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Identifying geospatial-, neighborhood- and healthcare system-related drivers of racial and ethnic disparities in lung cancer treatment in California

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#### UNIVERSITY OF CALIFORNIA SAN DIEGO

## SAN DIEGO STATE UNIVERSITY

Identifying geospatial-, neighborhood- and healthcare system-related drivers of racial and ethnic disparities in lung cancer treatment in California

> A dissertation submitted in partial satisfaction of the requirements for the degree Doctor of Philosophy

> > in

Public Health (Epidemiology)

by

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This dissertation of Chelsea A. Obrochta is approved, and it is acceptable in quality and form for

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University of California San Diego

San Diego State University

2021

## **TABLE OF CONTENTS**





## **LIST OF TABLES**





## **LIST OF FIGURES**



#### **ACKNOWLEDGMENTS**

Chapter 2, titled, "The Impact of Patient Travel Time on Disparities in Treatment for Early Stage Lung Cancer in California," by Chelsea A. Obrochta, Humberto Parada Jr., James D. Murphy, Atsushi Nara, Dennis Trinidad, Maria Rosario (Happy) Araneta, and Caroline A. Thompson, is under review at *PLOS One*. The dissertation author is the primary author of this material.

Chapter 3, titled, "Neighborhood Diversity and Racial/Ethnic Disparities in Lung Cancer Treatment," by Chelsea A. Obrochta, Humberto Parada Jr., James D. Murphy, Atsushi Nara, Dennis Trinidad, Maria Rosario (Happy) Araneta, and Caroline A. Thompson, is under review at *Lung Cancer*. The dissertation author is the primary author of this material.

Chapter 4, title, "Patient-Provider Engagement in Early Stage Lung Cancer Treatment Disparities: An Analysis of Cancer Registry-Linked Electronic Health Records," by Chelsea A. Obrochta, Humberto Parada Jr., James D. Murphy, Atsushi Nara, Dennis Trinidad, Maria Rosario (Happy) Araneta, and Caroline A. Thompson, is being prepared for submission to *Cancer Epidemiology, Biomarkers & Prevention*.

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## **Abstracts**

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patients in California. *Cancer Epidemiology Biomarkers and Prevention*. Jun; 29(6 Suppl\_2):D077.

2. **Obrochta CA**, Murphy JD, Nara A, Thompson CA (2019). Disparities in receipt of guideline-concordant treatment for early stage non-small cell lung cancer patients in California. *Journal of Clinical Oncology*. Sep;37(27\_Suppl):160.

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- 1. **Obrochta CA**, Humberto Parada Jr., James D. Murphy, Atsushi Nara, Dennis Trinidad, Maria Rosario (Happy) Araneta, Thompson CA. Travel Time to Treatment Facilities and Racial/Ethnic and Sociodemographic Disparities in Treatment for Early Stage Non-Small Cell Lung Cancer (NSCLC) Patients in California. *In Preparation.*
- 2. **Obrochta CA**, Humberto Parada Jr., James D. Murphy, Atsushi Nara, Dennis Trinidad, Maria Rosario (Happy) Araneta, Thompson CA. Neighborhood Diversity and Racial/Ethnic Disparities in Lung Cancer Treatment. *In Preparation.*
- 3. **Obrochta CA**, Humberto Parada Jr., James D. Murphy, Atsushi Nara, Dennis Trinidad, Maria Rosario (Happy) Araneta, Thompson CA. Patient Characteristics and Modifiable Healthcare System-Related Drivers on Racial and Ethnic Disparities in Early Stage Lung Cancer Treatment. *In Preparation.*

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## **Oral**

- 1. Offor P, **Obrochta CA**, Schumacher B, Thompson CA (2021). Evidence of Stage Shift in US Lung Cancer Diagnosis, 2009-2016. Society of Epidemiologic Research.
- 2. **Obrochta CA,** Chambers T, Bandoli G (2019). Psychological distress in pregnancy and postpartum. Epidemiology Research Exchange: Describing, Decomposing and Understanding the Causes of Health Disparities. San Diego, CA.
- 3. **Obrochta CA,** Thompson CA (2017). Addressing Missingness in the California Cancer Registry in the Form of Incomplete Dates. Society for Epidemiologic Research Digital **Conference**
- 4. **Obrochta CA,** Murphy J, Tsou MH, Thompson CA (2017). Ethnic and geographic disparities in the receipt of guideline concordant treatment in colorectal cancer patients.

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## **Poster**

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#### **ABSTRACT OF THE DISSERTATION**

Identifying geospatial-, neighborhood- and healthcare system-related drivers of racial and ethnic disparities in lung cancer treatment in California

by

Chelsea A. Obrochta

Doctor of Philosophy in Public Health (Epidemiology)

University of California San Diego, 2021 San Diego State University, 2021

Caroline A. Thompson, Chair

**Background:** Lung cancer is the leading cause of cancer-related death in the United States, but early diagnosis and evidence-based guideline-concordant treatment (GCT) can improve prognosis. However, disparities exist in who receives GCT for lung cancer which may be attributable to a patient's geography, social environment, or provider relationship. We studied the relative contribution of travel time, neighborhood diversity, and healthcare provider engagement on disparities in GCT among non-small cell lung cancer (NSCLC) patients in California.

**Methods:** For Aims 1 and 2, we analyzed geocoded California Cancer Registry linked American Community Survey data for  $\sim$ 23,000 stage I-II NSCLC patients (2006-2015). In Aim 3, we additionally linked these data to electronic health records (EHRs) for  $\sim$ 1,000 patients from a large healthcare delivery system. GCT was defined based on National Comprehensive Cancer Network guidelines. Driving and public transit travel times were estimated from a patient's residence to their treatment facility, neighborhood diversity was based on the racial/ethnic composition of the patient's neighborhood, and EHR variables reflecting healthcare engagement included provider sex and enrollment in an online patient portal. We used adjusted regression models to quantify the relative risks for undertreatment and delay (treatment initialization >45 days from diagnosis) associated with our target variables, stratified by detailed patient race/ethnicity.

**Results:** In Aim 1, we observed that longer travel times reduced risk of undertreatment and delay. This counterintuitive result, which we call a 'Travel Time Paradox', did not benefit all patients, with longer travel times leading to reduced quality care for some racial/ethnic groups. In Aim 2, we observed that patients living in neighborhoods that are mixed or discordant from their race/ethnicity increased risk of undertreatment and delay, but these findings also varied across race/ethnicities with some non-White patient groups living in racial/ethnic concordant neighborhoods at increased risk for undertreatment and delay. In Aim 3 we observed that patients enrolled in the online patient portal were at substantially decreased risk for undertreatment and delay, but most patients were not enrolled.

**Conclusion:** These results support the role of contextual drivers of inequitable treatment for cancer and highlight the importance of evaluating risk heterogeneity among multiethnic populations.

xvi

#### **CHAPTER 1: INTRODUCTION**

#### *Non-Small Cell Lung Cancer*

Lung cancer is the second most commonly diagnosed cancer and the most common cause of cancer related deaths in the United States (U.S.), accounting for approximately 25% of all cancer deaths<sup>1</sup>. Non-small cell lung cancer (NSCLC) is the most common type (80-85% of all cases) of lung cancer<sup>1</sup>. Prognosis for lung cancer patients is dismal. Favorable prognosis is highly dependent on a patient's stage of diagnosis and receipt of proper treatment in a timely manner<sup>2</sup>. Staging for NSCLC ranges from stage 0-IV and is dependent on whether the cancer is local or has spread from the lungs to the lymph nodes or other organs<sup>3</sup>. Unfortunately, most lung cancer cases are diagnosed in symptomatic patients. Symptoms for lung cancer do not appear until the disease has progressed to a later-stage in which the prognosis is poor<sup>3</sup>. The 5-year survival rate by stage ranges from:  $92\%$ for stage IA1, to < 1% for IV<sup>4</sup>. Only 16% of lung cancer patients are diagnosed at a localized stage, for which the 5-year survival rate is  $55\%$ <sup>4</sup>. Stratified by sex and race/ethnicity, the 5-year relative survival is 15.5% for White men, 13.4% for Black men, 18% for Asian American, Native Hawaiian and Pacific Islander (AANHPI) men, 16% for Hispanic men, 21.6% for White women, 19.1% for Black women, 25% for AANHPI women, and 25% for Hispanic women. California's 5-year survival rate is comparable to the national average<sup>5</sup>.

Smoking is the most common risk factor for lung cancer and in the U.S., smoking contributes to 80-90% of lung cancer deaths<sup>6</sup>. The most effective way of reducing lung cancer mortality among smokers is the early diagnosis of lung cancer through screening and receipt of proper treatment. In 2013, the U.S. Preventative Task Force began recommending lung cancer screening with low-dose spiral computed tomography for adults aged 55 to 80 years with at least a 30 pack-year smoking history, and who are current smokers or have quit within 15 years. Lung cancer screening efforts have resulted in earlier stage diagnosis for many tobacco users and evidence has shown that screening can reduce mortality by up to 20% with good adherence<sup>7</sup>. Unfortunately, lung cancer screening studies that have shown the benefit of screening of NSCLC patients have lacked diversity and may not be generalizable to vulnerable or underserved populations<sup>8</sup>.

Staging for NSCLC helps determine the severity of the cancer, including prognostic data related to the risk of recurrence and overall survival, and how to best treat it<sup>9</sup>. The American Joint Committee on Cancer (AJCC) TNM staging system considers the size and extent of the tumor (T), the spread to nearby lymph nodes (N), and the spread to distant sites (M), with higher numbers or letters after T, N, and M representing more advanced cancer<sup>9</sup>. The California Cancer Registry, California's statewide population-based cancer surveillance program, captures these tumor characteristics for all NSCLC diagnosed in California<sup>10</sup>. Stage I cancer is in the lung, less than 4 centimeters (cm), and has not spread to any lymph nodes. Stage II cancer is in the lung and has potentially spread to nearby lymph nodes. Stage III cancer is in the lung and in the lymph nodes in the middle of the chest, and Stage IV cancer has spread to both lungs, to the fluid around the lungs, or to another part of the body<sup>9,11,12</sup>. If NSCLC is detected at an early stage, increasingly more common since the introduction of lung cancer screening recommendations in 2013, and treated promptly, prognosis can be quite  $good<sup>4,7</sup>$ .

#### *Guideline-Concordant Treatment*

Timely diagnosis and treatment of lung cancer is critical. Evidence-based treatment can improve lung cancer prognosis, especially if it is detected at an early stage. Delays in lung cancer

care can lead to missed opportunities for both curative and life-prolonging therapies<sup>13</sup>. Receiving guideline-concordant treatment (GCT) for NSCLC increases survival time and lowers mortality risk, but it is unclear how the timeliness of this GCT impacts survival<sup>2</sup>. The National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines are the most widely recognized and used guidelines in oncology clinical policy around the world. These guidelines were developed from evidence-based and consensus-driven data to ensure clinicians can provide their patients with preventative, diagnostic, and supportive services that lead to the best outcomes<sup>14</sup>. Figure 1.1 presents NSCLC stage appropriate treatment based on NCCN guidelines<sup>3</sup>. Treatment for NSCLC is primarily based on the stage of the cancer, although other factors such as, but not limited to, patients overall health (comorbidities) and certain cancer traits, can influence treatment. The five main treatment options include surgery, radiation therapy, chemotherapy, targeted therapy, and immunotherapy<sup>15</sup>. The NCCN does not specify a maximum time between diagnosis and treatment, however, the Research ANd Development (RAND) Corporation suggests that treatment should begin within 6 weeks of diagnosis<sup>16</sup>. The Commission of Cancer (CoC) Quality of Care Measures recommends adjuvant treatment of chemotherapy to be administered within 6 months of surgery, when required $17$ .



Figure 1.1. NSCLC GCT based on NCCN guidelines.

For stage 1A-IIB NSCLC, an operable patients' initial treatment should be surgery within 45 days of diagnosis. If the patient is node 1 (N1), adjuvant chemotherapy (chemotherapy given after the primary treatment to reduce the likelihood of cancer recurrence) +/- radiation should be administered within 6 months of surgery. For inoperable patients, initial treatment differs by lymph node involvement. If the patient is node 0 (N0), initial treatment should be radiation within 45 days of diagnosis. If the patient is node 1 (N1), initial treatment should be chemoradiation within 45 days of diagnosis. If a patients' chemotherapy and radiation start date are within 2 weeks of one another, this will be considered chemoradiation.

#### *Lung Cancer Treatment Disparities*

Despite the existence of evidence-based guidelines for treatment, treatment disparities exist by race/ethnicity, socioeconomic status (SES), and geography. Disparities in who receives appropriate treatment for lung cancer have been observed across different racial/ethnic groups, among socioeconomically disadvantaged populations, and underserved rural populations. Ample research identifying age, race (Black verse White), and SES (often measured at the neighborhood/residential level) disparities in lung cancer stage at diagnosis and treatment (usually any treatment or specific treatment modalities; but not necessarily adherence to guidelineconcordant treatment) have been conducted. Lung cancer patients of older age, Black race, and lower SES are less likely to receive treatment or timely treatment<sup>2,18-33</sup>. Patients with rural residences have been shown to be less likely to receive radiation and chemotherapy, compared to patients with urban residences<sup>34</sup>. Patients with the lowest quartile educational attainment are less likely to receive surgery and chemotherapy, compared to the highest<sup>18</sup>. However, only one such study has taken place in California, limited to only White and Black patients<sup>25</sup>, and only one study included patients of Hispanic ethnicity $2^7$ .

Modifiable risk factors can be changed or treated. Unmodifiable risk factors are variables that we cannot change including age, gender, and race. The vast majority of cancer disparities research focuses on these factors. Modifiable risk factors or potentially modifiable risk factors such as health behaviors, health providers, or healthcare access, can be changed at an individuallevel or through policy. In this study, we consider neighborhood, geography, and healthcare provider characteristics to be potentially modifiable risk factors because these factors can be changed through additional and better health resources.

#### *Geospatial Disparities*

Residential proximity and ease of access to treatment facilities can impact guideline adherence for cancer treatment. A literature review published in 2015 examined distance as a barrier to cancer diagnosis and treatment, and (a) cancer stage at diagnosis (12 studies)<sup>35-46</sup>, (b) appropriate treatment (8 studies)<sup>47-54</sup>, outcome (4 studies)<sup>55-58</sup>, and (d) quality of life (1 study)<sup>59</sup>. Results revealed that increased travel requirements were associated with more advanced disease at diagnosis, inappropriate treatment, a worse prognosis, and worse quality of life<sup>60</sup>. Outside of the U.S., it has been shown that NSCLC patients who live remotely from cities and their closest associated cancer center are less likely to have major surgery and have poorer chances of survival due to a more advanced stage at diagnosis<sup>44,61</sup>.

Differential travel burden has been assessed in various US populations. Generally, higher travel burden is observed in rural residents and non-Caucasians<sup>62-66</sup>, although some studies see an inverse association<sup>67,68</sup>. Patients in rural areas use less medical care<sup>69</sup>, and patient's with a driver's license have more health care visits<sup>70</sup>. One study from 2011, using data from 10 states, found that women traveling further distances to receive mastectomies are doing so after bypassing local options<sup>53</sup>; meaning that an increased travel distance may be by choice. Additionally, affordable transportation to treatment facilities may influence receipt of cancer care. Patients, particularly minorities, may decline care due to lack of affordable transportation<sup> $71$ </sup>. On average, travel times are longer for public transportation compared to a private vehicle<sup>63</sup>, however, there is some evidence that treatment facilities are favorably located closer to neighborhoods with the lowest household access to a private vehicle<sup>64</sup>.

The relationship between travel burden and cancer care has not be reported consistently. There is evidence to suggest that an increased travel burden is associated with an increased diagnostic interval<sup>72</sup>, later stage diagnosis<sup>37,73</sup>, decreased GCT<sup>74</sup>, decreased surgery<sup>52,75</sup>, decreased radiation<sup>52,75-77</sup>, decreased chemotherapy<sup>75,78</sup>, decreased adjuvant chemotherapy<sup>79</sup>, increased mortality<sup>80</sup>, and decreased survival<sup>81,82</sup>. On the contrary, there is research showing an increased travel burden is associated with a more rapid cancer diagnosis<sup>82</sup>, lower overall mortality<sup>67</sup>, and increased survival<sup>83,84</sup>. Additionally, many studies show no association between travel burden and stage at diagnosis, treatment type, or long-term outcome<sup>62,75,85-87</sup>.

#### *Neighborhood Disparities*

Neighborhoods are key determinants of health. Neighborhood social and built environments can influence cancer across the continuum<sup>88,89</sup>. The social environment includes both the socioeconomic composition of the residents and the social aspects of the neighborhood such as crime and community support. The built environment is the man-made physical attributes that influence factors such as walkability and health-promoting resources<sup>88,90</sup>. Neighborhoods with lower SES have made less improvement gains in lung cancer incidence and survival compared to higher SES neighborhoods, with variations by race/ethnicity<sup>91-93</sup>. Disparities in healthcare utilization are related to both an individuals' racial/ethnic identity and the racial/ethnic composition on their community<sup>94</sup>.

Minority neighborhoods with increased segregation have poorer health resources. Residential segregation refers to the spatial separation of two groups, such as racial/ethnic groups, within a specific geographic region, such as neighborhood. Predominately Black neighborhoods have been shown to have poorer health facilities staffed by less competent physicians, higher

environmental exposures including ambient air toxins, and poorer built environments, and a higher primary care physician shortage<sup>95-98</sup>; Hispanic and Asian majority neighborhoods are less likely to have a primary care physician shortage<sup>97</sup>. Segregation contributes to worse access to a usual health care provider for both Blacks and Hispanics<sup>99</sup>. Very poor communities, often minority isolated spatially distinct neighborhoods, have less access to resources to maintain health, and little control over their environments.

