**RACIAL DISPARITIES IN LUNG CANCER SURVIVAL**

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**ABSTRACT**

Lung cancer is the second most common type of cancer that afflicts men and women.  Prostate and breast cancer are more common in men and women, respectively.  About 14% of all new cancers are lung cancers.  Lung cancer is the leading cause of cancer death amongst both men and women.  It is estimated that 1 out of 4 cancer deaths are from lung cancer.  In each year, more people die of lung cancer than of colon, breast and prostate cancers combined.  In 2017, the American Cancer Society projected that there will be about 222,500 new cases of lung cancer with about 155,870 deaths in the United States.  The overall chance of developing lung cancer in a lifetime is about 8% for a man and 6% for a woman.  The prevalence is significantly higher for African-American males and for lower socioeconomic classes.  The objective of this essay is to highlight important aspects of the racial disparities of lung cancer survival and to highlight specific goals the community should work towards bridging the gap.  In summary, we discover that African Americans have different smoking patterns and mistrust towards the medical community, which may negatively impact their increased propensity for developing lung cancer.  Even after removing the cancer, they experience increased morbidity and mortality, which corresponds with lower education and income. Such disparities highlight public health goals. First, in the social setting, plans need to be enacted to improve the education and socioeconomic status of the African American community.  Furthermore, the medical community must continue to build trust within this community to carry action plans to provide appropriate and equal medical education and healthcare.

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# 1.0 INTRODUCTION

The United States has made progress over the last several decades to address the racial and ethnic disparities that are prevalent throughout healthcare.  There is still a great amount of debate on how to fully eliminate the gap altogether.  Closing the gap will result in a healthier America as minorities would be receiving comparable care to their counterparts.  Secondly, racial and ethnic health disparities are associated with substantial economic losses nationally.  It was estimated that eliminating health disparities for minorities could potentially reduce direct medical care expenditures by about $230 billion for the years 2003-2006 1.

Lung cancer has one of the highest mortality rates of all cancers even after removal of the tumor.  Recently, it has been revealed that there are racial disparities that need to be addressed when it comes to the morbidity, mortality and treatment of lung cancer.  The purpose of this essay is to highlight specific disparities and propose interventions that may result in improved healthcare for the African American community.

## 2.**0 BACKGROUND**

## 2.1 Racial and Ethnic Disparities in Healthcare

The term disparities conjures up thoughts of unequal treatment of a group of people based on what defines them as population.  This could be based on gender, color or other types of patient characteristics.  One of the major goals of healthcare policy is the elimination of disparities amongst racial or ethnic groups.  However, it is quite difficult to have a standard measure or definition of such differences due to the multi-faceted nature of healthcare.  As defined by the Institute of Medicine, racial or ethnic disparities in healthcare are the differences in the quality of healthcare that are not due to access-related factors or clinical needs, preferences and appropriateness of intervention 2.

One of the major determinants of the distribution of healthcare is socioeconomic status.  Research has shown that persons of lower income, education and occupational status experience worse health and die earlier than those who are wealthier 3. In the United States, African-Americans make up a disproportionate fraction of those with lower socioeconomic status.  According to the US Census Bureau, in 2015, the median income for white Americans went up 4.4% and for black Americans, 4.1%.  The median household income for white Americans in 2015 was $63,000 which is approximately 70% more than the median household income of black Americans, which was $36,898 4.

When it comes to racial matters in healthcare distribution, socioeconomic status is not the only determinant involved. Increasingly more research has been done after the advent of the *Healthy People 2000* initiative 5 6 7 8. The CDC has published a series of reports reflecting the racial inequalities of education, housing, air quality, vaccinations and other issues 6.

## 2.2 Racial disparities in cancer

Cancer doesn’t discriminate” is a phrase that has been popularized by media.  It is true that several types of cancers afflict all races and genders.  However, a closer look at cancer incidence and death statistics reveals that certain groups in the United States are afflicted disproportionately by different types of cancers, including differences in morbidity and mortality 8. According to analysis of the Surveillance, Epidemiology and End Results Program (SEER) database, the incidence of African Americans developing cancer was 504.1 per 100,000 men and women.  The incidence of African Americans dying from cancer was 238.8 per 100,000 men and women.  For the entire population, incidence and death were 470.1 and 192.7, respectively.

