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Impact of Foreign born East Asian Density on Liver Cancer Incidence Rate among Neighborhoods in New York City during 2009 – 2013: Multilevel Analysis

by

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Abstract

Objective: To investigate the impact of the density of foreign born Asian population on geographical incidence rate of liver cancer in New York City during 2009 – 2013 in order to find specific geographic areas in NYC where liver cancer intervention should be targeted.

Method: We chose to employ cross-sectional and ecologic study design. We collected count data for liver cancer cases and sociodemographic characteristics from the 2010 U.S. census tracts (n = 2120) and health indicators from the United Hospital Funded neighborhoods (n = 34) in New York City during 2009 – 2013. We performed multilevel analysis in order to investigate the association between the density of foreign born Asian population and geographical incidence rate of liver cancer, controlling for sociodemographic characteristics at the census tract level and health indicators at the UHF neighborhood level.

Result: We found that for each one-percentage increase in the foreign born East Asian population in a census tract region, there is a significant increase in the expected incidence rate of liver cancer by 1.0%, controlling for other variables.

Conclusion: There was significant impact of the density of foreign born East Asian population on geographical incidence rate of liver cancer in NYC. We expected that the UHF neighborhoods with relatively high density of foreign born East Asian population and high liver cancer incidence rate should be targeted for the public health intervention of liver cancer.
Introduction

Liver cancer is a generic term for cancers of different cell types that originate in the liver\(^1\). Hepatocellular carcinoma (HCC) and bile duct cancer (cholangiocarcinoma) are the first and second most common types of liver cancer, respectively; approximately 80% of all liver cancer cases are HCC, and 10-20% are cholangiocarcinoma\(^1\). Hepatitis B and C virus infection is the most common cause of liver cancer; chronic hepatitis B virus infection causes at least 80% of liver cancer cases worldwide, while chronic hepatitis C virus infection is the leading cause of liver cancer in the U.S.\(^2\). Other risk factors, such as gender, race/ethnicity, cirrhosis, heavy alcohol use, tobacco use, obesity, type 2 diabetes, and socio-economic status, contribute to developing liver cancer as well\(^3\).

In 2012, there were approximately 782,000 new cases of liver cancer worldwide, which was the fifth most common cancer in men (554,000 cases) and the ninth in woman (228,000 cases)\(^4\). In addition, liver cancer was the second leading cause of cancer-related deaths, caused approximately 746,000 deaths worldwide\(^4\). In men, age-standardized incidence rate of liver cancer was the highest in the East Asian region (31.9 per 100,000), followed by South East Asia region (22.2 per 100,000) in 2012\(^4\). The rate for women, much lower than for men, was the highest in the East Asian region (10.2 per 100,000), followed by Western Africa region (8.1 per 100,000)\(^4\). Of all HCC cases for both men and women worldwide, 50% cases occurred in China\(^4\). Studies indicated that the high HCC rates in those Asian countries were attributed to high prevalence of hepatitis virus infection\(^5,6\).

In the United States, age-adjusted incidence rate of liver cancer was 8.2 per 100,000, and age-adjusted mortality rate of liver cancer among men and women was 6.0 per 100,000, based on
the data for 2008-2012\textsuperscript{7}. These represented less than 5% of all cancer cases and deaths\textsuperscript{7}. However, the liver cancer incidence rate and mortality rate have been increasing (rates of increase were 4.0\% and 2.7\%, respectively)\textsuperscript{7}. According to the National Cancer Institute, the age-adjusted incidence rate of liver cancer among Asians has been decreasing since 2000, while, age-adjusted incidence rate of liver cancer among all other race/ethnicity groups has been increasing\textsuperscript{8}. In 2012, the age-adjusted incidence rate of liver cancer among Hispanics was the highest; the age-adjusted incidence rate among Asians/Pacific Islanders was the second highest\textsuperscript{8}.

The increment of Asian population may be associated with the increase of liver cancer incidence rate in the US. A recent study reported a statistically insignificant increase in overall HCC incidence rate among Asians and Pacific Islanders in the US during 2000-2010, using data from the SEER 18 registries, which represented 28\% of the US population\textsuperscript{6}. The number of Asian immigrants has been increasing each year during 1980-2014, and Asian will be the largest foreign-born group by 2055\textsuperscript{9}. This indicates that the number of population at risk of liver cancer may be increasing in the US because those birth place among Asian population may be usually associated with hepatitis viral infections, and socioeconomic status (SES), and other risk factors (heavy drinking alcohol, smoking, and diabetes) may also contribute foreign born Asians to develop liver cancer.

