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Dr. Corrine Williams, Director of Graduate Studies

Impact of Health Insurance and Sociodemographic Characteristics on Survival for Women diagnosed with Breast Cancer in Kentucky

CAPSTONE PROJECT PAPER

A paper submitted in partial fulfillment of the
requirements for the degree of
Master of Public Health
in the
University of Kentucky, College of Public Health
By
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Lexington, Kentucky
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Pramila Rai

ABSTRACT

Introduction Objective of the study was to explore the impact of health insurance and socio-demographic factors on survival for breast cancer patients in Kentucky. Breast cancer is the most prevalent cancer among women in the US. Breast cancer survival is affected by various factors including health insurance, residence, age, race, geographical distance, income.

Methods The data were obtained from Kentucky Cancer Registry and included 47,128 women diagnosed with primary breast cancer between 2000 to 2014. The relationship of health insurance and other socio-demographic factors was analyzed using Cox regression.

Results The overall five-year survival proportion was 0.97, 0.76 and 0.71 respectively for privately insured, Medicaid and Medicare patients. Medicaid and Medicare patients had 1.89 (95% CI, 1.71-2.10), 1.96 (95% CI, 1.75-2.18) times higher hazard of dying respectively compared to privately insured patients. Patients who had no family history of breast cancer had a 15% (HR=1.15, p-value<0.001) higher hazard of dying compared to those having family history of breast cancer. Tobacco use and marital status also had significant effect on patient's survival. Other tumor related and biological factors were also included in the regression model. Sub group analysis by SEER summary stage also showed that Medicaid and Medicare patients significantly at disadvantage compared to privately insured patients for both in-situ and regional stage groups. Medicaid patients had 1.41(HR=1.41, p-value=0.0020) times higher hazard of death compared to privately insured patients whereas Medicare patients and the privately insured patients had no difference in hazard of death for distant stage group. Sub group analysis by age group also showed Medicare and Medicaid patients are disadvantaged compared to privately insured patients for all age groups.

Conclusion This study found that Medicaid and Medicare patients had higher hazard of dying compared to privately insured patients. This helps to inform public health professionals and policy makers for advocacy and design policies that bring equal health outcomes regardless of insurance types.

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ACRONYMS AND ABBREVIATIONS

KCR- Kentucky Cancer Registry

SEER- Surveillance Epidemiology and End Results

FFS- Fee for Service

HMO- Health Maintenance Organization

ER- Estrogen Receptor

PR- Progesterone Receptor

HR- Hazard Ratio

BACKGROUND

Breast cancer is one of the most commonly occurring cancers among women worldwide¹ and in the United States (US).² About one in eight women develop invasive breast cancer over the course of their lifetime² and an estimated 3,327,552 women were living with breast cancer in 2014³; and 236,968 women were diagnosed with breast cancer while 41,211 women died from breast cancer in the US in the same year.⁴ It is estimated that 266,120 women will be diagnosed with breast cancer in 2018. However, the relatively higher survival probability (i.e. 89.7%) of five years or more for breast cancer patients is positive outcome.⁵ Nevertheless, there is noticeable disparity in survival probability of patients depending on the type of health insurance and other socio-demographic factors.

Health insurance is a mechanism through which a person's health care expenses are financed. There are different types of health insurance coverage in the US. Health insurance policy can be broadly categorized into public and private health insurance plans, which can further be identified into different sub-types. Public health insurance is provided with Medicaid, Medicare and military coverage. Private health insurance is primarily provided with employer-based insurance, followed by direct-purchase private plan.⁶

Health insurance has been increasingly recognized as a modifiable policy determinant that affects the health of individuals. Studies have found that uninsured and Medicaid insured breast cancer patients have poorer outcomes than cancer patients with private insurance.⁷⁻¹¹ Health insurance not only affects the survival of a patient after diagnosis, it also affects the survival and quality of life through differential access to screening and thus stage at diagnosis. A higher proportion of uninsured and Medicaid patients are diagnosed with stage III and stage IV compared to privately insured patients.¹² Several factors including race, ethnicity, sociodemographic status, age, and reproductive factors affect the incidence and the mortality pattern of breast cancer in a population.^{13,14} Substantial and consistent disparities in quality of cancer care exist according to types of health insurance.¹⁵ Race, stage at the time of diagnosis, and type of tumor also influence the survival probability of patients. African-Americans are less likely to survive compared to other races, an effect mediated by tumor subtypes.¹⁶

Even after many advancements in treatment and greater focus on screening, still 32% of 5% breast cancer patients are identified respectively in regional and distant stage of

tumors in the U.S., resulting in poor outcomes and shorter survival. In addition, breast cancer may be characterized by different molecular subtypes with varying severity^{2,17,18} and survival rates, which contributes additional complexity.

Literature Review

Scientific literature was searched using databases from The National Library of Medicine Database (PubMed) and Google Scholar with query terms, “Breast cancer survival”, “Cancer survival” with “Disparity” “Health Insurance”, “Medicare”, “Medicaid”, “Managed care systems”, “Private health insurance”, “Sociodemographic status”, “Race”, “Income”.

A study conducted in metropolitan Detroit explored the relationship between race, socioeconomic status, and breast cancer treatment and survival, and found race was not significantly associated with survival. Low socioeconomic status, however, showed a clear association with late-stage breast cancer at diagnosis, type of treatment received and death.^{13,14} According to Surveillance, Epidemiology, and End Results (SEER) data in the 2000s, in the white population, breast cancer incidence was 127.4 per 100,000 annually, mortality was 12.3 per 100,000, and five-year survival was 90.4%. In the African American population, however, incidence was 121.4 per 1000 population, mortality rate was 18.2 per 100,000, and five- year survival was 78.6%, signifying huge disparities based on background characteristics.¹³

Furthermore, many studies highlighted that breast cancer survival and cancer screening are lower when breast cancer patients had no health insurance^{12, 19, 20} drawing the attention of health care professionals towards this issue. Not only the lack of health insurance, but the type of health insurance a patient has been found to play a role. Privately insured women have, in general, a more favorable stage of disease at breast cancer diagnosis than do women who are insured through Medicare or Medicaid whereas uninsured women have the least favorable outcome compared to other groups.¹⁴

A study conducted in California among the Latina ethnic group found lack of health insurance coverage to be strongest predictor of cancer screening underutilization.¹⁹ This gives rise to the number of women seeking health care at relatively advanced stage of the breast cancer further leading to risk of high mortality. Similarly, a study conducted in

Florida among female breast cancer patients diagnosed between 2007 and 2010 found that survival was worse for uninsured patients than privately insured patients with all stages.²⁰

In an older study conducted in 1993 by Ayanina et al., the adjusted risk of death in breast cancer patients was 49% higher for uninsured patients and 40% higher for Medicaid patients than for privately insured patients during the 54-89 months after diagnosis.²¹

