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An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
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2021

Abstract

Introduction: Prostate cancer is the most prevalent non epidermal cancer among American men, with an estimated 191,930 new cases and 33,000 deaths expected in 2020. In this study we aim to examine the association between area-level incarceration and prostate cancer mortality rates across the state of Georgia where incarceration rates are 4th in the nation.

Methods: The data was obtained from Surveillance, Epidemiology, and End Results (SEER). The study population was (n=65536), but after inclusion criteria (n=42215). Cox proportional hazard models and polytomous logistic regression were used.

Results: The overall association between incarceration and prostate cancer mortality was HR=2.60; 95% CI=0.86-1.07). Stratum specific hazard ratios for the association between arealevel incarceration and prostate cancer mortality for non-Hispanic Black vs. White men was 1.61 (95% CI=1.37-1.40) in areas of low incarceration and 2.03 (95% CI=1.74-2.36) in areas of high incarceration (defined as greater than the average rate). After accounting for covariates, the disparity in high incarceration areas was attenuated (HR=1.65; 05% CI=1.38-1.97). Incarceration was associated with development of stage III (vs. stage I) tumors (OR=1.18; 95% CI=1.07-1.31) and tumors that were undifferentiated (vs. well-differentiated) (OR=1.10; 95% CI=1.03-1.19). Conclusion: Incarceration was associated with increased mortality from prostate cancer. The race mortality disparity was most pronounced in areas of high incarceration but appear to be largely due to tumor and other neighborhood characteristics.

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Table of Contents

CHAPTER I: BACKGROUND/LITERATURE REVIEW	1
1.1 Incidence of Prostate Cancer	1
1.2 Risk Factors of Prostate Cancer	1
1.3 Disparities	1
1.4 Area level Incarceration	2
1.5 Pathophysiology	2
1.5 Mechanism of Stressors	3
1.6 Aims of Thesis	3
CHAPTER II: AREA-LEVEL INCARCERATION AS A DRIVER OF PR	OSTATE CANCER
MORTALITY IN GEORGIA	4
1.7 Abstract	4
1.8 Introduction	5
1.9 Methods	8
2.0 Results	10
2.1 Discussion	11
2.2 REFERENCES	15

2.3 TABLES	17
CHAPTER III:PUBLIC HEALTH IMPLICATIONS, DAG,	AND LITERATURE
REVIEW	21
2.4 Appendices	21
2.5 Appendix A	21
2.6 Appendix B	22
2.7 Appendix C	23

List of Tables

Table1: Patient demographic and Clinicopathological characteristics according to area-level incarceration

Table 2a: Age adjusted hazard ratios (HR) and 95% confidence intervals for the association between incarceration rates and prostate cancer specific deaths overall

Table 2b: Multivariable adjusted* hazard ratios (HR) and 95% confidence intervals for the association between incarceration rates and prostate cancer-specific death overall, and according to race

Table3: multivariable-adjusted odds ratios estimating the association between incarceration rates on prostate tumor characteristics and 95% confidence

CHAPTER I: BACKGROUND/LITERATURE REVIEW

1.1 Incidence and Risk Factors

Prostate cancer is the most prevalent non epidermal cancer among American men, with an estimated 191,930 new cases and 33,000 deaths expected in 2020(1). Globally it is the fifth leading cause of death worldwide with an estimated 1,276,106 new cases in 2018 (1). Although there has been meaningful advancement in prostate cancer treatment and mortality rates, Non-Hispanic Blacks have the highest death rate of 37.9 per 100,000 men per year with an incidence of 175.2 per 100,000 men per year (2).

The unmodifiable risk factors of prostate cancer established by many studies, are age, race, geography, family history and gene mutations. There are also other less confirmed risk factors such as diet, smoking, sexually transmitted infections, chemical exposures, and other socioeconomic factors (3).

1.2 Disparities

Though Non-Hispanic Blacks have genetic related factors that increase their risk of prostate cancer, almost all Genome wide associated study (GWAS) are conducted in men of European descent, only one GWAS has been conducted in men of African ancestry (7). Disparities in prostate cancer by race and ethnicity is a known public health issue, but the primary causes are not well documented. Several factors have been suggested as contributors such as differences in tumor characteristics, disease management and treatment, health care availability, sociodemographic and neighborhood characteristics (8,9,10).

Another epidemiologic study found that prostate cancer mortality rate was 1.5 times higher in men living in high-deprivation neighborhoods than in those living in the most affluent

neighborhoods. Mortality rates were connected to certain individual-level characteristics, such as age, marital status, family income, educational attainment, immigration status, urban/rural status, mobility, and comorbidity (12). Prior studies on neighborhood factors and prostate cancer proposed that neighborhoods with poor socioeconomic (SES) issues are related to high-grade prostate cancer regardless of individual-level exposures (13,14).

1.3 Area Level Incarceration and Health

The United states has the largest percentage of residents in jail or prison. The burden of mass incarceration is an important social determinant of health in urban communities because of persistent inequalities. Some of these urban centers are called urban "Million Dollar Blocks" because a large amount of tax income is spent every year incarcerating residents.

Neighborhoods with high incarceration rates have poor community health and higher crime rates. Several studies have examined the impact of individual and family member incarceration and found associations with adverse health outcomes (19,20). Homelessness, job security and poverty are common among people released from prison facilities and have been associated with mortality by several studies (15,16). Non-Hispanic Black men are exposed to many hard life experiences such as reduced access to quality education, lack of employment, and high rates of incarceration than any other racial group. Incarceration related stressors are important social determinants of health (21,22).