**Previous Research**

In the US, there were 40 million (12.9 percent of total population) foreign-born individuals in 2010\textsuperscript{10}. Both the number and percentage of foreign-born population in the U.S. greatly increased from 1960 to 2010; in particular, the foreign born population from Latin American and Asian countries grew rapidly (comprised 98 percent of the growth in the total foreign-born population during 1970 – 2010)\textsuperscript{10}. In 2010, Asian population constituted 5\% of the U.S. population\textsuperscript{11}, and
there were 11.3 million foreign-born Asians in the U.S. 71 percent of the Asian foreign-born population was from five countries –China, India, the Philippines, Vietnam, and Korea. In addition, according to the U.S. Census Bureau, Asian population growth is faster than for any other racial group; the categories for Asian alone and Asian combined with another race increased by 45.6 percent during 2000 – 2010 in the U.S.

Liver cancer is a public health issue for Asian population in NYC. Asian population heavily concentrates in the Western U.S. (45.5% in 2010), but NYC has the largest number of Asian population (Asian alone, and Asian in combination), followed by Los Angeles. In NYC, there were estimated 1,077,553 Asians, and estimated 778,410 Asians (or 72.2 percent of total population of Asian) were born outside the U.S. in 2013. In addition, according to a recent report on Asian population in NYC, Asian population growth tends to concentrate in the neighborhoods where Asian American population is the majority. Based on NYC annual population estimates from the US Census Bureau’s American Community Survey Public Use Micro-data Samples (2005 – 2009) and mortality data for 2001 – 2010 from the NYC Department of Health and Mental Hygiene’s Bureau of Vital Statistics, liver cancer was the second leading cancer-related cause of death among Asian/Pacific Islander (API) men in NYC (15.6 per 100,000). API men and women had the highest age-adjusted liver cancer mortality rate among all races and ethnicities. Korean men and women had the highest age-adjusted liver cancer mortality rate among API subgroups (25.3 per 100,000, 7.5 per 100,000, respectively).

Liver cancer incidence rate is associated with birth place in Asian population. Chang et al. found that the age-adjusted incidence rate of liver cancer was significantly higher among foreign born Asian groups by countries than US born Asian groups (reference group), which includes Chinese, Japanese, and combination of Filipino, Korean and Vietnamese - in California during
1997-2004 (IRR = 1.55, 95% CI [1.22-2.02]; IRR = 3.51, 95% CI [2.33 – 5.21]; IRR = 2.33, 95% CI [1.57 – 3.32], respectively). This study used the data from California Cancer Registry, which contained 4,115 male Asian cases and 1,694 female Asian cases\textsuperscript{15}.

Possible reasons for the high mortality and incidence rates of liver cancer in Asian population have been discussed in several studies. Asian Americans with liver cancer may be associated with liver cancer risk factors such as hepatitis viral infection, diabetes, tobacco use, alcohol consumption, and SES; especially, they are at higher risk for Hepatitis B virus infection\textsuperscript{14,16}.

**Hepatitis B**

Hepatitis B is an infectious disease caused by the hepatitis B virus (HBV) infection\textsuperscript{17}. HBV is the main risk factor of hepatocellular carcinoma (HCC) which is the most common type of liver cancer\textsuperscript{18}. In highly endemic areas, HBV transmission occurs when individuals are exposed to HBV infected blood, and perinatal transmission or horizontal transmission is the most common cause of hepatitis B virus infection\textsuperscript{17}. Prevalence of HBV is the highest in sub-Saharan African and East Asian countries\textsuperscript{6}. In the US, 1 out of 20 people are infected with HBV. Approximately, 2 million Americans are chronically infected with HBV\textsuperscript{19}.

Birth place among Asians may be associated with the prevalence of HBV in the US. Approximately 1 million Asian Americans and 1 in 10 foreign born Asians are infected with chronic HBV\textsuperscript{20}. In addition, the Centers for Disease Control and Prevention (CDC) reported that 67% of randomly selected chronic HBV infection cases (n = 180) occurred among Asian race/ethnicity groups in NYC during June 2008 – November 2009\textsuperscript{21}. A cross-sectional study by Quang et al. compared the prevalence of HBsAg between US-born API students (n = 145) and API-born students (n = 152) in a public university in California during 2007-2008\textsuperscript{22}. This study found that 1.4% of US-born APIs tested positive for HBsAg, while 3.3% of API foreign-born
students tested positive\textsuperscript{22}. The epidemic of chronic HBV among Asian group is remarkably shown in NYC. In a total of 7,272 Asian Immigrants aged 18 years and older in NYC, Pollack et al. found a highly elevated prevalence of HBV, and also a high risk of disease progression to HCC using data for January 2004 – June 2008\textsuperscript{23}. In addition, comparing to a Korea-born group, China- and Taiwan-born groups were significantly more likely to be infected with HBV (OR = 3.5, 95% CI [2.4 – 3.9] p = <0.001; OR = 4.4, 95% CI [2.0 – 10.0], p = <0.001, respectively)\textsuperscript{23}.

