ovarian cancer survival.

Methods: Using data from the Georgia Cancer Registry, all cases of malignant ovarian cancer among women in Georgia were identified. Based on the recommendations of the Public Health Disparities Geocoding Project, percentage of persons living in poverty by census tract was used an area-based measure of SES. Three-year cause-specific survival adjusted for age, race, marital status, stage, histology, grade, and treatment was estimated using Cox proportional hazards modeling. Three-year relative survival ratios were estimated using age and year-specific U.S life tables. Cause-specific and relative survival were estimated for cases with a single primary ovarian cancer and subsequently for all cases regardless of other cancer diagnoses.

Results: Women living in areas with the highest poverty had significantly lower 3-year cause-specific survival than women living in areas with little to no poverty. After controlling for covariates, the hazard ratio for women living in the highest poverty category was 1.44 (95% CI: 1.18, 1.76). Including cases with prior or subsequent cancer diagnoses also resulted in a significant association (HR (95% CI) = 1.48 (1.23, 1.78)). Compared to women living in areas with little to no poverty, three-year relative survival was lowest for women living in the highest poverty category (38% vs. 64%). This relationship held when higher order cancers were included in the analysis (39% vs. 65%).

Conclusions: This study identified SES as a significant factor in ovarian cancer survival among women living in Georgia. Women living in poverty are at greater risk of dying from ovarian cancer compared to women living low poverty. Future research should focus on decomposing this relationship to determine precisely how low SES negatively impacts ovarian cancer survival.

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Acknowledgements

I would like to thank my mentor and thesis advisor Dr. Kevin Ward. Without his guidance and support this thesis would not have been possible.

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Introduction

Socioeconomic status (SES) impacts health in several ways, as shown by Sir Michael Marmot's work on the social determinants of health(1). Differences in cancer survival have been attributed to socioeconomic status; however, the exact mechanisms through which SES imparts its effects are not fully understood. While stage at diagnosis and differences in treatment can explain some inequalities in survival due to socioeconomic status, even after controlling for these factors, unexplained differences remain in some studies(2).

Ovarian cancer is one of the most common gynecologic malignancies among women in the United States and is one of the leading causes of cancer death. Numerous studies have shown differences in survival for ovarian cancer patients across Europe and the United States(3-9). This study seeks to examine the impact of socioeconomic status on ovarian cancer survival among women in Georgia diagnosed with invasive ovarian cancer between 2001 and 2005 using population-based cancer registry data.

Background

Ovarian Cancer

The National Cancer Institute has estimated that 22,240 women will be diagnosed with ovarian cancer in the U.S. during 2013(10). Ovarian cancer is the ninth most common cancer among women, accounting for 3% of all new female cancer cases in 2012(11). From 2005-2009, the age-adjusted incidence rate for ovarian cancer was 12.7 cases per 100,000 women per year. White women had the highest age-adjusted incidence rate of 13.4 cases per 100,000 while Black and

Asian/Pacific Islander women had the lowest rate of 9.8 cases per 100,000(12). The median age at diagnosis during this same period was 63 years and 69.2% of women were diagnosed at age 55 or later. Ovarian cancer incidence has decreased in recent years. From 2001-2009, incidence decreased by 1.5%(13).

Despite relatively low incidence, ovarian cancer is the deadliest of the gynecological cancers and is the fifth leading cause of cancer death among women—accounting for 6% of all cancer deaths(11). In 2013, 14,030 women will die from the disease in the U.S(10). From 2005-2009, the age-adjusted mortality rate was 8.2 deaths per 100,000 women per year, with the highest age-adjusted mortality rate at 8.6 deaths per 100,000 for White women. Asian/Pacific Islander women had the lowest mortality rate at 5.0 deaths per 100,000(12). The median age at death was 71 years and 85.8% of ovarian cancer deaths occur at age 55 or later. Like incidence, ovarian cancer mortality rates decreased by 2.0% from 2002-2009(13).

Ovarian cancer has been termed the 'silent killer' because it is often extremely difficult to diagnose until the cancer has progressed to late stage. From 2002-2008, 61% of all ovarian cancer cases were diagnosed after the cancer had metastasized(13). Of the remaining diagnoses, 15% were localized, or confined to the primary site, 17% were diagnosed when the cancer had only spread to the regional lymph nodes, and 7% were diagnosed unstaged. The high proportion of women diagnosed at advanced stages is mostly due to the lack of effective screening tests for ovarian cancer and to the fact that most women do not notice any symptoms until the disease is advanced. Routine pelvic examinations cannot accurately detect changes in ovary size or volume, particularly in menopausal

women who are most at risk due to age(14). Furthermore, pelvic examinations are often normal in early stage ovarian patients and tend to only help diagnose advanced stage patients with larger abdominal masses(15). Researchers have proposed using levels of cancer antigen (CA) 125 in the blood and transvaginal ultrasounds as routine screening tests for ovarian cancer. However, these techniques have varied results for earlier diagnosis and have not impacted ovarian cancer mortality. While CA-125 levels are elevated for 80% of advanced stage ovarian cancer patients, only 50% of early stage patients have elevated levels(14). Additional prevention measures include testing for BRCA1 and BRCA2 gene mutations, and performing oophorectomies, hysterectomies, and tubal ligations in high-risk women. However, these additional prevention measures are not suitable for the entire population(15). Therefore, it is not surprising with the lack of effective screening tools and prevention measures that most women are diagnosed during the most advanced stages of disease.

As documented by the National Cancer Institutes' Physician Data Query(16-18), treatment for ovarian cancer depends highly upon the stage at diagnosis. For all ovarian cancers, including epithelial and germ cell, surgery is recommended. Surgery should include a complete hysterectomy, bilateral salpingo-oophorectomy, and omenectomy. For advanced stage epithelial ovarian cancers, surgery should also include debulking as much of the tumor as possible. Chemotherapy, including intraperitoneal and intravenous, may be required following surgery for advanced stage cancers. Radiation therapy may also be used to treat ovarian cancer.