In another study conducted in Kentucky the three-year relative survival proportion of patients with breast cancer was 91% for the privately insured and 78% for uninsured patients. This clearly indicates favorable outcome for privately insured patients. This study also discovered the patients with Medicaid insurance had lower survival proportion compared to privately insured patients with other cancers such as prostate cancer, colorectal cancer and lung cancer too.²²

Access to health insurance influences the frequency and quality of health care, types of health care services and providers. Thus the insurance status of cancer patients may play important role in their survival. A New Zealand study that included 14,468 patients, there were differences in the characteristics of the patients themselves and the risk of mortality depending upon the type of health care centers they utilized for the treatment. Patients, treated in public centers, were older, belonged to minority ethnic groups, resided in poor neighborhoods and rural areas were less likely to be diagnosed with early staged cancer and to receive timely cancer treatments compared to women, who utilized private health centers. They also had a higher (14% more) risk of mortality from breast cancer, even after controlling for baseline demographic, disease and treatment factors.²³ A retrospective cohort study conducted among patients registered in the Texas cancer registry found that those younger than 65 years without health insurance coverage had a significantly higher risk of mortality than those with private health insurance regardless of tumor stage, and treatment types.²⁴ The early detection and the survival rate also varied depending on the health care delivery systems type for patients enrolled under the same insurance program. For this purpose, researchers studied breast care patients enrolled in Medicare, an entitlement health insurance for older age citizen in US. The study found differential outcomes depending on if patients were managed through Health Management Organizations (HMOs) or the Fee for Service (FFS) system. Medicare patients enrolled in HMOs were diagnosed at an earlier stage than FFS patients. HMO patients diagnosed with

breast and colorectal cancer had improved survival, and these differences remained even after controlling for potential confounders such as stage at diagnosis, age, race, socioeconomic status, and marital status. Patients enrolled in HMOs had 9% greater survival in hazards ratio if they had breast cancer, and 6% greater survival if they had colorectal cancer.²⁵ Survival probability differs between blacks and whites even if they are diagnosed at similar stages of illness.²⁶

Similarly, the geographic residence of the patients also affects the survival of breast cancer patients. A study looking at the effect of distance from diagnostic hospital on screening found that 62% of total patients with distances greater than 20 km (n=347) had a late stage at diagnosis compared to 50% with distances less than 20 km. The risk of late stage at diagnosis significantly increased by 1.25-fold for each 30 Km increase in distance.²⁷

A study by Shi et al. found that compared to white patients, black patients had a 31% (1.31) increase, and other race had a 22% (0.78) decrease risk of death among breast cancer patients. Patients with higher comorbidity index ≥ 2 (2.27) and 1 (1.43) Charlson Comorbidity were more likely to die than those with no comorbid conditions.¹²

Other studies have also reported that insurance types, race/ethnicity, comorbidity, geographic region or residence were associated with tumor stage at the time of diagnosis and increased risk of deaths in breast cancer patients.^{16, 26,28,29} A study by Warner et al. found blacks had a 21% higher risk of breast cancer-specific death in multivariate adjusted models and the survival difference was prominent in estrogen receptor-positive tumors. Blacks were 76% and 56% more likely to die as a result of Luminal A-like and Luminal-B like tumors respectively, compared to their white counterparts.¹⁶ Survival was primarily different in those tumors for which survival could have been lengthened by hormonal treatment.

Previous research has shown that survival of female breast cancer patients is affected by numerous factors including health insurance, race, comorbidity, hormonal receptor status, stage at the time of diagnosis, and geographical location. Patients are likely to have better survival if they have private insurance followed by Medicare. The effect of insurance on cancer survival in Kentucky is understudied and this present study seeks to fill that gap by exploring the effect of health insurance for female breast cancer patients of Kentucky.

The primary objective of the study was to evaluate the effect of health insurance types on the survival of breast cancer patients, and type of treatment patients utilize. The secondary objective was to assess other socio-demographic, biological factors that affect survival of the patients.

Research Question. Do the types of health insurance affect survival of the breast cancer patients?

METHODS

This was a retrospective cohort study which included secondary analysis of existing data from the Kentucky Cancer Registry (KCR).

Study population. The study included women aged 19 or older with a primary diagnosis of breast cancer registered in the KCR. There were 47,128 total patients diagnosed with primary breast cancer from 2000 to 2015. Patients with missing information on health insurance status and types or insurance other than Medicare and Medicaid were excluded from the study. Patients, who were in TRICARE, military personnel or their dependents who are treated as a military facility, veterans who are treated in Veterans Affairs facilities, Indian/Public Health service patients who receives care at an Indian Health Service facility and costs are reimbursed by the Indian Health Service were also excluded from the study. Hence, there were 39, 271 patients had complete information on payer status.

Data source and study population. This study included women aged 19 and older diagnosed with primary breast cancer and registered in the Kentucky Cancer Registry from 2000 to 2015. Data was from Kentucky Cancer Registry (KCR). KCR is a statewide population-based registry that serves as the foundation for measuring the Kentucky cancer burden, comprehensive cancer control efforts, health disparities, progress in prevention, diagnosis, treatment and survivorship. Data are collected for the types of cancers, disease stage, types of first course treatment received by patients, and patient characteristics.

Study Variables

Outcome variable

The outcome variables for this study were five-year and ten-year survival. Length of survival was defined as time from the date of diagnosis to a 60 months and 120 months.

Independent variable

Primary independent variables. Health Insurance status of the breast cancer patients was the primary independent variable. The health insurance status of the patients at the time of diagnosis was categorized into three different levels: (1) Public Health Insurance e.g., Medicaid and Medicare (2) Private Health Insurance; and (3) No Health Insurance.

Secondary independent variables. In addition to type of treatment, the analysis included socio-demographic factors as well as specifics about cancer type (e.g., biological and tumor factors).

Type of treatment

For this analysis, four categories were defined: (1) no intervention, (2) surgery at primary site only, (3) other combination of treatment except surgery and (4) surgery at primary site and at least other type of therapies.

Socio-demographic factors

- Appalachia: Kentucky can be divided into geographical regions of Appalachia and non-Appalachia. Appalachian region is a cultural region of Appalachia that spreads along the spine of the Appalachian Mountains. The levels of Appalachia are residents of Appalachia=0, residents of non-Appalachia=1.
- Race: Depending on the proportion of racial groups, the participants were categorized into one of three categories: 0= African American, 1= Other, 2=Caucasian.
- Age of the patient at the time of diagnosis: Categorized into three groups (19-39, 40-64, equal to or over 65 years).
- Marital status: Classified into three categories (1) single; (2) married and not living with partners, including widowed, separated, divorced; and (3) married.
- Family history: Categorized into two groups as family history having breast cancer and without family history of breast cancer.