An ethnic enclave is a geographic area where a particular ethnic group is spatially clustered, distinct from the surrounding area. African Americans, immigrants, and ethnic minorities, such as Hispanics, Asian Americans, Native Hawaiians and Pacific Islanders, are more likely to live in enclaves<sup>100</sup>. Enclaves have worse walkability, fewer recreational exercise resources, worse safety, lower social cohesion, and lower neighborhood-based civic engagement<sup>101</sup>. Hispanic and Chinese enclaves report better health food availability and lower consumption of high-fat foods, but less physical activity among Hispanics<sup>101</sup>. Higher acculturation is associated with unhealthy behaviors such as alcohol use, smoking, and BMI, but conversely, increased exercise<sup>102</sup>. Residential segregation can influence cancer care. In highly segregated counties, an increase in Blacks or Hispanics is associated with a decrease in the availability and use of surgical services and an increase in emergency visits $103$ . Residential segregation by race is associated with lower rates of surgery, lower survival, and increased mortality in Black NSCLC patients<sup>104,105</sup>. Black segregation has been shown to both increases and decrease the risk for late-stage diagnosis<sup>73,106</sup>. Asian segregation has been shown to increased likelihood of late-stage diagnosis<sup>106</sup>. Black and Hispanic segregation is adversely associated with adequate cancer care, cause-specific mortality (lung, breast, and cardiovascular) and all-cause mortality<sup>103,107-113</sup>. The effect of segregation varies by patient race/ethnicity. Some research suggests that increased percent Black is often protective for Blacks<sup>108,111,114</sup>, and living in a neighborhood with a high racial/ethnic concentration as the one you identify, improves outcomes, potentially attributable to social cohesion or social capital<sup>115,116</sup>.

Neighborhood social cohesion has been linked to various improved health behaviors such as increased use of preventative health services<sup>117</sup>, but can sometimes be associated with worse health behaviors and outcomes<sup>118</sup>. Some U.S. research has shown that concentrations of Hispanics and Blacks have a negative impact on neighborhood social cohesion due to concentrated disadvantage resulting in higher crime and violence<sup>119</sup>, while others show that concentrations of Hispanics and Blacks increase neighborhood social cohesion such as social capital, safety, belonging, trust, and volunteering<sup>120</sup>. The relationship between the racial/ethnic composition of your neighborhood, neighborhood social cohesion, and health outcomes remains unclear.

#### *Healthcare System-Related Disparities*

A good relationship with a primary care provider (PCP) may improve a patient's adherence to guideline-concordant treatment. PCP across the U.S. have an active role in cancer patient management<sup>121</sup>. The patient-provider relationship, specifically communication, can influence patient engagement in their treatment and compliance, and improve patient health outcomes<sup>122,123</sup>. Having a usual source of healthcare may increase the odds of patient-provider discussion regarding lung cancer screening<sup>124</sup>. It has been shown that patients who felt that their physicians explained the risks of lung cancer treatment, discussed their chances of cure, discussed goals of treatment, or who were warm and friendly are more likely to undergo treatment<sup>125</sup>. Further, lower income or minority lung cancer patients may feel stigmatized. Lung cancer patients, especially current or past smokers experience more perceived stigma and self-blame than other non-lung cancer patients<sup>126-</sup>  $128$ . Stigma is associated with anxiety, depression, and lung cancer symptom severity $129$ .

Anticipated stigma can result in delays in seeking diagnosis and in turn, treatment<sup>130-132</sup>. A good patient-provider relationship may reduce lung cancer stigma, and improve poor psychosocial and medical outcomes<sup>133</sup>. Empathy is especially important in patient-provider communication. Past research has shown that physicians are rarely  $\left(\sim10\%$  of opportunities) empathic to concerns raised by lung cancer patients<sup>134,135</sup>. Empathy is important as is can improve patient satisfaction and adherence to physicians' recommendations<sup>135</sup>. Empathic responses are more prevalent in younger oncologists, and female physicians conduct longer visits, make more positive statements, made more partnership statements, asked more questions, made more back-channel responses, and smiled and nodded more<sup>134,136,137</sup>. Patients make more partnership statements and give more medical information to female physicians<sup>134</sup>. Patient/provider gender concordance, defined as a patient and their physician having the same gender, has not been clearly studied, although there is some evidence than gender concordance increases cancer screening<sup>138</sup>.

Language and cultural factors create additional barriers for timely and appropriate healthcare. Patients whose main spoken language is not English, are less likely to receive preventative services<sup>139</sup>. Spanish-speaking patients have been shown to be more likely to discuss diet and exercise modification with Spanish-speaking physicians<sup>140</sup>. Patients with language discordant physicians have also been shown to be more likely to omit medication, to miss office appointments, and to make at least one emergency room visit<sup>141</sup>. Conversely, there is some evidence that Spanish-speaking patients cared for by language concordant primary care physicians were no more likely to receive cancer screening<sup>142</sup>. Cultural factors may partially explain racial/ethnic disparities in treatment. Negative surgical beliefs, fatalism, and medical mistrust are more common among minorities and among late-stage lung cancer patients, and partially mediate the relationship between Black race and lower rates of stage appropriate treatment $143,144$ 

Active patient portals may be benefit to cancer patients through the ability to access/view electronic health records including test results, send and receive messages from their providers, request medication refills, and view provider visit notes and reminders. To our knowledge, there are no studies assessing the association between portal enrollment and cancer treatment, but research does show that disparities exist among cancer patient's enrollment in patient portals<sup>145,146</sup>. A longitudinal study that took place at the University of California, San Francisco showed that Black patients were 44% less likely than White patients to enroll in patient portals and enrollment decreased with increasing age. Additionally, men were less likely to initially enroll but eventually enrolled, and patients in which English was not was not their primary were less likely to enroll initially and over time<sup>147</sup>. Some research also shows that patients feel more involved in their care when they are able to view provider's notes from their visits<sup>148</sup>. Interventions to train patients on portal use has been proposed<sup>149</sup>, but barrier could include patients not having a computer or smartphones, not being comfortable with technology, or the portal not being translated to a patient's language.

#### *Conceptual Framework*



 Figure 1.2. Illustration of the impact of neighborhood-, geospatial-, and healthcare providercharacteristics on the cancer continuum.

Figure 1.2 illustrates how neighborhood-, geospatial-, and healthcare system-related factors can impact points across the cancer continuum. Some of the key components of geographical- and provider- predictors, as well as subcomponents of neighborhood-predictors are identified. For example, a patient's neighborhood may impact treatment; if a patient lives in a Hispanic enclave, where modesty and stigma may play a larger role, they may be less comfortable discussing their diagnosis and receiving treatment. The patient-provider relationship likely contributes to a patient's adherence to treatment as well; if a patient is modest, they may feel more comfortable with a provider of the same gender. Furthermore, a patient's health literacy relies on the patient and provider to speak the same language. Geography may also affect a patient's likelihood of receiving cancer treatment; barriers such as living far from the nearest treatment facility, lacking personal transportation, and unavailability of public transportation could all reduce a patient's chance of receiving care.

#### *Previous Studies*

California is a highly diverse state racially, socioeconomically, and geospatially. The state of California has one of the largest and most racially/ethnically diverse population in the U.S. Within California, the population identified as 38.4% White, 38.1% Hispanic, 5.1% Black, 13.9% Asian,  $2.9\%$  mixed, and  $0.9\%$  other<sup>150</sup>. The U.S. census population estimated that the percentage of Hispanics in California is 38.8% and surpassed the number of non-Hispanic Whites in 2014<sup>14</sup>. AANHPIs are the nation's fastest growing race or ethnic group. AANHPI's population increased by 2.9% in 2012, with California being one of the top three populated states<sup>151</sup>. To our knowledge, minimal research has been conducted to identify modifiable factors that explain treatment disparities, overall, or in California.

There are several studies, most taking place outside of the U.S., assessing travel burden and cancer care and survival, but the relationship is inconsistent. An increased travel requirements has been shown to be associated with more advanced disease at diagnosis, decreased and inappropriate treatment, a worse prognosis, and worse quality of life $37,52,60,73-82$ . But, there is evidence to the contrary<sup>67,82-84</sup>, and well as no association<sup>62,75,85-87</sup> previously reported. No previous research has been conducted in the U.S. assessing how distance to a patient's treatment facility effects receipt of GCT in lung cancer patients This research assesses this question in the context of racial/ethnic disparities and contributes to the U.S. research, specific to California's highly diverse population.

There are only two studies addressing residential segregation on NSCLC surgery and survival/mortality, but these only include White and Black patients. Residential segregation by race is associated with lower rates of surgery, lower survival, and increased mortality in Black NSCLC patients. These disparities vary by patient race<sup>104,105</sup>. Most past studies have failed to include Hispanics, and have assessed Asian Americans as one aggregate group, although we know there are important difference between Asian groups, especially with regard to cancer outcomes<sup>152</sup>. In this dissertation we incorporated Hispanics and disaggregated Asian groups, which is of utmost importance, especially in California. Past literature has identified census tract as a proxy for neighborhood<sup>153</sup>, but we had access to the census block group, which is the smallest geographic unit published by the U.S. Census Bureau. This allowed us to measure diversity at the census block group level, and nest block groups' diversity into census tracts (neighborhoods) to measure segregation.

To our knowledge, no past studies have examined patient-provider gender-, or languageconcordance, or enrollment in a patient portal on receipt of GCT, in NSCLC patients. However, electronic health records (EHRs) provide vast amount of longitudinal data which allows researchers access to details of care, including aspects of the patients' interaction with their health provider, before a cancer diagnosis and during treatment. For example, EHRs allow us to determine the presence of comorbidities which is considered to play a large role in treatment decisions and treatment outcomes, and a higher comorbidity index has been shown to decrease likelihood of curative treatment<sup>154-157</sup> and decrease survival<sup>157-159</sup> among cancer patients and NSCLC cancer patients specifically. Comorbidities may also play a role in the timing of cancer diagnosis as a highly comorbid patient may seek medical care sooner, leading to an earlier stage diagnosis, or alternately, cancer symptoms may be mistakenly considered a symptom of a patient's

comorbidities, leading to a delay in diagnosis<sup>154</sup>. Prior research has shown that lung cancer patients have a high number of comorbidities compared to other cancers<sup>160</sup>, which may be due to smoking being the number one risk factor for NSCLC. A study taking place in the Netherlands found that for early-stage NSCLC patient, an increasing number of comorbidities decreased surgical resection, increased radiotherapy, and had little impact of chemotherapy<sup>156</sup>. A study in Sweden also found that increased early-stage NSCLC patients with severe comorbidities were less likely to be offered surgery<sup>159</sup>. Variations in comorbidities among race/ethnicity groups may play a role in racial/ethnic disparities in receipt of GCT among NSCLC patients. By linking EHRs with a population-based cancer registry, we gain access to a more comprehensive picture, including the tumor characteristics and definitive treatment details, regardless of whether the treatment was recorded in the EHR.

Incorporating neighborhood social and built environment factors into cancer research is a new field and can help identify vulnerable populations to impact intervention and policy makers<sup>88</sup>. Geospatial, contextual, and multilevel research is integral to enhance cancer research across the cancer continuum.

#### *Specific Aims*

Lung cancer is the second most commonly diagnosed cancer and the leading cause of cancer-related death in the United States (U.S.), accounting for approximately 25% of all cancer deaths. The National Comprehensive Cancer Network provides evidence-based cancer treatment recommendations. However, there are disparities in who receives guideline-concordant treatment (GCT) for lung cancer. Evidence suggests that a patient's receipt of GCT increases survival, especially for screen-detected, earlier stage cancers. While there has been ample research identifying treatment disparities by race/ethnicity and sociodemographic factors, limited research has been done to identify modifiable factors that explain such treatment disparities.

Prognosis for patients with lung cancer is generally poor. However, evidence-based treatment can improve lung cancer prognosis, especially if it is detected at an early stage. Despite the existence of guidelines for treatment, treatment disparities exist by race/ethnicity, socioeconomic status, and geography. The mechanisms that drive such disparities are poorly understood. Contextualizing disparities through the lens of social determinants of health; i.e., the neighborhood and the built environment, the social and community context, and healthcare delivery, may illuminate important *modifiable* factors that drive systematic differences in evidence-based care. The objective of this proposal was to identify potentially modifiable predictors of treatment disparities in lung cancer in California. Specifically, we investigated the relative contribution of, geospatial-, neighborhood-, and healthcare system-related factors on racial/ethnic disparities in receipt of guideline concordant treatment.

**Aim 1.** Estimate the effect of patients' residential proximity and ease of accessibility to treatment facilities on racial/ethnic disparities in receipt of GCT for lung cancer.

**Aim 2.** Estimate the effect of neighborhood racial/ethnic composition and segregation on racial/ethnic disparities in receipt of GCT, independently and jointly with the patient's race/ethnicity.

**Aim 3.** Investigate healthcare system-related factors such as characteristics of the patient-provider dyad or the availability of patient portals that may explain racial/ethnic disparities in GCT for lung cancer.

The study database includes geocoded patient, tumor, and treatment data from the California Cancer Registry (CCR) for all non-small cell lung cancer patients diagnosed between 2006-2015. Neighborhood characteristics are derived from various sources including, but not limited to, the Census and American Community Survey. For Aim 3, we used cancer registrylinked electronic health records from a cohort of non-small cell lung cancer patients diagnosed between 2004-2013 from a large multi-specialty healthcare delivery system in Northern California. We applied modern quantitative methodology including measures of relative and absolute disparities and geospatial analysis.

California is a highly diverse state racially, socioeconomically, and geospatially. Minimal research has been conducted to identify modifiable factors that explain treatment disparities, overall, or in California. Geospatial, contextual, and multilevel research is integral to enhance cancer research across the cancer continuum. The results of this research provide actionable evidence on how to reduce disparities for underrepresented minorities experiencing early stage lung cancer, which is increasing in frequency due to improved uptake of recommended screening.

#### *Assurances*

This study was reviewed and approved by Institutional Review Boards (IRBs) at San Diego State University, the University of California San Diego, and the California Department of Public Health Committee for the Protection of Human Subjects. Aim 3 was additional approved by IRBs at University of California San Diego and Sutter Health.

# **CHAPTER 2: THE IMPACT OF PATIENT TRAVEL TIME ON DISPARITIES IN TREATMENT FOR EARLY STAGE LUNG CANCER IN CALIFORNIA**

#### **ABSTRACT**

**Background:** Travel time to treatment facilities may impede the receipt of guideline-concordant treatment (GCT) among patients diagnosed with early-stage non-small cell lung cancer (ES-NSCLC). We investigated the relative contribution of travel time in the receipt of GCT among ES-NSCLC patients.

**Methods:** We included 22,821 ES-NSCLC patients diagnosed in California from 2006-2015. GCT was defined using the 2016 National Comprehensive Cancer Network guidelines, and delayed treatment was defined as treatment initiation >6 versus ≤6 weeks after diagnosis. Mean-centered driving and public transit times were calculated from patients' residential block group centroid to the treatment facilities. We used logistic regression to estimate risk ratios and 95% confidence intervals (CIs) for the associations between patients' travel time and receipt of GCT and timely treatment, overall and by race/ethnicity and neighborhood socioeconomic status (nSES).

**Results:** Overall, a 15-minute increase in travel time was associated with a decreased risk of undertreatment and delayed treatment. Compared to Whites, among Blacks, a 15-minute increase in driving time was associated with a 24% (95%CI=8%-42%) increased risk of undertreatment, and among Filipinos, a 15-minute increase in public transit time was associated with a 27% (95%CI=13%-42%) increased risk of delayed treatment. Compared to the highest nSES, among the lowest nSES, 15-minute increases in driving and public transit times were associated with 33%  $(95\%CI=16\% - 52\%)$  and  $27\%$   $(95\%CI=16\% - 39\%)$  increases in the risk of undertreatment and delayed treatment, respectively.

**Conclusion:** The benefit of GCT observed with increased travel times may be a 'Travel Time Paradox,' and may vary across racial/ethnic and socioeconomic groups.

#### **INTRODUCTION**

Favorable early-stage non-small cell lung cancer (NSCLC) prognosis is highly dependent on receipt of timely guideline-concordant treatment  $(GCT)^2$ . Disparities in receipt of GCT have been observed among racial/ethnic minorities, those living in lower socioeconomic neighborhoods, and rural populations. An increased travel burden is associated with an increased diagnostic interval, more advanced disease at diagnosis, worse prognosis, and worse quality of life<sup>35-60</sup>, as well as nonadherence to  $GCT^{74}$  including undertreatment with surgery, radiation, chemotherapy, and adjuvant chemotherapy<sup>34,37,44,52,61,72,73,75-82</sup>. However, the reported relationships between travel burden and cancer outcomes have been inconsistent. In previous studies, an increased travel burden was associated with a more rapid cancer diagnosis, lower overall mortality, and increased survival<sup>67,82-84</sup>, while other studies show no association between travel burden and stage at diagnosis, treatment type, or long-term outcome<sup>62,75,85-87</sup>. One study reported that women traveling farther distances to receive mastectomies were doing so after bypassing local options<sup>53</sup>; suggesting that an increased travel distance may be by choice, for some.

Receipt of cancer care may be influenced by a high travel burden as a result of residing long distances from treatment facilities or lack of private transportation. A higher travel burden has been documented for patients without a driver's license or private vehicle<sup>70</sup> and for rural residents and non-Caucasians<sup>62-66</sup>. On average, travel times are longer for public transportation compared to a private vehicle<sup>63</sup>, however, there is some evidence that treatment facilities are favorably located closer to neighborhoods with the lowest household access to a private vehicle<sup>64</sup>.
The objective of this study was to investigate the relative contribution of patients' travel times to their treatment facilities on racial/ethnic and socioeconomic disparities in receipt of GCT among patients diagnosed with early-stage NSCLC in California. As higher travel burden has been observed in minority and lower socioeconomic groups, we hypothesized that the effect of travel time to treatment facilities on GCT differs by race/ethnicity and neighborhood socioeconomic status (nSES).

#### **METHODS**

#### **Data Source**

The California Cancer Registry (CCR) is a statewide population-based cancer surveillance program<sup>10</sup>. Cancer details, demographics, and social and clinical details were collected by the CCR. County 2013 rural-urban continuum codes were ascertained from the United States (U.S.) Department of Agriculture. To determine the location of a patient's cancer treatment facility, a list of complete addresses was compiled using Google and geocoded in ArcGIS PRO 2.4.