Despite the treatments that are available, survival from ovarian cancer is unfortunately quite poor. Overall, 75% of women survive one year after diagnosis, while the 5-year relative survival was only 43.7% from 2002-2008(13, 15). Despite higher incidence and mortality rates, White women had higher overall 5-year survival than Black women from 2002-2008 (43.5% vs. 36.0%). Like many other cancers, survival for ovarian cancer patients depends on the stage of cancer at diagnosis with the 5-year relative survival decreasing as stage advances. Women diagnosed with localized cancer have a 91.5% 5-year relative survival, while women diagnosed at advanced stages have only a 26.9% 5-year relative survival(13).

Disparities in Health

Understanding disparities in health outcomes is pertinent to improving overall population health. Mounting evidence over the past few decades has strengthened the debate for the importance of reducing disparities in health outcomes whether the disparities are geographic, social, racial, or gender based(1, 19, 20). The objectives of Healthy People 2020 emphasize the need to eliminate health disparities in order to achieve health equality(21). Despite this emphasis on reducing and eliminating health disparities, there is a lack of data available with which to measure health disparities due to SES in the U.S.(22). The Public Health Disparities Geocoding Project at Harvard University researched measures of socioeconomic status in order to remedy the lack of data. The project examined different area-based socioeconomic measures (ABSMs) to determine which measure and at which geographic level would most appropriately monitor

socioeconomic disparities in health. The results of the project recommended that census tract poverty level be used to track socioeconomic disparities in the U.S.(20).

Socioeconomic Status and Cancer Survival

Numerous studies have shown an association between cancer survival and SES. A review of 39 studies examining the association between SES and cancer survival in different settings found that SES is an important factor in cancer prognosis for many populations(2). Differences in cancer survival due to socioeconomic position have been attributed to stage at diagnosis and differences in treatment(23-29); however, some of the variation in cancer survival remains unexplained even after controlling for these factors(24, 25, 30-34). Most studies have shown only a moderate impact of SES on cancer survival, though in nearly all of the studies the relationship has been statistically significant. The majority of studies that have found no significant association between SES and cancer survival have either focused on pediatric cancers, were ecological studies, had small sample sizes, or assigned deprivation based on geographies with large heterogeneous populations. Overall, the studies provide a body of evidence supporting the hypothesis that socioeconomic position impacts cancer survival(2).

Two additional more recent studies have also provided supporting evidence regarding the relationship between cancer survival and SES. A study examining excess deaths from cancer due to socioeconomic inequalities found that 11% of the cancer deaths within three years of diagnosis for adult patients

diagnosed from 2004-2006 in England would have been avoided if all patients had the relative survival of the highest income group(35). Using data from the Norwegian Women and Cancer Study, socioeconomic differences in cancer survival for overall and site-specific survival were examined. Socioeconomic position was indexed through a combination of household income and years of education. Using Cox proportional hazard models to measure excess mortality as an analogue to survival, the authors found a significant linear trend of decreasing mortality with increasing SES level(36).

Socioeconomic Status and Ovarian Cancer Survival

A study in Northern California used data from the California Cancer Registry to study the impact of demographic, clinical, and provider characteristics on ovarian cancer survival in a cohort of Northern California women. A census-based SES measure at the block group level was applied to each patient based on the patient's residential address at time of diagnosis. Overall, living in low education and blue-collar neighborhoods was associated with lower 3-year and 5-year survival. The authors also conducted a multivariate analysis looking at age, race/ethnicity, neighborhood-level socioeconomic status, region of residence, cancer stage, grade, histology, chemotherapy, and type of provider. In the multivariate analysis, neighborhood-level SES was no longer a significant predictor of survival(4).

Two additional studies outside the U.S. have shown an association between SES and ovarian cancer survival. A study in England found that 9.6%, 12.1%, and 5.2% of ovarian cancer deaths within three years of diagnosis could

have been avoided for cases diagnosed from 1996-2000, 2001-2003, and 2004-2006, respectively, if all patients had the same relative survival as the highest income group(35). An additional study in Norway found that there was a significant declining linear trend in excess mortality due to ovarian cancer with increasing SES level(36).

Other Factors in Ovarian Cancer Survival

There are several additional factors which are likely impacted by SES that can also affect ovarian cancer survival. The type of treatment a woman receives can directly impact her survival and may also be impacted by her SES, though the relationship between SES and ovarian cancer treatment is not fully clear. The medical care a woman has access to in her region or can afford may affect the type of treatment and surgical care she receives (37-41). Additionally, the relationship between race and ethnicity and ovarian cancer survival has yet to be determined(5, 7, 42, 43). Some studies have shown there are no differences in stage of diagnosis among different racial groups; however, with the development of an effective screening tool for ovarian cancer differences may appear (7, 44). Finally, there is conflicting information regarding the impact of SES on delay of diagnosis. Some studies have found that SES has no effect on delay of diagnosis or intent to seek care while others have found that women in lower SES groups or diagnosed in later stages are less likely to seek treatment once diagnosed (8, 45-49).