- Tobacco use: Patients were categorized based on the history of tobacco use as tobacco user, non-user, or unknown.

Biological and tumor factors

- Surveillance, Epidemiology, and End Results (SEER) summary stage of breast cancer at diagnosis: SEER divides the breast cancer patients based on the extent of spread of cancer. It is defined as 1= In-situ and Localized, 2= Regional, 3= Distant.
- Estrogen Receptor (ER) and Progesterone Receptor (PR) status: Estrogen receptor status was dichotomized into 1= ER positive (ER+) and 2= ER negative (ER-). Cases recorded as having a borderline ER will also be classified as ER receptor-positive. Progesterone receptor status was also dichotomized into PR positive (PR+) and PR negative (PR-). Cases recorded as having a borderline PR status will also be classified as PR receptor-
- Menopausal status: Menopausal status was dichotomized into premenopausal status, and postmenopausal status.
- Tumor grade: Tumor grade was categorized into five categories as well differentiated, moderately differentiated, poorly differentiated, undifferentiated, non-high grade.

Data analysis

Data were analyzed using 9.4 version SAS software package. Kaplan-Meier curves and log-rank tests were used to assess the univariate association between breast cancer patient survival, and the types of health insurance. Impact of health insurance was further evaluated by controlling effects of socio-demographic variables, tumor and biological variables and health care related factors with multivariable Cox Proportional model. We also performed sub-group analysis by SEER summary stage and age group to find the effect of health insurance controlling effect of all other variables. We included observations with complete information about all the covariates in multivariable Cox regression. Multivariable Cox proportional hazards models was then used to assess the association between breast cancer patient survival and types of health insurance adjusting for aforementioned other factors. The backward model selection was performed. Significance was set at $p < 0.05$ (2-tailed). We also plotted map of counties of Kentucky corresponding to the number of deaths due to breast cancer during our study period.

Ethical Statement

IRB approval with an exempt application was obtained from the University of Kentucky, Office of Research Integrity and we applied to KCR for release of data along with application and approval letter from IRB, Kentucky Cancer Registry released the dataset upon approval for release. However, we couldn't obtain personal health information such as geographical location of the patient's residence and details about health care facilities and providers due to nature of ethical considerations we obtained and time constraints. KCR doesn't collect information on education and income.

RESULTS

There were 47,128 total female patients diagnosed with primary breast cancer from 2000 to 2015. However, there were only 39,271 observations were included in the study with complete information about the primary payer in file. Out of 39,271 patients, 11,663 had event of death.

The sample description is provided in Table 1. Comparatively higher proportion of the patients were covered under Medicare (47.71%) followed by private (40.84%) and Medicaid (11.45%) insurance scheme. A majority of the patients were Caucasian (92.13%) followed by African American (7.13%) and others constituted 0.74% of the total participants. About half (50.99%) of the patients belonged to 40-65 age category and 44.86% of the patients aged equal to or over 65 years. About a quarter (24.96%) of the total patients belonged to Appalachian region. Majority of the participants (66.90%) were in post-menopausal phase whereas 13.52% of the participants didn't have any information on menopausal status. Significant proportion of the patients (30.79%) had family history of breast cancer. However, 22.44% of the patients didn't have any information on family history. About half (53.14%) of the participants were married and 19.29% were widowed.

A higher percentage of patients (71.94%) had surgery at primary site and at least another type of treatment such as chemotherapy, radiotherapy or other type of therapy. A majority of the patients (53.24%) had localized staging of breast cancer according to SEER summary stage followed by regional, in-situ and distant respectively. Similarly, majority

of patients were estrogen receptor positive (71.26%) and progesterone receptor positive (61.55%). Fewer than half (30.93%) of the breast cancer patients had poorly differentiated tumor.

Table 1: Description of the study population from KCR, 2000 to 2015

Characteristics	Category	Frequency	Percent
Primary Payer	Medicaid	4497	11.45
	Medicare	18737	47.71
	Private	16037	40.84
Race	Caucasian	36182	92.35
	African American	2800	7.15
	Others	196	0.50
Age(years)	19-39	1629	4.15
	40-64	20024	50.99
	≥65	17618	44.86
Appalachia	Non-Appalachian	29469	75.04
	Appalachian	9802	24.96
Marital Status at Diagnosis	Single	3602	9.17
	Married	20869	53.14
	Separated	298	0.76
	Divorced	4508	11.48
	Widowed	7575	19.29
	Unmarried or domestic partner	39	0.10
	Unknown	2380	6.06
Family History	Yes	12090	30.79
	No	18366	46.77
	Unknown	8814	22.44
Menopausal Status	pre-menopausal	7692	19.59
	post-menopausal	26271	66.90
	Unknown	5308	13.52
SEER Summary Stage	In-situ	6225	16.01
	Localized	20701	53.24
	Regional	10001	25.72
	Distant	1953	5.02
ER Status	Positive	27979	71.26
	Negative	7275	18.53
	Unknown	4012	10.22
PR Status	Positive	24170	61.55
	Negative	10764	27.41
	Unknown	4332	11.03

Tumor Grade	Well differentiated	7353	18.72
	Moderately differentiated	15003	38.20
	Poorly differentiated	12145	30.93
	Undifferentiated	892	2.27
	Non-high grade	3878	9.87
Tobacco Use	Never user	19094	49.04
	Cigarette smoker	13331	34.24
	Cigar/pipe smoker	29	0.07
	Snuff/chew/smokeless tobacco user	47	0.12
	Mixed use of more than one type of tobacco product	21	0.05
	Unknown/ not recorded	6416	16.48
Treatment	No intervention	948	2.41
	Surgery at primary site only	8688	22.12
	Surgery at Primary site and other therapy	28253	71.94
	Other combination of therapies other than surgery	1382	3.52

We also mapped the fatality rate of counties to illustrate how deaths were distributed in Kentucky. Figure 1 shows the map of counties corresponding to hazard rate due to breast cancer per county during the period of 2000 to 2015. The hazard of death is most concentrated in counties in Appalachian region and western part of Kentucky.