This study was reviewed and approved by Institutional Review Boards (IRBs) at San Diego State University, the University of California San Diego, and the California Department of Public Health Committee for the Protection of Human Subjects.

#### **Study Population**

We included 23,571 patients diagnosed with first primary, stages I-II, NSCLC, as defined by the American Joint Committee of Cancer 7th edition, between 2006 and 2015, and alive at the time of diagnosis. Of these, we excluded patients due to the following reasons: missing lymph node (N) staging (n=122) or missing date of diagnosis (n=127), which were required to determine

receipt of GCT; missing race  $(n=43)$  or those who were classified as multiracial  $(n=288)$  or other Hispanics (n=9) due to race being required to assess differences by race, no validated methods to analyze multiracial categories, and a small sample size of other Hispanics; transsexual or transgender (n=4) individuals due to small sample sizes; missing residential census block group  $(n=20)$ , missing treatment facility  $(n=68)$ , or requiring a ferry for transit/driving time incalculable  $(n=3)$ , which were required to determine travel times; driving distance  $\geq$  250 miles (n=66), which were outliers for travel times. After applying these exclusions, the final study population comprised 22,821 patients.

#### **Assessment of GCT**

The primary outcome was receipt of GCT according to the 2016 National Comprehensive Cancer Network (NCCN) guidelines defined as the administration of proper initial and adjuvant surgery, chemotherapy, or radiation treatment(s) according to cancer site and stage. If a patient did not receive surgery, they were assumed inoperable and assessed for GCT according to lymph node staging (N0 or N1). Alternatively, undertreatment was less than minimum site- and stage- specific recommended treatment.

The secondary outcome was receipt of timely (versus delayed) GCT. The Research ANd Development Corporation recommends treatment initiation within 6 weeks of diagnosis<sup>16</sup> (i.e., the initiation of surgery, radiation, or chemotherapy within 45 days of diagnosis), and The Commission of Cancer Quality of Care Measures recommends adjuvant treatment of chemotherapy administration within 6 months of surgery, when required<sup>17</sup> (i.e., the initiation of chemotherapy +/- radiation within 6 months of initial surgery for N1 patients); Figure 1.1.

To determine receipt of GCT and timely treatment, full dates for diagnosis, surgery, radiation, and chemotherapy are required. If only month and year were available, the middle of the month day was imputed.

#### **Assessment of Travel Time**

Mean-centered travel time<sup>161,162</sup> to treatment facilities including driving and public transit travel times (minutes) to a patient's chosen treatment facility from their residence was calculated from the centroid of their census block group<sup>163</sup>. ArcGIS Online's *Connect Origins to Destinations* Analysis was used to compute driving travel time based on historical and live traffic data<sup>164</sup>. Public transportation was calculable for 11,607 patients living in census blocks with transit service available (nearest transit stop within 0.75 miles). The Google Maps Application Programming Interface with the *gmapsdistance* function in R was used to compute public transit travel time; *gmapsdistance* requires a future travel time and was specified as an arrival date and time of Monday, October 9<sup>th</sup>, 2020 at 5pm; 5pm was chosen to account for less traffic during the COVID-19 pandemic. Driving time was also calculated using *gmapsdistance* with the same specifications to compare the two methods of calculating driving travel time.

#### **Effect Modifiers**

Patient race/ethnicity and nSES were investigated as potential effect modifiers of the association between travel time and receipt of GCT. Race/ethnicity was classified as non-Hispanic White (NHW), non-Hispanic Black (NHB), Hispanic (including those who identify as White or Black), Native Hawaiian and Pacific Islander (NHPI), Chinese, Japanese, Filipino, Korean, Vietnamese, Asian Indian, Other Asian, or American Indian. Race/ethnicity data in the CCR is based on hospital records that use self-report, assumptions of hospital personnel, or extrapolation from birthplace, race/ethnicity of parent, maiden name, or surname<sup>165</sup>. nSES in the CCR is determined from the American Community Survey using a composite residential neighborhoodlevel index that combines census measures of education, income, occupation, and cost of living at the census block group level and categorized into quintiles<sup>166</sup>.

#### **Covariates**

Covariates included stage at diagnosis [IA (T1ab,N0), IB (T2a,N0), II, NOS (T2,N1), IIA (T2b,N0; T1ab,N1; T2a,N1), IIB (T2b,N1; T3,N0)], year of diagnosis, sex, age, insurance type (not insured, private insurance, Medicaid, Medicare, military, other/not otherwise specified), marital status (single/never married, married/unmarried or domestic partner, separated/divorced, widowed), whether or not the reporting facility with the earliest date of admission had an ACOSapproved cancer program, and rural-urban continuum codes. Rural-urban continuum codes (1-9) distinguishes metropolitan counties by the population of their metro area, and nonmetropolitan counties by degree of urbanization and adjacency to a metro area are assigned to each county<sup>167</sup>. To resolve unavailability of payer ( $n = 298$ ), marital status ( $n = 564$ ), and cancer program ( $n = 46$ ) information, we used multiple imputation, a valid statistical procedure for recovering missing data to create complete datasets that can then be analyzed through standard procedures<sup>168</sup>.

#### **Statistical Analysis**

Exposure, clinical and sociodemographic information were stratified by race/ethnicity. We quantified average disproportionality in receipt of GCT and timely treatment across categories of race/ethnicity, nSES, and driving and public transit travel times  $($ <15, 15–30, 30–60, and  $\geq 60$ minutes) using three disproportionality functions: Between-Groups Variance (BGV), The Theil Index (T), and Mean Log Deviation (MLD). BGV is a useful metric of absolute disparity for

unordered groups, such as race/ethnicity, because it weights by population size and is sensitive to larger deviations from the population average. T and MLD are entropy-based measures that quantify the relative disparity, meaning the disproportionate receipt of GCT and timely GCT across effect modifiers and exposures. T and MLD are complementary measures because T can be influenced by groups with high ratios of GCT and timely GCT in a group relative to the average GCT and timely GCT in the population, and MLD can be influenced by groups with larger population shares<sup>169</sup>; formulas provided in Figure 2.1.

$$
\text{BVG} = \sum_{j=1}^{J} p_j (y_j - \mu)^2
$$

Where  $p_j$  is groups j's population size,  $y_j$  is group j's average health status, and  $\mu$  is the average health status of the population.

$$
T = \sum_{j=1}^{J} p_j r_j \ln(r_j)
$$
  
MLD =  $\sum_{j=1}^{J} p_j [-\ln(r_j)]$ 

Where  $p_j$  is the proportion of the population in group j and  $r_j$  is the ratio of the mean health status in group j relative to the mean health status in the population.

Figure 2.1. Absolute and Relative Disparities Measure Formulas.

We used multivariable generalized logistic regression models (PROC GENMOD) with a Poisson distribution and log link function to explore all combinations of the following associations: outcomes (undertreatment and delayed GCT), exposures (mean-centered driving and public transit travel time), and effect modifiers (race/ethnicity and nSES), to estimate the impact of travel time to treatment facilities on both racial/ethnic and socioeconomic disparities in undertreatment and delayed GCT. The intraclass correlation coefficient (ICC) of treatment hospital was assessed to determine if treatment hospital needed to be included as a random effect. Driving and public transit travel times were mean-centered and rescaled to each represent a 15-minute increase from the population average. Patient racial/ethnic groups with less than 100 persons (NHPI, Asian Indian,

and American Indian) were excluded from models due to small sample sizes. In addition to disaggregating Asian groups with sufficient sample sizes, an aggregated Asian American, Native Hawaiian, and Pacific Islander (AANHPI) models was run separately including NHPIs and Asian Indians. Overall, we had 28 covariate-adjusted models. Models 1, 8, 15, and 22 regressed the outcomes (undertreatment and delayed GCT) on the effect modifiers (race/ethnicity and nSES). Models 2, 5, 9, 12, 16, 23, and 26 regressed the outcomes (undertreatment and delayed GCT) on the exposures (driving and public transit time). Models 3, 6, 10, 13, 17, 20, 24, and 27 combined the above models. Models 4, 7, 11, 14, 18, 21, 25, and 28 extended the previous models by adding an interaction term between the effect modifiers (race/ethnicity and nSES), and the exposures (driving and public transit time). The interaction models were the primary models of interest. nSES was not adjusted for when considering race/ethnicity as an effect modifier, but race/ethnicity was adjusted for when considering nSES as an effect modifier. Risk Ratios (RR) and 95% Confidence Intervals (CI) for the effect measure modifier analyses are presented in Table 2.6, while the betas and 95% CIs for all 28 models are available in Table 2.4 (effect modifier: race/ethnicity) and Table 2.5 (effect modifier: nSES). A sensitivity analysis considering driving time calculated using the *gmapsdistance* function were compared to the above results. All analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC).

#### **RESULTS**

Among the 22,821 early-stage NSCLC patients, 18,471 (80.94%) received GCT and, of these, 10,632 (57.56%) received timely GCT. Exposure, clinical and sociodemographic characteristics, stratified by race/ethnicity, are displayed in Table 2.1. Cells counts <5 are suppressed.

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#### *Clinical and Sociodemographic Characteristics*

Stage at diagnosis varied by race/ethnicity with NHBs having the highest proportion of Stage IIB diagnosis (14.9%). Females accounted for 54.5% of patients overall, but 64.4% of Japanese and 40.6% Vietnamese patients. The mean age at diagnosis was 70.4 years overall and ranged from 67.1 years for NHPI to 74.2 years for Japanese patients. Less than 1% of patients were uninsured, and half were married or in a domestic partnership. Most patients were treated at hospitals with an ACOS-approved cancer program (60.5%) with lower rates among NHBs (51.3%), NHPIs (51.5%), and Chinese (52.3%). nSES differed by race/ethnicity; overall, 14.2% of patients lived in the lowest nSES, but NHBs (29.7%), Hispanics (26.5%), and NHPIs (19.7%) proportions were much higher, and most patients lived in metro areas.

## *Travel time*

The mean ( $\mu$ ) driving time was 26 (standard deviation( $\sigma$ )=26.5) minutes with NHWs ( $\mu$ =26.8), Koreans ( $\mu$ =27.1), Asian Indians ( $\mu$ =29.4), and American Indians ( $\mu$ =26.9) having longer driving times than the average. Half (49.1%) of the population had no public transportation available with unavailability more frequent among NHWs (53.5%), Asian Indians (56.0%), and American Indians (56.3%). Among patients with available public transportation, the mean public transit time was 68.6 ( $\sigma$ =66.2) minutes with NHWs ( $\mu$ =71.3), Koreans ( $\mu$ =76.5), and Asian Indians  $(\mu=96.4)$  having longer than the average public transit times.

Table 2.1. Exposure variables and clinical and sociodemographic characteristics, stratified by patient race/ethnicity. Table 2.1. Exposure variables and clinical and sociodemographic characteristics, stratified by patient race/ethnicity.



Table 2.1. Exposure variables and clinical and sociodemographic characteristics, stratified by patient race/ethnicity. continued. Table 2.1. Exposure variables and clinical and sociodemographic characteristics, stratified by patient race/ethnicity. *continued.*





Table 2.1. Exposure variables and clinical and sociodemographic characteristics, stratified by patient race/ethnicity. continued. Table 2.1. Exposure variables and clinical and sociodemographic characteristics, stratified by patient race/ethnicity. *continued.*

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#### *Absolute and Relative Disparity Measures*

The proportions of receipt of GCT ranged from 76.35% among NHBs to 84.70% among Chinese and the proportions of receipt of timely treatment ranged from 49.80% among Filipinos to 72.06% among Other Asians. Patient's living in the highest nSES had the highest proportion of GCT (84.53%) and timely treatment (66.25%), followed by upper-middle, middle, lower-middle, and lowest SES (GCT=75.33%; timely GCT=50.43%) nSES (Table 2.2). Patients with a  $\geq 60$ minutes driving time had the highest percent GCT (86.90%) and timely treatment (64.95%), followed by 30–60, 15–30, and <15 minutes (GCT=77.36%; timely treatment=56.29%). Patients with a  $\geq 60$  minutes public transit time had the highest proportion of GCT (82.33%) and timely GCT (58.65%) (Table 2.3). BVG, Theil, and MLD values range from 0 to  $\infty$  (higher inequality) and should be used to compare the level of inequality across outcomes and groups. We observed more absolute disparity in rate of timely GCT, compared to GCT, between race/ethnicity (GCT=3.65; timely GCT=8.65) and nSES (GCT=10.10; timely GCT=28.35), with higher absolute disparity in nSES compared to race/ethnicity. There was more absolute disparity in GCT (driving=10.73; public transit=8.60) compared to timely GCT (driving=5.65; public transit =2.18), between travel times. There was very little relative disparity in rate of GCT and timely GCT.

GCT and Patient Race/Ethnicity ( $n = 22,821$ )									
<b>Patient Race/Ethnicity</b>	GCT(%)	<b>Population Proportion</b>	<b>BVG</b>	<b>Theil</b>	<b>MLD</b>				
non-Hispanic White (n=16450)	81.75	0.7208	0.4729	0.0072	$-0.0072$				
non-Hispanic Black (n=1463)	76.35	0.0641	1.3505	$-0.0035$	0.0037				
Hispanic (n=2263)	77.60	0.0992	1.1066	$-0.0040$	0.0042				
NHPI $(n=66)$	78.79	0.0029	0.0134	$-0.0001$	0.0001				
Chinese $(n=771)$	84.70	0.0338	0.4779	0.0016	$-0.0015$				
Japanese $(n=180)$	82.78	0.0079	0.0267	0.0002	$-0.0002$				
Filipino ( $n=632$ )	80.70	0.0277	0.0016	$-0.0001$	0.0001				
Korean $(n=195)$	78.46	0.0085	0.0523	$-0.0003$	0.0003				
Vietnamese $(n=360)$	78.61	0.0158	0.0858	$-0.0004$	0.0005				
Asian Indian (n=84)	80.95	0.0037	0.0000	0.0000	0.0000				
Other Asian $(n=325)$	78.77	0.0142	0.0669	$-0.0004$	0.0004				
American Indian (n=32)	81.25	0.0014	0.0001	0.0000	0.0000				
<b>All Groups</b>	80.94		3.6547	0.0003	0.0003				
Timely GCT and Patient Race/Ethnicity ( $n = 18,471$ )									
<b>Patient Race/Ethnicity</b>	Timely GCT (%)	<b>Population Proportion</b>	<b>BVG</b>	<b>Theil</b>	<b>MLD</b>				
non-Hispanic White (n=13448)	58.43	0.7281	0.5511	0.0111	$-0.0109$				
non-Hispanic Black (n=1117)	50.04	0.0605	3.4213	$-0.0074$	0.0085				
Hispanic ( $n=1756$ )	54.78	0.0951	0.7350	$-0.0045$	0.0047				
$NHPI(n=52)$	65.38	0.0028	0.1712	0.0004	$-0.0004$				
Chinese $(n=653)$	60.34	0.0354	0.2736	0.0018	$-0.0017$				
Japanese ( $n=149$ )	57.72	0.0081	0.0002	0.0000	0.0000				
Filipino $(n=510)$	49.80	0.0276	1.6620	$-0.0035$	0.0040				
Korean $(n=153)$	61.44	0.0083	0.1250	0.0006	$-0.0005$				
Vietnamese (n=283)	56.89	0.0153	0.0069	$-0.0002$	0.0002				
Asian Indian (n=68)	72.06	0.0037	0.7779	0.0010	$-0.0008$				
Other Asian $(n=256)$	65.63	0.0139	0.9052	0.0021	$-0.0018$				
American Indian (n=26)	53.85	0.0014	0.0193	$-0.0001$	0.0001				
<b>All Groups</b>	57.56		8.6486	0.0014	0.0013				
GCT and Neighborhood Socioeconomic Status ( $n = 22,821$ )									
nSES	$GCT$ $%$	<b>Population Proportion</b>	<b>BVG</b>	<b>Theil</b>	<b>MLD</b>				
Highest $(n=5132)$	84.53	0.2249	2.8985	0.0102	$-0.0098$				
Upper-Middle (n=5025)	83.24	0.2202	1.1649	0.0063	$-0.0062$				
Middle $(n=4927)$	81.10	0.2159	0.0055	0.0004	$-0.0004$				
Lower-Middle (n=4494)	78.13	0.1969	1.5547	$-0.0067$	0.0070				
Lowest $(n=3243)$	75.33	0.1421	4.4722	$-0.0095$	0.0102				
<b>All Groups</b>	80.94		10.0958	0.0008	0.0008				
		Timely GCT and Neighborhood Socioeconomic Status ( $n = 18,471$ )							
nSES	Timely GCT (%)	<b>Population Proportion</b>	<b>BVG</b>	<b>Theil</b>	$\bf MLD$				
Highest $(n=4338)$	66.25	0.2349	17.7387	0.0380	$-0.0330$				
Upper-Middle $(n=4183)$	57.95	0.2265	0.0345	0.0015	$-0.0015$				
Middle $(n=3996)$	55.56	0.2163	0.8652	$-0.0074$	0.0076				
Lower-Middle $(n=3511)$	53.60	0.1901	2.9811	$-0.0126$	0.0136				
Lowest $(n=2443)$	50.43	0.1323	6.7257	$-0.0153$	0.0175				
<b>All Groups</b>	57.56		28.3452	0.0042	0.0041				

 Table 2.2. Absolute and relative disparities in rate of GCT and Timely GCT between patient race/ethnicity groups and neighborhood socioeconomic status (nSES).