Methods

Study Population

Data from the Georgia Cancer Registry (GCR) were used to identify a cohort of invasive ovarian cancer cases diagnosed between January 1, 2001 and December 31, 2005 (n = 2812) with follow up through December, 31, 2008. The GCR is a population-based cancer registry that has attempted to register all incident cases of cancer in the state of Georgia since 1995. Eligible cases for the main analysis were diagnosed between the ages of 15 and 99 with a first and only primary invasive ovarian cancer diagnosis. Exclusions included cases with histologic codes for leukemia or lymphoma (n = 8) and cases with unknown census tract poverty level (n = 1), cause of death (n = 29), marital status (n = 78), race (n = 2), or treatment status (defined as chemotherapy, radiation, and/or surgery) (n = 193). Furthermore, cases reported only through an autopsy or death certificate were excluded as their contribution to overall survival was null (n = 1). A flow chart depicting exclusions for the main analytic cohort (n = 2037) is presented in Figure 1. A secondary analysis was conducted including cases with previous or subsequent cancer diagnoses to determine whether or not inclusion of second or higher primaries impacts the results of the analysis.

Socioeconomic Status

Using the recommendation of the Public Health Disparities Geocoding Project, the area-based socioeconomic measure of census tract poverty was used as the main exposure variable. Poverty status was categorized into four levels (0-<5%, 5-<10%, 10-<20%, and 20-100% of persons living below the FPL) with 0-

<5% representing the lowest level of area-based poverty and 20-100% representing the highest level of area-based poverty. Each eligible case was assigned a poverty level based on the 2000 U.S. Census.

Covariates

Additional data on age at diagnosis, race, martial status, date of diagnosis, last date of contact, vital status, histology, grade, stage, and treatment (chemotherapy, radiation, and/or surgery) were collected from the GCR. Age at diagnosis was coded as a continuous, numerical variable. Race (White, Black, or other), marital status (married vs. not married), vital status (alive vs. dead), stage (local, regional, distant, or unstaged), grade (low vs. high), and treatment (yes vs. no) were all coded as categorical variables. Survival time was calculated based on the date of diagnosis (month, day, year) and the last date of contact (month, day, year) and was censored at 36 months (3 years) for all subjects. The last date of contact is equivalent to the date of death for patients who died during the study period. Histology was grouped into three categories based on the predominant cell types for bladder cancers: epithelial tumors, sex cord tumors, and other tumors.

Statistical Analyses

All univariate, Kaplan-Meier, and cause-specific survival analyses were conducted using SAS 9.3 (SAS Institute, Cary, NC). Univariate analyses were conducted to investigate the relationship between covariates and both the exposure, census tract poverty level, and outcome, ovarian cancer survival.

Categorical covariates were assessed using chi-square tests and continuous covariates were assessed using t-tests or ANOVA. Covariates that had statistically significant associations with either the exposure or outcome were included in the full model. Collinearity diagnostics were conducted using a free SAS macro with an a priori cutpoint of 10 for Condition Indicies (CI) and 0.5 for variance decomposition proportions (VDP)(50). Collinearity was present if variables had both a high CI and VDP. After completion of the collinearity diagnostics, interaction assessment was performed using backward elimination to determine the statistical significance of potential two-way interaction between all covariates and all covariates with the exposure.

Descriptive statistics of the main analytic cohort were calculated including the mean and standard deviation for continuous variables and frequencies for categorical variables. Kaplan-Meier survival curves were estimated for each poverty level and compared using the log-rank test. Cox regression was used to model 3-year cause specific survival adjusted for age, race, marital status, stage histology, grade, treatment, and significant interaction terms for cases diagnosed from 2001-2005 with mortality follow up until 2008. The proportional hazards assumption was assessed using a goodness of fit approach with Schoenfeld residuals to test the significance of time-dependent variables ($p > 0.05$) and by comparing adjusted log-log survival curves. The proportional hazards assumption was met for all variables. Hazard Ratios (HR) for each poverty level (5% or greater) were estimated using the lowest poverty level as the reference group. Confounding was assessed in the final model by comparing HRs when systematically excluding potential confounders (age, race, histology, and grade)

from the model. Marital status, stage, and treatment were not assessed as potential confounders as significant interaction terms included these covariates. Though the HRs were not greatly altered by dropping any potential confounders, all potential confounders were kept in the model to control for any potential confounding.

Additionally, relative survival rates were estimated using age- and year-specific life tables for U.S. females for 2001-2008 from the National Center for Health Statistics(37). The London School of Hygiene and Tropical Medicine's Cancer Survival Group has created a relative survival module for STATA 12.0(39). This module was used to estimate unadjusted relative survival rates. Each analysis was conducted first using only cases with one primary cancer diagnoses. Secondary analyses were then conducted including cases with prior or subsequent cancer diagnoses.

Results

Table 1 provides descriptive characteristics of the cohort for the main analysis. Cases were distributed quite evenly across the poverty strata. Cases included in the main analysis were primarily older (61.8 years), White (76.8%), diagnosed in an advanced stage (57.7%), had epithelial or unknown histologies (94.5%), had high-grade tumors (poorly differentiated or undifferentiated) (77.6%), and had received some form of treatment (chemotherapy, radiation, and/or surgery) (85.3%). Approximately half were married (49.1%) and cases were diagnosed equally across the 5-year diagnosis period. A little over half of the cases were alive 3-years post- diagnosis (48.9%).

For women living in census tracts with the highest poverty, the average age at diagnosis was 63.3 years. Additionally, women living in high poverty were primarily White (53.4%), not married (single, divorced, separated, or widowed) (63.6%), diagnosed in an advanced stage (59.8%), had epithelial or unknown histologies (93.9%), had high-grade tumors (80.6%), and received treatment (76.6%). Similarly, the average age at diagnosis for women living in areas with little to no poverty was 59.8 years. The women living in these census tracts were predominantly White (88.5%) and married (59.6%). Like their counterparts living in high poverty, they were more likely to be diagnosed at an advanced stage (54.6%), have epithelial or unknown histologies (95.9%), have high-grade tumors (75.2%), and have had treatment (89.5%).