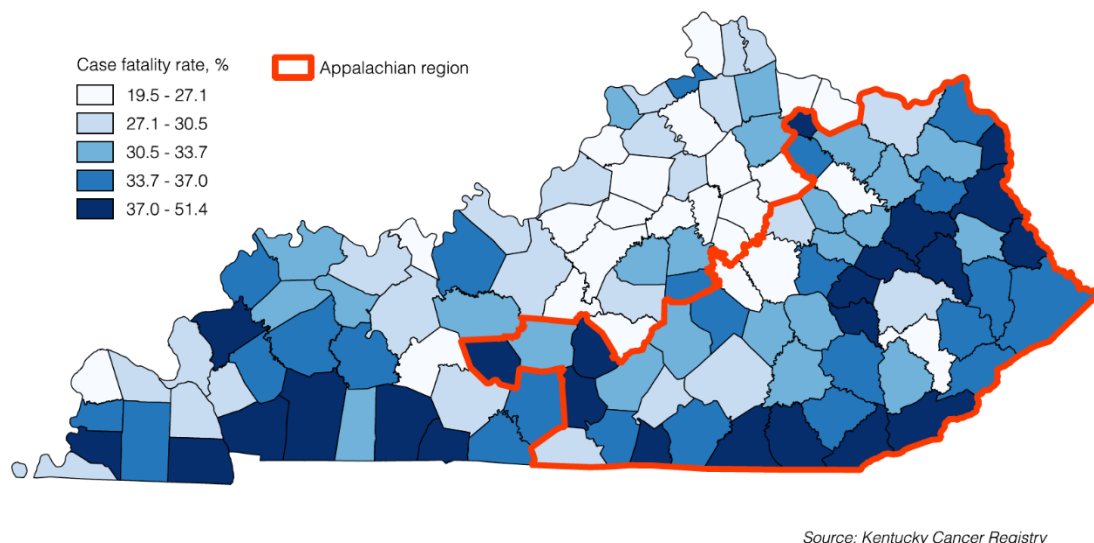


Figure 1: Case fatality rate for breast cancer by county among women, 2000 to 2015.

Univariate effect of health insurance policy on survival for breast cancer patients

We included 39,271 patients for univariate survival analysis using log rank test and a Kaplan Meier survival curves were produced. Out of total 4497 Medicaid enrolled women, 31.02% had event of death; out of 18,737 Medicare enrolled women, 43.81% had event of deaths and out of 16,037 women with private insurance, 12.84 % had event of deaths (Table 2).

Table 2: Number of events per health insurance policy

Insurance Scheme	Total	Death	Censored	Censored %	Death %
Medicaid	4497	1395	3102	68.98	31.02
Medicare	18737	8209	10528	56.19	43.81
Private	16037	2059	13978	87.16	12.84
Missing and other	7857	1895	5962	75.88	24.12

We performed log-rank test to analyze the effect of health insurance on survival probability of women and found significant difference in survival of women in three different health insurance policies. Women in Medicare group had the least survival probability whereas the women in private insurance had higher survival throughout the follow up duration as shown in Figure 2.

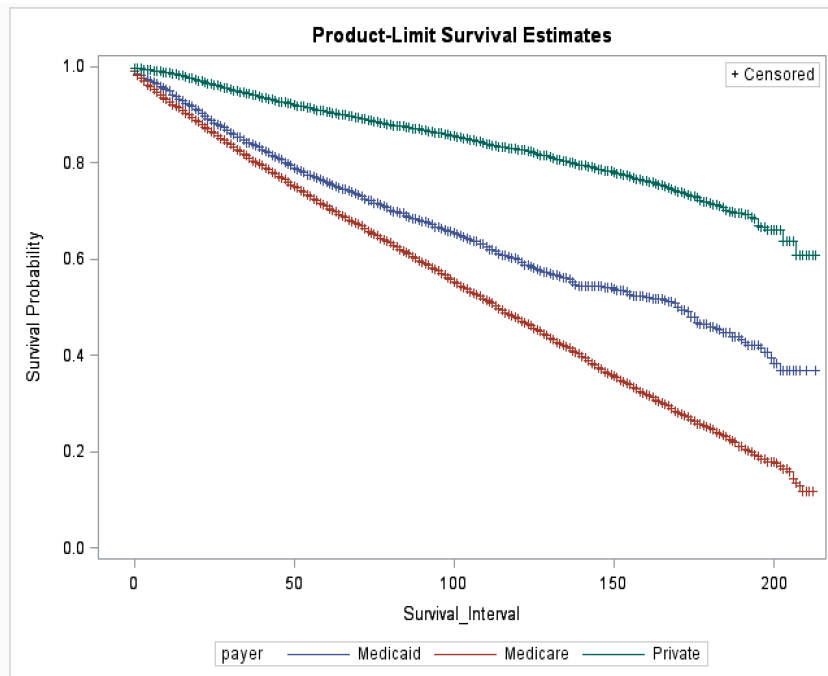


Figure 2: Kaplan Meier survival curve showing survival probability in three different insurance policy

There was a significant difference in survival for women between every one of insurance group with the other two groups of insurance schemes (Table 3).

Table 3: Log-rank test for multiple comparisons of health insurance groups				
Adjustment for Multiple Comparisons for the Log rank Test				
Strata Comparison		Chi-Square	p-value	
payer	payer		Raw	Tukey-Kramer
Medicaid	Medicare	1570.1	<.0001	<.0001
Medicaid	Private	1918.6	<.0001	<.0001
Medicare	Private	3485.9	<.0001	<.0001

The survival probability were 0.97, 0.76, and 0.71 for women with private, Medicaid and Medicare respectively, at 60 months whereas the survival probability was 0.82, 0.60 and 0.48 for women with private, Medicaid and Medicare respectively, at 120 months.

There were 21,473 total cases having complete information of the variables. Among them, 16,089 (74.93%) of the patients didn't have event of deaths due to loss to follow up and the study time frame, and 5384 (25.07%) patients had event of death. There were 21 parameters in the model and the number of events (5384) were enough for this multivariable cox regression.

Multivariable effect of health insurance types on survival for breast cancer patients

Table 4 displays the results of hazard ratio (HR) of death from a multivariable cox regression analysis. After adjusting for secondary factors, health insurance status had significant effect for overall survival of patients. Medicare and Medicaid payer status had significantly increased hazard of dying compared to private, with increase of 96% (HR =1.94 p-value<.0001), 89% (HR=1.88 p-value<.0001) respectively.

There were two direct health care related factors including treatment patients utilized and payer or health insurance status of the patients. Both factors were significantly associated with survival of patient in the hazard model. For the purpose of regression analysis, treatment was categorized into four different levels including a group of no intervention, combination of therapies other than surgery at primary site, surgery at primary

site only and the most comprehensive treatment of surgery at primary site along with at least other treatment alternatives. Compared to women who received no intervention, women having surgery at primary site and at least one other therapy had 0.15 (HR=0.15, p-value<.0001) times less hazard of death. Similarly, patients who got surgery at primary site only had significantly less hazard of death (HR=0.24, p-value<.0001) and patients who received other combination of therapies but no surgery had 0.46 (0.46, p-value<.0001) times less hazard of death compared to women having no intervention at all.