GCT and Driving Travel Time $(n = 22,821)$									
<b>Driving Travel Time</b>	GCT(%)	<b>Population Proportion</b>	<b>BVG</b>	<b>Theil</b>	<b>MLD</b>				
$<$ 15 minutes (n=8703)	77.36	0.3814	4.8882	$-0.0165$	0.0173				
15 - 30 minutes ( $n=8345$ )	81.41	0.3657	0.0808	0.0021	$-0.0021$				
30 - 60 minutes (n=4033)	85.10	0.1767	3.0579	0.0093	$-0.0089$				
$\geq 60$ minutes (n=1740)	86.90	0.0762	2.7067	0.0058	$-0.0054$				
<b>All Groups</b>	80.94		10.7336	0.0008	0.0009				
Timely GCT and Driving Travel Time $(n = 18,471)$									
<b>Driving Travel Time</b>	Timely GCT (%)	<b>Population Proportion</b>	<b>BVG</b>	<b>Theil</b>	<b>MLD</b>				
$15$ minutes (n=6733)	56.29	0.3645	0.5879	$-0.0081$	0.0081				
15 - 30 minutes (n=6794)	56.59	0.3678	0.3461	$-0.0060$	0.0063				
30 - 60 minutes (n=3432)	58.71	0.1858	0.2457	0.0038	$-0.0037$				
$\geq$ 60 minutes (n=1512)	64.95	0.0819	4.4727	0.0111	$-0.0099$				
<b>All Groups</b>	57.56		5.6524	0.0008	0.0008				
GCT and Public Transit Travel Time $(n = 11,607)$									
<b>Public Transit</b>	GCT(%)	<b>Population Proportion</b>	<b>BVG</b>	<b>Theil</b>	<b>MLD</b>				
<b>Travel Time</b>									
$<$ 15 minutes (n=476)	77.73	0.0410	0.4225	$-0.0009$	0.0009				
15 - 30 minutes (n=1891)	76.15	0.1629	3.7376	$-0.0067$	0.0070				
30 - 60 minutes (n=4186)	77.78	0.3606	3.6008	$-0.0077$	0.0079				
$\geq 60$ minutes (n=5054)	82.33	0.4354	0.8412	0.0158	$-0.0152$				
<b>All Groups</b>	79.50		8.6021	0.0004	0.0006				
Timely GCT and Public Transit Travel Time $(n = 9,227)$									
<b>Public Transit</b> <b>Travel Time</b>	Timely GCT (%)	<b>Population Proportion</b>	<b>BVG</b>	<b>Theil</b>	<b>MLD</b>				
$<$ 15 minutes (n=370)	52.97	0.0401	0.8448	$-0.0029$	0.0031				
15 - 30 minutes (n= $1440$ )	55.63	0.1561	0.5815	$-0.0044$	0.0046				
30 - 60 minutes (n= $3256$ )	56.76	0.3529	0.2259	$-0.0032$	0.0032				
$\geq 60$ minutes (n=4161)	58.64	0.4510	0.5260	0.0108	$-0.0106$				
<b>All Groups</b>	57.28		2.1782	0.0003	0.0003				

 Table 2.3. Absolute and relative disparities in rate of GCT and Timely GCT between driving travel time and public transit travel time.

To explain how driving and public transit time impacted the risk of undertreatment and delayed GCT, multivariable mean-centered models are described below. Treatment hospital had an intraclass correlation coefficient of < 5% and therefore was not included as a random effect.

# *Outcomes and Effect Modifiers*

Compared to NHWs, NHBs (beta(β)=0.21, 95%CI=0.11-0.30), Hispanics (β=0.20, 95%CI=0.12-0.28), and Vietnamese (β=0.34, 95%CI=0.15-0.54) had higher risks for undertreatment, and NHBs ( $\beta$ =0.15, 95%CI=0.09-0.22), Hispanics ( $\beta$ =0.08, 95%CI=0.03-0.14), and Filipinos (β=0.18, 95%CI=0.10-0.27) had higher risk for delayed GCT (Table 2.4). Compared to patients in the highest nSES, patients in the middle  $(\beta=0.13, 95\%CI=0.05-0.21)$ , lower-middle ( $\beta$ =0.23, 95%CI=0.15-0.31), and lowest ( $\beta$ =0.30, 95%CI=0.22-0.39) nSES had higher risk for undertreatment, and those in the upper-middle ( $\beta$ =0.19, 95%CI=0.14-0.25), middle ( $\beta$  = 0.24, 95%CI=0.18-0.29), lower-middle (β=0.27, 95%CI=0.22-0.33), and lowest (β=0.32, 95%CI=0.26- 0.38) nSES had higher risk for delayed GCT (Table 2.5).

#### *Outcomes and Exposures*

When considering all patients, a 15-minute increase (from the mean) in driving time was associated with a 5.48% (β=-0.06, 95%CI=-0.08, -0.04) and 3.10% (β=-0.03, 95%CI=-0.04, -0.02) decreased relative risk for undertreatment and delayed treatment, respectively, and a 15-minute increase in public transit times was associated with a 1.78% ( $\beta$ =-0.02, 95%CI=-0.03,-0.01) and 0.7% (β=-0.01, 95%CI=-0.01,0.00) decreased relative risk for undertreatment and delayed GCT, respectively (Table 2.5). However, increased travel times did not translate to improved care for all racial/ethnic or socioeconomic groups as evidenced by our joint exposure models.







Table 2.4. Effect of travel time to treatment facilities on racial/ethnic disparities in undertreatment and delayed GCT. continued. Table 2.4. Effect of travel time to treatment facilities on racial/ethnic disparities in undertreatment and delayed GCT. *continued.* Table 2.4. Effect of travel time to treatment facilities on racial/ethnic disparities in undertreatment and delayed GCT. continued. Table 2.4. Effect of travel time to treatment facilities on racial/ethnic disparities in undertreatment and delayed GCT. *continued.*





Table 2.4. Effect of travel time to treatment facilities on racial/ethnic disparities in undertreatment and delayed GCT. continued. Table 2.4. Effect of travel time to treatment facilities on racial/ethnic disparities in undertreatment and delayed GCT. *continued.*

\*Separate model with aggregate AANHPI which include NHPI and Asian Indians.

\*Separate model with aggregate AANHPI which include NHPI and Asian Indians.<br><sup>a</sup>Adjusted for age, year of diagnosis, stage at diagnosis, sex, insurance, marital status, cancer approved program, and rural-urban continuum cod bEstimates for race represent race effects as modified by a 15-minute increase in travel time (with product term to capture effect modification by travel time). aAdjusted for age, year of diagnosis, stage at diagnosis, sex, insurance, marital status, cancer approved program, and rural-urban continuum code



 Table 2.5 Effect of travel time to treatment facilities on socioeconomic disparities in undertreatment and delayed GCT. Table 2.5 Effect of travel time to treatment facilities on socioeconomic disparities in undertreatment and delayed GCT. Table 2.5 Effect of travel time to treatment facilities on socioeconomic disparities in undertreatment and delayed GCT. continued. Table 2.5 Effect of travel time to treatment facilities on socioeconomic disparities in undertreatment and delayed GCT. *continued.*

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\*Separate model with aggregate AANHPI which include NHPI and Asian Indians.

\*Separate model with aggregate AANHPI which include NHPI and Asian Indians.<br><sup>a</sup>Adjusted for age, year of diagnosis, stage at diagnosis, sex, insurance, marital status, cancer approved program, and rural-urban continuum cod bEstimates for race represent race effects as modified by a 15-minute increase in travel time (with product term to capture effect modification by travel time). aAdjusted for age, year of diagnosis, stage at diagnosis, sex, insurance, marital status, cancer approved program, and rural-urban continuum code

#### *Outcomes, Effect Modifiers, Exposures, and Interactions*

Considering a joint exposure that incorporates both travel time and race/ethnicity, a 15 minute increase in driving time for NHBs and Koreans increased their risk of undertreatment by 24% (95%CI=8%-42%) and 37% (95%CI=2%-82%), respectively, compared to NHWs. A 15 minutes increase in public transit time for NHBs, Hispanics, Vietnamese, and Other Asians increased their risk of undertreatment by 29% (95%CI=14%-46%), 32% (95%CI=16%-49%), 49% (95%CI=15%-93%), and 39% (95%CI=7%-82%) respectively, compared to NHWs. A 15-minute increase in driving time for NHBs and Filipinos increased their risk of delayed GCT by 17%  $(95\%CI = 7\% - 28\%)$  and  $27\%$   $(95\% CI = 15\% - 41\%)$ , respectively, compared to NHWs. A 15-minutes increase in public transit time for NHBs, Hispanics, and Filipinos increased their risk for of delayed GCT by 18% (95%CI=9%-28%), 12% (95%CI=4%-21%), and 27% (95%CI=13%-42%), respectively, compared to NHWs (Table 2.6).

Considering a joint exposure that incorporates both travel time and nSES, a 15-minute increase in driving time for patients in the lower-middle and lowest nSES increased their risk of undertreatment by 27% (95%CI=12%-44%) and 33% (95%CI=16%-52%) compared to patients in the highest nSES (P-for-trend<0.01), respectively. A 15-minute increase in public transit time for patients in the lower-middle and lowest nSES increased their risk of undertreatment by 31%  $(95\%CI=16\% - 49\%)$  and 39%  $(95\%CI=22\% - 59\%)$ , respectively, compared to patients in the highest nSES (P-for-trend $\leq 0.01$ ). A 15-minute increase in driving time for patients in the uppermiddle, middle, lower-middle, and lowest nSES increased their risk of delayed GCT by 26%  $(95\%CI=16\% - 36\%)$  to 44%  $(95\%CI=33\% - 56\%)$  compared to patients in the highest nSES (P-fortrend<0.01). A 15-minute increase in public transit time for patients in the upper-middle, middle, lower-middle, and lowest nSES increased their risk of delayed GCT by 13% (95%CI=4%-23%) to 27% (95%CI=16%-39%) compared to patients in the highest nSES (P-for-trend<0.01) (Table 2.4).

Sensitivity analyses considering driving time calculated using *gmapsdistance* were compared to the above results using ArcGIS Online's *Connect Origins to Destinations* Analysis. Estimates differed slightly, but groups at significantly increased risk for undertreatment and delayed GCT were consistent (Table 2.7).

 Table 2.6. Risk Ratios (RR) and 95 Confidence Intervals (CI) for race/ethnicity and neighborhood socioeconomic status (nSES) Table 2.6. Risk Ratios (RR) and 95 Confidence Intervals (CI) for race/ethnicity and neighborhood socioeconomic status (nSES) representing that effect as modified by a 15-minute increase in travel time. representing that effect as modified by a 15-minute increase in travel time.



\*Separate model with aggregate AANHPI which include NHPI and Asian Indians. \*Separate model with aggregate AANHPI which include NHPI and Asian Indians.

PRisk Ratio (Exponentiated Estimate) for Race/Ethnicity represents Race/Ethnicity effect (reference: non-Hispanic White with 15-minute increase in aRisk Ratio (Exponentiated Estimate) for Race/Ethnicity represents Race/Ethnicity effect (reference: non-Hispanic White with 15-minute increase in modified by a 15-minute increase in travel time (with product term to capture effect modification by travel time), adjusted for age, year of diagnosis, modified by a 15-minute increase in travel time (with product term to capture effect modification by travel time), adjusted for age, year of diagnosis, travel time) as modified by a 15-minute increase in travel time (with product term to capture effect modification by travel time, adjusted for age, travel time) as modified by a 15-minute increase in travel time (with product term to capture effect modification by travel time, adjusted for age, PRisk Ratio (Exponentiated Estimates) for nSES represent nSES effects (reference: Highest nSES with 15-minute increase in travel time) as bRisk Ratio (Exponentiated Estimates) for nSES represent nSES effects (reference: Highest nSES with 15-minute increase in travel time) as year of diagnosis, stage at diagnosis, sex, insurance, marital status, cancer approved program, and rural-urban continuum code. year of diagnosis, stage at diagnosis, sex, insurance, marital status, cancer approved program, and rural-urban continuum code. stage at diagnosis, sex, race/ethnicity, insurance, marital status, cancer approved program, and rural-urban continuum code stage at diagnosis, sex, race/ethnicity, insurance, marital status, cancer approved program, and rural-urban continuum code

 Table 2.7. Sensitivity Analysis: Risk Ratios (RR) and 95 Confidence Intervals (CI) for race/ethnicity and neighborhood socioeconomic status (nSES) representing that effect as modified by a 15-minute increase in driving time calculate using the *gmapsdistance* function.



**\***Separate model with aggregate AANHPI which include NHPI and Asian Indians.

<sup>a</sup> Risk Ratio (Exponentiated Estimate) for Race/Ethnicity represents Race/Ethnicity effect as modified by a 15-minute increase in travel time (with product term to capture effect modification by travel time, adjusted for age, year of diagnosis, stage at diagnosis, sex, insurance, marital status, cancer approved program, and rural-urban continuum code.

<sup>b</sup> Risk Ratio (Exponentiated Estimates) for nSES represent nSES effects as modified by a 15-minute increase in travel time (with product term to capture effect modification by travel time), adjusted for age, year of diagnosis, stage at diagnosis, sex, race/ethnicity, insurance, marital status, cancer approved program, and rural-urban continuum code

#### **DISCUSSION**

Racial/ethnic and socioeconomic disparities in receipt of GCT and timely treatment exist among early-stage NSCLC patients in California. NHBs experienced the lowest rate of GCT and Filipinos and NHBs experienced the lowest rates of timely treatment, and patients living in the highest nSES experienced the highest rate of timely GCT with a linear decreasing trend with decreasing nSES. On average, a 15-minute increase in travel time was associated with a decreased risk for undertreatment and delayed treatment. This protective effect observed from increased travel times was unexpected and may be a "Travel Time Paradox," but this paradox was not uniform across all groups.

 NHBs and Hispanics were at higher relative risk as compared to Whites for undertreatment and delayed treatment. NHBs and Hispanics had shorter travel times and the highest proportions of patients in lower nSES. Interestingly, when considering the interaction between travel time and race/ethnicity, a 15-minute increase in driving time for Hispanics attenuated the risk of undertreatment and delayed treatment, compared to NHWs. This could be explained by healthcare facilities near Hispanic neighborhoods being poorer. Opposing, a 15 minute increase in public transit time for Hispanics increased the magnitude of risk of undertreatment and delayed treatment, compared to NHWs. It is unclear why this "Travel Time Paradox" would not hold in Hispanics for public transit, but it may be that patients requiring public transit are less likely to travel farther for better care when travel times are already three times longer than driving. Further, a 15-minute increase in driving and public transit time for NHBs increased the magnitude of risk of undertreatment and delayed treatment, compared to NHWs. This supports a racial/ethnic disparity that is not overcome by a farther, more qualified, healthcare facility.

In aggregate, AANHPIs were not at increased relative risk for undertreatment or delayed treatment, however, by disaggregated Asian groups important heterogeneity was illuminated. Compared to NHWs, Koreans and Vietnamese were at higher risk for undertreatment and Filipinos were at higher risk for delayed treatment. Filipinos and Vietnamese had shorter travel times and relatively average nSES. For Vietnamese, however, a 15-minute increase in driving time for Vietnamese appears to protect against undertreatment compared to NHWs and reveals the benefit for Vietnamese to travel farther for better cancer care. On the other hand, a 15-minute increase in public transit time for Vietnamese increases the risk of undertreatment, compared to NHWs. A 15 minute increase in driving and public transit time for Filipinos attenuates the risk of undertreatment and exaggerates the risk of delayed treatment, compared to NHWs. Lastly, Other Asians are at higher risk for undertreatment and lower risk for delayed treatment compared to NHWs, but a 15 minute increase in travel time significantly increases risk for undertreatment and delayed treatment, compared to NHWs.

We observed a linear relationship between increased travel time and risk of undertreatment and treatment delay by decreasing quintile of nSES. For patients in the lowest nSES, a 15-minute increase in travel time resulted in 33-39% and 27-44% increased risks of undertreatment and delayed treatment, respectively. This may be explained by lower socioeconomic patients not having as good of choices, even if traveling farther. Interestingly, a 15-minute increase in driving time for non-highest nSES patients increases the risk of delayed treatment and a 15-minute increase in public transit time for the non-highest nSES patients attenuates the risk of delayed treatment, compared to the highest nSES patients. This may be due to patients in lower nSES wanting to drive farther for better care, but it simply taking longer to find the time.

In previous U.S. studies<sup>170-172</sup>, increased travel distance within urban areas decreased receipt of timely treatment, while within rural areas, the inverse relationship was found. These studies considered distance as opposed to time, which may have influenced results as driving the same distance in an urban setting likely takes longer than in a rural setting. Our public transit time results generally represent urban areas in which this 'Travel Time Paradox' holds, although attenuated compared to driving time, and contradictory to the above studies' findings. Most other U.S. studies considered assessed travel distance as opposed to travel time, and found that increased travel distance decreased likelihood of treatment<sup>74,77-79</sup>.

This "Travel Time Paradox" has not been previously reported in U.S. patients. In one Australian study, early-stage NSCLC patients living farther away were less likely to have surgery and more likely to attend a general hospital rather than a specialist hospital. But, for patients that were treated in specialist hospitals, the relationship with distance was inverse showing a protective effect with longer distance<sup>54</sup>. Although our study is not directly comparable due to differences in healthcare systems, our study supports the hypothesis that patients may choose, if resources allow, to travel farther for better cancer care, and the closest hospital may not have the resources to provide proper treatment. Further, two recent U.S. studies showed that early-stage NSCLC who were treated at an academic facility compared to a community facility had significantly higher median overall survival, and Black patients were more likely to undergo surgery at academic facilities<sup>173,174</sup>. Our study controlled for ACOS-approved cancer program to try and account for quality of care and the importance of facility type, but also found no random effect by treatment facility.

We considered a patient's chosen treatment facility as opposed to the nearest facility, as often examined47-56,63,64,73,74,76,78,84,170-172. Considering the nearest treatment facility may make sense in countries with universal healthcare or clearly defined catchment regions, but this topic is much more complex in the U.S. where patients' healthcare utilization is driven by insurance, choice, and convenience<sup>175</sup>. Thus, our observed 'Travel Time Paradox' may be driven by a patient's choice to travel further for improved cancer care.

The findings from this study should be interpreted in light of the limitations. The CCR does not provide patient refusal or comorbidities preventing treatment which could result in outcome misclassification. Further, a patient's ability to get appropriate care may be attributable to more than just proximity to care. One consideration is that wealthier patients may choose to travel farther for their cancer care than a poorer patient. We tried to unpack this by assessing nSES as an effect modifier, but due to limited sample sizes, we were unable to stratify our results by both race/ethnicity and nSES. A strength of this study includes the presentation of disaggregated Asian groups; aggregating Asians into one group masks heterogeneity between groups. Additionally, we consider a patient's chosen treatment facility, as opposed to nearest treatment facility, and so our exposure is representative of the treatment facility a patient chose to attend.