HBV vaccination is the most effective way to prevent hepatitis B infection\textsuperscript{24}. HBV vaccination is recommended for every individual. According to the CDC, HBV vaccination is recommend for all children and adolescents because it contributed to a 96% decline in the incidence of acute HBV infection among those groups\textsuperscript{25}. It is also strongly recommended that adults who are at high risk and not vaccinated receive HBV vaccination, because approximately 95% of new HBV infections occur among adults\textsuperscript{26}. In addition, HBV vaccination was found to reduce the risk of primary liver cancer and other liver diseases. According to Qu et. al, a nested case-cohort study of Hepatitis B intervention containing 850,255 person years in the control group (IR = 1.41) and 954,886 person years in the vaccination group (IR = 0.21), the efficacy of HBV vaccination for incidence rate of HBV-related primary liver cancer was significantly higher among the vaccination group than the control group (HR = 0.16; 95% CI 0.03 – 0.11) with 84% (95% CI 23% - 97%) protective efficacy\textsuperscript{27}.

In general, however, awareness of HBV in populations around the world is low, and immigrants in particular are less likely to be aware of HBV\textsuperscript{28}. To our knowledge, we are not aware of any recent national data describing HBV knowledge among APIs. However, some studies addressed awareness of HBV vaccination among APIs in their study subjects. In a literature review study, Nguyen et al. found that many Asian Americans, including Chinese, Vietnamese, and
Cambodian, were not aware of the importance of HBV vaccination. Accordingly, in 1999, only 35% Chinese and 38% of Cambodian reported previous HBV screening. The proportions of HBV vaccinated population among susceptible Cambodian women, Chinese women, and Vietnamese men were 33%, 39%, and 71%, respectively. Quang et al. described that one third of 207 API-born and US-born API students attending a public university in California were not clearly aware of their Hepatitis B vaccination status. Therefore, it appears that a large proportion of Asian Americans are not vaccinated or unsure about their vaccination status, and that their risks of HBV infection and subsequent development of liver cancer are elevated.

**Hepatitis C**

Hepatitis C virus (HCV) is a blood-borne virus which causes HCV infection in the liver. Chronic HCV infection is the major cause of chronic liver disease and a risk factor for development of hepatocellular carcinoma (HCC). Vaccine for HCV has not been found, and therapy is capable to cure only a proportion of people at risk of developing advanced liver disease. Generally, approximately 70% of acute HCV infections become chronic liver disease, approximately 20% of acute HCV infections develop liver cirrhosis within 20 years, and approximately 5% of acute HCV infections cause deaths from the consequence of chronic liver disease. In 2015, the World Health Organization (WHO) reported that there were approximately 130 – 150 million chronic HCV cases, and the infection of HCV contributed to approximately 500,000 deaths worldwide. The prevalence of HCV infection varied by geographical regions worldwide. According to the 2017 Global Hepatitis Report by the WHO, Eastern Mediterranean region, European region, and Africa region were estimated the top three high prevalence of HCV infection regions (2.3%, 1.5%, 1.0%, respectively); South-East Asian region had the lowest prevalence with 0.5%.
In the US, the CDC estimated that 29,713 HCV infection cases occurred in 2013, 2.7-3.9 million people had chronic HCV in 2016, and HCV infection contributed to 19,659 deaths in 2014\textsuperscript{30}. The incidence rate of acute HCV among Asian/Pacific Islanders was lower than any other race/ethnicity including American/Indian Alaska Native, non-Hispanic Black, non-Hispanic White, and Hispanic during 2000-2014\textsuperscript{37}. Tohm et al. compared HCV infection between Asian Americans and other race/ethnicities\textsuperscript{38}. The study used the data from the Racial and Ethnic Approaches to Community Health across the US Risk Factor Survey conducted during 2009 – 2010 in 28 minority communities within 17 states, and four racial and ethnic minorities were included - such as non-Hispanic Blacks, Hispanics, Asian, and American Indian/Alaska Native\textsuperscript{38}. In this study, among the 9,972 Asian American respondents, 6.8% reported being told that they had HCV infection by a health care provider (non-Hispanic Blacks, 9.2%; Hispanics, 8.3%; American Indian/Alaska Native, 6.4%)\textsuperscript{38}. In addition, a proportion of diagnosis with HCV infection among US-born Asians (4.5%) were insignificantly lower than foreign-born Asians (7.5%) (foreign-born Asians as reference group; adjusted OR = 0.62, 95% CI = [0.27 – 1.45])\textsuperscript{38}.

