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The Determinants of colorectal cancer survival disparities in Nevada

Lucas N. Wassira
University of Nevada, Las Vegas

THE DETERMINANTS OF COLORECTAL CANCER SURVIVAL DISPARITIES IN NEVADA

by

Lucas Nyamanda Wassira

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Paulo Pinheiro, Committee Chair

James Symanowski, Committee Member

Michelle Chino, Committee Member

Sheniz Moonie, Committee Member

Patricia Alpert, Graduate Faculty Representative

Ronald Smith, Ph.D., Vice President for Research and Graduate Studies and Dean of the Graduate College

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ABSTRACT

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by

Lucas Nyamanda Wassira

Dr. Paulo Pinheiro, Examination Committee Chair
Assistant Professor, Epidemiology
University of Nevada, Las Vegas

Different population groups across Nevada and throughout the United States suffer disproportionately from colorectal cancer and its after-effects. Overcoming cancer health disparities is important for lessening the burden of cancer. There has been an overall decline in the incidence of and mortality from colorectal cancer (CRC). This is likely due, in part, to the increasing use of screening procedures such as Fecal Occult Blood Test (FOBT) and/or endoscopy, which can reduce the risk of CRC mortality by fifty percent. Nevertheless, screening procedures are routinely used by only fifty percent of Americans aged fifty years and older. Despite overall mortality decreasing over time, there continues to be a widening disparity in CRC incidence and survival between races and ethnicities. To assess CRC survival disparities across race and ethnicity in Nevada, data from the statewide Nevada Central

Cancer Registry (NCCR) was used. We examined a cohort of men and women [n=11,459] who were diagnosed with CRC from 1995 through 2006 in Nevada. Cause-specific survival analyses were performed to ascertain the determinants of CRC disparities. Hazard ratios were calculated and stratified by race/ethnicity groups. The five years age adjusted survival rates were compared for 1995 – 1998, and 1999 - 2001. In the univariate model type three tests (Wald=24.71, df=5, p=.0002), race/ethnicity was statistically significant implying that there are survival disparities between race/ethnicity groups. African Americans had 20.6% risk ratio of CRC death in relation to Whites [HR = 1.21, 95% CI=1.05 – 1.39]. However, after adjusting for gender, age groups, health insurance type, period of diagnosis, stage of diagnosis, and sub-location within the colon and rectum in a multivariate analysis, Blacks and Hispanics had an increased risk of death in relation to Whites [HR = 1.24, p=0.004 for Blacks, and Hispanics HR=1.12, p=0.04] . More aggressive screening and equal treatment opportunities would do much to remedy the survival disparity seen among race/ethnic groups.

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CHAPTER 1

INTRODUCTION

Colorectal carcinoma (CRC) is the cancer that forms in the tissues of the colon or rectum. Cancers of the colon or rectum have many features in common and are discussed together in this project.

Altekruse et al. (2010) on their cancer statistic review published on the Surveillance Epidemiology and End Results Program (SEER), it was identified that CRC is the second deadliest cancer, and third most commonly diagnosed cancer in the United States. For the year 2010, Altekruse et al., estimated 142,570 new cases in the United States (72,090 in men and 70,480 in women) would be diagnosed with and 51,370 would die of CRC.

In a cancer statistics report by Murray et al. (2003), the authors reported CRC accounts for ten percent of annual cancer-related deaths in the United States.

Between 2002 and 2006, Nevada had an annual age-adjusted incidence rate of 49.1 per 100,000 (C.I = 47.7 - 50.4) versus 50.4 [C.I = 50.3 - 50.5] per 100,000 men and women for the whole United States (Altekruse et al., 2010). The authors also reported an annual age-adjusted mortality rate of 19.6 [C.I = 18.7 – 20.5] per 100,000 person-years for

Nevada versus 18.2 [C.I = 18.1 – 18.3] per 100,000 person-years for the whole United States in the same period [table 1 and 2].

Table 1: Colon and Rectum Age Adjusted Incidence Rates and 95% Confidence Intervals. Nevada and United States 2002 – 2006

Geographic Area	All Races	White	Black	Hispanic*
United States	50.4 C.I = 50.3 - 50.5	49.5 C.I = 49.4 - 49.6	58.1 C.I = 57.6 - 58.5	41.6 C.I = 41.2 - 42.0
Nevada	49.1 C.I = 47.7 - 50.4	49.3 C.I = 47.9 - 50.8	51.7 C.I = 46.0 - 57.8	39.8 C.I = 35.6 - 44.3

Table 2: Colon and Rectum Age Adjusted Death Rates and 95% Confidence Intervals. Nevada and United States 2002 – 2006