Similarly, other socio-demographic factors such as age, marital status, tobacco use, family history of breast cancer were significantly associated with the hazard of death from breast cancer. However, the geographical location of patients as Appalachia and non-Appalachia and the race of the patients didn't have a significant relationship with the survival of the breast cancer patients when adjusted with other covariates. Women in the 19-39 age group had a 33% (HR=0.67, p-value<.0001) decreased hazard of death compared to women equal to or over 65 years old. Similarly, women in the 40-64 age group had a 41% (HR=0.59, p-value<0.0001) less hazard of death compared to women in the 65 years and older age group.

Patients with no history of tobacco use had a decreased hazard of hazard compared to tobacco users, with a significant decrease of 24% (HR=0.76, p-value<.0001). Women having no family history had a 15% (HR=1.15, p-value≤.0001) higher hazard of death compared to women having family history of breast cancer. Married women or those living with their partners had a 26% (HR =0.74, p-value<.0001) less hazard of death compared to single women whereas women who were widowed, divorced or separated had a 17% (HR=1.17, p-value=0.0045) higher hazard of death from breast cancer compared to single women. Similarly, women in post-menopausal phase had a 16% (HR=1.16, p-value=0.0041) higher hazard of death compared to pre-menopausal women even after adjusting with other covariates.

The tumor and biological co-variates which included tumor grade, estrogen receptor status, progesterone receptor status, SEER summary stage were also significantly associated with survival of breast cancer patient in this cox proportional hazard model. Patients with moderately differentiated and poorly-differentiated tumor grade had statistically increased hazard of death with significant increase of 14% (HR=1.14, p-value

=0.0024) and 39% (HR=1.39, p-value<0.0001) respectively. However, women with undifferentiated and non-high grade tumor didn't have significant effect on hazard of death. Women with estrogen receptor negative breast cancer had a 14% (HR=1.14, p-value=0.0032) higher hazard of death compared to women with estrogen receptor positive breast cancer. Likewise, progesterone receptor negative breast cancer had a 25% (HR=1.25, p-value<.0001) higher hazard of death compared to progesterone receptor positive breast cancer. SEER summary stage also had significant impact on survival for breast cancer patients controlling effect of other variables. Women with distant stage of cancer had a 245% (HR=3.45, p-value<.0001) higher hazard of death whereas women with in-situ and localized cancer had a 53% (HR=0.47, p-value <.0001) less hazard of death respectively compared to women with regional stage of breast cancer.

Table 4: Multivariable Cox Proportional Regression: Hazard Ratio and 95% CI of Hazard ratio per covariate

Group of Covariates	Co-variates and Levels	Level of Covariates	Hazard Ratio	95% CI of Hazard ratio		p-value
				Lower	Upper	
Health care access covariates	Health Insurance	Medicaid	1.89**	1.71	2.10	<.0001
		Medicare	1.96**	1.75	2.18	<.0001
		Private	Ref.			
		Medicaid vs Medicare	0.97	0.86	1.09	
	Treatment	Surgery at Primary site and other therapy	0.15**	0.13	0.18	<.0001
		Surgery at Primary site only	0.24**	0.20	0.29	<.0001
		Other combination of therapies other than surgery	0.46**	0.38	0.56	<.0001
		No intervention	Ref.			
*Socio-Demographic	Age	19-39	0.67**	0.55	0.82	<.0001
		40-64	0.59**	0.54	0.66	<.0001
		≥65	Ref.			
	Appalachia	Appalachia	1.02	0.96	1.09	0.5483
	Non-Appalachia	Non-Appalachia	Ref			
	Race	African-American	1.71	0.91	3.20	0.0940
		Caucasian	1.65	0.89	3.07	0.1143
Others		Ref				

Tumor and Biological Characteristics	Tobacco use	Never user	0.76**	0.72	0.80	<.0001
		Tobacco user	Ref.			
	Family history of breast cancer	No family history	1.15**	1.09	1.22	<.0001
		Have family history	Ref.			
	Marital status	Married	0.74**	0.67	0.81	<.0001
		Not with partners (widowed, divorced, separated)	1.17**	1.06	1.29	0.0045
		Single	Ref.			
	Menopausal status	Post-menopausal status	1.16**	1.05	1.28	0.0041
		Pre-menopausal status	Ref.			
	Tumor grade	Moderately differentiated	1.14**	1.05	1.24	0.0024
		Non-high grade	1.03	0.91	1.16	0.6112
		Poorly-differentiated	1.39**	1.27	1.52	<.0001
		Undifferentiated	0.94	0.75	1.18	0.6060
		Well differentiated	Ref.			
	ER status	Negative	1.14**	1.05	1.25	0.0032
		Positive	Ref.			
	PR status	Negative	1.25**	1.16	1.35	<.0001
		Positive	Ref.			
	SEER summary stage	Distant	3.45**	3.09	3.85	<.0001
		In-situ & localized	0.47**	0.44	0.50	<.0001
	Regional	Ref.				

* KCR doesn't collect information on Education and Income of the patients.

**significance at p-value <0.01

Effect of health insurance types on survival for patients with subgroup analysis by SEER summary stage

We also performed sub-group analysis by SEER summary stage in multivariable Cox hazard model to find the effect of health insurance on survival for the patients in different groups of SEER summary stage (Table 5).

Having private insurance is a highly protective factor for patients in all stages for survival of the patients. Medicaid and Medicare patients had 2.13 (HR=2.13, p-value<.0001) and 2.12 (HR=2.12, p-value<.0001) times higher hazard of death compared to privately insured patients for in-situ and localized groups. Medicaid and Medicare patients had 1.75 (HR=1.75, p-value<.0001) and 1.92 (HR=1.92, p-value<.0001) times higher hazard of death compared to privately insured patients for regional stage group and Medicaid patients had 1.41(HR=1.41, p-value=0.0020) times higher hazard of death compared to privately insured patients whereas Medicare patients and the privately insured patients had no difference in hazard of death for distant stage group.

Having some treatment decreased hazard of death for all stages of cancer. Surgery at primary site and at least one other therapy had lowest hazard of death compared to surgery at primary site only group for patients in all summary stage. Patients, who received surgery at primary site and at least one other therapy had an 88%, 87% and 81% lower hazard of death compared to patients who received no treatment respectively for in-situ, regional and distant stage.

When survival rate was analyzed by stratifying the patients based on summary stage of cancer, age had significant effect on survival for patients with in-situ and localized and regional stage whereas the effect of age was not significant for patients with distant stage. Patients with in-situ and localized stage in age category of 19-39 had a 59% lower hazard of death compared to those in the 65 years or older age group.

Appalachian patients with in-situ and localized breast cancer stage had a 10% (HR=1.10, CI=1.21-1.01) higher hazard of dying compared to non-Appalachian patients whereas the Appalachia status had minimal effect on patients with regional and distant stage. Marital status had significant association with survival of patients in all the stages. Married patients had consistently lower hazard of death compared to single and the participants not living with partners had a comparatively higher hazard of dying.