Socioeconomic Status

Socioeconomic status (SES), which is a measure of person’s social, economic and occupational status, is a strong indicator for liver cancer incidence and survival\textsuperscript{39}. People with higher SES are likely to receive better health care service including frequent cancer screening. They are also more likely to live in a better environment that can protect them from risk factors of cancer\textsuperscript{39}. In a cohort study of 548,530 Korean male service workers aged 30-59 years, Joshi et al. found a significant association between SES, which is comprised of four categories (upper, upper middle, lower middle, and low), and liver cancer mortality (upper class as a reference category: RR = 1.35, 95% CI [1.13-1.61]; RR = 1.54, 95% CI [1.13 – 1.61]; RR = 1.72, 95% CI [1.45 –
The contextual effects of neighborhood SES can indirectly affect individuals’ health status. For instance, health care service is less likely to be provided in lower SES neighborhoods, which subsequently affect individuals’ health status due to having less chances to see a doctor. Jacqueline et al. examined the geographical variation in chronic liver disease and hepatocellular carcinoma by contributions of socioeconomic deprivation, alcohol retail outlets, and lifestyle using a multilevel cox proportional hazard regression model with the data from the National Institutes of Health-American Association of Retired Persons (NHI-AARP) Diet and Health study cohort. The data contained 343 HCC cases, 494,477 non-cases, and 805 chronic liver disease deaths. The measurement of contextual effects was represented by area socioeconomic deprivation, of which an index was created using percent of families below the poverty level, percent unemployed, percent with no high school diploma, and the Gini coefficient from the census data. The area socioeconomic deprivation index was significantly associated with increased risk of HCC and chronic liver disease (HR = 1.48, 95% CI [1.03 – 2.14]; HR = 2.36; 95% CI [1.79 – 3.11], respectively).

Disparity in liver cancer incidence by neighborhood SES exists in foreign-born Asian populations. Asian immigrants tend to have high socioeconomic achievement in the US. In a study using the national mortality and census data (1979 – 2003) and the 1993 and 2003 National Health Interview Survey, it was found that Asian immigrants had higher educational attainment, a higher proportion of managerial and professional occupations, and a higher proportion of family income >= $50,000 than any other ethnic-immigrant groups, including Whites/European, Black and Hispanic immigrants. However, Asian immigrants were more likely to lack health insurance and less likely to receive preventive care than US-born Asians. Chang et al. found that contextual
SES was significantly associated with liver cancer incidence rate in Asian immigrant population. In this study, age-adjusted incidence rates of liver cancer in Asian immigrants in low SES neighborhoods was significantly higher compared to Asian immigrants in high SES neighborhoods in California during 1998 - 2002 (IRR = 1.21, 95% CI [1.10 – 1.34]).