Table 2 provides the descriptive characteristics of the main analytic cohort by outcome, 3-year cause-specific survival. Women who died within 3 years of diagnosis were more likely to live in high poverty areas than women who survived

3 years post-diagnosis (25.0% vs. 15.9%). Additionally, women who died were significantly more likely to be older (67.8 vs. 55.5 years), black (23.6% vs. 19.5%) not married (61.4% vs. 39.7%), diagnosed at an advanced stage (72.8% vs. 41.8%), diagnosed with epithelial or other histologies (98.5% vs. 90.4%), have high-grade tumors (85.7% vs. 69.2%), and have not received treatment (25.5% vs. 3.3%) than women who survived 3 years after their diagnosis.

Figure 2 provides three-year cause-specific Kaplan-Meier survival curves for the four levels of poverty. The survival probability is highest for the cases living in census tracts with 0-<5% poverty, and decreases as the percent of poverty increases. A log-rank test showed that the four Kaplan Meier curves were significantly different from each other ($X^2 = 32.36$, p-value <.0001).

Three-year relative survival was calculated for each poverty category using year and age-specific life tables for U.S. females. Additionally, 3-year unadjusted cause-specific survival estimates were calculated for comparison. Table 3 compares the 3-year cause-specific and relative survival estimates and the associated 95% CIs. Women living in the highest poverty level category had the lowest 3-year relative survival and relative survival decreased as poverty level increased (63.5% vs. 55.2% vs. 50.5% vs. 38.4%). When higher order cancers were included in the analysis, 3-year relative survival increased for the highest poverty level, but a similar pattern of decreasing survival with increasing poverty was seen (64.6% vs. 56.0% vs. 52.0% vs. 38.6%). Cause-specific survival was higher than relative survival for women in the two lowest poverty categories (0-<5% and 5-<10%), but higher than relative survival for women in the two highest

poverty categories (10-<20% and 20-100%). A similar result was found when higher order cancers were included in the analysis.

Three-year adjusted cause-specific survival was estimated using Cox proportional hazards modeling for cases diagnosed from 2001-2005 with mortality follow-up until 2008. Hazard Ratios (HR) by poverty level were adjusted for age at diagnosis, race, marital status, histology, grade, stage, treatment, and significant interaction terms. There was statistically significant interaction of marital status with treatment and treatment with stage. Table 4 provides the results of the 3-year cause-specific analysis. The highest poverty category (20-100%) had a significant HR of 1.44 (95% CI: 1.18, 1.76) when compared to the lowest poverty category (0-<5%). When cases with higher order cancers were included in the analysis, the HR for the highest poverty level was significant and increased to 1.48 (95% CI: 1.23, 1.78). Similarly, the HR for cases living in census tracts with 5-<10% was also significant (HR (95% CI) = 1.20 (1.00, 1.43)). For cases living in census tracts with 10-<20% poverty, the HR was borderline significant (HR (95%CI) = 1.17 (0.99, 1.38)).

Women who were diagnosed at regional or distant stage or with an epithelial or unknown histology had significantly higher HRs than women who were diagnosed with localized cancer or with germ cell or sex cord-stromal tumors. Women with poorly differentiated and undifferentiated tumors also had significantly higher HRs than women with well differentiated or moderately differentiated tumors. Age at diagnosis was also a significant predictor of survival, with each year of age significantly associated with a higher HR. Finally, not receiving treatment significantly decreased survival when controlling for

significant interaction terms. Similar results were found when the analysis included second or higher order.

Discussion

Disparities in several health outcomes are partially attributable to differences in SES(1). In addition to previous research on socioeconomic disparities in health, studies have also shown that SES can negatively impact cancer survival. Most studies attribute socioeconomic disparities in cancer survival due to delays in diagnosis and differences in treatment, however, these two factors do not fully explain the disparities observed (2). Relatively little is known about the impact of SES on ovarian cancer survival in particular, however. The results from this analysis show that poverty level is significantly associated with ovarian cancer survival. This relationship holds for women living in areas with high poverty (20-100%) even when the results are adjusted for age at diagnosis, race, marital status, stage at diagnosis, histology, grade, and treatment. Furthermore, when the analytic dataset is expanded to include higher order cancers two poverty levels are significantly associated with lower 3-year cause-specific survival.

Disparities in health outcomes are becoming an increasingly important topic to public health professionals. Healthy People 2020, the Department of Health's agenda for improving the health of the U.S. population over the next decade, includes achieving health equity and eliminating health disparities(51). This study supports the goals of Healthy People 2020 by identifying the disparities in ovarian cancer survival in Georgian women. Though this study was limited to the state of Georgia due to the fact that census based poverty does not exist in publically available national datasets, similar results may be found in different settings throughout the U.S.

The area-based measure of SES used for this analysis was the percent of persons in a given census tract living below the Federal Poverty Level. Cancer registries do not routinely collect individual-level socioeconomic data, such as income or education level. Thus, studies typically use an area-based measure of socioeconomic status for each case. The Public Health Disparities Geocoding Project researched different area-based measures in order to determine which measure was the most appropriate for examining health disparities and found that census tract poverty level was the best method as it was the most robust measure and was easy to interpret. It accurately and consistently found expected gradients in various health outcomes due to SES. Additionally, this study used the same categories for poverty level as suggested by the Public Health Disparities Geocoding Project (0-<5%, 5-<10%, 10-<20%, and 20% or greater)(20).

Cancer patients with a prior or subsequent primary cancer diagnosis may have lower overall survival than patients with only one primary diagnosis. Previous research has excluded these cases in the analysis; however, a more recent trend is to include all higher order cancers except those from the same cancer site(52, 53). This study conducted a secondary analysis to determine if including higher order cancers in the analytic cohort would alter the results. We found that with the addition of higher order cancers SES remained a significant predictor of ovarian cancer survival for high poverty and become a significant predictor of survival for moderate poverty.