Geographic Area	All Races	White	Black	Hispanic*
United States	18.2 C.I = 18.1-18.3	17.7 C.I = 17.6-17.7	25.4 C.I = 25.1-25.7	13.0 C.I = 12.8-13.3
Nevada	19.6 C.I = 18.7-20.5	20.0 C.I = 19.1-21.0	21.3 C.I = 17.5-25.5	10.5 C.I = 8.3-13.1

Note:

- (*) Hispanic origin is not mutually exclusive from category race (white, black)
- Rates are per 100,000 persons.
- Source(U.S. Cancer Statistics Working Group, 2010)

Based on rates from 2005-2007 (Altekruse et al., 2010), the authors noted that 5.12% of men and women born today will be diagnosed with CRC at some time during their

lifetime. Meaning, 1 in 20 men and women will be diagnosed with CRC during their lifetime. When looking at the probability of developing CRC between genders for the same age periods, Altekruse et al. reported 2.04 percent of men compared to 1.53 percent of women will develop cancer of the colon and rectum between their 50th and 70th birthdays.

For survival, Altekruse et al. (2010) reported that overall 5-year CRC relative survival for 1999-2006 from 17 SEER geographic areas was 65.0%. Five-year relative survival by race and sex was: 66.0% for white men; 65.7% for white women; 55.6% for black men; 56.6% for black women.

The study of cancer health disparities has been documented in many populations and cancer types. The causes of these inequalities are not well understood but may include disease and patient characteristics, treatment differences and health service factors. CRC health disparities are differences in the incidence, prevalence, mortality, and survival of adverse health conditions, in the context of disenfranchised segments of the population. Understanding these disparities is a potential public health component for intervention towards lessening CRC burden.

There are striking differences between racial and ethnic groups in both mortality and survival for colorectal cancer in Nevada and the United States in general. As many population groups across Nevada and around the United States suffer disproportionately from CRC and its after-effects, overcoming CRC health disparities is of ut-most significance.

The reasons for disparity in survival have not been elucidated and may include many factors such as differences in access to preventive medical care, as well as quality and type of care received after diagnosis.

The purpose of this study was to ascertain the determinants of colorectal cancer survival disparities that exist in selected populations of Nevada, and ultimately suggest ways to minimize those disparities. Secondary objectives includes: 1) To quantify the effects of CRC stage of diagnosis, gender, type of health insurance, and colorectal sub-location on CRC racial/ethnic survival disparities, and 2) To assess change in CRC survival over time by race/ethnicity stratified by age and stage of diagnosis,

Findings of the study were used to answer the research question, what are the determinants of colorectal cancer

survival disparities among Nevadans? Further, in answering this question it was hypothesized that: 1) Blacks will have lower 5-year age-adjusted survival rates than non-Hispanic whites, 2) Increasingly advanced stage will be inversely associated with survival 3) Increasing age will be inversely associated with survival 4) Blacks will have a higher relative risk of death compared to Whites and 5) CRC patients on Medicaid and those with lack of health insurance will have/show a higher relative risk of death compared to CRC patients on private insurance.

Data from the Nevada Central Cancer Registry (NCCR) was used for the study. NCCR is the population-based registry that collects and maintains data on all cancer patients within the State of Nevada. The Registry began collecting cancer incidence data in 1989, and continues to collect data on all reportable cancers in accordance with the National Program for Cancer Registries (NPCR) and the North American Association of Central Cancer Registries (NAACCR) Standards. The study population was all Nevada residents who were diagnosed with CRC from 1995-2006, with follow up through December 31, 2006, and registered in the Nevada Central Cancer Registry.

CHAPTER 2

LITERATURE REVIEW

There has been reported overall decline in the incidence of and mortality from CRC (Espey et al., 2007). This is likely due, in part, to the increasing use of screening procedures such as Fecal Occult Blood Test (FOBT) and/or endoscopy, which can reduce the risk of CRC mortality by 50 percent (Walsh, 2004). However, screening procedures are routinely used by only 50 percent of Americans age 50 years or older.

Despite overall incidence and mortality decrease over time (U.S Cancer Statistics, 2010), Irby (2006) found a continue widening disparity in CRC survival between races and ethnicities. For the year 2002 – 2006, United States Cancer Statistics (2010) reported the age-adjusted death rate per 100,000 in Nevada males was 26.2 (C.I = 19.8-33.8) in Blacks compared with 23.6 (C.I = 22.2-25.2) in Whites and 13.1 (C.I = 9.2-17.8) in Hispanics. For females, the death rate was 17.7 (13.3-23.0) in Blacks compared with 16.8 (C.I = 15.6-18.0) in Whites and 8.9 (C.I = 6.2-12.1) in Hispanics.

In the same 2002-2006 period, according to the American Cancer Society (2007), stage-specific survival rates were

96%, 87%, 55%, and 5% for CRC stages: In Situ, Local, Regional, and Distant, respectively. When CRC is detected at an early localized stage, the five-year relative survival rate is 90%; however, only 39% of CRC's are discovered at this stage (ACS, 2007).