**Other risk factors (heavy alcohol consumption, diabetes, and tobacco use)**

Heavy alcohol consumption, and tobacco use are well established risk factors of chronic liver diseases, and diabetes increases the risk of developing HCC. They may contribute to the association between liver cancer incidence and foreign-born status in Asians-Americans. Asian Americans overall are less likely to drink alcohol than other races. According to a report from the CDC, based on the 2008-2010 National Health Interview Survey (NHIS) data, the percentage of Asian adults who were current drinkers (48%) was the second lowest, following Native Hawaiians and other Pacific Islanders (45.5%). The percentage of Asian adults who had five or more drinks in 1 day at least once in the past year (11.2%) was lower than for any other race. In addition, the prevalence of heavy drinking is not higher in foreign-born Asian population than US-born Asian Americans. According to a study by Lo et al. which used the data from the 2008-2011 National Health Interview Survey (NHIS), US-born Asians were more likely to engage in heavy drinking than foreign-born Asian. However, in NYC, Haung et al. found that the contribution of alcohol use on liver cancer mortality rate varied by subgroups of Asian Americans. The percentage of binge drinking in individuals of Korean decent was almost 4 times higher than in individuals of Chinese decent during 2002 – 2008 (23.5%, 5.8%, respectively). The percentage of heavy drinking in individuals of Korean decent was also higher compared to individuals of Chinese decent (3.4%, 1.3%, respectively). The study demonstrated that the synergism between alcohol consumption and chronic HBV infection can possibly increase the liver cancer mortality in Koreans in NYC.
Diabetes status and tobacco use may be weakly related to liver cancer in Asian immigrants. According to the American Diabetes Association, prevalence of diagnosed diabetes in Asian American adults (8.0%) was the second lowest of five race/ethnicity groups in the US (American Indians/Alaskan Natives - 15.1%; non-Hispanic Blacks – 12.7%; Hispanic – 12.1%; non-Hispanic Whites – 7.4%)48. In addition, according to a study using the 1997-2005 NHIS data on 34,456 immigrants, diabetes prevalence among male and female Southeast Asian immigrants was the fifth highest among nine region of birth groups – including Europe, combination of Mexico, Central America, Caribbean, South America, Russia, Africa, Middle East, Indian subcontinent, and Central Asia (5.06%, 4.00%, respectively). However, it also found that prevalence of diabetes in both male and female Southeast Asia immigrants was significantly higher than Europe immigrants after controlling for age, poverty, income ratio, duration of residence, and body mass index (men: OR = 1.89, 95% CI [1.12 – 3.17]; women: OR = 2.30, 95% CI [1.36 – 3.89])49. Prevalence of tobacco use among non-Hispanic Asians (9.5%) is the lowest among all racial/ethnic groups in the US50. Li et al. investigated the prevalence of smoking Among Asians in NYC using the data from the REACH US Risk Factor Survey (RFS) which contained 3,405 individuals. They found that prevalence of tobacco use in foreign-born Asian population was not significantly higher than US-born Asian population in NYC during 2009 - 2011 (19.8% versus 10.5%, respectively; OR = 0.74, 95% CI [0.45-1.21])51.

However, diabetes, tobacco use and alcohol outlet density impact on chronic liver disease mortality (CLD) rate by SES. Jacqueline et al. investigated whether individual-level risk factors, such as obesity and diabetes, and alcohol outlet density within a census tract contribute to the socioeconomic disparities in HCC incidence and chronic liver disease (CLD) morality rate. This study found that individual-level obesity (5.14%) and diabetes (8.55%), and alcohol outlet density
(9.51%) respectively contributed to the differences in the risk of chronic liver disease (CLD) mortality by SES after accounting for age, sex, and race\textsuperscript{42}. Density of alcohol outlets (Jacqueline et al. scaled alcohol outlet density per 1000 people) is positively associated with frequency of alcohol consumption\textsuperscript{52–54}. Combination effects of alcohol outlet density, diabetes, obesity, demographics and health risk behaviors (includes education, marital status, cigarette smoking, perceived health status, alcohol consumption, non-alcohol energy, total meat intake, total fruit intake, total vegetable intake, and saturated fat intake) contributed to 39.07\% of changes in the association between neighborhood socioeconomic deprivation and CLD mortality\textsuperscript{42}. The study does not directly imply the possible impact of those risk factors on the association between Asian immigrants and liver cancer incidence rate. However, the result of this study suggests that such risk factors are important confounders which should be controlled in statistical analysis.

In sum, we assumed that the liver cancer may be a rising public health issue corresponding to the increase number of Asian immigrants in the US. In addition, we found that the risk factors of liver cancer – such as hepatitis B and C infection, SES, diabetes, heavy alcohol use, and tobacco use – are either positively or negatively associated with both liver cancer incidence and Asian immigrants. We hypothesize that the liver cancer incidence is more likely to be higher in a region of a high density of Asian immigrants compared with a region with a low density of Asian immigrants, controlling for the known liver cancer risk factors. Therefore, the purpose of this study is to investigate the association between the density of foreign born Asian population from East and South Eastern Asia countries (China, Japan, Korea, Cambodia, Indonesia, Laos, Malaysia, Burma, Philippines, Singapore, Thailand, Vietnam, and other South Eastern Asia Countries) and the incidence rate of liver cancer. We chose a cross-sectional and ecologic study design in order to explore the overall impact of those foreign born East Asian populations on the liver cancer
incidence rate. First, we will investigate the distribution of defined Asian population and liver cancer incidence rate among United Hospital Fund (UHF) neighborhoods in NYC. Second, the impact of density of foreign born East Asian population (main effect) on regional incidence rate of liver cancer (outcome) will be examined. Data for risk factors of liver cancer at the corresponding community level will be collected, and determine which risk factors significantly explain the outcome with the main effect. At the conclusion of this research, we expect to find specific geographic areas in NYC where public health prevention should be targeted to efficiently reduce new cases of liver cancer in the future.