Looking more specifically at different types of cancers, African-American women were more likely to die from cervical and breast cancers compared to their Caucasian counterparts 6. Meanwhile, African-American men had a higher incidence and death rates of prostate cancer.  Colorectal cancer affects both genders and has a higher rate of incidence and death in African Americans compared to Caucasians.  Finally, when it comes to lung cancer, once again, a similar trend continues.  The incidence and death rates per 100,000 men and women for African-Americans was 76.6 and 62.0, respectively.  Caucasians have incidence and death rates from lung cancer of 65.7 and 55.0, respectively 8.

If cancer does not discriminate, these cancers should not have different incidence and death rates for difference groups.  So, does nature discriminate?  Some populations of people show an increased propensity for developing diseases based on their genetic makeup.  For example, Ashkenazi Jews are certainly more affected by Tay-Sachs disease 9. For cancer, there are certainly familial diseases that result in increased risk of cancer.  Generally, cancer is a disease of aging and of lifestyle decisions.  Essentially, our body deteriorates resulting in difficulty in repairing ourselves microscopically.  To further exacerbate things, we as a population are exposed to carcinogens daily.  Some may suggest that there are social biases as well that result in poorer or delayed care for minorities.

## 2.3 What is lung cancer?

### 2.31 Epidemiology

Lung cancer is the second most common type of cancer that afflicts men and women.  Prostate and breast cancer are more common in men and women, respectively.  About 14% of all new cancers are lung cancers 10. Lung cancer is the leading cause of cancer death amongst both men and women. Approximately 25% of all deaths caused by cancer are due to lung cancer 11. In each year, lung cancer results in more deaths than colon, breast and prostate cancers combined.  In 2017, the American Cancer Society projected that there will be about 222,500 new cases of lung cancer with about 155,870 deaths in the United States.  The overall chance of developing lung cancer in a lifetime is about 8% for a man and 6% for a woman 12. The prevalence is significantly higher for African-American males and for lower socioeconomic classes.

As the general population continues to live longer and longer due to advances in medicine, more and more cancers have begun to show up.  Lung cancer is mainly a disease of the elderly, with an average age of 70 at time of diagnosis.  Only less than 2% of those diagnosed with lung cancer are younger than age 45 13.

### 2.32 Risk Factors

By far the leading risk factor for lung cancer is smoking. Before cigarettes were so prevalent, lung cancer was a relatively rare illness. About 80% of lung cancer deaths are thought to result from smoking. Cigarette smoke results in the respiration of a myriad of mutagens and carcinogens 14. The relative risk of lung cancer for a current smoker is 20, meaning a current smoker is 20 times more likely to eventually have lung cancer. Cessation of smoking does mitigate some of this risk. However, prior smoking is a risk factor with a relative risk of 9. Furthermore, being around others who smoke (secondhand smoke), also portends an increase risk of 1.3 15.

Other environmental factors increase the risk of lung cancer.  For instance, asbestos fibers were used as insulating material since the Industrial Revolution.  During the 20th century, increasing evidence linked asbestosis to increased risk of lung cancer in groups of asbestos-exposed workers 16. A naturally occurring gas that is radioactive and results in a significant risk of lung cancer is radon.  This gas leaks into homes and exposes its inhabitants.  It is estimated that radon is the cause of approximately 21,000 cases of lung cancer per year 17.

### 2.33 Treatment

There are generally 5 treatment options for lung cancer. One is surgery. The goal of surgery is to completely remove the lung lesion and nearby lymph nodes. Surgical resection must remove the tumor as well as healthy tissue surrounding it in order to obtain a “negative margin.” The types of surgery include a lobectomy, wedge resection, segmentectomy or pneumonectomy. A lobectomy is the removal of an entire lobe of the lung and is currently thoughts to be the gold standard of surgery 18. Segmentectomy is another way the cancer can be removed, by removing a segment of the lung with its associated artery and vein. Studies have shown that anatomic segmentectomy and lobectomy have similar outcomes in early stage lung cancer 19. However, wedge resections have poorer outcomes compared both of those procedures 20. Kent and colleagues showed that if a tumor is simply just “wedged” out without removing associated arteries and veins, there was a smaller lung cancer margins and lower yield of lymph nodes 20. Because of this, a wedge resection may not be as “complete” of a resection compared to segmentectomy and lobectomy. If the tumor is too close to the center of the chest, the surgeon may need to remove the entire lung 21.