1.4 Pathophysiology

The prostate is a male reproductive organ about 3 cm long and weighing about 1 ounce. It is a gland that plays an important role in the production of seminal fluids. It is located above the pelvic floor muscles and underneath the bladder. The prostate gland is covered by a pericarp of

connective tissue of smooth muscle fibers and elastic connective tissue, also located on inside of the prostate. The glandular tissue produces over 30% of the semen and provides an alkaline medium for sperm to survive (30,31). Prostate adenocarcinoma develops mostly in the glandular parts of the prostate cells and begin to grow out of control due to a mutation. The cancer frequently metastasizes in the lymph nodes and bones (31).

1.5 Mechanism of Neighborhood Factors and Prostate Cancer

New research has indicated that inflammation is a likely pathway for prostate cancer progression (14). Environmental stress is a pathway for many primary neighborhood factors, such as area level incarceration, which can affect health. Chronic stress has been identified as potential pathways that increase the risk of disease and may be connected to general social economic status (17). Stress associated with poverty increases the risk of many chronic illnesses such as cancers. As stress response is prolonged it results in a suppressed immunity and reduces protection against diseases. It can also affect reproductive hormones and immune responses (14,17,).

1.6 Aims of Thesis

Working Aim 1. To examine the association between neighborhood incarceration rates and prostate cancer mortality among men diagnosed with invasive prostate cancer in Georgia.

Working Aim 2. To explore potential heterogeneity in the association between neighborhood incarceration rates and prostate cancer mortality by sociodemographic characteristics including race.

Hypothesis: High incarceration rate is associated with prostate cancer mortality with non-Hispanic Blacks associated with the highest risk and disparities.

CHAPTER II: AREA-LEVEL INCARCERATION AS A DRIVER OF PROSTATE CANCER MORTALITY IN GEORGIA

1.7 Abstract

Introduction: Prostate cancer is the most prevalent non epidermal cancer among American men, with an estimated 191,930 new cases and 33,000 deaths expected in 2020. In this study we aim to examine the association between area-level incarceration and prostate cancer mortality rates across the state of Georgia where incarceration rates are 4th in the nation.

Methods: The data was obtained from Surveillance, Epidemiology, and End Results (SEER). The study population was (n=65536), but after inclusion criteria (n=42215). Cox proportional hazard models and polytomous logistic regression were used.

Results: The overall association between incarceration and prostate cancer mortality was HR=2.60; 95% CI=0.86-1.07). Stratum specific hazard ratios for the association between arealevel incarceration and prostate cancer mortality for non-Hispanic Black vs. White men was 1.61 (95% CI=1.37-1.40) in areas of low incarceration and 2.03 (95% CI=1.74-2.36) in areas of high incarceration (defined as greater than the average rate). After accounting for covariates, the disparity in high incarceration areas was attenuated (HR=1.65; 05% CI=1.38-1.97). Incarceration was associated with development of stage III (vs. stage I) tumors (OR=1.18; 95% CI=1.07-1.31) and tumors that were undifferentiated (vs. well-differentiated) (OR=1.10; 95% CI=1.03-1.19). Conclusion: Incarceration was associated with increased mortality from prostate cancer. The race mortality disparity was most pronounced in areas of high incarceration but appear to be largely due to tumor and other neighborhood characteristics.

1.8 Introduction

Prostate cancer is the most prevalent non epidermal cancer among American men, with an estimated 191,930 new cases and 33,000 deaths expected in 2020 (1). Globally it is the fifth leading cause of death worldwide with an estimated 1,276,106 new cases in 2018 (1). Although there has been meaningful advancement in prostate cancer treatment and mortality rates, Non-Hispanic Blacks have the highest death rate of 37.9 per 100,000 men per year with an incidence of 175.2 per 100,000 men per year (2). The unmodifiable risk factors of prostate cancer established by many studies, are age, race, geography, family history and gene mutations. There are also other less confirmed risk factors such as diet, smoking, sexually transmitted infections, chemical exposures, and other socioeconomic factors (3). Societal and environmental factors that contribute to prostate cancer risk are not well-known.

Several studies have shown that non-Hispanic Blacks have the highest likelihood of developing prostate cancer in their lifetime. They are also more predisposed to have advanced disease at the time of diagnosis and have twice the mortality rate than White men. They are also more likely to be diagnosed at younger ages and succumb to their cancer(5).

An epidemiological study using The Prostate Cancer Outcomes Study resources has been instrumental in our current understanding of Black White differences in prostate cancer (4). Non-Hispanic Blacks within the cohort were generally younger with age < 60 and had not completed high school, were poorer, likely uninsured, unemployed, likely to not have a previous PSA test and also more likely to have urinary symptoms (4,5). Non-Hispanic Blacks had more comorbidities, highest PSA levels and high rate of poorly differentiated cancers. Non-Hispanic Blacks who did not complete high school and lacked insurance were more likely than non-

Hispanic Whites to have advanced prostate cancer. Even with high socioeconomic status, the rate of advanced disease still increased in Non-Hispanic Blacks (4,5,6).

Though Non-Hispanic Blacks have genetic related factors that increase their risk of prostate cancer, almost all Genome wide associated study (GWAS) are conducted in men of European descent, only one GWAS has been conducted in men of African ancestry (7). An epidemiologic study showed that 38 out of 68 prostate cancer SNPs have higher risk allele frequencies in African populations, however, 9 out of 13 most divergent SNPs have higher risk allele frequencies in African populations than in non-African populations (7).