Participants, who were not living with partners, with localized stage had a 27% (HR=1.27, CI=1.09, 1.48) higher hazard of death compared to single participants.

Never using tobacco was a positive factor for survival for patients with localized and regional stage whereas tobacco use was not significant for survival of patient with distant stage. Patient who never used tobacco were 29% and 26% less likely to die compared to patient who had history of tobacco use for localized and regional stage group respectively. Similarly, having family history of breast cancer had a protective effect on survival for patients diagnosed in localized and regional stage. However, family history had no significant effect for patients with distant stage. Patients with localized breast cancer in post-menopausal phase had a 33% greater hazard of death compared to women in pre-menopausal phase.

Compared to well differentiated tumor grade, patients in distant stages with moderately differentiated tumor had a significantly (82%) higher hazard of death. Similarly, patients with non-high grade in regional and distant stage had a 31% and 68% higher hazard of death. Patients with poorly-differentiated tumor in localized, regional and distant stages had a 1.28, 1.37, and 2.23 times higher hazard of death, respectively. Remarkably, patients with localized cancer with undifferentiated tumor grade had a 24% lower hazard of death compared to patients with well differentiated tumor grade. Negative estrogen receptor status had increased hazard of dying in patients with regional (17%) and distant (33%) stages whereas negative progesterone receptor status had increased hazard of death in patients with localized (21%), regional (30%) and distant (31%) stages.

Estrogen receptor status and race had no significant effect on survival for women with in-situ and localized summary stage patients. Appalachia, menopausal status and race had no significant effect on survival for patients with regional summary stage. Race, menopausal status, tobacco status, family history, Appalachia, and age had no significant effect on survival for women with distant summary stage.

Table 5: Effect of covariates on survival for the patients by SEER summary stage with multivariable Cox proportional hazard model

Covariates	In-situ and Localized			Regional			Distant		
	Hazard ratio	95% CI	p-value	Hazard ratio	95% CI	p-value	Hazard ratio	95% CI	p-value
Health Insurance									
Medicaid	2.13**	1.78,2.54	<.0001	1.75**	1.50,2.03	<.0001	1.41**	1.13,1.76	0.0020
Medicare	2.21**	1.87,2.61	<.0001	1.92**	1.61,2.29	<.0001	1.26	0.95,1.67	0.1078
Private	Ref.			Ref.			Ref.		
Treatment									
Surgery at primary site and other therapy	0.12**	0.09,1.17	<.0001	0.13**	0.08, 0.20	<.0001	0.19**	0.14, 0.25	0.0001
Surgery at Primary site only	0.20**	0.15,0.27	<.0001	0.21**	0.13, 0.32	<.0001	0.45**	0.30, 0.67	<.0001
Other combination of therapies other than surgery	1.03	0.69,151	0.8947	0.39**	0.24, 0.63	<.0001	0.44**	0.34, 0.57	<.0001
No intervention	Ref.			Ref.			Ref.		
Age									
19-39	0.41**	0.28, 0.62	<.0001	0.84	0.64, 1.11	0.2225	0.68	0.43, 1.07	0.0977
40-64	0.49**	0.47, 0.57	<.0001	0.70**	0.59, 0.82	<.0001	0.77	0.59,1.00	0.0524
≥65	Ref.			Ref.			Ref.		
Appalachia									
Appalachia	1.10	0.99, 1.20	0.0543	0.99	0.89, 1.10	0.8427	0.95	0.80,1.12	0.5138
Non-Appalachia	Ref.			Ref.			Ref.		
Race									
African American	1.48	0.55, 3.99	0.4371	2.50	0.80, 7.86	0.1159	1.00	0.31, 3.20	0.9998
Caucasian	1.65	0.62, 4.41	0.3156	2.21	0.71, 6.86	0.1721	0.93	0.30, 2.95	0.9075
Other	Ref.			Ref.			Ref.		
Tobacco use									
Never user	0.71**	0.65, 0.76	<.0001	0.74**	0.67, 0.81	<.0001	1.03	0.89, 1.19	0.7111
Tobacco user	Ref.			Ref.			Ref.		
Family History									
No family history	1.14**	1.05, 1.24	0.0012	1.21**	1.10, 1.33	<.0001	1.06	0.91, 1.24	0.4487
Have family history	Ref.			Ref.			Ref.		
Marital Status									
Married	0.70**	0.60, 0.82	<.0001	0.84*	0.72, 0.99	0.0383	0.77*	0.62, 0.96	0.0203
Not with partners(widowed, divorced, separated)	1.26**	1.08, 1.47	0.0034	1.17	0.99, 1.37	0.0568	1.03	0.82, 1.30	0.7831
Single	Ref.			Ref.			Ref.		
Menopausal Status									
Post-menopausal status	1.33**	1.12, 1.58	0.0012	1.10	0.95, 1.28	0.1985	1.02	0.81,1.30	0.8349
Pre-menopausal status	Ref.			Ref.			Ref.		
Tumor Grade									
Moderately differentiated	1.07	0.97, 1.18	0.1811	1.10	0.95, 1.28	0.1985	1.82**	1.28, 2.58	0.0009
Non-high grade	0.91	0.76, 1.08	0.2698	1.31**	1.10, 1.56	0.0029	1.68**	1.16, 2.43	0.0058
Poorly-differentiated	1.28**	1.14, 1.44	<.0001	1.37*	1.07, 1.76	0.0121	2.23**	1.56, 3.18	<.0001
Undifferentiated	0.74*	0.55, 0.99	0.0438	1.67**	1.40, 2.00	<.0001	1.90	0.99, 3.67	0.0543
Well differentiated	Ref.			Ref.			Ref.		
ER status									
Negative	1.04	0.91, 1.19	0.5746	1.17*	1.02, 1.34	0.0289	1.33**	1.06, 1.66	0.0124
Positive	Ref.			Ref.			Ref.		
PR status									
Negative	1.21**	1.08, 1.35	0.0010	1.30**	1.15, 1.48	<.0001	1.31**	1.07, 1.61	0.0086
Positive	Ref.			Ref.			Ref.		

*Significant at p-value<.05 **Significant at p-value<.01

Effect of health insurance types on survival for patients with subgroup analysis by age group

We further analyzed the effect of insurance types on hazard of death by age groups (Table 6). Of the total 1629 patients in the youngest (19-39 years) age group, 948 patients were included in the regression analysis, 182 (19.19%) had event of death. Of the total 17,618 patients in the oldest age group (≥ 65 years), 9531 patients were included in the regression analysis and 3527 (37%) patients had event of death. In the 40-64 age group, (total of 20,024 patients), 10,994 were included in the regression analysis, 1675 (15.24%) had event of death.