Multivariate survival analysis is beneficial because it allows the researcher to simultaneously adjust for several different covariates in an analysis. The

primary purpose of this study was to examine the impact of SES on cause-specific survival adjusting for potential confounding variables. Some researchers have argued that cause-specific survival may not be the most accurate methodology for analyzing cancer survival, and instead relative survival analysis should be used(54). Relative survival compares the total observed mortality of a cohort – including deaths from causes other than the cancer of interest – to their expected background mortality based on relevant life tables. Cause-specific survival analysis, however, counts only deaths from the specific cancer of interest as an event, thus the accuracy of cause-specific survival relies upon accurate and consistent coding of causes of death on death certificates. Recent improvements in coding of cause of death have been incorporated into cancer registries, improving the accuracy of cause-specific survival. The newer cause of death coding considers sequence of tumor occurrence, site of the original primary cancer diagnosis and the underlying cause of death. This coding allows deaths that were attributable to the cancer but not necessarily coded as a cause-specific death to be coded correctly and consistently as a cause-specific death(55). Additionally, because ovarian cancer is particularly fatal, there is less of a chance for misclassification of death, thus, improving the reliability of cause-specific estimates.

Though methods for multivariate regression modeling for relative survival have recently been developed, appropriate life tables are needed to conduct an accurate analysis(56). The National Center for Health Statistics produces age-, race-, and sex-specific national life tables for the U.S., but does not have state-specific or SES-specific life tables. Therefore, 3-year relative survival was

estimated using age- and year-specific life tables without adjusting for additional covariates and compared with 3-year unadjusted cause-specific survival. Relative survival overestimated 3-year survival for the analysis for women living in the two highest poverty categories and underestimated survival for women living in the two lowest poverty categories. This overestimation is likely due to the use of life tables not specific to different deprivation levels and women living in the two highest poverty categories having a higher background mortality rate than the national average included in the life table. Similarly, the underestimation is likely due to the fact that women living in low poverty have lower background mortality than the national average.

Strengths

The impact of SES on ovarian cancer survival has not been researched in detail. This work addresses a gap in ovarian cancer research by assessing the impact of SES on ovarian cancer survival. This study used census tract poverty level which has previously been shown as the best area-based measure of SES for measuring health disparities. The sample size for analysis was large (n=2037) and came from a population-based cancer registry.

Limitations

One of the limitations of this study is the lack of individual-level SES data. While an adequate area-based measure was used, this measure may not be an accurate measure of SES for each individual case and could be categorizing individuals incorrectly. Furthermore, deprivation-specific life tables are not

available for the U.S. population. Therefore, for the relative survival analysis background mortality was calculated assuming that mortality remained the same for each poverty category. Because SES has been shown to negatively impact health, the use of life tables that are not deprivation-specific may not be appropriate. Furthermore, the life tables used were for the entire country and not specific to the state of Georgia. While the impact of SES on treatment and stage at diagnosis is relatively unknown, the relationship between SES and ovarian cancer survival could be biased due to overadjustment if SES directly affects these variables. Additionally, we were unable to adjust for insurance status, which could influence survival. When conducting the secondary analysis including second or higher primaries, we did not adjust for higher order cancers in our analysis. Finally, our study is limited to women diagnosed in Georgia and may not be representative of the U.S. as a whole.

Future Directions

This study has shown that living in poverty can negatively impact ovarian cancer survival among Georgian women. Further research is needed to determine if this relationship holds in different populations. Additionally, research is needed to decompose the relationship between SES and survival to determine what interventions are needed and would be successful. Furthermore, this study supports the development of deprivation- and state-specific life tables for the U.S. in order to conduct an accurate relative survival analysis.

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Tables

Table 1. Descriptive characteristics of Ovarian Cancer Cases Diagnosed in Georgia from 2001-2005 by Poverty Level.

	Total	% Below Poverty Level				
		0-<5%	5-<10%	10-<20%	20-100%	
	(n = 2037)	(n = 436)	(n = 483)	(n = 700)	(n = 418)	
Outcome and Covariates	n(%)	n(%)	n(%)	n(%)	n(%)	**p-value**
Died from Ovarian Cancer†						<.0001*
No	995 (48.85)	255 (58.49)	250 (51.76)	332 (47.43)	158 (37.80)	
Yes	1042 (51.15)	181 (41.51)	233 (48.24)	368 (52.57)	260 (62.20)	
Age at Diagnosis (Years)						0.0001**
mean(SE)	61.81 (15.88)	59.79 (15.33)	60.75 (15.16)	62.89 (16.25)	63.31 (16.38)	
Race						<.0001*
White	1564 (76.78)	386 (88.53)	402 (83.23)	553 (79.00)	223 (53.35)	
Black	440 (21.60)	37 (8.49)	70 (14.49)	140 (20.00)	193 (46.17)	
Other	33 (1.62)	13 (2.98)	11 (2.28)	7 (1.00)	2 (0.48)	
Marital Status						<.0001*
Married	1002 (49.19)	260 (59.63)	279 (57.76)	311 (44.43)	152 (36.36)	
Not Married	1035 (50.81)	176 (40.37)	204 (42.24)	389 (55.57)	266 (63.64)	
Year of Diagnosis						<.0001*
2001	437 (21.45)	113 (25.92)	97 (20.08)	154 (22.00)	73 (17.46)	
2002	419 (20.57)	91 (20.87)	104 (21.53)	151 (21.57)	73 (17.46)	
2003	390 (19.15)	84 (19.27)	85 (17.60)	143 (20.43)	78 (18.66)	
2004	389 (19.10)	98 (22.48)	99 (20.50)	115 (16.43)	77 (18.42)	
2005	402 (19.73)	50 (11.47)	90 (20.29)	137 (19.57)	117 (27.99)	

*Chi-square test, 0.05 significance level

**ANOVA test, 0.05 significance level

†Cause-specific death from ovarian cancer within three years of diagnosis, otherwise censored and assumed alive.