These findings help elucidate the cancer-related health disparities within California's highly diverse population. Undertreatment and delayed treatment for early-stage NSCLC disproportionately affect minorities and those living in lower socioeconomic status neighborhoods. The protective effect observed from increased travel times may be a 'Travel Time Paradox'. This paradox effect may be partially explained by patients choosing to travel farther for better care or having to travel farther to receive treatment. However, a patient's ability to travel farther for care could be prohibited for many reasons such as lack of time or personal transportation thus additional healthcare facilities may not be the solution. Instead, accessible high-quality healthcare facilities that offer surgery, radiation, and chemotherapy are required.

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# **CHAPTER 3: NEIGHBORHOOD DIVERSITY AND RACIAL/ETHNIC DISPARITIES IN LUNG CANCER TREATMENT**

#### **ABSTRACT**

**Background:** Disparities in healthcare utilization are related to an individuals' racial/ethnic identity and the racial/ethnic composition of their community. We studied the effect of neighborhood diversity on racial/ethnic disparities in receipt of guideline-concordant treatment (GCT) among early-stage non-small (ES-NSCLC) patients.

**Methods:** We studied 22,890 ES-NSCLC patients diagnosed in California (2006-2015). We quantified absolute (Between-Groups Variance) and relative (Theil and Mean Log Deviation) disparities in receipt of GCT and timely GCT across patient race/ethnicity and patientneighborhood concordance, defined as the racial/ethnic composition of a neighborhood being predominately concordant, mixed, or discordant with the patient's race/ethnicity. Logistic regression was used to estimate the relative risk (RR) of patient race/ethnicity and neighborhood diversity on undertreatment and treatment delay, independently and jointly with patient race/ethnicity.

**Results:** We observed higher absolute disparities in timely GCT compared to GCT, and across patient race/ethnicity compared to patient-neighborhood concordance. Blacks, Hispanics, and Vietnamese were at 22-44% and Blacks, Hispanics, and Filipinos were at 8-20% increased risk for undertreatment and treatment delay, respectively, compared to Whites. Overall, living in mixed  $(RR=1.08, 95\% CI=1.01-1.16)$  and discordant  $(RR=1.13, 95\% CI=1.02-1.25)$  neighborhoods was associated with an increased risk of undertreatment. This linear trend did not hold across patient race/ethnicities. Hispanics in predominately concordant neighborhoods (RR=1.47, 95%CI=1.25-

1.73) had higher RR of undertreatment than Hispanics in mixed neighborhoods (RR=1.29,  $95\%CI=1.13-1.48$ ).

**Conclusion:** Minority patients living in neighborhoods with high racial/ethnic concordance were at increased risk for undertreatment and delayed treatment, possibly due to poorer social and built environments, compared to Whites living in concordant neighborhoods.

### **INTRODUCTION**

Lung cancer is the second most commonly diagnosed cancer and the leading cause of cancer-related deaths in the United States (US), accounting for approximately 25% of all cancer deaths<sup>1</sup>. Favorable prognosis after lung cancer is highly dependent on a patient's stage at diagnosis and receipt of appropriate and timely treatment as recommended by the National Comprehensive Cancer Network  $(NCCN)^{2,14}$ . If detected at an early stage, increasingly more common since the introduction of lung cancer screening recommendations in 2013, and treated promptly, prognosis can be quite  $\text{good}^{4,7}$ .

Unfortunately, despite the availability of evidence-based treatment guidelines, it is welldocumented that lung cancer patients of non-White race and lower socioeconomic status are less likely to receive appropriate or timely treatment<sup>2,18-31</sup>. Such disparities in healthcare utilization are attributable to multiple levels: an individuals' racial/ethnic identity, the racial/ethnic composition of their community, and the socioeconomic conditions in which a patient resides<sup>94</sup>. For example, minority neighborhoods and ethnic enclaves with increased segregation more often have less access to health-promoting resources and little control over their environments<sup>95-99</sup>. Previously reported findings of the relationship between living in segregated communities, social cohesion, and healthcare utilization or health outcomes have been mixed and variations by race/ethnicity have been noted<sup>103,104,107-115,117,176-178</sup>.

While disparities attributed to unmodifiable factors such as a patient's race/ethnicity are well-understood<sup>2,18-31</sup>, the modifiable mechanisms that drive such disparities are not. Contextualizing these disparities through the lens of social determinants of health, including neighborhood characteristics, may illuminate important factors amenable to intervention that drive these racial/ethnic disparities in cancer outcomes, such as receipt of timely appropriate treatment among individuals diagnosed at an early stage. The objective of this study was to estimate the effect of neighborhood diversity on racial/ethnic disparities in receipt of timely GCT among earlystage non-small cell lung cancer (ES-NSCLC) patients in California.

# **METHODS**

#### *Data Source*

This study used individual-level data from the California Cancer Registry (CCR), California's statewide population-based cancer surveillance program<sup>10</sup>. CCR variables include patient demographics tumor characteristics, treatments received in the 6 months following diagnosis, including surgery, radiation, and chemotherapy, treating hospital, and residential census block based on the patient address at the time of diagnosis.

We constructed a two-level database where individuals were nested within their neighborhoods, which was assigned at the block group-level. The database was augmented with contextual neighborhood-level data including proportions of each racial/ethnic group (tract- and block group-level) and population density (tract-level) from the 2010 Census Demographic Profile

Summary, the 2010 Environmental Systems Research Institute (ESRI) Diversity Index (tract- and block group-level)<sup>179,180</sup>, neighborhood socioeconomic status (nSES; block group-level, included in the CCR), tract-level percent uninsured from the 2008-2012 ACS, Area Deprivation Index (ADI; block group-level) as developed by the University of Wisconsin School of Medicine and Public Health in 2013<sup>181,182</sup>, the California Health Places Index (HPI) from the Public Health Alliance of Southern California<sup>183</sup>, 2013 Rural-Urban Continuum Codes (RUCC) developed by the US Department of Agriculture<sup>184</sup>, physician density from the California Health Care Foundation (county-level)<sup>185</sup>, and neighborhood (block group-level) street intersection density from the US Environmental Protections Agency's Smart Location Database<sup>186</sup>.

This study was reviewed and approved by Institutional Review Boards (IRBs) at San Diego State University, the University of California San Diego, and the California Department of Public Health Committee for the Protection of Human Subjects.

#### *Study Population*

We initially included 23,571 patients diagnosed with stage I-II NSCLC, as defined by the American Joint Committee of Cancer 7th edition<sup>187</sup>, between 2006 and 2015, and alive at the time of diagnosis. Patients were excluded for the following reasons: (1) missing lymph node (N) staging  $(n=122)$ ; (2) missing date information required to determine GCT or timely treatment  $(n=127)$ ; (3) sex categorized as "other", Transsexual or Transgender, or unknown  $(n=4)$ ; (4) missing race  $(n=43)$ ; (5) 2+ races documented  $(n=288)$ ; (6) other Hispanics  $(n=9)$ ; (7) missing residential census block at diagnosis ( $n=20$ ); and (8) missing treatment facility ( $n=68$ ). Our final analytic sample comprised 22,890 patients.

#### *Outcomes*

The primary study outcome, receipt of GCT, was defined according to the 2016 NCCN Guidelines as the administration of proper initial and adjuvant treatment(s) according to cancer site and stage<sup>14</sup>, and measured using CCR variables on surgery, chemotherapy, and radiation. Patients were classified as receiving "undertreatment" if they received no treatment or less than the minimum recommended treatment, or "GCT" if they received at least the minimum recommended treatment for their stage. A secondary study outcome was receipt of timely treatment. The Research ANd Development (RAND) Corporation recommends treatment initiation within 6 weeks of diagnosis<sup>16</sup> (i.e., the initiation of surgery, radiation, or chemotherapy within 45 days of diagnosis) and The Commission of Cancer (CoC) Quality of Care Measures recommends that adjuvant treatment of chemotherapy be administered within 6 months of surgery, if appropriate<sup>17</sup> (i.e., the initiation of chemotherapy  $+/-$  radiation within 6 months of initial surgery for N1 patients). Patients who received GCT were classified as having received either delayed treatment or timely treatment (Figure 1.1).

To determine adherence to GCT and timely treatment, full dates for diagnosis, surgery, radiation, and chemotherapy were required. If only month and year were available, the middle of the month was imputed.

#### *Exposures*

We examined six measures of neighborhood diversity:

**Diversity (1 and 2):** Block group and tract diversity was calculated using multi-group entropy score (E), calculated as:

 $E = \sum_{r=1}^{r} (\pi_r) \ln[1/\pi_r]$ ; where  $\pi_r$  is a racial/ethnic group's proportion of the whole neighborhood (block group or tract). We used eight racial/ethnic groups (White, Black, Hispanic, Asian, Pacific Islander, American Indian/Alaskan Native, other, and mixed)<sup>188</sup>, and therefore the maximum entropy was  $ln(8) = 2.079$  which occurs when all 8 racial/ethnic groups have equal representation in the block group or tract. E is influenced by the relative size of the various racial/ethnic groups<sup>189</sup>.

**Segregation (3):** Neighborhood (tract) segregation was measured using the multi-race information theory index (H), calculated as:

 $H = \sum_{i=1}^{n} \frac{t_i (E - E_i)}{F_i^T}$  $ET$  $\frac{n}{i=1} \frac{t_i (E-E_i)}{ET}$ ; where  $t_i$  is total population of tract t, T is the census tract population size, n is the number of block groups, and  $E_i$  and E represent block group i's diversity (entropy) and census tract diversity, respectively.

Block group residents are nested in neighborhoods (tracts). H measures how evenly racial/ethnic groups at the block group-level are distributed across neighborhoods, regardless of the size of each group. H ranges from 0 (all block groups have the same composition as the neighborhood) to 1 (maximum segregation) $189$ .

**Diversity Index (4 and 5):** The block group and tract Diversity Indices were ascertained from the ESRI Diversity Index<sup>179,180</sup>, calculated as the likelihood that two people, chosen from the same area at random, belong to the same racial or ethnic group. The Diversity Index ranges from 0 (no diversity) to 100 (complete diversity)<sup>190</sup>.

**(6) Patient-Neighborhood Racial/Ethnic Composition Concordance:** Neighborhood (tract) racial/ethnic composition was compared to a patients' race/ethnicity to classify concordance

as predominately concordant, mixed concordant, or discordant. Predominately concordant was defined as  $\geq$  50% patient race/ethnicity and  $\leq$  20% any other racial/ethnic group, mixed concordant as  $\geq$  20% patient race/ethnicity,  $\geq$  20% one or two other racial/ethnic group, and  $\leq$  20% any other racial/ethnic group, and discordant as neighborhoods that did not fit into the above categories.

A detailed description of all patient-neighborhood racial/ethnic compositions seen in our population, definitions, the number (%) of patients in our population who are residents of each neighborhood type, and concordant race/ethnicities are available in Table 3.1.


 Table 3.1. Robust Description of Neighborhood Racial/Ethnic Composition Concordance within our Study Population.

## *Covariates*

Individual- and neighborhood-level covariates shown to be associated with receipt of GCT in published literature were selected *a priori*103,104,107-115,176-178. Individual-level covariates included patient race/ethnicity classified as: non-Hispanic White (NHW), non-Hispanic Black (NHB), Hispanic (including those who identify as White or Black race), Asian Americans and Pacific Islanders (AAPI) aggregated as one race as well as disaggregated into specific ethnicities (Chinese, Japanese, Filipino, Korean, Vietnamese, Asian Indian, Other Asian, Native Hawaiian and Pacific Islander (NHPI)), and American Indian/Alaska Native (AIAN); stage at diagnosis, year of diagnosis, sex, age, insurance type (not insured, private insurance, Medicaid, Medicare, military, or other/not otherwise specified), marital status (single, married or domestic partner, separated/divorced, or widowed), whether or not the reporting facility with the earliest date of admission had an ACOS-approved cancer program, and whether a patient's treatment hospital had surgery, radiation, or chemotherapy services available.

Neighborhood-level covariates included population density, nSES, percent uninsured, ADI state rank, HPI percentile, RUCC, intersection density, and physician density (oncology, general surgery/surgical oncology, radiation oncology, primary care, and specialists per 100,000 population) as a measure of the variety of nearby treatment facility options. nSES uses a composite residential neighborhood-level index that combines census measures of education, income, occupation, and cost of living at the census block group level and categorized into quintiles<sup>166</sup>. California ADI (ranked 1-10 (most disadvantaged)) is a factor-based score from 17 census-block level markers of SES for each neighborhood including domains of income, education, employment, and housing quality<sup>191</sup>. HPI (percentile ranking  $0-100$  (most disadvantaged)) integrates multiple data sources including  $25$  economic, social, and environmental indicators<sup>192</sup>.

RUCC (1-9 (rural)) distinguishes metropolitan counties by the population of their metro area, and nonmetropolitan counties by degree of urbanization and adjacency to a metro area are assigned to each county<sup>167</sup>.

Missing covariate data were multiply imputed, a valid statistical procedure for recovering missing data to create complete datasets that can be analyzed using standard procedures<sup>168</sup>, using five imputations.

## *Statistical Analysis*

We tabulated exposures, individual-, and neighborhood-level characteristics overall and by patient race/ethnicity. We quantified average disproportionality in receipt of GCT and timely treatment across patient race/ethnicities and patient-neighborhood racial/ethnic composition concordance using three commonly used disproportionality functions: 1) Between-Groups Variance (BGV); 2) The Theil Index (T); and 3) Mean Log Deviation (MLD). Absolute (BVG) and relative (T and MLD) values range from 0 to  $\infty$  (higher level of inequality); formulas are provided in Figure 2.1.

To quantity the relative risks (RRs) and 95% confidence intervals (CIs) of the associations between neighborhood diversity and risk of undertreatment and delayed treatment, we fit multivariable logistic regression models using PROC GENMOD with a Poisson distribution and log link function. We used direct acyclic graphs (Figure 3.1) to guide our covariate selection and chose two sets of covariates. Model 1 included only individual-level covariates and Model 2 added neighborhood-level covariates. We excluded neighborhood-level covariates from Model 1 because these variables could be intermediates on the causal pathways from the individual race/ethnicity to the outcomes. The intraclass correlation coefficient (ICC) of treatment hospital was assessed in intercept-only models for each outcome to determine if treatment hospital needed to be included as a cluster variable; the ICC for treatment hospital was <5% and therefore not included as a cluster variable. Variables for diversity, segregation, and the Diversity index were rescaled to reflect a 10% increase per unit change. To examine joint effects with patient race/ethnicity, a statistical interaction between the neighborhood exposure and patient race/ethnicity was included, with "joint effect" results reported by patient race/ethnicity. We also calculated the interaction contrast ratio (ICR), a measure of departure from additivity, and attributable portion (AP), a measure of the proportion of risk in the doubly exposed group that is due to the interaction considering the exposed group to be non-White patients living in mixed and discordant neighborhoods<sup>193,194</sup>. Our final models included (1) all subjects, (2) joint effects with NHPI, Asian Indian, and AIAN patients removed from the models due to populations <100 (Undertreatment n=22,707; Delayed GCT n=18,381), and (3) joint effects with patient race/ethnicity with AANHPI included as an aggregate group (n=22,857; Delayed GCT n=18,381).



Y: Undertreatment and Delayed Guideline Concordant Treatment A: Individual-level covariates **B:** Neighborhood-level covariates



All analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC). Statistical significance was assessed at  $p<0.05$ . ICR and AP 95% CIs were calculated using bootstrapping with 500 repetitions.

# **RESULTS**

# *Population and Neighborhood Characteristics*

Over half of case population was female; 64.4% of Japanese and 40.6% of Vietnamese patients were female. The mean age at diagnosis was 70.4 among all patients and was 74.2 among Japanese patients. NHBs had the highest proportion of Stage IIB at diagnosis at 14.9%. Few patients were uninsured, and most were married. Over 60% of hospitals had an ACOS-approved cancer program and over 93% of hospitals offered surgery, radiation, or chemotherapy services (Table 3.2).

Table 3.2. Exposures, Individual- and Neighborhood-level characteristics, stratified by patient race/ethnicity. Table 3.2. Exposures, Individual- and Neighborhood-level characteristics, stratified by patient race/ethnicity.







3.2. Exposures, Individual- and Neighborhood-level characteristics, stratified by patient race/ethnicity. continued. 3.2. Exposures, Individual- and Neighborhood-level characteristics, stratified by patient race/ethnicity. *continued.*



At the neighborhood level, block group and tract diversity and diversity indices varied by patient race/ethnicity. Neighborhood segregation was low with no variation by patient race/ethnicity, indicating that the racial/ethnic composition of a block group is very similar to the tract it falls within. Most patients lived in predominately White and mixed White and Hispanic neighborhoods (Table 3.1). The percentage of patients living in predominately concordant neighborhoods was highest among NHWs, followed by Hispanics.

Fourteen percent of patients lived in the lowest nSES and most patients lived in metro areas. Intersection density was lower for NHW, Asian Indian, and AIAN patient neighborhoods, and much higher in NHB patient neighborhoods. By ADI, Chinese patients lived in the least and AIAN patients lived in the most disadvantaged neighborhoods. By HPI, Asian Indian patients lived in the least and AIAN and NHB patients lived in the most disadvantaged neighborhoods. (Table 3.2).

Among the 22,890 ES-NSCLC patients, 18,528 received GCT and, of these, 10,671 received timely treatment. GCT was lowest among NHBs (76.31%) and highest among Chinese (84.72%). Timely treatment was lowest among Filipinos (49.71%) and highest among Asian Indians (72.06%). Patients living in predominately concordant neighborhoods had the highest percent of GCT (82.43%) and timely treatment (60.87%), followed by mixed concordant, and discordant. We observed higher levels of absolute disparity in receipt of timely treatment compared to GCT, and higher levels across patient race/ethnicity groups compared to patientneighborhood concordance types. We observed low relative disparity (Table 3.3).