Disparities in prostate cancer by race and ethnicity is known public health issue, but the primary causes are not well documented. Several factors have been suggested as contributors such as differences in tumor characteristics, disease management and treatment, health care availability, sociodemographic and neighborhood characteristics (8,9,10). An epidemiologic study showed that a 24% of this survival disparity was attributable to differences in diagnosis stage, 14% was due differences in marital status, and 7% was explained by neighborhood SES. The adjusted covariables explained 48% of the overall disparities in prostate cancer survival across all racial groups (8). Another epidemiologic study found that prostate cancer mortality rate was 1.5 times higher in men living in high-deprivation neighborhoods than in those living in the most affluent neighborhoods. Mortality rates were connected to certain individual-level characteristics, such as age, marital status, family income, educational attainment, immigration status, urban/rural status, mobility, and comorbidity (12).

Prior studies on neighborhood factors and prostate cancer proposed that socially and economically improvised neighborhoods are more likely to have high-grade prostate cancer regardless of individual-level exposures (13,14). The United States has the largest percentage of

residents in jail or prison, the burden of mass incarceration is an important social determinant of health in urban communities because of persistent inequalities. Some of these urban centers are called urban "Million Dollar Blocks" because a large amount of tax income is spent every year incarcerating residents.

Neighborhoods with high incarceration rates have poor community health and higher crime rates. Several studies have examined the impact of individual and family member incarceration and found associations with adverse health outcomes (19,20). Homelessness, job insecurity and poverty are common among people released from prison facilities and have been associated with mortality by several studies (15,16). Non-Hispanic Black men are more exposed to many hard life experiences such as reduced access to quality education, lack of employment, and high rates of incarceration than any other racial group. Incarceration related stressors are important social determinants of health (21,22). Stress associated with societal and environmental factors can increase the risk of many chronic diseases. The mechanism by which a stressful environment affects the inflammation processes is not well known, but chronic stress and stressors have been identified as a potential pathway for cancer. Neighborhood deprivation, urbanization, poverty, education, residential racial segregation, social disorder, population density and incarceration may influence health-related outcomes at both the individual and community levels. (14,17,18).

In this thesis we aim to examine the association between area-level incarceration and prostate cancer mortality rates across the state of Georgia where incarceration rates are 4th in the nation with 490 per 100,000 people incarcerated and 1 in 33 black adult males. The state has 34% black residents, but 51% of people in jail and 60% of people in prison are black, and there remain disparities in prostate cancer severity and outcomes (25).

1.9 Methods

Study Population

The data was obtained for all cases of invasive prostate cancer among Non-Hispanic Blacks and Non-Hispanic Whites diagnosed between 2010 and 2014 from Surveillance, Epidemiology, and End Results (SEER). The Program provides information on cancer statistics to reduce the cancer burden in the United States. It is supported by the Surveillance Research Program (SRP) in NCI's Division of Cancer Control and Population Sciences (DCCPS). It contains data from 9 population-based cancer registries (Connecticut, Detroit, Atlanta, San Francisco-Oakland, Hawaii, Iowa, New Mexico, Seattle-Puget Sound, and Utah). The SEER program is funded by the National Institutes of Health and the National Cancer Institute. Prostate cancer-specific mortality was obtained from SEER using active and passive surveillance for various Georgia counties. Overall survival was calculated from the date of cancer diagnosis to date of death, or censored (23). Censured individuals are those that died from causes other than the specified outcome (prostate cancer) or their cause of death was not verified as related the outcome due to site of metastasis been attributed as cause of death. The inclusion criteria include men 45-69 years of age with a complete history of diagnosis, treatment, and tumor grade. Men were excluded if their prostate cancer was diagnosed after death, outside the age criteria, missing data on covariates or have an incomplete treatment history and tumor characteristics. Neighborhood characteristics were collected from the American community survey (ACS), which is an important source for detailed population and housing information. The data from ACS represents all 159 Georgia counties. The study population was (n=65536), but after inclusion criteria (n=42215).

Exposure

The main exposure of interest is area level incarceration. This was obtained using ACS survey and area-level characteristics were assigned based on residential address from the date of cancer diagnosis, using a validated census tract composite index.

Outcome

The outcome was prostate cancer survival, defined as the period from start of treatment to death. This dependent variable was accessed across different race groups. Anatomic location and histology were coded using the International Classification of Diseases for Oncology (ICD-O) edition during diagnosis period (24).

Covariates

The covariates include race, age at diagnosis, tumor characteristics, and treatment type(radiation/Chemotherapy). Tumor characteristics used in this analysis included cancer stage at diagnosis, and tumor grade. The tumor grade was categorized as well differentiated, moderately differentiated, poorly differentiated, and undifferentiated. The stage at diagnosis was classified as distant (stage3), localized (stage1), regional (stage2), and upstaged. The neighborhood covariates, median household income and area level education, were obtained from ACS as previously described.

Statistical Analysis

Cox proportional hazard models were used to calculate age adjusted hazard ratios and 95% confidence intervals for the association between incarceration rate and prostate cancer specific death, and multivariable adjusted hazard ratios and 95% confidence intervals to examine the association between area level incarceration and prostate cancer specific mortality overall.

The association between incarceration and tumor characteristics was also examined. Hazard

ratios were calculated and corresponding 95% confidence intervals reported. Death from disease was the end point. Polytomous logistic regression was also used to estimate multivariable-adjusted odds ratios (OR) and corresponding 95% confidence intervals of the association between incarceration rates and prostate tumor characteristics.