Table 1. Descriptive characteristics of Ovarian Cancer Cases Diagnosed in Georgia from 2001-2005 by Poverty Level.

	Total	% Below Poverty Level				
		0-<5%	5-<10%	10-<20%	20-100%	
	(n = 2037)	(n = 436)	(n = 483)	(n = 700)	(n = 418)	
Outcome and Covariates	n(%)	n(%)	n(%)	n(%)	n(%)	**p-value**
Summary Stage at Diagnosis						0.2232*
Localized	308 (15.12)	78 (17.89)	67 (13.87)	107 (15.29)	56 (13.40)	
Regional	409 (20.08)	96 (22.02)	94 (19.46)	145 (20.71)	74 (17.70)	
Distant	1175 (57.68)	238 (54.59)	291 (60.25)	396 (56.57)	250 (59.81)	
Unstaged	145 (7.12)	24 (5.50)	31 (6.42)	52 (7.43)	38 (9.09)	
Histology						0.1567*
Germ Cell/Sex Cord-Stromal	112 (5.50)	18 (4.13)	33 (6.83)	33 (4.71)	28 (6.70)	
Epithelial/Other	1925 (94.50)	418 (95.87)	450 (93.17)	667 (95.29)	390 (93.30)	
Grade						0.2668*
Low	456 (22.39)	108 (24.77)	105 (21.74)	162 (23.14)	81 (19.38)	
High	1581 (77.61)	328 (75.23)	378 (78.26)	538 (76.86)	337 (80.62)	
Received Treatment						<.0001*
Yes	1738 (85.32)	390 (89.45)	430 (89.03)	598 (85.43)	320 (76.56)	
No	299 (14.68)	46 (10.55)	53 (10.97)	102 (14.57)	98 (23.44)	

*Chi-square test, 0.05 significance level

**ANOVA test, 0.05 significance level

†Cause-specific death from ovarian cancer within three years of diagnosis, otherwise censored and assumed alive.

Table 2. Descriptive characteristics of Ovarian Cancer Cases Diagnosed in Georgia from 2001-2005 by Vital Status.

	Total	Died from Ovarian Cancer†		
		No	Yes	
	(n = 2037)	(n = 995)	(n = 1042)	
Exposure and Covariates	n(%)	n(%)	n(%)	**p-value**
Poverty Level				<.0001*
0-<5%	436 (21.40)	255 (25.63)	181 (17.37)	
5-<10%	483 (23.71)	250 (25.13)	233 (22.36)	
10-<20%	700 (34.36)	332 (33.37)	368 (35.32)	
20-100%	418 (20.52)	158 (15.88)	260 (24.95)	
Age at Diagnosis (Years)				<.0001**
mean(SE)	61.81 (15.88)	55.49 (15.14)	67.83 (14.14)	
Race				0.0140*
White	1564 (76.78)	780 (78.39)	784 (75.24)	
Black	440 (21.60)	194 (19.50)	246 (23.61)	
Other	33 (1.62)	21 (2.11)	12 (1.15)	
Marital Status				<.0001*
Married	1002 (49.19)	600 (60.30)	402 (38.58)	
Not Married	1035 (50.81)	395 (39.70)	640 (61.42)	
Year of Diagnosis				0.2389*
2001	437 (21.45)	222 (21.31)	215 (21.61)	
2002	419 (20.57)	208 (19.96)	211 (21.21)	
2003	390 (19.15)	215 (20.63)	175 (17.59)	
2004	389 (19.10)	206 (19.77)	183 (18.39)	
2005	402 (19.73)	191 (18.33)	211 (21.21)	

*Chi-square test, 0.05 significance level

**Two-sample independent t-test, 0.05 significance level

†Cause-specific death from ovarian cancer within three years of diagnosis, otherwise censored and assumed alive.

Table 2. Descriptive characteristics of Ovarian Cancer Cases Diagnosed in Georgia from 2001-2005 by Vital Status.

	Total	Died from Ovarian Cancer†		
		No	Yes	
	(n = 2037)	(n = 995)	(n = 1042)	
Exposure and Covariates	n(%)	n(%)	n(%)	**p-value**
Summary Stage at Diagnosis				<.0001*
Localized	308 (15.12)	278 (27.94)	30 (2.88)	
Regional	409 (20.08)	259 (26.03)	150 (14.40)	
Distant	1175 (57.68)	416 (41.81)	759 (72.84)	
Unstaged	145 (7.12)	42 (4.22)	103 (9.88)	
Histology				<.0001*
Germ Cell/Sex Cord-Stromal	112 (5.50)	96 (9.65)	16 (1.54)	
Epithelial/Other	1925 (94.50)	899 (90.35)	1026 (98.46)	
Grade				<.0001*
Low	456 (22.39)	307 (30.85)	149 (14.30)	
High	1581 (77.61)	688 (69.15)	893 (85.70)	
Received Treatment				<.0001*
Yes	1738 (85.32)	962 (96.68)	776 (74.47)	
No	299 (14.68)	33 (3.32)	266 (25.53)	

*Chi-square test, 0.05 significance level

**Two-sample independent t-test, 0.05 significance level

†Cause-specific death from ovarian cancer within three years of diagnosis, otherwise censored and assumed alive.