 Table 3.3. Absolute and Relative Disparities in receipt of GCT and Timely GCT between Patient Race/Ethnicity Groups and Neighborhood Racial/Ethnic Composition Concordance Groups.

GCT and Patient Race/Ethnicity Groups $(n = 22,890)$										
<b>Patient Race/Ethnicity</b>	GCT(%)	<b>Population Proportion</b>	<b>BVG</b>	Theil	<b>MLD</b>					
non-Hispanic White (n=16509)	81.76	0.7212	0.4849	0.0073	$-0.0073$					
non-Hispanic Black (n=1465)	76.31	0.0640	1.3720	$-0.0036$	0.0038					
Hispanic ( $n=2266$ )	77.63	0.0990	1.0847	$-0.0040$	0.0041					
AANHPI $(n=2617)*$	81.24	0.1143	0.0103	0.0004	$-0.0004$					
NHPI $(n=66)$	78.79	0.0029	0.0134	$-0.0001$	0.0001					
Chinese $(n=772)$	84.72	0.0337	0.4815	0.0016	$-0.0015$					
Japanese $(n=180)$	82.78	0.0079	0.0267	0.0002	$-0.0002$					
Filipino $(n=635)$	80.47	0.0277	0.0061	$-0.0002$	0.0002					
Korean $(n=195)$	78.46	0.0085	0.0523	$-0.0003$	0.0003					
Vietnamese $(n=360)$	78.61	0.0157	0.0852	$-0.0004$	0.0005					
Asian Indian $(n=84)$	80.95	0.0037	0.0000	0.0000	0.0000					
Other Asian $(n=325)$	78.77	0.0142	0.0669	$-0.0004$	0.0004					
AIAN $(n=33)$	81.82	0.0014	0.0011	0.0000	0.0000					
<b>All Groups</b>	80.94		3.6748	0.0003	0.0003					
Timely treatment and Patient Race/Ethnicity Groups ( $n = 18,528$ )										
<b>Patient Race/Ethnicity</b>	Timely GCT (%)	<b>Population Proportion</b>	<b>BVG</b>	<b>Theil</b>	<b>MLD</b>					
non-Hispanic White (n=13498)	58.48	0.7285	0.5770	0.0113	$-0.0112$					
non-Hispanic Black (n=1118)	50.09	0.0603	3.3919	$-0.0073$	0.0084					
Hispanic $(n=1759)$	54.80	0.0949	0.7387	$-0.0045$	0.0047					
AANHPI $(n=2126)$ *	58.33	0.1147	0.0628	0.0015	$-0.0015$					
NHPI $(n=52)$	65.38	0.0028	0.1699	0.0004	$-0.0004$					
Chinese $(n=654)$	60.24	0.0353	0.2479	0.0017	$-0.0016$					
Japanese $(n=149)$	57.72	0.0080	0.0001	0.0000	0.0000					
Filipino $(n=511)$	49.71	0.0276	1.7138	$-0.0035$	0.0041					
Korean $(n=153)$	61.44	0.0083	0.1230	0.0006	$-0.0005$					
Vietnamese $(n=283)$	56.89	0.0153	0.0075	$-0.0002$	0.0002					
Asian Indian $(n=68)$	72.06	0.0037	0.7747	0.0010	$-0.0008$					
Other Asian $(n=256)$	65.63	0.0138	0.8921	0.0021	$-0.0018$					
AIAN $(n=27)$	51.85	0.0015	0.0494	$-0.0001$	0.0002					
<b>All Groups</b>	57.59		8.6861	0.0015	0.0012					
GCT and Patient-Neighborhood Racial/Ethnic Composition Concordance Groups (n = 22,890)										
<b>Neighborhood Concordance</b>	GCT(%)	<b>Population Proportion</b>	<b>BVG</b>	<b>Theil</b>	<b>MLD</b>					
Predominately Concordant (n=7717)	82.43	0.3371	0.7486	0.0063	$-0.0062$					
Mixed Concordant (n=11391)	80.62	0.4976	0.0509	$-0.0020$	0.0020					
Discordant (n=3782)	78.90	0.1652	0.6879	$-0.0041$	0.0042					
	80.94		1.4875	0.0002	0.0000					
<b>All Groups</b> Timely treatment and Patient-Neighborhood Racial/Ethnic Composition Concordance Groups (n = 18,528)										
<b>Neighborhood Concordance</b>	Timely GCT (%)	<b>Population Proportion</b>	<b>BVG</b>	<b>Theil</b>	<b>MLD</b>					
Predominately Concordant (n=6361)	60.87	0.3433	3.6966	0.0201	$-0.0190$					
Mixed Concordant (n=9183)	56.20	0.4956	0.9570	$-0.0118$	0.0121					
Discordant (n=2984)	54.89	0.1611	1.1744	$-0.0074$	0.0077					
	57.59		5.8280	0.0009	0.0008					
<b>All Groups</b>										

## **Models for Patient Race/Ethnicity**

In Model 1, NHBs, Hispanics, and Vietnamese were at increased risk for undertreatment (RRs ranged from 1.22-1.44) and NHBs, Hispanics, and Filipinos were at increased risk for delayed treatment (RRs ranged from 1.08-1.20), compared to NHWs (Table 3.4).

Table 3.4. Effects of Patient Race/Ethnicity and Diversity and Segregation on Undertreatment and Delayed GCT. Table 3.4. Effects of Patient Race/Ethnicity and Diversity and Segregation on Undertreatment and Delayed GCT.



Table 3.4. Effects of Patient Race/Ethnicity and Diversity and Segregation on Undertreatment and Delayed GCT. continued. Table 3.4. Effects of Patient Race/Ethnicity and Diversity and Segregation on Undertreatment and Delayed GCT. *continued.*



\* RR correspond to a 10% increase in the exposure variable.

 $*$  RR correspond to a 10% increase in the exposure variable.<br>1 Separate model with aggregate AANHPI which include NHPI and Asian Indians. ϯ Separate model with aggregate AANHPI which include NHPI and Asian Indians.

#### **Models for Diversity, Segregation, and the Diversity Index Indices**

RR's of the associations between neighborhood diversity and receipt of GCT and timely treatment are reported in Table 3.4.

In Model 1, compared to NHWs, when assessing the joint effects with patient race/ethnicity, a 10% increase in block group and tract diversity in NHBs and Hispanics increased risk of undertreatment by 59-78% and a 10% increase in neighborhood segregation increased the risk of undertreatment in Hispanics by 33%. In Model 1, we observed a 4% increased risk of undertreatment with a 10% increase in the block group and tract diversity index overall, and an 77%-88% increased risk of undertreatment in NHBs, compared to NHWs.

In Model 1, we observed a 3% increased risk of delayed GCT with a 10% increase in block group and tract diversity overall, and a 67% increased risk of delayed treatment in Filipinos and a 22-24% increased risk of delayed treatment in Hispanics, compared to NHWs. A 10% increase in neighborhood segregation increased the risk of delayed GCT in NHBs by 31%, compared to NHWs. In Model 1, we observed a 4% increased risk of delayed GCT with a 10% increase in the block group and tract diversity index overall.

Overall, RRs were attenuated after adjustment for neighborhood-level variables in model 2, but RRs increased in magnitude for undertreatment with a 10% increase in the block group and tract diversity index for NHBs and Hispanics.

## **Models for Patient-Neighborhood Racial/Ethnic Composition Concordance**

RRs, ICRs, and APs of the associations between patient-neighborhood racial/ethnic composition concordance and receipt of GCT and timely treatment are reported in Table 3.5.

Table 3.5. Effects of Patient Race/Ethnicity on Patient-Neighborhood Racial/Ethnic Composition Concordance on Undertreatment and Delayed GCT. Table 3.5. Effects of Patient Race/Ethnicity on Patient-Neighborhood Racial/Ethnic Composition Concordance on Undertreatment and Delayed GCT.



Table 3.5. Effects of Patient Race/Ethnicity on Patient-Neighborhood Racial/Ethnic Composition Concordance on Undertreatment Table 3.5. Effects of Patient Race/Ethnicity on Patient-Neighborhood Racial/Ethnic Composition Concordance on Undertreatment and Delaved GCT. continued. and Delayed GCT. *continued.*



ϯ Separate model with aggregate AANHPI which include NHPI and Asian Indians.

f Separate model with aggregate AANHPI which include NHPI and Asian Indians.<br>"The interaction contrast ratio is a measure of departure from additivity due to the interaction and is interpreted as a positive or negative add bThe attributable proportion is the proportion of risk in the doubly exposed group that is due to the interaction considering the exposed group to be non-White patients aThe interaction contrast ratio is a measure of departure from additivity due to the interaction and is interpreted as a positive or negative additive interaction. living in mixed and discordant neighborhoods and is interpreted as an increased or decreased proportion of risk, compared to non-Hispanic Whites.

In Model 1, patients living in mixed and discordant neighborhoods compared to predominately concordant neighborhoods were at 8% and 13% increased risk, respectively, for undertreatment. When compared to NHWs living in predominately concordant neighborhoods, Hispanics in predominately concordant neighborhoods were at 47% increased risk for undertreatment. For mixed versus predominately concordant neighborhoods, ICRs and APs indicated a negative additive interaction and 22.09% decreased proportion of risk for Hispanics, and a positive interaction and 38.13% increased proportion of risk for Filipinos and 43.20% increased proportion of risk for Vietnamese, compared to NHWs. For discordant versus predominately concordant neighborhoods, ICRs and APs indicated a decreased proportion of risk for NHB, Hispanic, and Chinese patients.

In Model 1, patients living in mixed and discordant neighborhoods, compared to predominately concordant neighborhoods, were at 10% and 12% increased risk, respectively, for delayed treatment. When compared to NHWs living in predominately concordant neighborhoods, Hispanics and Vietnamese in predominately concordant neighborhoods were at 25% and 95% increased risk, respectively, for delayed treatment. For mixed versus predominately concordant neighborhoods, ICRs and APs indicated a decreased proportions of risk for Hispanics, AANHPI, Chinese, Korean, and Vietnamese patients, and for discordant versus predominately concordant neighborhoods, a decreased proportion of risk for Hispanic, AANHPI, Chinese, and Vietnamese, and an increased proportion of risk for Japanese patients, compared to NHWs.

After further adjustment for neighborhood-level covariates in Model 2, ICRs and AP attenuated for negative additive interactions and increased for positive additive interactions.

## **DISCUSSION**

Considering 10 years of ES-NSCLC diagnoses in California, we found disparities in the proportion of patients who received GCT and timely treatment by patient race/ethnicity and neighborhood racial/ethnic composition. NHBs had the lowest rate of GCT and Filipinos and NHBs had the lowest rate of timely treatment. Patients living in predominately concordant neighborhoods had the highest rate of GCT/timely treatment. We expected the linear trend of decreased risk by patient-neighborhood racial/ethnic composition concordance to hold across patient race/ethnicities, but we instead found that many non-White race/ethnicity groups living in predominately concordant neighborhoods were at higher relative risk for undertreatment and delayed treatment than those living in mixed concordant and discordant neighborhoods.

This study aimed to uncover the underlying mechanisms, specifically neighborhood characteristics, that drive these racial/ethnic disparities. To our knowledge, this is the first study to examine the effect of patient-neighborhood racial/ethnic composition on racial/ethnic disparities in receipt of lung cancer treatment. Previous research suggests entanglement of racial segregation, income inequality, and health problems<sup>153,195</sup>, which produces inequalities that contribute to socioeconomic inequalities, and thus health inequalities<sup>196</sup>. Neighborhoods are key determinants of health and the incorporation of neighborhood social and built environment factors into cancer research can help identify vulnerable populations amenable to intervention or policy changes such as increasing health education in the community and creating new clinics $88$ .

Previous studies examining neighborhood characteristics and cancer outcomes have reported mixed findings, with variations by race/ethnicity<sup>176,177</sup>. Similar to our study, two studies among NSCLC patients in Florida and Georgia found decreased odds of receipt of surgery for Black patients living in Black segregated areas<sup>104,178</sup>. Residential segregation by race has also been associated with lower survival in Black NSCLC patients<sup>104,105</sup>. In highly segregated counties, an increase in Blacks or Hispanics has been shown to be associated with a decrease in the availability and use of surgical services and an increase in emergency visits $103$ . Black and Hispanic segregation was shown to be adversely associated with adequate cancer care, cause-specific mortality and allcause mortality among lung cancer patients<sup>103,107-113</sup>. Some advantages to neighborhood diversity have also been observed. Increased percent Black has been shown to be protective for outcomes in Blacks<sup>108,111,114</sup>. Living in a neighborhood with a high racial/ethnic concentration as the one you identify has been shown to improve outcomes, potentially attributable to social cohesion or social capital $115,116$ .

In our study, non-White race/ethnic groups living in a neighborhood with high racial/ethnic concordance were at increased risk for undertreatment and delayed treatment. We also found that increased diversity, or equal representation of racial/ethnic groups in neighborhoods, increased risk for undertreatment and delayed treatment for some non-White racial/ethnic groups. This may be attributed to predominately White neighborhoods having better social and built environment, such as accessible high-quality healthcare facilities. Meaning, minority patients who live in predominately White neighborhoods may be protected. Minority neighborhoods with increased segregation have been found to have poorer health resources, which may partially explain the harmful effect of neighborhood segregation. Predominately Black neighborhoods are more likely to have poorer health facilities staffed by less competent physicians, a greater primary care physician shortage, higher environmental exposures including ambient air toxins, and poorer built environments<sup>95-98</sup>. Hispanic and Asian majority neighborhoods are generally less likely to have a primary care physician shortage<sup>97</sup>.

A strength of this study included the large sample size which allowed us to present the effects of disaggregate Asian groups. A limitation is that the 2010 Census Demographic Profile Summary File in which the proportions of each racial/ethnic group were ascertained only provided aggregate AANHPI and thus our exposures did not consider disaggregate Asian groups. When considering our exposure patient-neighborhood racial/ethnic composition concordance, predominately Black and Asian neighborhoods are scarce in California, and thus this measure may not provide actionable evidence at this time. Additionally, we used a patient's census block group, which provides high spatial resolution compared to zip code or census tract, allowing us to use more precise neighborhood characteristics. Another limitation is that we were unable to account for patient refusal of treatment or comorbidities preventing GCT. Minorities have a higher prevalence of comorbidities compared to NHWs, which could create a degree of misclassification in receipt of GCT dependent on patient race/ethnicity.

This study on the relative contributions of neighborhood-related factors on racial/ethnic disparities in receipt of GCT for early-stage NSCLC provides actionable evidence on how to reduce disparities for underrepresented minorities with lung cancer. Neighborhoods are key but modifiable determinants of health. By understanding the role that neighborhoods play in healthcare utilization, specifically receipt of proper cancer treatment, we can begin to identify vulnerable neighborhoods and implement individual-level and group-level interventions or policy changes to reduce the lung cancer disparities in the US.

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# **CHAPTER 4: PATIENT-PROVIDER ENGAGEMENT IN EARLY STAGE LUNG CANCER TREATMENT DISPARITIES: AN ANALYSIS OF CANCER REGISTRY-LINKED ELECTRONIC HEALTH RECORDS**

## **ABSTRACT**

**Background:** Disparities in who receives timely guideline-concordant treatment (GCT) for earlystage non-small cell lung cancer (ES-NSCLC) have been observed. Primary care physicians (PCP) across the United States have an active role in cancer care delivery, and patient-provider engagement may improve adherence to treatment recommendations. We investigated the impact of modifiable factors of patient-provider engagement in receipt of timely GCT in a convenience sample of ES-NSCLC patients of a Northern California health system.

**Methods:** We studied 988 ES-NSCLC patients diagnosed from 2004-2013 who had an assigned Sutter Health PCP and a health system encounter within 90 days of their diagnosis, using cancer registry linked electronic health records. GCT was defined according to the 2016 National Comprehensive Cancer Network guidelines and timely treatment was defined as treatment initialization within 45 days of diagnosis, using cancer registry variables. We used adjusted logistic regression models to quantify the relative risks (RRs) and 95% confidence intervals (CI%) for undertreatment and delay on patient characteristics and patient-provider engagement factors including language- and gender-concordance, and patients' enrollment in an online patient portal.

**Results:** Hispanics were at increased risk for undertreatment (RR=2.56, 95%CI=1.18-5.55) and Asians were at decreased risk for delay (RR=0.57, 95%CI=0.34-0.97). Unpartnered patients were at increased risk for undertreatment (RR=1.67, 95%CI=1.15-2.43) and delay (RR=1.57, 95%CI=1.15-2.13). Patients with gender-discordant PCP appeared to be at slight increased risk for undertreatment (RR=1.21, 95%CI=0.81-1.83) and delay (RR=1.23, 95%CI=0.88-1.72) and language discordance was difficult to assess due to few language discordant patients. Patients with an active patient portal were at decreased risk for undertreatment (RR=0.29, 95%CI=0.16-0.52) and delay (RR=0.70, 95%CI=0.49-0.99). More recently diagnosed, younger, partnered, and Asian cancer patients were more likely have an active online patient portal.

**Conclusion:** Active patient portals protect against undertreatment and delayed treatment in NSCLC patients in one Northern California healthcare system. Patients enrollment in a patient portal should be encouraged especially among underserved populations with newly diagnosed, treatable cancers.

## **INTRODUCTION**

Lung cancer is the leading cause of cancer related deaths in the United States (US) and non-small cell lung cancer (NSCLC) is the most common type (80-85%) of lung cancer<sup>1</sup>. Treatment for NSCLC is primarily based on the stage of the cancer, although other factors such as, but not limited to, patients overall health (comorbidities) and certain cancer traits, can influence treatment. Outcomes are favorable for patients who are diagnosed early and treated promptly. The National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines provides evidence-based guidelines to ensure clinicians can provide their patients with preventative, diagnostic, and supportive services that lead to the best outcomes<sup>14</sup>. Despite these evidence-based guidelines, disparities in who receives guideline-concordant treatment (GCT) has been observed.