Rabeneck et al. (2003) found that overall and stage-specific five year CRC survival rates were higher for Whites compared with African Americans, and differences were largely attributable to the stage of disease at diagnosis.

In another study by Mostafa et al. (2004), the authors found that African Americans tended to present with an advanced disease stage and having a poorer clinical outcome than do Whites. Other studies, however, have shown that even with a similar distribution of tumor stage by race or after statistical adjustment for stage, survival disparities between African Americans and Whites persisted (Govindarajan et al., 2003).

Moreover, Marcella and Miller (2001) found CRC survival disparity among race and ethnicity groups remained even after controlling for socioeconomic, comorbid, and treatment factors.

In a study about SES impact on CRC survival, Marcella and Miller (2001) also found that SES differences explained a large portion of the racial disparity in CRC survival. Nevertheless, in a meta-analysis of SES influences on CRC survival racial differences, Du et al. (2007) demonstrated that after adjusting for SES, no significant survival disparity was observed.

Among patients with CRC, Bach (2002) and Mostafa (2004) found that Blacks had higher death rates than Whites, even when stage of cancer is controlled for.

Banerjee et al. (2009) in their study on the effect of demographics, clinical factors, and socioeconomic status on CRC racial disparities, they found African Americans had a significantly increased risk of death (HR, 1.13; 95% CI, 1.07-1.20) from CRC as compared to Whites. However, when simultaneously adjusted for age, sex, marital status, SES, tumor grade, SEER stage, and surgical treatment in a multivariate model, race was no longer significantly associated with survival (HR, 1.00; 95% CI, 0.92-1.09).

Conversely, in many other studies (Mayberry, 1995), stage of diagnosis was consistently shown to be the strongest predictor of excess risk of death for CRC

patients accounting for greater than 50% of the excess mortality.

Further, Banerjee et al. (2009) found the determinants: increasing age at diagnosis, tumor grade, marital status, and treatment disparity are significantly associated with decreased survival among individuals with colorectal cancer.

In a Danish study by Johansen et al. (1998), being married was found to have a positive influence on survival among CRC patients.

In the studies by Ward (2008) and Ayanian (1993), the authors found that patients diagnosed with colorectal cancer who were either uninsured or on Medicaid had worse survival than patients with private health insurance.

Cardinez et al. (2004) identified income, education, and health insurance coverage influences access to appropriate early detection, treatment, and palliative care for CRC.

In the studies of screening and CRC, other studies have found being Blacks is associated with a lower screening rate for CRC. Additionally, Etzioni et al. (2006) found that screening disparity exists amongst Blacks and Whites with positive family history.

Similarly, James et al. (2002) in their study about the relationship of perception to screening behavior, the authors found that African-Americans' perceptions of sigmoidoscopy and colonoscopy differ from fecal occult blood testing (FOBT) with respect to perceived benefits versus barriers. Specifically, the authors found barriers were significantly and negatively associated with FOBT and sigmoidoscopy. However, in the same study the authors found a significant positive association between perceived benefits and sigmoidoscopy or colonoscopy but not with FOBT.

Higher educational status and greater knowledge of flexible sigmoidoscopy were found to predict greater adherence to screening flexible sigmoidoscopy guidelines (Lawsin, 2007); whereas, greater knowledge of FOBT and doctor recommendation predicted greater adherence to FOBT screening guidelines in an East Harlem Blacks population (Lawsin et al., 2007).

Schroy et al. (2008) found knowledge status about colorectal cancer is lower in African Americans than in Whites. In addition, Schroy et al. also found that African Americans who adhered to the screening guidelines were tended to be more knowledgeable about colorectal cancer and

held more positive beliefs about the benefits of screening than those who were not up-to-date with screening.

In another study by Peterson et al. (2008), the authors found having either a screening sigmoidoscopy or colonoscopy is positively associated with education status, being married, higher household income, recent medical visit, higher age, and public or private insurance among Blacks.

Mayberry et al. (1995), on the other hand, found the risk of death from invasive CRC among Blacks patients was fifty percent higher than among Whites patients [HR = 1.5 (95% CI = 1.2 - 1.9)]. However, after adjustment for age, sex, and location, in that particular study, subsequent analyses with all potential explanatory variables in the model did not show any significant interactions of race separately with age, sex, location, and poverty index.

Additionally, Mayberry et al. (1995) also found Blacks were more likely than Whites to be diagnosed with advanced disease. After adjustment for stage, however, the disparity diminished. There was no racial difference in survival for patients with distant stage metastatic disease.