Method

Data source

We included all populations in NYC since the purpose of this study aimed at investigating the overall impact of density of foreign-born East Asian American on liver cancer incidence in communities in NYC. A hierarchic approach was employed to adjust important risk factors of liver cancer at different geographical levels so as to precisely investigate the association between geographical liver cancer incidence rate and geographical density of foreign born Asian population. We determined to collect 2-level of hierarchically structured data: sociodemographic characteristics table and liver cancer case table at 2010 census tract level (micro level) and health indicators at United Hospital Fund (UHF) neighborhood level (macro level). The number of liver cancer cases and population estimates by gender for census tracts in NYC, during 2009 - 2013, were obtained from the New York State Cancer Registry (NYSCR). Corresponding to the geographical unit of the outcome variable, which is stratified by 2010 census tracts, we retrieved data for 2009 - 2013 estimated percentage of sociodemographic characteristics - such as foreign born East Asian, age 65 years and older, low education.
attainment, household income below the poverty level, not working, and other than married status - among all census tracts in NYC from the United States Census Bureau website (American Factfinder). We defined foreign born East Asian population as the total population of foreign born East and Southeast Asians from the census tracts within NYC obtained from the United States Census Bureau. Data for health indicators, which contribute to the liver cancer incidence, exist only at 34 UHF neighborhoods (the department aggregated 42 neighborhoods into 34 neighborhoods); tables for percentages of health indicators - such as diabetes ever, obesity, self-reported health status, current smoker, heavy drinking alcohol, and physical inactivity collected by health community surveys during 2009 - 2013 were retrieved from the NYC DOHMH website; tables for percentage of chronic HBV infection and chronic HCV infection were retrieved from 2011 Communicable Disease Surveillance Data from the DOHMH website. Definition of each variable is specified in table 1.

**Stratifying UHF Neighborhood by the 2010 Census Tract**

A list of the 2010 population census tracts stratified by UHF Neighborhoods was obtained from the NYSCR. NYC consists of 42 UHF neighborhoods and 2168 census tracts. Originally, each UHF neighborhood was the aggregation of ZIP code Tabulated Areas (ZCTAs), and NYSCR traditionally published cancer data based on this neighborhood definition in NYC. However, NYSCR recently started to use new UHF neighborhood which is based on the 2010 census tract definition. With the list, health indicators at the UHF neighborhood level were merged into other variables at the census tract level so as to perform the hierarchic analysis.
Multilevel Analysis and Mapping

For purpose of this study, we employed a multilevel analysis to examine the association between the density of foreign born East Asian population and geographical liver cancer incidence rate, adjusting for socioeconomic status variables at census tract level (micro level) and health indicators at UHF neighborhood level (macro level). All sequences of analysis were performed using SAS 9.4 software. In addition, the distribution of liver cancer incidence rate and the density of foreign born East Asian population among 34 UHF neighborhoods were mapped using QGIS 2.18 software.

Poisson regression analysis method must be employed since we have count outcome. In order to determine whether the Poisson regression model fits, we analyzed the liver cancer incidence rate at the census tract level using PROC UNIVARIATE statement. The distribution of the outcome variable violated the Poisson distribution assumption since its variance was greater than the mean. Negative binomial model is usually employed to solve the over-dispersion problem in Poisson regression model. However, the variance of Pearson Residual in our initial multilevel Poisson regression model was 0.986, which indicates that the over-dispersion may be adjusted in the model, we decided to employ Poisson regression analysis method.

Other variables, such as sociodemographic variables and health indicators, were also analyzed using the PROC UNIVARIATE statement. The results of the univariate analysis are presented in Table 1, which shows: overall percentage, median and its 95% confidence interval, and the first and the third quartiles for each variable at their level. In addition, we depicted distribution of all variables among 34 UHF neighborhoods where rates (per 100,000) were classified into five classes with equal intervals. Those classes were numbered from 1 to 5, corresponding with the lowest to the highest. In addition, we grouped class 4 and 5 as high rate,
class 3 as middle rate, class 1 and 2 as low rate. The incidence rate of liver cancer was age-adjusted using the 2000 US standard population which consists of 19 age categories. We used SAS 9.4 software for the calculation, and created maps of distribution using QGIS software. Vector files for creating maps were retrieved from the United State Census Bureau website.