Our previous findings indicate racial/ethnic disparities in who receive timely appropriate treatment for early-stage (ES) NSCLC in California. Black, Hispanic, and Vietnamese patients were less likely to receive appropriate treatment for ES-NSCLC and among those that did, Blacks,

Hispanics, and Filipinos were less likely to receive that treatment in a timely manner. Other research has also identified lung cancer patients of older age, Black race, and lower socioeconomic status as less likely to receive treatment or timely treatment<sup> $2,18-33$ </sup>.

Primary care physicians (PCP) across the United States (US) have an active role in cancer patient management<sup>121</sup> and a good relationship with a PCP may improve patient adherence to cancer treatment recommendations and mitigate treatment disparities. The patient-provider relationship, specifically communication, can influence patient engagement in their treatment and compliance, and improve patient health outcomes<sup>122,123</sup>. It has been shown that patients who felt that their physicians explained the risks of lung cancer treatment, discussed their chances of cure, discussed goals of treatment, or who were warm and friendly are more likely to undergo treatment<sup>125</sup>. There is also some evidence to suggest that patient-provider gender-concordance increases cancer screening<sup>138</sup>, language-concordance had no impact on cancer screening<sup>142</sup>, and enrollment in a patient portal increases screening<sup>197,198</sup>, but to our knowledge, no past studies have examined patient-provider gender- or language- concordance, or enrollment in a patient portal on receipt of GCT, in NSCLC patients.

A patient can choose their PCP and therefore the patient-provider relationship is modifiable. We believe that patient-provider gender- and language- concordance and enrollment in patient portals may help improve adherence to GCT, through an improved patient-provider relationship. The objective of this study is to investigate the effect of modifiable patient engagement-related factors in receipt of timely GCT in ES-NSCLC patients in Northern California. We leveraged a data resource that links cancer registry data, a definitive source of cancer and treatment details, with electronic health records from a large, multispecialty healthcare delivery system to obtain additional information on factors that might improve patient-provider engagement during the cancer treatment episode.

## **METHODS**

## *Data Source*

The California Cancer Registry (CCR) is a statewide population-based cancer surveillance program<sup>10</sup>. Cancer details, demographics, and social and clinical details were collected by the CCR. Sutter Health is a not-for-profit health system that delivers healthcare coverage in 19 California counties across 150 ambulatory medical clinics, with more than 3 million patient and over 10 million outpatient visits per year. The demographics of Sutter Health's patient population is generally representative of the underlying population with respect to sex, age, and race/ethnicity, and patients can remain in the system with their own physicians regardless of change in employerprovided health plan. Patients' enrollment in a patient portal (voluntary patient program that facilitates online interaction between the patient and provider), patients' primary care physician (PCP) at the time of diagnosis, provider language, provider gender, and patient medical and billing history were extracted. This study leveraged an existing CCR-Sutter linked cohort that linked electronic health record (EHR) data with lung cancer incidence data from the statewide, population-based CCR.

## *CCR-Sutter Linkage*

This existing CCR-Sutter linked cohort was developed and validated by Thompson et al. and explained in detail previously<sup>199,200</sup>. Adult patient's identifying information from EHR data (2006-2013) from five Sutter Health Medical Foundations (Palo Alto Medical Foundation (PAMF), Sutter East Bay Medical Foundation, Sutter Pacific Medical Foundation, Sutter Gould Medical Foundation, and Sutter Medical Foundation) were extracted. The EpicCare EHR has been active at PAMF since 2000, and all medical foundations as of 2010. Individuals diagnosed with cancer in the CCR (1988-2013) were extracted. LinkPlus software was used to identify CCR-Sutter patient matches. The importance of this linkage is the ascertainment of information from two different data sources. The CCR reflects adjudicated demographics and treatment for all cancer cases in California, regardless of where the patient received care<sup>10</sup>. The Sutter EHRs provides key Sutter-provided data elements that the CCR lacks, including patient encounters that allows us to determine comorbidities. Thus, as an example, a Sutter patient may receive surgery elsewhere, which is common for cancer patients, which would not be captured in the Sutter EHRs, while the CCR would provide information of this surgery received from a different facility, allowing us more comprehensive data.

## *Study Population*

Stage I-II NSCLC tumors, as defined by the American Joint Committee of Cancer 7th edition, diagnosed between 2004 and 2013, in patients alive at the time of diagnosis, and assigned a valid Sutter primary care physician at the time of their tumor diagnosis were initially included (n=1,196). If a unique patient had multiple tumors, only the most severe tumor was included (n=113). A handful of patients were also excluded due to missing date information required to determine GCT or timely GCT (n=5), missing race/ethnicity (n=1) required for analyses, and American Indian race  $(n=2)$  due to a small sample size. Lastly, as we want to understand the patient-provider dyad and enrollment in a patient portal, we only want to consider patients that were patients of Sutter Health at the time of their cancer diagnosis. Thus, patients were required to have a Sutter Health encounter within 90 days of cancer diagnosis (n=87). Our final study population includes 988 patients.

## *Variables Definitions*

The primary outcome was receipt of GCT according to the 2016 National Comprehensive Cancer Network (NCCN) guidelines according to cancer site and stage (Figure 1.1). Administration of proper initial and adjuvant treatment was measured using surgery type, chemotherapy type, and radiation type provided in the CCR. If a patient did not receive surgery, they were assumed inoperable and assessed for GCT according to lymph node staging (N0 or N1). Alternatively, undertreatment was less than minimum site- and stage- specific recommended treatment.

The secondary outcome was receipt of timely treatment (versus delayed treatment). The Research ANd Development Corporation suggests treatment initiation within 6 weeks of diagnosis<sup>16</sup> (i.e., the initiation of surgery, radiation, or chemotherapy within 45 days of diagnosis), and The Commission of Cancer Quality of Care Measures recommends adjuvant treatment of chemotherapy administration within 6 months of surgery, when required<sup>17</sup> (i.e., the initiation of chemotherapy +/- radiation within 6 months of initial surgery for N1 patients) (Figure 1.1). Timely treatment was calculated by the day interval between the date of diagnosis and the date when the first treatment started for initial treatment, and the day interval between the date of surgery and date of chemotherapy for adjuvant treatment. The date of diagnosis and the dates of treatment initiation (i.e., surgery, radiation, and chemotherapy) were ascertained from the CCR.

The patient characteristics of interest captured from the CCR were patient race/ethnicity (non-Hispanic White (NHW), non-Hispanic Black (NHB), Hispanic (including those who identify as White or Black), and Asian American, Native Hawaiian, and Pacific Islander (AANHPI); distinct AANHPI groups were aggregated due to insufficient sample sizes to investigate specific Asian ethnicities of interest), insurance type (Private insurance, Medicaid, Medicare, and Other), and marital status (partnered (married/unmarried or domestic partner) or unpartnered (single/never married, separated/divorced, widowed)). Patients' Charlson's comorbidity index (CCI) prior to initiation of first cancer treatment was calculating from ICD-9 codes reflecting encounters, surgery, and other procedures included in each patient's EHRs. A CCI of zero indicate no comorbidities and the higher the score, the more comorbidities<sup>201</sup>,

 The provider engagement variables of interest were patient-provider language concordance, patient-provider gender concordance, and patients' enrollment in MyHealthOnline, the Sutter online patient portal (active versus inactive). Online patient portal enrollment was directly derived from EHRs. To determined patient-provider language concordance and patientprovider gender concordance, both CCR and EHR fields were considered. Patient sex was extracted from the CCR and patient primary language was extracted from EHRs. Provider gender (male or female) and languages or dialects spoken at a language competency of "Very Good", "Excellent", or "Fluent" were extracted from EHRs<sup>197</sup>. Patient-provider gender concordance was classified as concordant if a patient and their PCP had the same sex/gender; if a provider's gender was missing, patient-provider gender concordance was classified as unknown. Patient-provider language concordance was classified as concordant is the patient's primary language was English or if a patient's language was not English, but their provider spoke the primary language of the patient based on exact language matches (e.g. Mandarin matches only with Mandarin).

 Covariates for confounding control included stage at diagnosis, year of diagnosis, age, and sex which were all captured from the CCR, in addition to patient characteristics (race/ethnicity, insurance type, marital status, and CCI).

Payer ( $n=55$ ) and marital status ( $n=13$ ) was unavailable for some subjects. To resolve this, we used multiple imputation (PROC MI) using SAS version 9.4 (SAS Institute, Cary, NC) with 6 imputed datasets, a valid statistical procedure for recovering missing data to create complete datasets that can then be analyzed through standard procedures<sup>168</sup>.

#### *Statistical Analysis*

All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC). Patient characteristics and engagement-related variables were tabulated overall, and by patient race/ethnicity. We tabulated GCT and timely treatment between 2004-2008 compared to 2009- 2013 overall, and by patient race/ethnicity and patient portal enrollment.

 We used multivariable generalized logistic regression models (PROC GENMOD) with a Poisson distribution and log link function to quantify the relative risks (RRs) and 95% confidence intervals (CI) of the associations between patient characteristics (race/ethnicity, insurance type, marital status at diagnosis, and CCI) and provider engagement variables (gender concordance, language concordance, and online patient portal enrollment) and undertreatment and delayed treatment using two sets of covariates: Model 1 (M1) and Model 2 (M2). M1 is minimally adjusted for stage at diagnosis, year of diagnosis, age, and sex. M2 additionally adjusted for race/ethnicity, insurance type, marital status, and CCI. To assess how patient characteristics and provider engagement variables relate to online patient portal enrollment, all descriptive statistics were also tabulated by patient portal enrollment.

#### **RESULTS**

Our patient population was primarily NHW (80.1%) and stage at diagnosis was lower among NHWs. Medicare was the most common insurance type overall, but Hispanics primarily had private insurance which may be due to a lower age at diagnosis. Most patients were partnered, expect among NHBs (39.2%). Comorbidity scores were highest along NHBs and lowest among AANHPIs (Table 4.1).

 Table 4.1. Patient Characteristics of the Study Population, overall and stratified by Race/Ethnicity.

	All	<b>Patient Race/Ethnicity</b>						
	$(N = 988)$	non-Hispanic White (n=791)	non-Hispanic Black $(n=51)$	Hispanic $(n=47)$	<b>AANHPI</b> $(n=99)$			
<b>Patient Characteristics</b>	$n$ (%) or *Mean, SD							
<b>Stage</b>								
Ι.	823 (83.3)	666 (84.2)	41 $(80.4)$	37(78.8)	79 (79.8)			
$\mathbf{I}$	165(16.7)	125(15.8)	10(19.6)	10(21.3)	20(20.2)			
Year of diagnosis*	2009.6, 2.7	2009.1, 2.7	2010.4, 2.7	2009.6, 2.6	2009.7, 2.9			
$2004 - 2008$	351 (35.5)	288 (36.4)	13(25.5)	18(38.3)	32(32.3)			
$2009 - 2013$	637(64.5)	503 (63.6)	38 (74.5)	29(61.7)	67(67.7)			
<b>Sex</b>								
Male	409 (41.4)	323 (40.8)	18(35.3)	24(51.1)	44 (44.4)			
Female	579 (58.6)	468 (59.2)	33(64.7)	23(48.9)	55 (55.6)			
$Age$ groups*	72.1, 10.9	72.8, 10.1	71.2, 10.0	66.3, 15.0	69.5, 13.3			
18 through 45	24(2.4)	13(1.6)		5(10.6)	5(5.1)			
46 through 60	100(10.1)	68 (8.6)		7(14.9)	21(21.2)			
61 through 75	459 (46.5)	372(47.0)	33 (64.7)	22(46.8)	32(32.3)			
$76 +$	405(41.0)	338 (42.7)	13(25.5)	13(27.7)	41(41.4)			
<b>Insurance Type</b>								
Private Insurance	319 (32.3)	243 (30.7)	13(25.5)	21(44.7)	42 (42.4)			
Medicaid	13(1.3)	7(0.9)			--			
Medicare	560 (56.7)	458 (57.9)	34(66.7)	19(40.4)	49 (49.5)			
Other	41 $(4.2)$	35(4.4)			$- -$			
Missing	55(5.6)	48(6.1)						
<b>Marital Status</b>								
Partnered	551 (55.8)	433 (54.7)	20(39.2)	27(57.5)	71(71.7)			
Unpartnered	424 (42.9)	349 (44.1)	29(56.9)	20(42.6)	26(26.3)			
Missing	13(1.3)	9(1.1)	$\overline{a}$		$\overline{a}$			
<b>Charlson Comorbidity Index*</b>	0.68(1.0)	0.69(1.0)	1.04(1.5)	0.68(1.2)	0.41(0.8)			
$\mathbf{0}$	574(58.1)	446 (56.4)	27(52.9)	30(63.8)	71(71.7)			
	263(26.6)	223(28.2)	10(19.6)	10(21.3)	20(20.2)			
2	77(7.8)	66(8.3)	6(11.8)		$\overline{a}$			
3	51(5.2)	38(4.8)	5(9.8)	5(10.6)				
4	12(1.2)	11(1.4)	$\overline{a}$					
$5+$ $\sim$ 11 $\rightarrow$	11(1.1)	7(0.9)						

-- Cell sizes < 5 are suppressed.

Most patients had a gender concordant (52.1%) and language concordant (97.9%) PCP. One hundred and four patients were missing gender concordance due to 40 PCP's missing sex/gender information. 97.48% of our patient population spoke English resulting in this high level of language concordance. Other patient primary languages spoken are provided in Table 4.2. Patient's enrollment in an online patient portal was low (25.3%), with the highest rate among AANHPIs (41.4%) (Table 4.3).



Table 4.2. Patient Primary Languages Spoken.

 Table 4.3. Provider Engagement of the Study Population, overall and stratified by Race/Ethnicity.



Between 2004-2008, the overall rate of GCT was 80.34% and timely treatment was 59.93%. Between 2009-2013, the overall rate of GCT was 79.75% and timely treatment was 60.43%. Percent GCT and timely treatment varied by race/ethnicity with the rate of GCT decreasing among Blacks, Hispanics, and AANHPIs, and the rate of timely treatment decreasing among Hispanics and AANHPIs over time. Percent GCT and timely treatment was much higher for patients with an active patient portal compared to an inactive patient portal, although the percent GCT and timely treatment decreased over time for patients with both active and inactive patient portals (Table 4.4).

patient race/ethnicity and patient portal enrollment. GCT (%) **Timely Treatment (%) 2004-2008 2009-2013 2004-2008 2009-2013 All (N=988)** 80.34 79.75 59.93 60.43

Table 4.4 GCT and timely treatment between 2004-2008 compared to 2009-2013 overall, and by



There were 468 different PCP in our study population of 988 subjects. Thus, clustered variance within PCPs could not be considered. Black patients were at increased relative risk for undertreatment (M1 RR=1.42, 95%CI=0.68-2.98) and delayed treatment (M1 RR=1.21, 95%CI=0.62-2.36) with a decreased magnitude for undertreatment and an increased magnitude for delayed treatment in fully adjusted models. Hispanics were at significantly increased risk for undertreatment (M1 RR=2.56, 95%CI=1.18-5.55) with similar RRs and CIs in both models. Hispanics also appear to be an increased risk for delayed treatment (M1 RR=1.62, 95%CI=0.78-3.38) with decreased magnitude in fully adjusted models. AANHPI were at decreased risk for undertreatment (M1 RR=0.83, 95%CI=0.45-1.54) and delayed treatment (M1 RR=0.57, 95%CI=0.34-0.97); in fully adjusted models, AANHPI's decreased risk is slightly attenuated. In minimally adjusted models, compared to patients with private insurance, patients with Medicare appear to be at slightly decreased risk for undertreatment (M1 RR=0.80, 95%CI=0.52-1.20) and delayed treatment (M1 RR= $0.87$ ,  $95\%$ CI= $0.61$ -1.25); the direction and magnitude of this association is consistent in fully adjusted models. Compared to patients with private insurance, patients with Medicaid appear to be at increased risk for delayed treatment in both M1 (RR=1.79, 95%CI=0.50-6.36) and M2 (RR=1.50, 95%CI=0.41-5.50). Patients who are partnered are at decreased risk for undertreatment (M1 RR=1.67, 95%CI=1.15-2.43) and delayed treatment (M1 RR=1.57, 95%CI=1.15-2.13), compared to patients who are unpartnered; the direction and magnitude of this association is consistent in fully adjusted models. Increasing comorbidities slightly increased risk for undertreatment (M1 RR=1.06, 95%CI=0.91-1.24) and delayed treatment (M1 RR=1.14, 95%CI=0.98-1.32) (Table 4.5).



Table 4.5 Effect of Patient Characteristics on Undertreatment and Delayed Treatment.

a minimally adjusted for stage at diagnosis, year of diagnosis, age, and sex.

<sup>b</sup> fully adjusted for stage at diagnosis, year of diagnosis, age, sex, for race/ethnicity, insurance type, marital status, and Charlson Comorbidity Index.

Compared to patients with a gender concordant PCP, patients with a gender discordant PCP may be at slightly increased risk for undertreatment (M1 RR=1.21, 95%CI=0.81-1.83) and delayed treatment (M1 RR=1.23, 95%CI=0.88-1.72), which held in fully adjusted models. Compared to patients with a language concordant PCP, patients with a language discordant PCP may be at increased risk for undertreatment (M1 RR=2.02, 95%CI=0.74-5.48) and decreased risk for delayed treatment (M1 RR=0.43, 95%CI=0.11-1.62), although we had few patients with discordance. Patients with an active patient portal are at significantly decreased risk for undertreatment (M1 RR=0.29, 95%CI=0.16-0.52) and delayed treatment (M1 RR=0.70, 95%CI=0.49-0.99), compared to patients with an inactive patient portal, with slight attenuation in fully adjusted models (Table 4.6).



Table 4.6. Effect of Provider Engagement Variables on Undertreatment and Delayed Treatment.

<sup>a</sup> minimally adjusted for stage at diagnosis, year of diagnosis, age, and sex.

<sup>b</sup> fully adjusted for stage at diagnosis, year of diagnosis, age, sex, for race/ethnicity, insurance type, marital status, and Charlson Comorbidity Index.