In the study describing racial and ethnic patterns of cancer-specific survival and relative risks (RRs) of cancer

death, Clegg et al. (2002) found survival rates improved between 1988 and 1997 for virtually all racial and ethnic groups. However, racial or ethnic differences in RRs of cancer death persisted after controlling for age for all cancers combined and for age and stage for specific cancer sites ($P<.01$). Additionally, it was also found that Blacks, American-Indian, Alaskan-Native, and Hawaiian-Native patients tended to have higher RRs of cancer death than the Whites. American-Indians and Alaskan-Natives generally exhibited the highest RRs of cancer death, except for colorectal cancer in males.

CHAPTER 3

METHODOLOGY

Study Population

The study population in this study comprised men and women diagnosed with a first primary colon or rectal/rectosigmoid junction carcinoma from 1995 through 2006, identified through the Nevada Central Cancer Registry (NCCR) and followed for vital status until December, 31st 2006.

Data Sources

Cancer incidence statistics were obtained from (NCCR) through the Bureau of Health Planning and Statistics. Death records came from the Office of Vital Records (OVR), also within the Bureau of Health Planning and Statistics. CRC cause of death was classified based on ICD-9 for all deaths which occurred on and before 1998 and ICD-10 for deaths after 2000.

CRC Classification

CRC cancer site and morphology were coded according to the International Classification of Diseases for Oncology (ICD-O) coding structure codes C18.0-20.9(WHO, 1990) that includes topography as well as morphology. Cancers with

histologic codes 9590 through 9989 which include intestinal lymphomas were excluded (Ries, 2000).

CRC Stage of Diagnosis Classification

Surveillance Epidemiology and End Results Program (SEER) summary staging (localized, regional, and distant) was used to categorize the extent of the disease.

Statistical Techniques

Variables determined at diagnosis that were assessed for prognostic significance for survival included age, gender, stage (SEER), payer, race and ethnicity, CRC sub-location, and time period of diagnosis.

Statistical analyses were carried out using likelihood ratio chi-square tests to compare the demographics, stage of diagnosis and accessibility to healthcare for race and ethnicity groups. G-statistic P-values less than .05 were considered statistically significant.

Survival rates were calculated using the actuarial method. Partial likelihood tests were used to estimate the regression coefficients. Test statistic results were reported using Wald test value and Wald Chi-square p-values.

Cox Proportional Regression Modeling

A univariate model was first performed to assess the impact of race/ethnicity alone on CRC survival. A multivariable model was executed next to account for other covariates in the model.

In the multivariable model, adjusted hazard ratios (HR) and their corresponding 95 percent confidence intervals (CI) were estimated using the Cox proportional hazards regression. To assess independent prognostic importance, each factor included in the model was tested for significance based on the Wald Chi-square test incorporating the appropriate degrees of freedom. Additionally, for each factor, subgroup level hazard ratios were estimated and corresponding Wald Chi-square p-values were reported.

CRC Survival

Cancer-specific survival was defined as the time between the date of diagnosis and either the date of death due to CRC or the last follow-up date whichever occurred first. The cause-specific survival rate, which estimates the likelihood of surviving cancer during a specified time period if CRC is the only cause of death, was used for this

study (Clegg et al., 2002). Survival time was calculated in years. Patients who died of causes other than the CRC or of unknown causes prior to the cut-off follow-up date of 31December2006 were censored at time of death. All others, if not dead by CRC or if alive after December 31 2006 were censored at the date of last linkage with the State Vital Statistics up until the cutoff date of December 31, 2006.

Age Categorization

Age at diagnosis was categorized into the following 5 categories: <44, 45-54, 55 – 64, 65 – 74, and ≥75 years old.

CHAPTER 4

RESULTS

A total of 11,459 diagnoses of CRC from 1995 through 2006 were included in the study. Of those diagnoses, 53.6 percent [n=6139] were male and the remaining 46.4 percent [n=5320] were female. Whites made up the largest proportion of the patients in Nevada, constituting 83.9 percent [n=9610]. Other racial-ethnic groups included Blacks 5.6 percent [n=644], Asian 3.3 percent [n=378], and Hispanics 5.9 percent [n=662].

For the period 1995 through 2006, the mean age for colon and rectum diagnoses in Nevada for both gender and race/ethnicity was 68 years with a standard deviation of 12.5. The minimum age of diagnosis was 11 and maximum age was 103. Most people, 35.5 percent, were diagnosed at the regional stage. 30.6 percent were diagnosed at localized stage, 17.9 percent at distant stage, and 13.2 percent diagnoses were unstaged.

Of 11,459 CRC diagnoses, 24.1 percent of the patients had private health insurance at the time of diagnosis. 11.9% had Medicare, 5.2% were on Medicaid, and 4.8% were uninsured. The largest proportion of patients, 54.1%, had unknown health insurance at the time of their diagnosis.

Table 3: Patients' Demographic and Clinical Characteristics by Race/Ethnicity [n = 11,294].