**Building Multilevel Model**

In this study, we have hierarchically structured data, which is composed of variables at two regional levels: the census tract (micro) level and the UHF neighborhood (macro) level; by hierarchy, regions at census tract level are nested within or grouped into regions at the UHF neighborhood level. Multilevel model is a useful statistical analysis tool that allows hierarchically structured data to be employed\(^5\). The generalized linear mixed effect model (GLMM) which is based on a generalization of ordinary least square (OLS) regression and allows the outcome probability distribution to be any member of an exponential family of distributions\(^5\), was employed since we have count outcome. Like multilevel linear model, GLMM can take into account the intra-class correlation coefficient (ICC), which is the measure of within-group homogeneity or between group heterogeneity, in hierarchically structured data by allowing random coefficients in the model\(^5\). The model consists of fixed effect, random effect, and link function; random intercept is a micro-level intercept varies across macro-level units; fixed effect is the effect of the micro-level variables on dependent variable that does not vary across groups; random effect is the effect of the micro-level variables on dependent variable that does vary across groups; link function connects the linear predictors to the mean of the outcome distribution, which includes the family of exponential distributions\(^5\).
By default, PROC GLIMMIX in SAS 9.4 software estimates the maximum likelihood of GLMM using a linearization method, which is also called a pseudo-likelihood method. Unlike Multilevel Linear Model, GLMM is a nonlinear multilevel model which cannot directly maximize the likelihood or restricted likelihood since the integrated distribution of the random effect is usually unknown. SAS generates pseudo-data from original data by approximating likelihood function, and approximate GLMM using normal linear mixed model estimates repeatedly. However, the deviance statistic from the linearization-based method cannot be used for model comparison since the iterative model is estimated using pseudo-data constructed from original data. Therefore, based on the result of modeling using PROC GLIMMIX statement, we need to re-build multilevel model using PROC NLMIXED which is exclusively based on numerical methods. Consequently, the deviance statistic or -2LL as well as Akaike’s information criterion (AIC) and Bayesian information Criterion (BIC) could be used for model comparison.

We took five steps to build a final multilevel Poisson regression model. First, we ran an empty model, which contained a dependent variable without any explanatory variable, to assess within-group homogeneity or between-group heterogeneity and explore the grand mean of the outcome measure. If the result of empty model implies the existence of significant within group observation dependence or ICC, then it indicates that the multilevel model should be employed. Second, we expanded the empty model by adding macro level explanatory variables since it is logical to add macro level variables into the model to explain the significant unexplained variation in the mean outcome across the neighborhoods. The Generalized Chi-square/DF statistic and the variance of the Pearson-type residuals for conditional Poisson distribution would be compared between the current model and the previous model in order to investigate the over-
dispersion problem. Third, census tract level explanatory variables were added as a fixed effect to the model that is built in the second step. The statistic fit for this model would be investigated as comparing the generalized Chi-square/DF statistic and the variance of the Pearson-type residuals for conditional Poisson distribution of the previous model. Fourth, we identified the random micro level slope coefficients in the model. This is because, the relationship between census tract level explanatory variables and the liver cancer incidence measure may vary across UHF neighborhoods. Significance testing for variance in macro level residual variance/covariance implies the randomness of corresponding micro level slope coefficient. Finally, we assessed the cross-level interactions. This is because, the significant random micro level slope coefficients were identified and their variation could be systematically and partially explained by macro level explanatory variables.

Results of multilevel poisson regression analysis are presented in table 3 and table 4. We used backward stepwise selection for building final model of the association between density of foreign born East Asian population and liver cancer incidence rate. Noteworthy models, especially for showing the process of building the final model, are presented in table 3. Table 4 presents the association between health indicators at UHF neighborhood level and liver cancer incidence rate controlling socioeconomic status variables as well as the density of foreign born East Asian population variable at census tract level.

Results

Table 1 presents the result of univariate analysis for each variable at its level. There are nine variables at the census tract level and eight variables at the UHF neighborhood level. Population variable, a continuous variable, shows its count, mean, 95% confidential interval; all other variables show overall percentage, median (a region of the geographical unit has median
percentage) and its 95% confidence interval, and the first and the third quantiles. Of 2,168 census tracts, 2,120 census tracts were selected; 48 census tracts were excluded because no resident was counted in those census tracts.

There were 8,282,725 people in NYC; the average population size of a census tract was 3,906; and on average 243,609 people lived in a UHF neighborhood. Of the total population in NYC, 0.012% was diagnosed with liver cancer during 2009 - 2013; the median percentage was 0.01% (95% CI 0.01 - 0.011), and the Interquartile Range (IQR) was 0.013%. Of total population in NYC, it was estimated that 6.642% were foreign born East Asian during 2009 - 2013. The median was 2.425% (95% CI 2.138 - 2.625), and the IQR was 6.662%.