In this regression model, the hazard of death was significantly higher for patients with Medicaid and Medicare compared to women with private insurance in the (18-39)-year age group and 40-65 age group. However, for patients over or equal to 65-year age group, there was no significant difference in hazard of death between patients enrolled in private and in Medicaid insurance.

In the 19-39 age group, the hazard of death is 84% and 116% higher for patients enrolled in Medicaid, Medicare respectively compared to patients with private insurance. Appalachia, race, family history, tobacco status, marital status, menopausal status, estrogen receptor status, progesterone receptor status, and weren't associated with the survival of women in the 19-39 age group.

The hazard of death was significantly higher for patients with Medicaid and Medicare insurance compared to women with private insurance in 40-64 age group with increased hazard of 91% and 127% respectively. Appalachia and race weren't associated with survival of patients in the 40-64 age group.

Patients enrolled in Medicare had significantly (45%) higher hazard of death compared to women with private insurance in the 65 years or older age group. Appalachia, menopausal status, race, and estrogen receptor status had no significant impact on survival for patients 65 years or older (Table 6).

Table 6: Effect of Covariates on Survival for breast cancer patients by Age groups with Multivariable Cox Proportional Hazard Model

Covariates	19-39 years			40-64 years			≥65 years		
	Hazard ratio	CI	p-value	Hazard Ratio	CI	p-value	Hazard ratio	CI	p-value
Health Insurance									
Medicaid	1.84**	1.31, 2.60	0.0005	1.91**	1.69, 2.15	<.0001	1.30	0.89,1.89	0.1820
Medicare	2.16*	1.05, 4.44	0.0352	2.27**	1.97, 2.60	<.0001	1.45**	1.20, 1.75	0.0001
Private	Ref.			Ref.			Ref.		
Treatment									
Surgery at Primary site and other therapy	27343.95	0,1.25E298	0.9764	0.12**	0.08, 0.18	<.0001	0.14**	0.11,0.17	<.0001
Surgery at Primary site only	21140.69	0, 9.66E297	0.9770	0.15**	0.10, 0.22	<.0001	0.23**	0.19, 0.29	<.0001
Other combination of therapies other than surgery	151479.6	0, 6.92E298	0.9724	0.30**	0.20, 0.46	<.0001	0.45**	0.36, 0.56	<.0001
No intervention	Ref.			Ref.			Ref.		
Appalachia									
Appalachia	1.32	0.92, 1.89	0.1274	1.04	0.93, 1.17	0.4624	0.99	0.92, 1.08	0.8787
Non-Appalachia	Ref.			Ref.			Ref.		
Race									
African American	1.66	0.39, 7.07	0.4954	2.06	0.76, 5.56	0.1550	1.69	0.63, 4.55	0.2998
Caucasian	1.02	0.25, 4.23	0.9738	2.10	0.78, 5.61	0.1398	1.66	0.62, 4.44	0.3115
Other	Ref.			Ref.			Ref.		
Tobacco Use									
Never user	0.72*	0.52, 0.99	0.0448	0.70**	0.64, 0.78	<.0001	0.78**	0.73, 0.84	<.0001
Tobacco user	Ref.			Ref.			Ref.		
Family History									
No family history	0.88	0.65, 1.19	0.4149	1.19**	1.07, 1.31	0.0008	1.16**	1.08, 1.24	<.0001
Have family history	Ref.			Ref.			Ref.		
Marital Status									
Married	0.84	0.58, 1.22	0.3578	0.86	0.74, 1.01	0.0588	0.67**	0.58, 0.77	<.0001
Not with partners(widowed, divorced, separated)	0.99	0.62, 1.59	0.9870	1.15	0.98, 1.34	0.0954	1.15	0.99, 1.31	0.0515
Single	Ref.			Ref.			Ref.		
Menopausal Status									
Post-menopausal status	1.32	0.76, 2.28	0.3243	1.15**	1.03,1.27	0.0109	0.91	0.49, 1.69	0.7550
Pre-menopausal status	Ref.			Ref.			Ref.		
Tumor Grade									
Moderately differentiated	1.66	0.65, 4.25	0.2914	1.29**	1.08, 1.54	0.0039	1.11*	1.01,1.22	0.0280
Non-high grade	2.12	0.69, 6.52	0.1881	1.13	0.89, 1.43	0.3095	1.02	0.88,1.17	0.8133
Poorly-differentiated	2.44	0.96, 6.20	0.0615	1.58**	1.32, 1.89	<.0001	1.36**	1.22, 1.51	<.0001
Undifferentiated	4.16*	1.16,14.86	0.0284	1.10	0.73, 1.66	0.6495	0.87	0.65,1.16	0.3445
Well differentiated	Ref.			Ref.			Ref.		
ER status									
Negative	1.10	0.68, 1.77	0.7062	1.25**	1.07, 1.45	0.0045	1.08	0.96,1.20	0.1999
Positive	Ref.			Ref.			Ref.		

PR status									
Negative	1.18	0.73, 1.90	0.4958	1.38**	1.20, 1.59	<.0001	1.20**	1.09, 1.32	0.0001
Positive	Ref.			Ref.			Ref.		
SEER stage									
Distant	2.06*	1.09, 3.90	0.0260	4.27**	3.61, 5.05	<.0001	3.02**	2.60,3.51	<.0001
Localized	0.23**	0.15, 0.35	<.0001	0.35**	0.31, 0.39	<.0001	0.56**	0.52,0.60	<.0001
Regional	Ref.			Ref.			Ref.		

*Significant at p-value<0.05 **Significant at p-value<0.01

DISCUSSION

The purpose of this study was to evaluate the effect of types of health insurance and other socio-demographic factors on survival for women with breast cancer. We included women with breast cancer to understand their survival based on their health insurance types and other covariates. We found that the survival is highest among patients with private insurance while the patients with Medicaid and Medicare had comparatively lower survival probability post-diagnosis. Effect of health insurance on hazard of death was still present even after controlling other socio-demographic factors, tumor and biological characteristics and treatment factors in the regression model. The hazard ratio was higher for Medicare patients (94% vs 88%) than Medicaid patients compared to patients with private health insurance. Previous studies have shown that uninsured and Medicaid enrolled patients are at increased hazard of death compared to privately insured breast cancer patients. A study by Gorey et. al. (2011) using a California population and another study using data from Texas Cancer Registry by Zhang et.al. (2015) concluded that privately insured women were at an advantage on survival compared to the uninsured or those insured by Medicaid.^{11, 24} Other studies have focused on the differential effect on survival due to private and Medicaid insurance. However, Medicare patients are also significantly disadvantaged for survival compared to patients with private health insurance as depicted in this study.