Characteristic	White N =9610	Black N =644	Asian N =378	Hispanic N = 662	P-value*
Age at diagnosis					<.0001
<44	3.5	5.3	7.1	9.1	
45 – 54	9.1	16.8	17.5	15.9	
55 – 64	19.7	28.6	23.5	24.5	
65 – 74	31.7	28.4	29.1	27.2	
75^{+}	36.0	21.0	22.6	23.4	
Gender					0.004
Male	53.9	53.3	44.4	53.6	
Female	46.1	46.7	55.6	46.4	
Stage of Diagnosis					0.07
Local	31.1	27.8	25.4	28.6	
Regional	35.7	34.8	38.9	34.6	
Distant	17.5	21.6	19.8	21.0	
Unstaged	13.2	13.0	12.4	12.8	
Payer at Diagnosis					<.0001
Medicare	11.5	9.3	9.0	7.1	
Medicaid	2.3	6.2	5.3	5.6	
Private	26.1	32.6	35.2	35.6	
Uninsured	4.5	7.0	6.1	7.3	
Unknown	55.6	44.9	44.44	44.41	
Tumor sub-location					<.0001
Proximal	40.6	49.8	33.6	32.9	
Sigmoid Colon	20.6	20.2	27.0	25.8	
Rectosigmoid and Rectum	27.8	18.2	28.4	30.8	
Colon NOS	11.1	11.8	10.6	10.4	

**Likelihood ratio chi-square p-value*

There were 5,514 (48.1%) deaths in Nevada for the period 1995 – 2006; 3,388 (29.6%) deaths occurred due to colorectal cancer.

Demographically, Blacks, Asians, and Hispanics were more likely than Whites to be diagnosed at a younger age, 16.8 percent, 15.9 percent, and 17.5 percent respectively versus 9.1 percent for Whites. Blacks were more likely to be uninsured than other races/ethnicity.

With regard to clinical variables, Blacks were more likely than White to present with distant stage disease at the time of diagnosis, 21.6 percent versus 17.5 percent for Whites. Asians were diagnosed at a distant stage in 19.8 percent, and Hispanics 21.0 percent.

Survival Analyses

In this particular study, it was found the median overall survival for the entire cohort was 5.4 years with a 5-year survival rate of 53.4 percent. For CRC cause-specific survival, the unadjusted analysis showed that Blacks patients had a significantly increased risk of death for CRC (HR = 1.21, CI = 1.05 – 1.39, p=0.009) compared with White patients (Table 4). The model was significant with a Wald Chi-square statistic value of 24.71, p = .0002.

Table 4: Univariate Survival Analysis Results to Assess Individual Prognostic Importance

Analysis of Maximum Likelihood Estimates

Parameter	HR	95% C.I of the HR LL	UL	P-value
Ref = White	1			
Blacks	1.206	1.047	1.390	0.0094
Hispanic	1.060	0.916	1.227	0.4313
Asian	1.005	0.825	1.225	0.9601

Type 3 Tests

Effect	DF	Wald Chi-Square	ChiSq p-value
race_eth	5	24.7050	0.0002

Note
LL = Lower Limit
UL = Upper Limit
HR = Hazard Ratio

Conversely, in the multivariate model (Table 5) when simultaneously adjusted for age group, gender, SEER stage, health insurance type, period of diagnosis, sub location of the tumor, race and ethnicity was significantly associated with increased risk of death($p = 0.0001$). For Blacks and Hispanics compared to Whites it was estimated that the increase in risk of death was 22%, and 15% respectively.

Patients in age group 75 years and above had higher increased hazards of death (HR=2.1) as opposed to the younger group, less than age 44. Also, age groups 55 – 64, and 65 – 74 (HR = 1.25, and 1.41) respectively had increased hazards of death in relation to those less than 44 years old.

Additionally, we also found in the study female patients had better survival than males, with an 8.4 percent decreased risk of death [HR = 0.92].

Using localized Stage as the reference group, patients diagnosed in regional, distant and unstaged CRC had increased risks of death compared with those diagnosed in localized stage. Compared with localized stage, patients diagnosed in regional stage had HR of 2.75 with 95 percent C.Is of 2.42 and 3.12. Distant stage conveyed HR of 10.98, with 95% C.Is of 9.66 – 12.47 in relation to the localized stage.

This study also found Blacks had lower 5-year age adjusted survival rates than White when compared across two periods of diagnosis 1995 – 1998 and 1999 – 2001(Figure 1).