For each analysis, the referent group was based on which group had the lowest risk of outcome. All analyses were conducted using SAS version 9.4 (SAS Institute, Cary, USA).

2.0 Results

Table1 shows demographic characteristics according to area level incarceration rate (cut points < or > median 0.0422). The median age at diagnosis for the cohort was 62 years for both high and low incarceration quartiles. The average length of follow up (survival) was 54 years in areas of high incarceration and 53 in low incarceration areas. Non-Hispanic Blacks had the higher representation in the cohort at 53.7% (11272), non-Hispanic Whites were 46.3% (9717). Non-Hispanic Blacks were 1.81 times more likely to die from prostate cancer when compared to Non-Hispanic Whites (1.81 CI:1.63-2.01). Localized prostate cancer or stage 1 was the highest at 84.1% for individuals with high incarceration and 82.7% for individuals with low incarceration. A large portion of the cohort had moderately differentiated tumors at 43.3%, followed by poorly differentiated tumors at 42.86% in areas of high incarceration. For both low and high incarceration areas, receipt of chemotherapy was high. There were a greater proportion of individuals with median income ≥ \$46,000 in areas of low incarceration.

Table 2a provided the age adjusted hazard ratios and 95% confidence intervals for the association between area level incarceration and prostate cancer specific death. The overall hazard ratio for incarceration was 2.60(CI: 0.86-1.07). Stratum specific hazard ratios for the

association between area-level incarceration and prostate cancer mortality for non-Hispanic Black vs. White men was 1.61 (95% CI=1.37-1.40) in areas of low incarceration and 2.03 (95% CI=1.74-2.36) in areas of high incarceration (defined as greater than the average rate). The corresponding interaction p-value was 0.0425.

Table 2b shows the multivariable adjusted hazard ratios (HR) and 95% confidence intervals for the association between incarceration rates and prostate cancer-specific deaths overall, and according to race. The overall hazard ratio and 95% confidence intervals for incarceration rate in the model was 2.59 (CI: 0.83-1.08). We saw no stratum specific differences in mortality by race in multivariable models.

Table 3a shows multivariable-adjusted odds ratios estimating the association between incarceration rates on prostate tumor characteristics. Individuals living in areas of high incarceration were slightly more likely to develop stage III tumors (OR=1.18; 95% CI=1.07-1.31) and tumors that were undifferentiated (OR=1.10; 95% CI=1.03-1.19).

2.1 Discussion

Incarceration was associated with increased mortality from prostate cancer. In our study, Non-Hispanic Blacks were almost twice likely to have increased mortality from prostate cancer than non-Hispanic Whites. There was an interaction between race and incarceration in age-adjusted models. In the multivariable model interaction did not persist. Incarceration was associated with increased odds of developing stage 3 prostate cancer, and we observed a monotonic increase in tumor aggressiveness according to grade. At high incarceration rates individuals were more likely to develop undifferentiated tumors.

These findings make a number of contributions to existing research. Several studies have examined the relationship between incarceration and many individual-level health outcomes. The findings from (Schnittker et al) found that individuals with a history of incarceration have more chronic health problems after their period of incarceration than before. The authors concluded that incarceration was associated with a negative change in health status (26). They also found that the length of incarceration was not a factor but incarceration itself affected health negatively (26). In our study we extend these observations to persons living in areas of high incarceration, which we found to be associated with prostate cancer mortality. High area-level incarceration was associated with poor tumor characteristics including late-stage disease and undifferentiated tumors which are more aggressive and harder to treat.

Another epidemiologic study found that those who had been incarcerated disproportionately suffer from infectious diseases and stress-related illness (22), which may burden not only the individuals but families, neighborhoods, and entire communities. Parental incarceration leads to poor health outcomes for children by increasing the possibility that children will embrace behaviors associated with poor health (22). Lee et al., found that having a family member incarcerated increased the probability of experiencing poor health outcomes such as heart attack and stroke. Another study suggested that tumor grade in African Americans may be particularly affected neighborhood influences (29). There is limited research that has explored the association between incarceration rates and relative poverty rates on a crossnational level, but there is some evidence that higher rates of incarceration may be associated with higher rates of relative poverty (27,28). Our study did not look at how county level income affected the association between incarceration rate and mortality.

Living in areas with high incarceration may be a chronic stressor, which has been identified as potential pathways that increase risk of chronic diseases such as cancer and cardiovascular disease. As stress response is prolonged it results in suppressed immunity and reduces protection against diseases. It can also affect reproduction of hormones and immune responses. Many cellular and molecular pathways that promote cancer development like DNA repair mechanisms could be damaged because of stress. Stress affects the expression of viral oncogenes and the replication of tumorigenic viruses. It can also promote tumor proliferation providing blood supply to the tumors (14,17). Research have also shown that chronic exposure to hostile conditions is associated with immune dysfunction (28). We found that tumor proliferation was associated with high incarceration rates and is consistent which these prior observations. Although our study made some interesting findings there were several limitations. Most significantly, the models and results are based on county level data from Georgia. This makes it difficult to intervene person to person, but we can have health intervention on community levels. We did not account for other area-level factors such as education or access to care and did not obtain individual-level characteristics which may impact our findings. We similarly did not account for variations in incarceration races, area-level characteristics, or mortality rates over time. Despite the limitations, our study made some contributions to existing research. It provides the first evidence that area-level incarceration is associated with increased mortality from prostate cancer. The study also showed that high incarceration rates was associated with

Conclusions

Our findings yield opportunity for understanding the ways in which the criminal justice system impacts the health of neighborhoods. This work may also inform future thinking about how

undifferentiated tumors which is known to increase tumor aggressiveness.

structural factors (such as incarceration) mechanistically impact tumor aggression. Given that non-Hispanic Blacks disproportionately reside in neighborhoods with high incarceration rates, open dialogue and intervention is needed to reduce racialized incarceration. We anticipate efforts to reduce area-level incarceration would have downstream impacts on poverty, crime, income, and education, thus improving overall health in communities most impacted.