With later year of diagnosis, participation in the online portal increased. As patients age at diagnosis increased, participation in the online portal decreased. Patients with Medicare and patients with 2+ comorbidities were less likely to have an active patient portal, which may be due to increased age. Patients who were partnered, compared to unpartnered, were more likely (30.3% verse 19.1%) to have an active patient portal. Hispanic patients were the least likely (19.2%) and AANHPI patients the most likely (41.4%) to have an active patient portal (Table 4.7).



 Table 4.7. Patient Characteristics and Provider Engagement Variables of the Study Population, overall and stratified by Patient Portal (Active versus Inactive) status.
## **DISCUSSION**

Leveraging 10 years of CCR-Sutter linked EHRs (2004-2013), which allowed us to evaluate the relationship between healthcare system variables that reflect patient-provider engagement and receipt of treatment based on registry data reflecting complete initial treatment histories, we observed treatment disparities in early stage non-small cell lung cancer patients. Compared to Whites, Blacks and Hispanics were at increased risk and Asians were at decreased risk for undertreatment and delayed treatment. These convenience sample findings are fairly consistent with our previous studies findings using all ES-NSCLC cases in California (2006-2015), which assessed disaggregated Asian groups as well as aggregated Asians, and found that Blacks, Hispanics, and Vietnamese were at increased risk for undertreatment and Blacks, Hispanics, and Filipinos were at increased risk for delayed treatment, although Asians as an aggregated group were not found to be at decreased risk.

We also noted that compared to patients with private insurance, patients with Medicare may be at slightly decreased risk for undertreatment and delayed treatment and patients with Medicaid may be at increased risk for delayed treatment. Unpartnered patients were at increased risk for undertreatment and delayed treatment, compared to partnered patients, and increasing comorbidities also slightly increased risk for both undertreatment and delayed treatment.

With an eye to evaluating the importance of the patient-provider relationship on receipt of high-quality care for cancer, our study also quantified patient-provider engagement factors including gender- and language-concordance and the benefit of patient portal enrollment among NSCLC patients. Patients with gender-discordant PCP appeared to be at slight increased risk for undertreatment and delayed treatment and language discordance was difficult to assess due to few language discordant patients. Importantly, we observed that online patient portal enrollment was highly protective against undertreatment and treatment delay and patients who were diagnosed later, were younger, partnered, and Asian were more likely to have an active online patient portal. Interestingly, in fully adjusted models when we are further adjusting for race/ethnicity, insurance type, marital status, and comorbidities, this protective effect of online portal activation is slightly attenuated, meaning that race/ethnicity and marital status likely partially explains the association between online patient portal enrollment and cancer treatment.

Active patient portals may be beneficial in the receipt of timely appropriate treatment through the ability to access/view electronic health records including test results, send providers messages, request medication refills, and view provider visit notes. The Centers for Medicare & Medicaid Services (CMS) has defined goals for "Meaningful Use" with electronic health records, including an incentive program for the meaningful use of certified EHR technology<sup>202</sup>. Most physicians and practices offer online patient portals $203,204$ , although patient adoption remains low<sup>203</sup>. Barriers to activation could include personal factors such as age, race/ethnicity, education, and health literacy<sup>205</sup> or patients not having a computer or smartphones, not being comfortable with technology, or the portal not being translated to a patient's language<sup>206,207</sup>. Dr. Ratanawongsa, Chief Medical Informatics Officer at the University of California, San Francisco (UCSF), states that patient portals across the US are largely not available for non-English speakers and that she only knows of a handful of portals available in Spanish and one in English<sup>208</sup>. Among the 988 ES-NSCLC patients in our population, 963 patients spoke English and 7 patients spoke Spanish as their primary language. Sutter only offers their patient portal in English, but key sections of the patient portal are available in Spanish<sup>209</sup>. Thus, as our population overwhelmingly spoke English, patient portal language translation was not a key deterrent to patient portal enrollment in our study.

We were unable to locate any other studies assessing the association between portal

enrollment and cancer treatment, but one Northern California EHR study found that enrollment in a patient portal was associate with timely cervical and mammography screening completion $197$  and research does show that disparities exist among cancer patient's enrollment in patient portals<sup>145,146</sup>. A study that took place at the UCSF showed that Black patients were 44% less likely than White patients to enroll in patient portals and enrollment decreased with increasing age. Additionally, men were less likely to initially enroll but eventually enrolled, and patients in which English was not was not their primary were less likely to enroll initially and over time<sup>147</sup>. Some research also shows that patients feel more involved in their care when they are able to view provider's notes from their visits<sup>148</sup>. Interventions to train patients on portal use has been proposed<sup>149</sup>.

Our results also replicate the benefit of being partnered, including married/unmarried or domestic partner, on receipt of cancer treatment, which has been described in previous literature. A study by Aizer et al. using the Surveillance, Epidemiology and End Results (SEER) program data found that married cancer patients, including lung cancer patients, were more likely to receive definitive therapy compared to unmarried patients, and that the benefit associated with marriage was greater for males than females<sup>210</sup>. An older study assessing epithelial cancer in New Mexico using the SEER database found than unmarried patients were more likely to be untreated for cancer<sup>211</sup> and a study that also used the CCR found that unmarried breast cancer patients have a higher overall mortality than married patients. Unmarried patients have also been shown to be more likely to be diagnosed at a regional or distant stage<sup>210,211</sup> and have decreased survival<sup>210-213</sup>.

 A limitation of this study is that although primary care physicians play a large role in the cancer continuum, they may not be a patient's treating physician for cancer, which is usually comprised of a team of physicians. A strength was the ability to calculate and control for a patients comorbidity index before receiving cancer treatment, as comorbidities may impact a patients

ability to receive specific treatment modalities, with the limitation of comorbidity indices only being calculated based on information available in the electronic health records, and thus reflect only care received at Sutter Health. Additionally, due to small sample sizes, we were unable to disaggregate AANHPI which may have masked heterogeneity between Chinese, Japanese, Filipino, Korean, Vietnamese, Asian Indian, Other Asian, and Native Hawaiian and Pacific Islander patients.

Our results demonstrate that enrollment in an online patient portal protects against undertreatment and delayed treatment in NSCLC patients in one Northern California hospital system. Patient enrollment in a patient portal should be encouraged by a patient's PCP, and a good patient-provider relationship may increase activation. Active patient portals may be beneficial through the ability to access/view electronic health records including test results, send providers messages, request medication refills, and view provider visit notes. Patient portal enrollment is a modifiable healthcare system-related driver of treatment and the results of this research provides actionable evidence on how to reduce treatment disparities.

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## **CHAPTER 5: DISCUSSION**

Lung cancer accounts for the greatest proportion of cancer deaths in the United States. Inequities in lung cancer outcomes exist at multiple levels ranging from fixed individual characteristics such as age, gender, and race/ethnicity to contextual risk factors such as healthcare access and providers that can be changed at an individual-level or through policy. With the introduction of population-level screening recommendations and resulting improvement of prognosis due to shifting trends towards earlier stage at diagnosis <sup>214</sup>, understanding the drivers of lung cancer treatment disparities is of critical importance to improve outcomes for lung cancer patients. The objective of this dissertation was to identify modifiable contextual predictors of treatment disparities in lung cancer by space, place, and provider, in California. Specifically, we investigated the relative contribution of geospatial-, neighborhood-, and healthcare system-related factors on racial/ethnic disparities in receipt of timely appropriate treatment.

This effort reflects a new field of research on contextual determinants of disparities, which has been enhanced by the availability of high quality cancer registry data, geographical information systems with high spatial resolution, representative survey data to characterize the patient context, and the novel use of electronic health records to better understand patient healthcare engagement. Additionally, by studying patients in California, a highly diverse state, we demonstrate the importance of racial and ethnic disaggregation and the complex heterogeneity of results that can often arise when studying multiethnic populations. To our knowledge, ours is the first study to identify modifiable factors, specifically neighborhood-, geospatial-, and healthcare system-related factors that affect adherence with timely receipt of guideline concordant treatment (GCT) for non-small cell lung cancer (NSCLC), and vary in their impact across racial/ethnic groups, including non-Hispanic Whites, non-Hispanic Blacks, Hispanics, American Indian/Alaska Native (AIAN), and Asian American, Native Hawaiian and Pacific Islander (AANHPI) disaggregated as Chinese, Japanese, Filipino, Korean, Vietnamese, Asian Indian, Other Asian, Native Hawaiian and Pacific Islander (NHPI).

The outcome for this dissertation was receipt of timely, guideline concordant treatment for patients with early stage non-small cell lung cancer which we defined two ways: receipt of recommended treatment and timeliness of treatment initiation among patients who receive the minimum recommended treatment. Healthy People recommends the use of quantitative measures of disproportionality to monitor and communicate overall public health burden of health disparities, which allows comparisons across disease outcomes and social groups, over time<sup>169,215</sup>. We identified disparities in the receipt of GCT and timely treatment by patient race/ethnicity and socioeconomic status. Specifically, we observed more absolute disparity in rate of timely GCT, compared to GCT, between race/ethnicity and neighborhood socioeconomic status (nSES) with higher absolute disparity in nSES compared to race/ethnicity. There was very little relative disparity in rate of GCT and timely GCT.

Further, we found that compared to patients who are non-Hispanic White, patients who are Black or Hispanic are at increased risk for undertreatment and delayed treatment, and among Asian American patients, Vietnamese are at elevated risk for undertreatment, and Filipinos are at increased risk for delayed treatment. Compared to patients living in the highest socioeconomic neighborhoods, patients across all races living in the lowest through upper-middle socioeconomic neighborhoods are at increased risk for both undertreatment and delayed treatment. These findings establish the premise of the dissertation, that disparities in GCT for early stage lung cancer exist in diverse populations and will contribute to the literature reflecting unmodifiable risk factors for poor quality care. In each of the three dissertation aims, we identified that GCT also varied by modifiable risk factors including travel time to treatment facilities, neighborhood diversity, and patient online portal enrollment, although the direction of the association was not always as hypothesized and often varied by specific patient group.

In Aim 1, we asked the question, what is the relative contribution of travel time in receipt of timely GCT? Our results indicate that, on average, an increase in travel time was associated with a decreased risk for undertreatment and delayed treatment, which reflects a counterintuitive result – that longer travel times improve care. This protective effect was unexpected and may be a "Travel Time Paradox," but we noted that this paradox was not uniform across all groups. Our interaction analysis in which we allowed the travel time benefit to vary with race/ethnicity revealed important heterogeneity. For some non-White patient groups, an increase in travel time exaggerated the risk of undertreatment and delayed treatment. For non-highest nSES patients, an increase in driving time exaggerates and an increase in public transit time attenuates the risk of delayed treatment.

In Aim 2, we asked the question, what is the effect of neighborhood diversity in receipt of timely GCT? Our results indicate that patients living in predominately concordant neighborhoods had the highest rate of GCT and timely treatment, but unfortunately, many non-White race/ethnicity groups living in predominately concordant neighborhoods were at higher relative risk for undertreatment and delayed treatment than those living in mixed concordant and discordant neighborhoods. We also found that increased diversity, or equal representation of racial/ethnic groups in neighborhoods, increased risk for undertreatment and delayed treatment for some non-White racial/ethnic groups. While White neighborhoods may have more, or better, healthcare resources<sup>95-99</sup>, living in an enclave may be protective due to social cohesion<sup>117</sup>.

In Aim 3, we asked the question, what is the impact of patient-provider engagement in receipt of timely GCT in one Northern California health care system? While language concordance was difficult to assess as almost all of our patient populations' primary language was English, this aim revealed that patients with gender-discordant primary care physicians appear to be at slight increase risk for undertreatment and delayed treatment. Further, results revealed active online patient portals protect against undertreatment and delayed treatment and that more recently diagnosed, younger, partnered, and Asian cancer patients were more likely have an active online patient portal. Active online patient portals may be beneficial through the ability to access/view electronic health records including test results, send providers messages, request medication refills, and view provider visit notes, but barriers to activation could include limited computer or smartphones access, technology illiteracy, or the portal not being translated to a patient's language<sup>206,207</sup>.

Adopting a "precision public health" interpretation of our results<sup>216</sup>, we now consider three hypothetical patients and what our results might tell us about how their context affects their treatment (and as a result prognosis):

(1) A Black, male, early stage NSCLC patient with a high number of comorbidities<sup>217</sup> living in a lower socioeconomic neighborhood that is predominately Black may be at increased risk for undertreatment and delayed treatment. This patient is more likely chose to receive cancer treatment at a treatment facility in or near their neighborhood, but unfortunately, their neighborhood likely has poorer healthcare resources, and even if this patient chose to travel to a further, more qualified, treatment facility, they would still receive lower quality care than a non-Hispanic White patient traveling the same distance. This patient's risk of undertreatment and delayed treatment may be reduced if they are enrolled in a patient portal, with increased likelihood of enrollment if they are younger and married, but enrollment may be difficult based on their access to a computer or smartphone<sup>218</sup>.

- (2) A Hispanic, female, early stage NSCLC patient in California is likely to live in a predominately Hispanic or mixed White and Hispanic neighborhood and be of lower socioeconomic status. Living in a mixed White and Hispanic neighborhood may confer some protection against undertreatment for this patient because her neighborhood may have better healthcare resources compared to a predominately Hispanic neighborhood<sup>95-99</sup>. Traveling as little as 15-minutes more by private vehicle could protect against undertreatment and delayed treatment for this patient. However, if this patient has young children, taking time to travel to treatment may be difficult, and childcare options may be helpful<sup>219</sup>. If this patient does not have access to a private vehicle and requires public transit, our results suggests choosing a closer treatment facility. Her prognosis may also be improved by enrolling in her healthcare system's patient portal, and some online portals, including the one provided by Sutter Health offers key sections of the patient portal in Spanish<sup>209</sup>.
- (3) A non-Hispanic White or Asian American patient is more likely to be wealthier and live in predominately White neighborhoods with better healthcare resources<sup>95-99</sup>. Wealthier White patients also have the resources to choose to travel further for higher quality cancer care, but lower socioeconomic White patients are still at higher risk for both undertreatment and delayed treatment and may benefit from being partnered and enrolled in a patient portal. Asian American groups may be at an advantage due to lower comorbidities<sup>220</sup>, although elderly Vietnamese and Filipinos have been shown to have poorer health than Chinese, Japanese, and Koreans in California<sup>221</sup>, and higher enrollment in patient portals, although not supported in other literature<sup>206</sup>, but there is important variability between distinct groups of Asian

Americans. For example, while Chinese and Japanese patients appear to largely be protected from undertreatment and delay, a Vietnamese American patient is at increased risk for undertreatment. They likely have a shorter travel time and lower SES, but benefit from traveling further for better cancer care, assuming they have access to a private vehicle. They would also benefit from living in a predominately Asian neighborhood but are more likely to live in a mixed neighborhood.

Strengths of this dissertation include the large sample size which allowed us to present the heterogeneity of effects across disaggregated Asian groups, and our results add to a growing body of research demonstrating that aggregating Asians into one group masks important heterogeneity. Our GIS enabled analyses used the patient's census block group, which provides higher spatial resolution compared to zip code or census tract, allowing us to use more precise travel time calculations and neighborhood characteristics. Additionally, this allowed us to measure diversity at the census block group level, and nest block groups' diversity into census tracts (neighborhoods) to measure segregation in Aim 2. We incorporated nine neighborhood-level data sources, such as the Census and American Community Survey, which provided us with data rich in neighborhood contextual factors. Further, the incorporation of electronic health records (EHRs) with populationbased registry data is a novel source of research data, with the limitation of this linked data being a convenience sample. CCR-EHR linked data provided us with detailed patient and healthcare provider interactions, allowing us to calculate and control for comorbidities, as well a tumor characteristics and definitive treatment details, regardless of the treatment facility. Lastly, we incorporated modern quantitative methodology such as measures of relative and absolute disparities and geospatial analyses.

An important limitation of this dissertation is the potential misclassification of the outcome, GCT. Our primary outcome data source, the CCR does not collect information on patient refusal of treatment or comorbidities preventing treatment which could result in outcome misclassification – i.e., a patient did not receive all recommended treatment because it was contraindicated. In Aim 3, we noticed that NHBs are more likely to have more comorbidities, and AANHPIs had less comorbidities, which could create a type of differential misclassification in receipt of GCT that is dependent on patient race/ethnicity. Further, the CCR only collects information reflecting treatments received in the 6 months following the cancer diagnosis.<sup>10</sup>. Thus, for operable node 1 (N1) patients, when adjuvant treatment of chemotherapy +/- radiation should be administered within 6 months of surgery, adjuvant treatment may not be captured within the CCR if that treatment occurred more than 6 months after cancer diagnosis. Despite this concern, we believe the potential for this misclassification remains low. We note that only 3.1% (Aim 1), and 3.7% (Aim 2) of the study population could have been misclassified due to missing adjuvant treatment that more than 6 months after cancer diagnosis. This is supported by our calculations of the average time from surgery to adjuvant treatment, which was 47.35 days (median = 39, maximum = 1353) for Aims 1 and 2 and 44.4 days (median  $= 37$ , maximum  $= 448$ ) for Aim 3. Accordingly, since the average time from surgery to adjuvant treatment was roughly 6 weeks and adjuvant treatment was captured far after the required 6 months, we believe the true number of patients with this type of outcome misclassification is low.

This results from this dissertation elucidate the lung cancer-related health disparities within California's highly diverse population. Undertreatment and delayed treatment for early-stage NSCLC disproportionately affect minorities and those living in lower socioeconomic status neighborhoods. In summary, traveling further for cancer treatment is beneficial for some and

harmful to others, minority patients appear to be protected when living in predominately White neighborhoods, and active online patient portals protect against undertreatment and delayed treatment. These findings solicit the need for accessible high-quality healthcare facilities that offer surgery, radiation, and chemotherapy. Accessibility is many-sided including knowledge of higherquality facilities, adequate health insurance, ability to take time of work or find childcare, and transportation including private vehicle, public transit, or even cancer treatment transportation options219,222. Additionally, enrollment in online patient portals may encourage a better patientprovider relationship and increase guideline-concordant treatment and timely treatment, and online patient portal availability in more languages and dialects are needed.

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