Table 5: Multivariate Predictors of CRC Survival Using Cox Proportional Hazard Modeling

Analysis of Maximum Likelihood Estimates

Parameter	Subgroup HR	95% C.I of the HR		Subgroup P-value
		LL	UL	
Race/Ethnicity	1			
Ref = White				
Blacks	1.216	1.054	1.403	0.0073
Asian	1.059	0.867	1.293	0.5744
Hispanic	1.142	0.984	1.324	0.0796
Stage				
Ref = Localized				
Regional	2.746	2.415	3.123	<.0001
Distant	10.975	9.661	12.469	<.0001
Unstaged			8.765	<.0001
Payer				
Ref = Private				
Medicaid	1.191	0.943	1.503	0.1420
Medicare	1.302	1.116	1.518	0.0008
Uninsured	1.227	1.045	1.441	0.0127
Unknown	1.193	1.080	1.318	0.0005
Age Group				
Ref = Less than 44				
45 – 54	1.127	0.898	1.415	0.3012
55 – 64	1.221	0.989	1.506	0.0627
65 – 74	1.381	1.123	1.699	0.0022
75+	2.002	1.630	2.458	<.0001
Gender				
Ref = Male				
Female	0.919	0.856	0.986	0.0194
Tumor sub-location				
Ref = Proximal				
Colon NOS	1.954	1.761	2.167	<.0001
Rectosigmoid and Rectum	0.960	0.874	1.055	0.3935
Sigmoid Colon	0.922	0.831	1.022	0.1207

Type 3 Tests

Group Effect	DF	Wald Chi-Square	Group p-value
Race/eth	5	25.1670	0.0001
Stage	3	1798.1097	<.0001
Gender	1	5.4650	0.0194
Payer	4	16.8730	0.0020
Diag Period	1	14.6261	0.0001
Age Group	4	148.6613	<.0001
Sub-Location	3	226.1119	<.0001

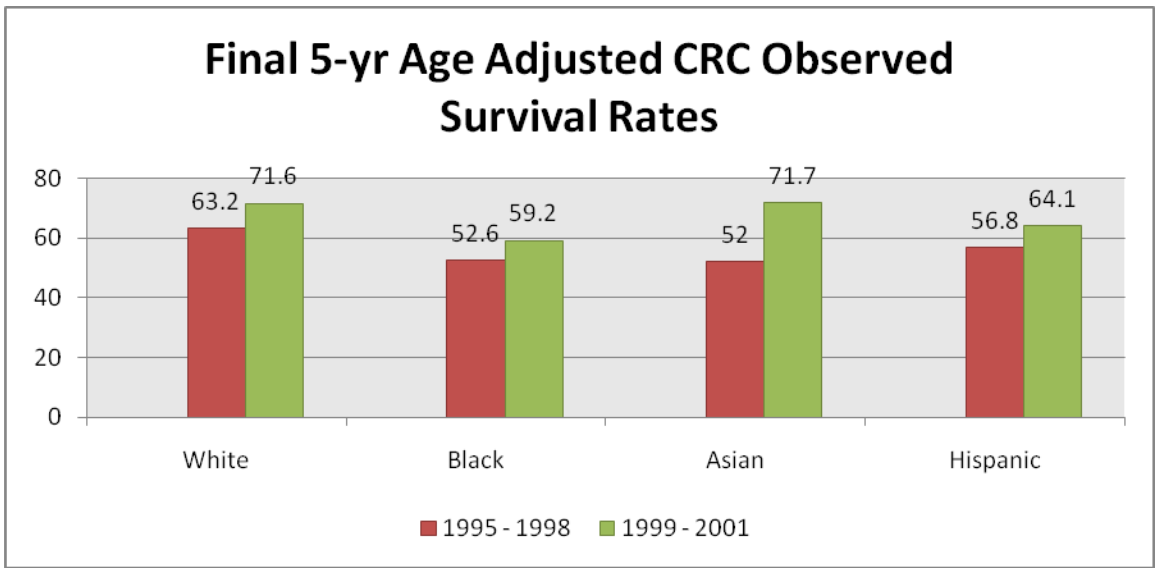

Figure 1: Age-Adjusted CRC Survival Rates After Five Years Compared Between Diagnosis Periods.

CHAPTER 5

DISCUSSION

Numerous studies have been conducted to evaluate CRC survival differences between African Americans and White. These studies showed overall poorer survival for African Americans compared to Whites (Ries et al, 2000; Marcella et al., 2001; Govindarajan et al., 2003; Clegg et al., 2002).

In this study, initial univariate analysis demonstrated Blacks patients with CRC had significantly worse survival than White patients. After controlling for age groups, gender, period of diagnosis, sub location of the tumor, type of health insurance, and stage of diagnosis, these survival differences persisted for African Americans. In addition, a significant disadvantage was shown for Hispanics in relation to the univariate model.

Studies (Swan et al., 2003; Cheng et al., 2001) have consistently reported stage at diagnosis as the strongest predictor of excess risk of death for CRC patients. Swan et al. and Cheng et al. reported in their studies that stage of diagnosis accounts for greater than 50 percent of the excess mortality. However, this was not found in our study as the final model accounted for all covariates and not

stage of diagnosis alone. Stage of diagnosis by far was shown to be the strongest predictor of CRC survival disparity in this study.