2.2 References

- 1. Rawla, Prashanth. "Epidemiology of Prostate Cancer." *World journal of oncology* vol. 10,2 (2019): 63-89. doi:10.14740/wjon1191
- 2. Kelly, Scott P et al. "Trends in the Incidence of Fatal Prostate Cancer in the United States by Race." *European urology* vol. 71,2 (2017): 195-201. doi:10.1016/j.eururo.2016.05.011
- 3. American Cancer Society: https://www.cancer.org/cancer/prostate-cancer/causes-risks-prevention/risk-factors.html
- 4. Richard M. Hoffman, Frank D. Gilliland, J. William Eley, Linda C. Harlan, Robert A. Stephenson, Janet L. Stanford, Peter C. Albertson, Ann S. Hamilton, W. Curtis Hunt, Arnold L. Potosky, Racial and Ethnic Differences in Advanced-Stage Prostate Cancer: the Prostate Cancer Outcomes Study, *JNCI: Journal of the National Cancer Institute*, Volume 93, Issue 5, 7 March 2001, Pages 388–395, https://doi.org/10.1093/jnci/93.5.388
- 5. Dess RT, Hartman HE, Mahal BA, et al. Association of Black Race With Prostate Cancer–Specific and Other-Cause Mortality. *JAMA Oncol.* 2019;5(7):975–983. doi:10.1001/jamaoncol.2019.0826
- 6. Jemal, Ahmedin et al. "Geographic Patterns of Prostate Cancer Mortality and Variations in Access to Medical Care in the United States." *Cancer Epidemiology Biomarkers & Prevention* 14 (2005): 590 595.
- 7. Lachance, Joseph et al. "Genetic Hitchhiking and Population Bottlenecks Contribute to Prostate Cancer Disparities in Men of African Descent." *Cancer research* vol. 78,9 (2018): 2432-2443. doi:10.1158/0008-5472.CAN-17-1550
- 8. Ellis, Libby et al. "Racial and Ethnic Disparities in Cancer Survival: The Contribution of Tumor, Sociodemographic, Institutional, and Neighborhood Characteristics." *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* vol. 36,1 (2018): 25-33. doi:10.1200/JCO.2017.74.2049
- 9. Lai Y, Wang C, Civan JM, et al.: Effects of cancer stage and treatment differences on racial disparities in survival from colon cancer: A United States population-based study. Gastroenterology 150:1135-1146, 2016
- 10. Aizer AA, Wilhite TJ, Chen MH, et al.: Lack of reduction in racial disparities in cancer-specific mortality over a 20-year period. Cancer 120:1532-1539, 2014
- 11. DeRouen MC, Schupp CW, Yang J, et al. Impact of individual and neighborhood factors on socioeconomic disparities in localized and advanced prostate cancer risk. *Cancer Causes Control*. 2018;29(10):951-966. doi:10.1007/s10552-018-1071-7
- 12. Li X, Sundquist K, Sundquist J. Neighborhood deprivation and prostate cancer mortality: a multilevel analysis from Sweden. *Prostate Cancer Prostatic Dis.* 2012;15(2):128-134. doi:10.1038/pcan.2011.46
- 13. Diez Roux AV, Mair C. Neighborhoods and health. Annals of the New York Academy of Sciences. 2010;1186(1):125–45
- 14. Zeigler-Johnson C, Tierney A., Rebbeck TR, Rundle A. Prostate Cancer Severity Associations with Neighborhood Deprivation. Prostate Cancer 2011
- 15. Mathew P, Elting L, Cooksley C, Owen S, Lin J. Cancer in an incarcerated population. *Cancer*. 2005;104(10):2197-2204. doi:10.1002/cncr.21468