Radiation therapy can also be used, particularly if the patient has higher stage lung cancers or cannot tolerate surgical intervention. Using high energy x-ray beams, a radiation oncologist focuses them at a tumor to kill the tumor cells. Radiation can also harm healthy cells as some patients may experience skin irritation similar to sunburns. As with surgery, this technique cannot be used to treat widespread tumors 22. When tumors have spread to lymph nodes or other parts of the body resulting in advance staged lung cancer, treatment usually will include chemotherapy. Chemotherapy is the use of drugs that destroy cancer cells by inhibiting their growth and division. These medications are usually given systemically to treat the micrometastatic disease. Like radiation, chemotherapy can also harm healthy cells in the body. It can cause fatigue, depletion of cells within the body, infections, nausea, vomiting, loss of appetite and other side effects 23. In addition to these therapies, oncologists can also use targeted immunotherapies. Targeted immunotherapy is a treatment that targets specific genes or proteins that affect cancer growth and survival 24.

### 2.34 Prognosis

 Patients diagnosed with non-small cell lung cancer (NSCLC), squamous cell carcinoma and adenocarcinoma generally have better five-year survival rates compared to those diagnosed with SCLC. Usually at time of diagnosis, patients with small-cell lung cancer (SCLC) have advance stage with metastasis. For NSCLC, the 5-year survival for Stage I is approximately 65%; for Stage 2, it is 35%; for Stage 3A, it is 15%; and for Stage 4, it is <10%. For SCLC, the survival is much worse. For disease that has not spread to lymph nodes or other parts of the body, the median survival is 18-20 months with a 5-year survival of 10%. For patients with extensive disease, the median survival is 10-12 months with a 5-year survival of 1-2% 25.

# 3.0 LUNG CANCER DISPARITIES IN AFRICAN AMERICANS

There have been major efforts to reduce smoking in the last 50 years. Some of these efforts can been seen in the incidence rates of lung cancer, as they continue to decrease in the last several years. However, racial disparity still exists with regard to incidence rates of lung cancer, as African American men have about a 50% higher incidence than Caucasians 26. Between 1999 and 2012, age-adjusted incidence rates in lung cancer have decreased in all states and regions. However, Caucasians continue to have a lower age-adjusted incidence rate for lung cancer compared to African American males in all states and in most of the United States Geographic regions. In 2012, the incidence rate for white males developing lung cancer was approximately 75 cases per 100,000. It was approximately 90 cases per 100,000 for African American males 27.

Lung cancer is a multifactorial disease. In order to understand the mechanism behind the increased incidence rates of lung cancer in African Americans, it is important to analyze risk factors. The major risk factor for lung cancer is smoking. Smoking differences between races can explain some of the disparities. African Americans who are diagnosed with lung cancer are significantly more likely to be intermittent or light smokers compared to their Caucasian counterparts 28. Haiman and colleagues showed that African Americans and Native Hawaiians who smoked no more than 11-20 cigarettes per day had a significantly greater risk of lung cancer than did the other groups with a relative risk of 0.21 to 0.39 28.

African Americans are also more likely to start smoking later in life 29. As the body becomes older, it has less of an ability to repair genetic mutations because of exposures. Even when smoking rates are matched between African Americans and Caucasians, African Americans still experience a higher incidence of lung cancer. Though African Americans were more likely to be lighter smokers, it also seems they are less likely to quit as well. This results in having a longer cumulative exposure to tobacco 30.

Furthermore, African Americans are more likely to smoke menthol cigarettes. According to the Food and Drug Administration, 70-80% of African Americans use menthol cigarettes as opposed to 20-30% seen in Caucasians. Menthol cigarettes are associated with a decreased odds of quitting 31. In conclusion, though African Americans smoke later in life and fewer cigarettes, they have significantly lower quit rates and have a longer cumulative duration of smoking.

Cultural factors come into play as well when it comes to lung cancer care. Lin and colleagues looked to determine associations between cultural factors and disparities in lung cancer treatment. From 2008 to 2011, Lin and colleagues surveyed patients from four medical centers in New York City about their beliefs regarding lung cancer, fatalism and medical mistrust. African Americans were signifincantly less likely to receive stage-appropriate therapies compared to their Caucasian counterparts after adjusting for age, sex, marital status, insurance, income, comorbidities and performance status. African Americans also had a more negative connotation when it comes to surgery and death 32.