Certainly, besides the obvious benefits of early stage at diagnosis, detecting tumors earlier reduces both short-term and long-term morbidity and mortality by increasing the chances of successful curative surgeries and decreasing the number of treatment-related complications such as bowel obstruction, perforation, or excessive bleeding (Yan et al., 2008). Our study could not look at clinical factors such as surgery, or chemotherapy due to incompleteness of clinical information in the registry.

Through screening, CRC can be detected at early stages which are also treatable. According to Swan et al. (2003) data from the 2000 National Health Interview Survey indicated that Blacks and Whites report similar rates of screening with either occult blood stool sampling or colorectal endoscopy.

In addition, between 1987 and 2000, Cheng et al. (2001) reported Blacks improved their rates of screening for colon cancer as compared with Whites. These findings, along with data suggesting that Blacks present with more proximal tumors (Cheng et al.,2001) and at a younger age, has

heralded the suggestion among some experts to recommend that African Americans receive colonoscopies as first-line screening starting at age 45 (Agrawal et al.,2005). Due to lack of screening data in cancer database, this study could not analyze information about CRC screening. For future studies, better ways should be designed that will link cancer registry and other population databases that collect information on CRC screening.

Furthermore, although the relatively poor outcomes associated with advanced stage did not account for all of the excess mortality experienced by Blacks and Hispanic patients seen in our study, we found significant differences in age adjusted survival rates by diagnosis period (Figure 1). The clinical implications of these findings are unavailable or/unknown, although it is possible that the higher mortality associated with advanced disease takes its full toll closer to the time of diagnosis, and if patients survive beyond the first few years of their disease, other factors such as comorbid diseases may make a greater contribution to mortality.

Obviously, many prior studies have aimed at elucidating reasons for the noted racial disparity in CRC survival, and multiple factors have been implicated including differences

in stage at diagnosis, tumor biology, and socioeconomic status (SES) among others (Du et al.,2007). Although stage at diagnosis is consistently more advanced among Blacks CRC patients compared with Whites, adjustment for stage alone does not explain all of the racial disparity in survival (Roetzheim et al., 2000). These findings are also supported by our findings.

Previous reports showed that African Americans diagnosed with colorectal cancer are more likely to reside within lower SES areas than their White American counterparts, suggesting that race may act as a proxy for the influence of SES on survival (Polite et al., 2006).

Other studies (Du et al. 2007), have looked at SES as one of the determinant of CRC survival disparity amongst race/ethnicity groups. SES was not analyzed in our study. Additionally, it is important to note that individual SES is unavailable in large cancer databases such as SEER, and that SES has been inconsistently defined in several studies, being most often based on neighborhood data (Krieger et al., 1997).

Moreover, marital status has also been one of the known determinants of colorectal cancer survival outcomes. Nevertheless, the relation between marital status and colon

cancer survival has not been completely explained, and data on the subject are sparse. Our data did not analyze marital status variable. For future improvement of this study we look forward to as well study marital status data in the cancer registry.

Inequalities in access to and receipt of quality health care and/or differences in comorbidities have been constantly mentioned as determinants for CRC differential survival among race and ethnicities. This study was able to look at the type of health insurance at diagnosis. However, data quality for health insurance type was uncertain at best, with more than 50 percent of the patients in the study recorded with unknown insurance type. This can bias the results of the analysis specifically in predicting survival disparity using types of health insurance. Besides, this study partly compensates the problem of comorbidities, at least for the most fetal one, by considering cause-specific survival.

Studies are inconsistent in explaining the extent to which factors other than stage of diagnosis contribute to the overall differential survival among race and ethnicities. Yet, some studies suggest that African Americans who receive cancer treatment and medical care

similar to that of whites experience similar outcomes (Ghafoor et al., 2002). For future studies, type of treatments can be studied to justify the persisting racial/ethnicity survival disparity of CRC seen in Nevada.

In the study by Mayberry (1995), the authors found that Blacks were more likely than Whites to be diagnosed with advanced disease. After adjustment for stage, however, the disparity diminished. There was no racial difference in survival for patients with distant stage metastatic disease. These results substantially support the hypothesis that black/white differences in colon cancer survival are due to later stage of disease at diagnosis among Blacks. In this study, however, after adjustment for all covariates a disparity in CRC survival was found for both Blacks and Hispanics.

Age at diagnosis is also an important predictor of survival for patients with CRC (Dominitz et al.,1998; Du et al.,2007; Roetzheim et al.,2000; Agrawal et al.,2005) and our data clearly supports this observation.