- 16. Binswanger, Ingrid A et al. "Clinical risk factors for death after release from prison in Washington State: a nested case-control study." *Addiction (Abingdon, England)* vol. 111,3 (2016): 499-510.
- 17. Baum A, Garofalo JP, Yali AM. Socioeconomic status and chronic stress. Does stress account for SES effects on health? *Annals of the New York Academy of Sciences*. 1999;896:131–144.
- 18. Chang VW. Racial residential segregation and weight status among US adults. *Social Science and Medicine*. 2006;63(5):1289–1303
- 19. Rose DR, Clear TR. Incarceration, social capital, and crime: implications for social disorganization theory. Criminology. 1998;36(3):441–480
- 20. Sealy-Jefferson, Shawnita et al. "Neighborhood-Level Mass Incarceration and Future Preterm Birth Risk among African American Women." Journal of urban health: bulletin of the New York Academy of Medicine vol. 97,2 (2020): 271-278. doi:10.1007/s11524-020-00426-w
- 21. Massoglia M. Incarceration as exposure: the prison, infectious disease, and other stressrelated illnesses. J Health Soc Behav 2008;49(1):56–71
- 22. Xanthos Clare et al." Social determinants of health among African—American men". doi:10.1016/j.jomh.2009.12.002
- 23. Howlader N, Noone AM, Krapcho M, et al., eds. SEER Cancer Statistics Review, 1975–2012. Bethesda, MD: National Cancer Institute; 2015. http://seer.cancer.gov/csr/1975 2012/. Accessed June 10, 2016.
- 24. World Health Organization. International Classification of Diseases for Oncology. 3rd ed.Geneva, Switzerland: World Health Organization Press; 2000.
- 25. Vera institute of Justice: Derived on March 24th, 2021.https://www.vera.org/downloads/pdfdownloads/state-incarceration-trendsgeorgia.pdf
- 26. Enduring stigma: the long-term effects of incarceration on health. Schnittker J, John A J Health Soc Behav. 2007 Jun; 48(2):115-30.
- 27. A heavy burden: the cardiovascular health consequences of having a family member incarcerated. Lee H, Wildeman C, Wang EA, Matusko N, Jackson JS Am J Public Health. 2014 Mar; 104(3):421-7.
- 28. Massoglia, Michael, and William Alex Pridemore. "Incarceration and Health." Annual review of sociology vol. 41 (2015): 291-310. doi:10.1146/annurev-soc-073014-112326
- 29. Subramanian SV, Kubzansky L, Berkman L, Fay M, Kawachi I. Neighborhood effects on the self-rated health of elders: uncovering the relative importance of structural and service-related neighborhood environments. Journals of Gerontology—Series B. 2006;61(3):S153–S160.
- 30. Goh CL, Saunders EJ, Leongamornlert DA et al. Clinical implications of family history of prostate cancer and genetic risk single nucleotide polymorphism (SNP) profiles in an active surveillance cohort. BJU Int 2013; 112: 666–73
- 31. Tortajada JF, Castell JG, Tornero OB, Garcia JAO. Constitutional risk factor in PCa. Acta Urol Esp. 2011; 35(5):282-8.

2.3 TABLES

Table 1: Patient demographic and Clinicopathological characteristics according to area-level incarceration

	Incarcera	Incarceration high		Incarceration low	
	(n=20989)		(n=26775)		
Characteristic	Median	SD	Median	SD	
Age at Diagnosis	62	5.78	62	5.76	
Length of Follow-up	54	35.41	35.49	53	
Time to outcome	29	26.92	30	27.39	
	N	%	N	%	
Race/ethnicity					
White	9717	46.3	20936	72.11	
Black	11272	53.7	5839	27.89	
Stage					
Distant	881	4.2	707	3.38	
Localized	17651	84.1	17313	82.69	
Regional	1982	9.44	2509	11.98	
Un-staged	475	2.26	407	1.94	
Tumor characteristics (Grade)					
Well differentiated	1947	9.3	2054	9.82	
Poorly differentiated	8996	42.96	18062	41.88	

Moderately	9095	43.43	9306	44.51
Undifferentiated	37	0.18	21	0.1
Unknown	867	4.14	771	3.69
Chemotherapy				
Yes	217	1.04	197	0.86
No/Unknown	20725	98.96	20757	99.14
Radiation				
Yes	16659	39.46	9045	43.09
No/unknown	25556	60.54	11944	56.91
Median Income				
<\$30,000	62	0.3	0	0
\$30,000-\$34,999	201	0.96	86	0.41
\$35,000-\$45,999	5796	27.61	1594	7.61
≥\$46,000	14930	71.13	19256	91.98

Table 2a Age adjusted hazard ratios(HR) and 95% confidence intervals for the association between incarceration rates and prostate cancer specific deaths overall

	Deaths (N)	Overall HR (95% CI)		aths N)	Stratified Effects HR (95% CI)
	Overall	,	NHW	NHB	
Incarceration					
Low	656	referent	431	225	1.61(1.37-1.40)
High	768	2.60(0.86- 1.07)	249	516	2.03(1.74-2.36)
					Interaction p-value = 0.0425

^{*}adjusted for age

Table 2b: Multivariable adjusted* hazard ratios (HR) and 95% confidence intervals for the association between incarceration rates and prostate cancer-specific death overall, and according to race.

	Deaths (N)	Overall HR (95% CI)	Dea (N		Stratified Effects HR (95% CI)
	Overall	,	NHW	NHB	
Incarceration					
Low	656	referent	431	225	1.43(1.19-1.72)
High	768	2.59(0.83- 1.08)	249	516	1.65(1.38-1.97)
_					Interaction p-value =
					0.2663

^{*}Adjusted for: age, race, income, grade, stage

Table 3a. Multivariable-adjusted odds ratios estimating the association between incarceration rates on prostate tumor characteristics

Stratified Effects OR (95% CI)

high vs. low incarceration

Stage

I referent

II 0.79(0.74-0.84)

III 1.18(1.07-1.31)

Tumor differentiation

Well differentiated referent

Moderately 1.06(0.99-1.14)

Undifferentiated 1.10(1.03-1.19)

^{*}adjusted for age, income, incarceration

CHAPTER III: PUBLIC HEALTH IMPLICATION, DIRECTED ACYLIC GRAPH(DAG) AND LITERATURE REVIEW

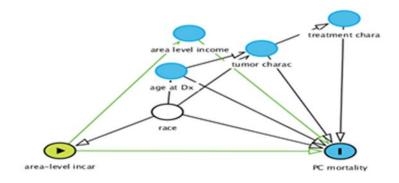
2.4 Appendices

2.5 Appendix A

Public Health Implications

The goal of this thesis was to improve the understanding of the relationship between area level incarceration and prostate cancer mortality and the disparities that impact mortality and morbidity. The findings can help in understanding the process in which the criminal justice system negatively impacts community health and how neighborhood factors are also affected. It can also further help in the discussion of social economic disparities and how they affect neighborhood health. This work may also contribute to future research about how structural factors such as incarceration affect tumor aggression and survival.