There was also increased mistrust of the medical community by minorities 32. Mistrust in the medical community results in fewer African Americans seeking out medical care which will negatively impact their survival rates for lung cancer. However, is there a difference in access to care for African Americans compared to Caucasians? Backhus and colleagues examined US county level data for age-adjusted lung cancer mortality rates from 2003-2007. They discovered that providers of lung cancer care were unevely distributed throughout the US. Almost three times as many Africans Americans compared to Caucasians live in counties considered to be high lung cancer mortality zones. These zones correlated with fewer number of thoracic surgeons compared to zones with better mortality rates 33.

## 3.1 Racial Disparities of lung cancer survival after surgery

Surgical resection remains the gold standard for lung cancer treatment. It results in better long-term survival in patients with early stage non-small cell lung cancer. After overcoming some of the barriers of diagnosis and treatment, what are the results of patients who undergo treatment such as surgery to remove the tumor? Once the tumor is completed surgically eradicated, is there a disparity between African Americans and Caucasians in in-hospital mortality after the surgery? Is there a disparity between their quality of life after discharge?

Harrison et al. looked specifically at in-hospital mortality after lobectomy, the surgery of choice for lung cancer 34. Between the years 2008-2011, 23,058 patients in the United States who had received a lobectomy for lung cancer were discharged. The study excluded patients who had a redo operation, improper coding, deaths in the operating room, missing in-hospital mortality and hospital details. Furthermore, if information on the patient’s race, income or insurance information, he/she was missing, he/she was excluded. At the end of the study, 6,154 patients had undergone a minimally invasive video-assisted thoracoscopic (VATS) approach, while 13,199 had open surgery 34.

According to Harrison et al., those who had a median income of <$39,000 had a significant increase in in-hospital mortality after surgery compared to those with a median income of >$39,000, 2.5% vs. 1.9%, p=0.014. African Americans were also more likely to die in the hospital after surgery compared to all other races, 2.8% vs. 1.9%, p=0.021. African Americans were 66% more likely to die in-hospital after lobectomy than other races. One of the limitations of this study is it cannot account for surgical bias; that is, it did not determine if patients of different racial or economic backgrounds were offered surgery at difference rates? 34

Another study done by Poghosyan looked at racial disparities in health-related quality of life (HRQOL) after lung cancer surgery. HRQOL data were obtained using patient surveys and analysis of medical records obtained from clinical data. These data were then divided into a physical and mental component score (PCS/MCS). Mean time to initial assessment after surgery was 4.1 months, second assessment was 12.7 months 35.

Of the 650 patients analyzed, 80.5% were Caucasian, 8.8% were African Americans and 10.7% were other races. Analysis of PCS scores showed no significant differences between Caucasians and African Americans. However, at the second assessment, multivariable analysis showed a significantly lower MCS in African Americans compared to their Caucasian counterparts. Other interesting findings from this analysis showed that education and income were significantly different between the two groups, with African American having disproportionately more patients with only a high school degree or less and making <$20,000 per year. A major limitation of this study is that the physical and mental health variables were self-reported 35.

It is difficult to explain these results shown by Harrison et al. and Poghosyan et al. In terms of in-hospital mortality, it is unfortunate that we do not have the medical profiles of the patients in the study done by Harrison. Multiple factors could contribute to these results. First, as mentioned before, African Americans are more likely to be smokers and have longer term smoking 36. This continued smoking impacts perioperative mortality. Patients who are active smokers at time of surgery have a more difficult time of recovering from the operation. It also increases risks of other medical problems at the time of surgery, such as coronary artery disease or other vascular disease. This puts the patient at risk of having a myocardial infarction or stroke in the hospital, leading to their demise 37.

Proportionally, in the Poghosyan et al., the African Americans who had surgery were less educated and had lower income. Multiple studies have shown that education and income affect the mental health of the patient 38. Impaired mental health, whether it be depression or anxiety, it increases morbidity of the patients suffering from a wide range of conditions 39. Therefore, this racial disparity highlights the need for interventions to improve the mental health of the African Americans undergoing lung cancer surgery. One can argue that such a study should be applied globally and suggests that mental health issues should be improved throughout the United States.