Aging is associated with decrease in many bodily functions and the elderly generally do not have as much physical reserve to combat a serious illness such as CRC as do their younger counterparts (Krieger et al., 1997;

Rabeneck et al., 2003). In addition, proximal colon cancers became relatively more common as age increases and such tumors are less likely to be diagnosed at an early stage, potentially leading to increased mortality rates seen among older patients with CRC (Krieger et al., 1997; Rabeneck et al., 2003). Blacks are more likely to be diagnosed at a younger age than White (Swan et al., 2003), which is supported by our data (table 3). The implications of this are uncertain, but, coupled with the increased likelihood that Blacks have proximal colon tumors led the American College of Gastroenterology to recommend colonoscopy as a primary screening tool for colorectal cancer in African Americans along with starting screening at an earlier age. In our study, 49.8 percent (largest to all race/ethnic groups) of Blacks were diagnosed with proximal colon.

In regards to treatment, age alone does not increase the risks associated with primary tumor resection as described by McGinnis (1994), and aggressive surgical options should be considered, regardless of age, depending on the presence of comorbidities.

Furthermore, Meyerhardt ,Giovannucci and Holmes et al.,(2006) and Meyerhardt, Heseltine, and Niedzwiecki et al.,(2006) reported that low levels of physical activity

and the metabolic syndrome, which includes obesity, are associated with higher rates of CRC, decreased overall CRC survival, and increased rates of recurrence. Other studies by (Flegal et al., 2002; Kuczmarski et al., 1994) the authors found that Blacks are more likely to be obese and physically inactive than White. To what extent these and other comorbid conditions contribute to the excess mortality observed for Blacks with CRC is uncertain. Future studies can investigate the association of physical activity, obesity, and diet on CRC racial and ethnic survival disparities.

Conclusion and Limitations

This study provides an examination of survival disparities among individuals with CRC for the first time in the state of Nevada. The NCCR includes adequate number of race and ethnic groups which allowed for the study of CRC survival disparities. In addition to a large sample size, it allowed for a more comprehensive assessment of cancer-specific survival.

There were a number of limitations experienced in the study including: limited follow-up time (2006) and its passive characteristics, as well as low quality of NCCR registry data with the majority of patients having unknown

types of insurance; also, low quality of death certificates in identifying cause of death, as well as the absence of a linkage with out-of-state deaths. All these made it difficult for accurate analysis of cancer survival rates.

In summary, this study shows that while multiple factors may account for a decreased CRC survival, they do not explain the survival disparity observed between Whites and Blacks and Hispanics in the study. This means that in Nevada the effect of race and ethnicity is still present even when accounted for all covariates. In essence, the disparity related to race and ethnic group should be further studied with improved data on health insurance and treatment.

Advanced stage at diagnosis contributed to poorer survival experience for all patients, especially in the first few years after CRC diagnosis, but other factors, including health insurance type, gender, tumor sub-location, age, and diagnosis period (Cox regression model) were also associated with decreased survival. As lack of insurance severely limits one’s ability to obtain adequate screening opportunities and appropriate treatment, it was found that CRC survival disparities existed among those

with different types of health insurance(private versus Medicare), and uninsured patients.

More aggressive screening and equal treatment opportunities would do much to remedy the survival disparity seen among Blacks and White American individuals with colorectal cancer. More public health intervention programs should focus on increasing CRC screening awareness as well as ensuring equal accessibility to health care and treatments service. Early identification of CRC cases will ultimately cut down incidence cases and improve survival.

APPENDIX

IRB APPROVAL

UNLV
UNIVERSITY OF NEVADA LAS VEGAS

Biomedical IRB – Exempt Review

Deemed Exempt

DATE: November 2, 2010

TO: **Dr. Paulo Pinheiro,** Community Health Sciences

FROM: Office of Research Integrity – Human Subjects

RE: Notification of review by Dr. John Mercer, Chair

Protocol Title: **The Determinants of Colorectal Cancer Survival Disparities in Nevada** Protocol # 1006-3492M

This memorandum is notification that the project referenced above has been as indicated in Federal regulatory statutes 45CFR46.

The protocol has been reviewed and deemed exempt from IRB review. It is not in need of further review or approval by the IRB.

Any changes to the exempt protocol may cause this project to require a different level of IRB review. Should any changes need to be made, please submit a **Modification Form**.

If you have questions or require any assistance, please contact the Office of Research Integrity – Human Subjects at IRB@unlv.edu or call 895-2794.

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VITA

Graduate College
University of Nevada, Las Vegas

Lucas N. Wassira

Degree:
Bachelor of Arts, Medical Sociology
University of Dar es Salaam, Tanzania

Special Honors and Awards:
James F. Adams/GPSA Scholarship, 2010

Thesis Title: The Determinants of Colorectal Cancer Survival Disparities in Nevada

Thesis Examination Committee:
Chairperson, Paulo Pinheiro, MD Ph.D.
Committee Member, James Symanowski, Ph.D.
Committee Member, Michelle Chino, Ph.D.
Committee Member, Sheniz Moonie, Ph.D.
Graduate Faculty Representative, Patricia Alpert, Dr.PH.