When multivariable Cox regression was performed to evaluate effect of health insurance controlling effects of other covariates by age group, the hazard was insignificant between patients with Medicaid and private insurance in older than 65-year age group. However, the hazard of death was significantly higher (45%) for patients with Medicare compared to patients with private insurance. Even though some other socio-demographic factors, tumor and biological factors lost their significance in the multivariable model,

health insurance and treatment type remained consistently significant in the model in all age groups. These findings highlight the importance of these health care factors in affecting survival of the breast cancer patients.

A study by Shi et al (2013) found the survival outcome was different for patients enrolled in Medicaid and private health insurance even when patients got the same type of treatment administered by the clinicians in a public hospital.³⁰ This differential outcome could be attributed to the fact that patients without private health insurance are diagnosed in the later stage of disease. The relationship of personal characteristics of the patient and the enrollment in the health insurance policy should also be taken into consideration.

Some studies also implied differential quality of treatment rendered to patients depending upon their insurance coverage. A study done by Parikh-Patel et al. found that breast cancer patients in all other insurance groups including Medicare, Medicaid, uninsured group had significant lower odds (16-25%) of receiving radiation after breast conserving surgery (BCS) compared with the privately insured group.¹⁵ Similarly, for patients with four or more positive lymph nodes, uninsured and dual eligible patients had significantly lower odds of receiving radiation therapy after mastectomy.¹⁵ This finding was further supported by other studies conducted to assess impact of insurance types on the treatment pattern among breast cancer patients.³⁰⁻³⁴ Another study conducted in Florida by Voti et al. found that women with Medicaid at the time of diagnosis were 29% less likely to receive recommended treatment for breast cancer compared to patients with private insurance.³⁵ Those finding suggest role of insurance in determining quality of health care they received and these findings should be taken into account while deciphering the mechanism by which health insurance affect the survival of the patients.

Even within insurance types, differences in outcomes have been seen in patients in capitated and fee-for-service systems. A study by Kirsner et al., found that 13.1% of HMO patients were diagnosed in an in-situ stage compared with 10.8% of FFS patients for breast cancer.²⁵ Similarly, Medicare patients enrolled in HMO healthcare delivery systems had greater survival when diagnosed with breast cancer, either as a first cancer diagnosis or subsequent cancer diagnosis compared with patients enrolled in FFS systems.²⁹ The differences remained even after controlling for potential confounders.

One study hypothesized Medicaid patients would have a higher likelihood of late-stage disease at diagnosis and a lower likelihood of receiving radiation therapy compared to women not insured by Medicaid. The difference being due to circumstances beyond the control of insurance status as such patients insured by Medicaid may have comorbid conditions that interfere with cancer screening and treatment and physicians may be reluctant to recommend routine screening or cancer treatment for low-income women, even those who are insured.¹⁴

The effect of geographical distribution of the patients did not have any significant effect on survival of the patients though Appalachian patients had significantly higher hazard ratio compared to non-Appalachian patients in univariate Cox regression. Being married or living with partners were found to be a protective factor for survival of breast cancer patients. This finding could be related to the fact that having partner shortens the delay in seeking health care as was found in a population-based study done using register-sampled cancer patients in the Aarhus County, Denmark implying partner support to be significantly associated with shorter patient delay in health seeking among cancer patients.³⁶ Partner support explains one way of advantage being in relationship at the time of diagnosis and subsequent care of breast cancer patients.

Conclusion and Limitation

This study is based on secondary data analysis of breast cancer patients to determine the impact of health insurance on survival of breast cancer patients. This research project also depends on the only available structured information that limits potential of the researcher and the project to explore in depth mechanism by which health insurance affects survival. Original research with primary data could answer several questions about the quality and accessibility of health care services by the breast cancer patients. Health insurance ensures the access of health care when needed. Hence, including components of health care access such as appointments to care providers, type of health care providers, and treatment as intermediary model could be more useful to understand the pathways of disparities in survival probability due to health insurance. Lack of information about education and income might also affect the overall impact of health insurance on survival as their effect are not controlled in the regression model.

This issue has attained considerable attention from the government and other medical professionals and allied health care organizations. In the meantime, assessing the effect of health insurance on breast cancer patients underlines its importance in improving survival, and helps demonstrate the disparities in survival rates of breast cancer patients, as well as provides evidence regarding the discrepancy of health insurance types and their effects. Given the high burden and mortality of breast cancer among US women, this should be high priority among policymakers and health care professionals to ensure the availability and affordability of health care when needed to decrease the mortality and to increase the quality of life among survivors.

This study shows a higher hazard of death in patients with Medicaid and Medicare compared to privately insured patients requiring an action to understand thoroughly how they are varied. This study also validates health insurance as an imperative modifiable factor of survival of breast cancer patients. Health insurance has been highly debated policy issues of US health care system and with expansion of Medicaid, it is pushed as right of every individual. However, our research supports that having health insurance is not sufficient enough, policy makers should be aware about how quality of health care and health outcome are affected by health insurance policies. It is highly recommended to ensure that those insurance policies provide at least the same basic level of coverage that brings equal health outcome for the disease.

Recommendations

A detailed study to find out the financing detail in each insurance policy for treatment of breast cancer is recommended to understand any factors motivating care provider's behavior. Further study detailing physician perspectives on how they recommend treatment and their perception about consideration of insurance while recommending treatment and patients perspectives on how they are recommended treatment based on insurance could help in understanding impact of health insurance in real life scenario. Hence, large scale original research projects could be performed to extract views and perceptions of those patients covered with different insurance types. Policy analysis of health insurance organizations regarding coverage of breast cancer patients can be carried out to understand policies of health insurance companies.

In conclusion, the findings from this study can help to inform public health professionals and policy makers about impact of health insurance on survival of female breast cancer patients and help to design policies that reduce disparity in health outcome depending on types of health insurance. Improving provision of health care services under Medicare and Medicaid may improve breast cancer outcomes.

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BIOGRAPHICAL SKETCH

Pramila Rai was born and raised in Sankhuwasabha district of Nepal. She received her B.Sc. Nursing and MPH from B. P. Koirala Institute of Health Sciences (BPKIHS) in Nepal. She has worked as a faculty for more than 5 years in School of Public Health, BPKIHS, where she taught and mentored public health, medical and nursing students. She has also worked in other research projects as principal and co-investigator. She writes regularly on public health issues in her blog, 'Dimensions of Public Health'. She was awarded Fulbright scholarship for pursuing MPH (Health Policy and Management) and Graduate Certificate in Biostatistics in University of Kentucky, College of Public Health. She is interested in health system, women's health, survival analysis, secondary data analysis and health disparity. She plans to pursue leadership role in health system of Nepal by contributing her knowledge and skills in creating efficient and equitable health system.