## 3.2 Racial differences in cancer genes

Genetics play a significant role in lung cancer as well. Family, twin and genome wide studies have shown that genetics of lung cancer is heritable 36. Genetics thus predispose a patient to lung cancer, and life choices, such as smoking, will exacerbate that risk. Furthermore, recent studies have shown that certain families have a higher risk of developing lung cancer with a higher mortality rate 40. The oncogene that is very well studied is k-ras. Mutations in k-ras are associated with earlier distant metastatic disease and poorer prognosis 41. Epidermal growth factor receptor (EGFR) is a protein on the surface of cells. It normally helps the cell grow and divide. It has been observed that some cancer cells have too much EGFR, which makes the cells grow faster and without inhibition. It has also been observed to mutate in lung adenocarcinomas in smokers and non-smokers 42. Such discoveries are highly important as this improves diagnostics and broadens the scope of treatment of lung cancer.

Are there racial differences in the genetics of lung cancer? In 2005, Cote and colleagues wanted to measure lung cancer aggregation and estimate lifetime risk among relatives who patients who had early-onset lung cancer and compare it to a population-based control. Their study showed that relatives of African American patients who had early-onset lung cancers were significantly more at risk of developing lung cancer than their Caucasian counterparts after adjusting for age, sex, pack years of smoking, pneumonia and COPD (odds ratio, 2.07, 95% confidence interval, 1.29-3.32) 43. Are there differences between specific genes related to cancer with respect to race? Studies have conflicting results, as many of these genetic mutations not only occur in utero, but also because of environmental exposures. One genetic difference seen by Hunt et al. was k-ras. In a study using lung tumor specimens, k-ras mutations were more common in African Americans compared to Caucasians 44.

# 4.0 CONCLUSION

Lung cancer is a difficult disease to manage by both patients and their physicians. Like other aspects of healthcare, there are still racial disparities that must be addressed in the treatment and management of lung cancer. There continues to be differences in incidence rates and morbidity/mortality after surgical resection. These studies also highlight the social aspects of lung cancer, as African Americans generally have lower education and lower income compared to their Caucasian counterparts 45. Smoking in the African American community is also an issue, as they are less likely to quick smoking as well 28. Lastly, the African American community also harbors more mistrust in the medical community 32.

There are limitations to this review. It is difficult to quantify behavioral biases. For example, Lin and colleagues reports that African Americans were signifincantly less likely to receive stage-appropriate therapies compared to their Caucasian counterparts. It is difficult to determine if decisions were made by the patient or physician to pursue a different therapy. Furthermore, the multifactorial aspects of lung cancer make it difficult to formulate a specific intervention that may or may not affect these disparities.

Bridging the gap between the racial disparities of lung cancer starts even before the cells begin to mutate into tumor cells. It starts initially at a social level. One must understand why African Americans are more prone to start smoking at a later age compared to their Caucasian counterparts and why they continue to smoke. Essentially, assuming they are exposed to the same efforts, are the current efforts of preventing smoking effective towards this population? At a later age, they should be as educated, if not more well-versed to make an educated decision.

Other social issues also need to be addressed because lung cancer care today is not distributed equally. Lower education and income are associated with a decreased survival rate in lung cancer 45. The more education one has, the more likely one can understand the dangers of lung cancer and its risk factors. A common cause of depression and mental health issues, which predicts poorer cancer survival, is financial stability. In addition to this, financial security may also allow for patients to pursue better care. For example, it may allow someone to travel out of state to a more experienced surgeon.

The medical community can also improve its relations with African Americans. Mistrust in medicine is still a major issue in the African American community due to studies like the Tuskegee Study of Untreated Syphilis in the Negro Male from 1932 to 1972. We have to improve the confidence of this population in the medical community in order for them to seek medical care, screening and maintain surveillance. The medical community also needs to primary care physicians, specialists and surgeons to recognize that there is this disparity that needs to be addressed.

Improvement in relations does not rest solely on the medical community but also US agencies. Relations have been improving. In the Healthy People 2020 initiative, there is a focus on the social determinants of health 46. There is a recognition that health starts in homes, schools, workplaces and communities. The goal of this focus is to “create social and physical environments that promote good health for all” 46. The government must continue to provide programs and additional funding to improve the social disparities, such as with education and income. Furthermore, funding and resources should be provided to improve lung cancer care and appropriate screening for those who are at risk in counties that are considered high mortality zones of lung cancer. The US is home to some of the most advanced medical centers in the world. It is important to evenly distribute these resources throughout the US to create a healthier America. Eliminating racial disparities will not only reduce medical costs for the country, but it will allow for improved healthcare for our African American community.