2.6 Appendix B



- exposure
- outcome
- ancestor of exposure
- ancestor of outcome
- ancestor of exposure and outcome
- O adjusted variable

2.7 Appendix C

Lead auth year	nor, J, name pub	Study Design	Study Population	End Point	Results	Comments
	I	Prostate Cancer Mor	tality and Disp	arity		
M G of Pr M O 35	letcher SA, Marchese M, Cole AP, et al. Geographic Distribution f Racial Differences in rostate Cancer Mortality. <i>JAMA Netw Open.</i> 2020;3(3):e2018 9. oi:10.1001/jamanetwo kopen.2020.1839	cohort study used the Surveillance, Epidemiology, and End Results (SEER)	U.S men	Disparity and mortality	Black men had the highest risk of mortality (AHR, 1.39; 95% CI, 1.30-1.48). These findings are consistent with the idea that racial differences in prostate cancer survival are subject to geographic variation.	Black men were more likely than men of other races to be uninsured (black: 1057 men [3.0%]; white: 2059 men [1.2%]; other: 204 men [1.2%]), have low education level (black: 21 731 men [62.1%]; white: 83 655 men [47.0%]; other: 7261 men [43.9%]), and have low income (black: 21 318 men [60.9%]; white: 85 582 men [48.0%]; other: 6047 men [36.5%])
MAAR:	Dess RT, Hartman HE, Mahal BA, et al. Association of Black Bace with Prostate Cancer—Specific and Other-Cause Mortality. JAMA Dicol. 2019;5(7):975—83. oi:10.1001/jamaoncol. 019.0826	SEER Cohort	U.S men	Mortality and Disparity	median age of black men was 2 to 3 years younger than in each cohort, and had 30% relative increased sub distribution PCSM hazard in the age adjusted IPW model (sHR, 1.30; 95% CI, 1.23-1.37; <i>P</i> < .001	In our study, black race was not associated with worse PCSM outcomes in men with newly diagnosed nonmetastatic prostate cancer treated within health care systems with standardized access
3. G E, K ar m ac sy 20	Graham-Steed T, Uchio J, Wells CK, Aslan M, To J, Concato J. 'Race' and prostate cancer nortality in equal-ccess healthcare ystems. <i>Am J Med</i> . 013;126(12):1084-088. 0i:10.1016/j.amjmed.2 13.08.012	Literature Review	U.S	Mortality and Disparity	Among 5 reports providing quantitative results for the association of race and mortality among men with prostate cancer in equalaccess systems	Mortality among black and white patients with prostate cancer is similar in equal-access healthcare systems. Studies that find racial differences in mortality (including cause-specific mortality)

4.	Tewari, Ashutosh K et al. "Effect of socioeconomic factors on long-term mortality in men with clinically localized prostate cancer." <i>Urology</i> vol. 73,3 (2009): 624-30. doi:10.1016/j.urology.2 008.09.081	All cases (n = 2046) of clinically localized prostate cancer diagnosed from 1990 to 2000 at the Henry Ford Health System and the Henry Ford Medical Group	U. S Mortality and No	Disparity and mortality	Of the 2046 cases, 1243 were white and 803 were black. Black patients were more likely to have lower incomes, a greater baseline prostate-specific antigen level, and greater comorbidities.	In this cohort, socioeconomic factors were sufficient to explain the disparity in survival between white and black patients
5.	Derouen MC, Schupp CW, Koo J, et al. Impact of individual and neighborhood factors on disparities in prostate cancer survival. <i>Cancer Epidemiol</i> . 2018;53:1-11. doi:10.1016/j.canep.2018.01.003	Individual-level data from the California Collaborative Prostate Cancer Study, a population-based study of non-Hispanic White (NHW), Hispanic, and African American prostate cancer cases (N = 1800) diagnosed from 1997 to 2003,	U.S	Mortality and Neighborhood factors	African American men had worse survival than NHW men, which was attenuated by nSES. Increased risk of death was associated with residence in lower SES neighborhoods (quintile 1 (lowest nSES) vs. 5: HR = 1.56, 95% CI: 1.11-2.19) and lower education (<high 95%="" ci:<="" college:="" hr="1.32," school="" td="" vs.=""><td>Multivariable, stage- stratified Cox proportional hazards regression models with cluster adjustments were used to assess education and nSES main and joint effects on overall survival, before and after adjustment for social and built environment factors</td></high>	Multivariable, stage- stratified Cox proportional hazards regression models with cluster adjustments were used to assess education and nSES main and joint effects on overall survival, before and after adjustment for social and built environment factors
6.	Ellis, Libby et al. "Racial and Ethnic Disparities in Cancer Survival: The Contribution of Tumor, Sociodemographic, Institutional, and Neighborhood Characteristics." Journa l of clinical oncology: official journal of the American Society of Clinical Oncology vol. 36,1 (2018): 25-33. doi:10.1200/JCO.2017. 74.2049	California Cancer Registry data were used to estimate population-based cancer-specific survival for patients diagnosed with breast, prostate, colorectal, or lung cancer between 2000 and 2013	U.S	Mortality disparity and neighborhood characteristic	In baseline models, black patients had the lowest survival for all cancer sites, and Asian American and Pacific Islander patients had the highest, compared with whites. Mediation analyses suggested that stage at diagnosis had the greatest influence on overall racial/ethnic survival disparities accounting for 24% of disparities in breast cancer, 24% in prostate cancer, and 16% to 30% in colorectal cancer	Neighborhood SES was an important factor in all cancers, but only for black and Hispanic patients. The influence of marital status on racial/ethnic disparities was stronger in men than in women. Adjustment for all covariables explained approximately half of the overall survival disparities in breast, prostate, and colorectal cancer, but it explained only 15% to 40% of disparities in lung cancer.
7.	Zeigler-Johnson, Charnita M et al. "Prostate cancer severity associations with neighborhood deprivation." <i>Prostate</i> <i>cancer</i> vol. 2011 (2011): 846263. doi:10.1155/2011/8462	Pennsylvania Department of Health was provided on prostate cancer patients diagnosed in the Commonwealth of Pennsylvania from 1995 to 2007	U.S	Disparities	There were significant ethnic differences for all neighborhood-level variables (<i>P</i> < 0.001). Compared to Caucasians patients (38-39%), African Americans (86–89%) were more likely to live in low-SES neighborhoods, characterized by belowsample median income and education. The neighborhoods of African American cases were also	Compared to Caucasians, African Americans were younger (66 versus 68 years), less likely to be married (57% versus 77%), and more likely to have unfavorable prostate cancer characteristics (high- stage, 15% versus 12%, and high Gleason Score, 28% versus 22%).