Table 3. Three-year Cause-Specific and Relative Survival By Poverty Level

	First Cancer Only					
% Poverty Level	Cause-Specific Survival (%)	95% CI Lower	95% CI Upper	Relative Survival (%)	95% CI Lower	95% CI Upper
0-<5%	61.43	59.05	63.81	63.50	58.32	68.22
5-<10%	54.03	51.72	56.34	55.23	50.27	59.89
10-<20%	51.62	49.67	53.57	50.51	46.36	54.51
20-100%	43.26	40.71	45.81	38.41	33.35	43.44

	First and Higher Order Cancers					
% Poverty Level	Cause-Specific Survival (%)	95% CI Lower	95% CI Upper	Relative Survival (%)	95% CI Lower	95% CI Upper
0-<5%	62.79	60.69	64.89	64.58	60.01	68.76
5-<10%	55.13	53.07	57.19	56.03	51.63	60.20
10-<20%	52.94	51.15	54.73	52.03	48.21	55.71
20-100%	43.66	41.27	46.05	38.62	33.85	43.36

Table 4. Three-year Adjusted Hazard Ratios (HR)† for Ovarian Cancer Cases in Georgia.

	First and Only				First and Higher Order			
	HR	95% CI Lower	95% CI Upper	P-value	HR	95% CI Lower	95% CI Upper	P-value
% Poverty Level								
0-<5%	1.00			*ref*	1.00			*ref*
5-<10%	1.15	0.95	1.40	0.1504	1.20	1.00	1.43	0.0448
10-<20%	1.16	0.96	1.39	0.1174	1.17	0.99	1.38	0.0629
20-100%	1.44	1.18	1.76	0.0003	1.48	1.23	1.78	<.0001
Age at Diagnosis	1.03	1.02	1.03	<.0001	1.03	1.02	1.03	<.0001
Race								
White	1.00			*ref*	1.00			*ref*
Black	1.14	0.97	1.33	0.1075	1.14	0.99	1.31	0.0762
Other	1.10	0.62	1.96	0.7393	1.07	0.62	1.85	0.8206
Marital Status								
Married	1.00			*ref*	1.00			*ref*
Not Married	1.15	0.84	1.57	0.3780	1.01	0.77	1.31	0.9638

†Significant interaction terms (marital status and treatment; treatment and stage) included in the model

Table 4. Three-year Adjusted Hazard Ratios (HR)† for Ovarian Cancer Cases in Georgia.

	First and Only				First and Higher Order			
	HR	95% CI Lower	95% CI Upper	P-value	HR	95% CI Lower	95% CI Upper	P-value
Summary Stage								
Local	1.00			*ref*	1.00			*ref*
Regional	6.13	3.66	10.25	<.0001	6.83	4.23	11.03	<.0001
Distant	6.81	4.70	9.87	<.0001	6.85	4.88	9.62	<.0001
Unstaged	3.89	2.17	6.97	<.0001	3.20	2.11	4.86	<.0001
Histology								
Germ Cell/Sex Cord	1.00			*ref*	1.00			*ref*
Epithelial/Other	1.96	1.18	3.25	0.0091	1.84	1.13	2.99	0.0148
Grade								
Low Grade	1.00			*ref*	1.00			*ref*
High Grade	1.23	1.03	1.47	0.0244	1.25	1.06	1.48	0.0071
Received Treatment								
Yes	1.00			*ref*	1.00			*ref*
No	4.66	3.46	6.28	<.0001	0.20	0.15	0.26	<.0001

†Significant interaction terms (marital status and treatment; treatment and stage) included in the model