# BIBLIOGRAPHY

1 LaVeist TA, Gaskin D, Richard P. Estimating the economic burden of racial health inequalities in the United States. Int J Health Serv 2011; 41:231-238

2 American Board of Regents. Racial and Ethnic Disparities in Health Care, Updated 2010. American College of Physicians 2010

3 Fiscella K, Williams DR. Health disparities based on socioeconomic inequities: implications for urban health care. Acad Med 2004; 79:1139-1147

4 Redden MK, J. Wage gap between white and black Americans is worse today than in 1979. . New York 2016

5 U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics (NCHS). Healthy people 2000 final review. 2001. 2001

6 U.S. Department of Health and Human Services, Centers for Disease Control and Preventions. health disparities and inequalities report—United States, 2011. Morbidity and Mortality Weekly Report 2011

7 Agency for Healthcare Research and Quality. US Department of Health and Human Services. 2009 national healthcare disparities report. .Publication no. 10-0004. 2010

8 . Surveillance Epidemiology and End Results (SEER) Program (<http://www.seer.cancer.gov>) \*Stat Database: Incidence—SEER 17 Regs Limited-Use, Nov 2006 Sub (2000-2004)—Linked To County Attributes—Total U.S., 1969-2004 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2007, based on the November 2006 submission.

9 Triggs-Raine BL, Feigenbaum AS, Natowicz M, et al. Screening for carriers of Tay-Sachs disease among Ashkenazi Jews. A comparison of DNA-based and enzyme-based tests. N Engl J Med 1990; 323:6-12

10 Dela Cruz CS, Tanoue LT, Matthay RA. Lung Cancer: Epidemiology, Etiology, and Prevention. Clinics in chest medicine 2011; 32:10.1016/j.ccm.2011.1009.1001

11 Ridge CA, McErlean AM, Ginsberg MS. Epidemiology of Lung Cancer. Seminars in Interventional Radiology 2013; 30:93-98

12 American Cancer Society. Cancer Facts & Figures 2017. Atlanta GACS.

13 Brown JS, Eraut D, Trask C, et al. Age and the treatment of lung cancer. Thorax 1996; 51:564-568

14 Pinsky PF, Church TR, Izmirlian G, et al. The National Lung Screening Trial: results stratified by demographics, smoking history, and lung cancer histology. Cancer 2013; 119:3976-3983

15 Pesch B, Kendzia B, Gustavsson P, et al. Cigarette smoking and lung cancer – relative risk estimates for the major histological types from a pooled analysis of case-control studies. International Journal of Cancer. Journal International du Cancer 2012; 131:1210-1219

16 Heintz NH, Janssen-Heininger YMW, Mossman BT. Asbestos, Lung Cancers, and Mesotheliomas: From Molecular Approaches to Targeting Tumor Survival Pathways. American Journal of Respiratory Cell and Molecular Biology 2010; 42:133-139

17 Scott BR. Residential Radon Appears to Prevent Lung Cancer. Dose-Response 2011; 9:444-464

18 Lackey A, Donington JS. Surgical Management of Lung Cancer. Seminars in Interventional Radiology 2013; 30:133-140

19 Schuchert MJ, Pettiford BL, Keeley S, et al. Anatomic segmentectomy in the treatment of stage I non-small cell lung cancer. Ann Thorac Surg 2007; 84:926-932

20 Kent M, Landreneau R, Mandrekar S, et al. Segmentectomy versus wedge resection for non-small cell lung cancer in high-risk operable patients. Ann Thorac Surg 2013; 96:1747-1754; discussion 1754-1745

21 Mizushima Y, Noto H, Sugiyama S, et al. Survival and prognosis after pneumonectomy for lung cancer in the elderly. Ann Thorac Surg 1997; 64:193-198

22 Kong F-M, Zhao J, Wang J, et al. Radiation dose effect in locally advanced non-small cell lung cancer. Journal of Thoracic Disease 2014; 6:336-347