			more likely to have higher than median percentages of poverty, single female head of households, no car ownership, and households on public assistance	
Identified Pennsylvania Cancer Registry cases diagnosed between January 2000 and December 2015. Totally, 128,568 participants	U.S	Neighborhood and Mortality	Most participants were diagnosed with localized disease (85%). Participants in greener neighborhoods (Q5) had lower population density, higher census Block Group income and median home value than participants in less green neighborhoods (Q1)	Estimated proportions of racial disparity in mortality that would be eliminated by fixing residential greenness to the 75th percentile of NDVI (White) were modest for all-cause (5.3%) and prostate-specific (23.2%) mortality. However, for CVD mortality, we estimated a relative 50.5% increase in the racial disparity after this hypothetical intervention
Pennsylvania Cancer Registry data were linked to U.S. Census data.	U.S	Neighborhood variable and prostate cancer	17 new neighborhood variables associated with PCA. These variables represented income, housing, employment, immigration, access to care, and social support. The top hits or most significant variables related to transportation (OR = 1.05;CI = 1.001–1.09) and poverty (OR = 1.07;CI = 1.01–1.12)	Findings confirm some previous associations, but also provide new insights into the role of neighborhood in prostate cancer and suggest the potential value of NWAS to inform public health interventions and multilevel studies
Prostate Cancer	and Mortality ar	nd (Incarceration or	Prison)	
Nested case control study of people released from prison.	U.S	Mortality	factors for all-cause mortality included homelessness (Odds Ratio [OR] 1.53, 95% Confidence Interval [CI] 1.06, 2.23 medications before release (OR 2.37, 95% CI 1.71, 3.29). Independent risk factors for overdose mortality included substance dependence (OR	study identified important clinical and social risk factors for all-cause and overdose death after release from prison homelessness upon release
	Pennsylvania Cancer Registry cases diagnosed between January 2000 and December 2015. Totally, 128,568 participants Pennsylvania Cancer Registry data were linked to U.S. Census data. Prostate Cancer Nested case control study of people released	Pennsylvania Cancer Registry cases diagnosed between January 2000 and December 2015. Totally, 128,568 participants Pennsylvania Cancer Registry data were linked to U.S. Census data. Prostate Cancer and Mortality ar Nested case control study of people released	Pennsylvania Cancer Registry cases diagnosed between January 2000 and December 2015. Totally, 128,568 participants U.S Neighborhood variable and prostate cancer Prostate Cancer and Mortality and (Incarceration or Nested case control study of people released And Mortality And Mortality Incarceration or And Mortality And Mortality	Identified

11. Zhou Y, Bemanian A, Beyer KM. Housing Discrimination, Residential Racial Segregation, and Colorectal Cancer Survival in Southeastern Wisconsin. Cancer Epidemiol Biomarkers Prev. 2017;26(4):561- 568. doi:10.1158/1055- 9965.EPI-16-0929	Cancer incidence data were obtained from the Wisconsin Cancer Reporting System for two southeastern Wisconsin metropolitan areas	U. S	Housing discrimination and Mortality	For all-cause mortality, racial bias in mortgage lending was significantly associated with a greater hazard rate among blacks [HR = 1.37; 95% confidence interval (CI), 1.06-1.76] and among black women (HR = 1.53; 95% CI, 1.06-2.21	Our findings indicate that black women in particular experience poorer colorectal cancer survival in neighborhoods characterized by racial bias in mortgage lending, a measure of institutional racism
12. Hayanga AJ, Zeliadt SB, Backhus LM. Residential segregation and lung cancer mortality in the United States. <i>JAMA Surg</i> . 2013;148(1):37-42. doi:10.1001/jamasurger y.2013.408	A retrospective, population-based study using data obtained from the 2009 Area Resource File and Surveillance, Epidemiology and End Results program	U. S	Mortality). Each additional level of segregation was associated with a 0.5% increase in lung cancer mortality for blacks (P < .001) and an associated decrease in mortality for whites (P = .002)	Poisson distribution and log link were used to examine the association between residential segregation and lung cancer mortality from 2003 to 2007 for black and white populations