Figures

Figure 1. Exclusions flow chart

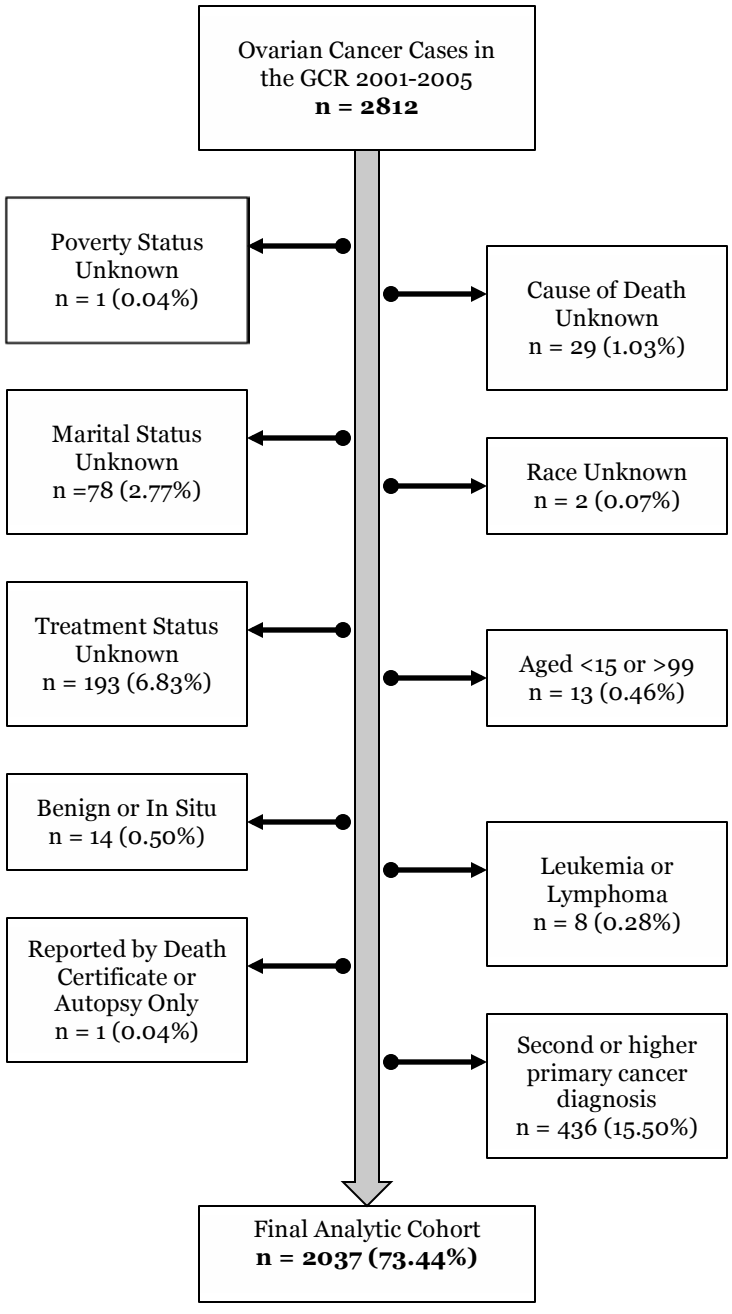
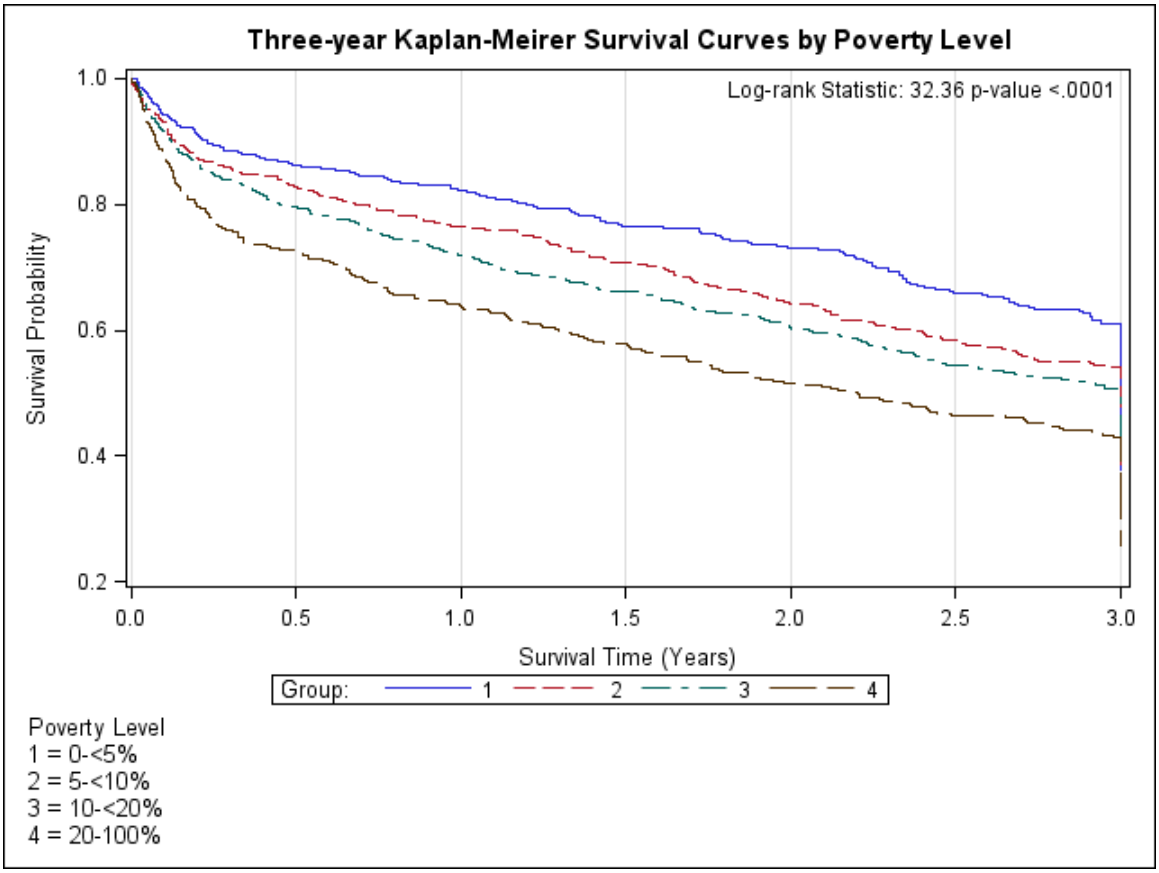


Figure 2. Kaplan-Meier Survival Curves by Poverty Group



EMORY UNIVERSITY

Institutional Review Board

TO: Lisa Matz
Principal Investigator
Public Health

DATE: December 7, 2012

RE: **Expedited Approval**
IRB00062327
The impact of socioeconomic status on ovarian cancer outcome among Georgia women.

Thank you for submitting a new application for this protocol. This research is eligible for expedited review under 45 CFR.46.110 and/or 21 CFR 56.110 because it poses minimal risk and fits the regulatory category F5 as set forth in the Federal Register. The Emory IRB reviewed it by expedited process on 12/6/2012 and granted approval effective from **12/6/2012** through **12/5/2013**. Thereafter, continuation of human subjects research activities requires the submission of a renewal application, which must be reviewed and approved by the IRB prior to the expiration date noted above. Please note carefully the following items with respect to this approval:

- A full waiver of consent/HIPAA was granted

Any reportable events (e.g., unanticipated problems involving risk to subjects or others, noncompliance, breaches of confidentiality, HIPAA violations, protocol deviations) must be reported to the IRB according to our Policies & Procedures at www.irb.emory.edu, immediately, promptly, or periodically. Be sure to check the reporting guidance and contact us if you have questions. Terms and conditions of sponsors, if any, also apply to reporting.

Before implementing any change to this protocol (including but not limited to sample size, informed consent, study design, you must submit an amendment request and secure IRB approval.

In future correspondence about this matter, please refer to the IRB file ID, name of the Principal Investigator, and study title. Thank you

Andrea Goosen, MPH, CIP

Research Protocol Analyst
This letter has been digitally signed

CC: There are no items to display

Ward Kevin Epidemiology

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