23 Waller D, Peake MD, Stephens RJ, et al. Chemotherapy for patients with non-small cell lung cancer: the surgical setting of the Big Lung Trial. Eur J Cardiothorac Surg 2004; 26:173-182

24 Massarelli E, Papadimitrakopoulou V, Welsh J, et al. Immunotherapy in lung cancer. Translational Lung Cancer Research 2014; 3:53-63

25 Detterbeck FC, Boffa DJ, Tanoue LT. The new lung cancer staging system. Chest 2009; 136:260-271

26 Meza R, Meernik C, Jeon J, et al. Lung cancer incidence trends by gender, race and histology in the United States, 1973-2010. PLoS One 2015; 10:e0121323

27 Tabatabai MA, Kengwoung-Keumo JJ, Oates GR, et al. Racial and Gender Disparities in Incidence of Lung and Bronchus Cancer in the United States: A Longitudinal Analysis. PLoS One 2016; 11:e0162949

28 Haiman CA, Stram DO, Wilkens LR, et al. Ethnic and racial differences in the smoking-related risk of lung cancer. N Engl J Med 2006; 354:333-342

29 White HR, Jarrett N, Valencia EY, et al. Stages and sequences of initiation and regular substance use in a longitudinal cohort of black and white male adolescents. J Stud Alcohol Drugs 2007; 68:173-181

30 Holford TR, Levy DT, Meza R. Comparison of Smoking History Patterns Among African American and White Cohorts in the United States Born 1890 to 1990. Nicotine Tob Res 2016; 18 Suppl 1:S16-29

31 Nonnemaker J, Hersey J, Homsi G, et al. Initiation with menthol cigarettes and youth smoking uptake. Addiction 2013; 108:171-178

32 Lin JJ, Mhango G, Wall MM, et al. Cultural factors associated with racial disparities in lung cancer care. Ann Am Thorac Soc 2014; 11:489-495

33 Backhus LM, Hayanga AJ, Au D, et al. The effect of provider density on lung cancer survival among blacks and whites in the United States. J Thorac Oncol 2013; 8:549-553

34 Harrison MA, Hegarty SE, Keith SW, et al. Racial disparity in in-hospital mortality after lobectomy for lung cancer. Am J Surg 2015; 209:652-658

35 Poghosyan H, Stock S, Kennedy Sheldon L, et al. Racial Disparities in Health-Related Quality of Life After Lung Cancer Surgery: Findings From the Cancer Care Outcomes Research and Surveillance Consortium. J Thorac Oncol 2015; 10:1404-1412

36 Ryan BM. Lung Cancer Health Disparities. Carcinogenesis 2018

37 Mason DP, Subramanian S, Nowicki ER, et al. Impact of smoking cessation before resection of lung cancer: a Society of Thoracic Surgeons General Thoracic Surgery Database study. Ann Thorac Surg 2009; 88:362-370; discussion 370-361

38 Golberstein E. The effects of income on mental health: evidence from the social security notch. J Ment Health Policy Econ 2015; 18:27-37

39 Ghoneim MM, O'Hara MW. Depression and postoperative complications: an overview. BMC Surg 2016; 16:5

40 Westcott PM, To MD. The genetics and biology of KRAS in lung cancer. Chin J Cancer 2013; 32:63-70

41 Westcott PMK, To MD. The genetics and biology of KRAS in lung cancer. Chinese Journal of Cancer 2013; 32:63-70

42 Siegelin MD, Borczuk AC. Epidermal growth factor receptor mutations in lung adenocarcinoma. Lab Invest 2014; 94:129-137

43 Cote ML, Kardia SL, Wenzlaff AS, et al. Risk of lung cancer among white and black relatives of individuals with early-onset lung cancer. Jama 2005; 293:3036-3042

44 Hunt JD, Strimas A, Martin JE, et al. Differences in KRAS mutation spectrum in lung cancer cases between African Americans and Caucasians after occupational or environmental exposure to known carcinogens. Cancer Epidemiol Biomarkers Prev 2002; 11:1405-1412

45 LaPar DJ, Bhamidipati CM, Harris DA, et al. Gender, race, and socioeconomic status affects outcomes after lung cancer resections in the United States. Ann Thorac Surg 2011; 92:434-439

46 Koh HK, Blakey CR, Roper AY. Healthy People 2020: a report card on the health of the nation. Jama 2014; 311:2475-2476