Figure 1 and figure 2 show the distribution of age-adjusted incidence rate of liver cancer per 100,000 and density of foreign born East Asian population per 100,000, respectively. There are a total of six neighborhoods with high age-adjusted incidence rates of liver cancer; three neighborhoods (UHF 103, 104, and 309/310) were categorized as class 4; three neighborhoods (UHF 105/106/107, 205, and 303) were categorized as class 5. There are a total of three neighborhoods with high rate of foreign born East Asian population; two neighborhoods (UHF 205 and 404/406) were categorized as class 4; UHF 403 was categorized as class 5. All other maps, which depict the distribution of each variable, are presented in appendix – 2.

Other variables at census tract level were examined. Of the total NYC population, 47.557% was male; the median percentage was 47.715% (95% CI 47.500 - 47.900); the IQR was 3.7%. Overall estimated percentage of people at age 65 or over was 12.455%; the median was 11% (95% CI 10 - 10); the IQR was 7.7%. Overall estimated percentage of low educational attainment, which was defined as the population that attained education diploma less than high school, was 13. 841%; the median percentage was 12.361% (95% CI 11.95 - 12.735); the IQR
was 10.995%. Overall estimated percentage of population whose poverty was below the poverty line was 20.088%; the median percentage was 15.771% (95% CI 15.008 - 16.510); the IQR was 18.24%. Overall estimated percentage of population who have not been working for last 12 months was 20.066%; the median percentage was 19.754% (95% CI 19.380 - 20.070); the IQR was 7.67%. Overall estimated percentage of population whose marital status was other than married was 50.154%; the median percentage was 49.512% (95% CI 48.7 - 50.2); the IQR was 16.5%.

Likewise, health indicators and chronic hepatitis B and C virus infection variables at the UHF neighborhood level were examined. Overall incidence rate of Chronic HBV infection was 0.090%; the median percentage was 0.056% (95% CI 0.04 - 0.072); the IQR was 0.06%. Overall incidence rate of Chronic HCV infection was 0.094%; the median percentage was 0.078% (95% CI 0.072 - 0.106); the IQR was 0.042%. Overall estimated percentage of diabetic, which was defined as people who have been told by a doctor, nurse or other health professional that they have diabetes was 10.569%; the median percentage was 13.505% (95% CI 11.436 - 15.514); the IQR was 4.82%. Overall estimated percentage of obesity, which is defined as population whose body mass index (BMI, calculated based on respondents self-reported weight and height) was equal to or greater than 30, was 25.97%; the median percentage was 25.970% (95% CI 22.434 - 30.532); the IQR was 11.446%. Overall estimated percentage of heavy drinker, which was defined as people who drink an average of more than 2 drinks per day for men and more than 1 drink per day for women, was 4.615%; the median percentage was 3.939% (95% CI 3.82 - 4.654); the IQR was 1.404%. The overall percentage of current smoker was 14.048%; the median was 14.023% (95% CI 13.109 - 16.152); the IQR was 3.996%. Overall estimated percentage of physical inactivity, which was defined as people who participate in any physical
activities or exercise - such as running, calisthenics, golf, gardening, or walking for exercise - other than their regular job during the past 30 days, was 25.674%; the median percentage was 26.028% (95% CI 25.164 - 27.657); the IQR was 4.751%.

Table 2 presents results of crude association between covariates and the outcome using multilevel Poisson regression model. Each variable at census tract level – such as Age at 65 and higher (RR 1.021; 95% CI 1.016 – 1.026), Male population (RR 0.988; 95% CI 0.979 – 0.998), Low Education Attainment (RR 1.031; 95% CI 1.026 – 1.035), Unemployment Status (RR 1.021; 95% CI 1.017 – 1.026), Other than Married Status (RR 1.008; 95% CI 1.005 – 1.012), and Below Poverty Level (RR 1.011; 95% CI 1.014) - was significantly associated with the outcome. Of eight variables at UHF neighborhood level, five variables - such as Incidence rate of Chronic HBV infection (RR 2.335; 95% CI 1.274 – 4.278), Incidence rate of Chronic HCV infection (RR 46.899; 95% CI 5.940 – 370.295), Current smoker (RR 1.038; 95% CI 1.005 – 1.072), Physical Inactivity (RR 1.019; 95% CI 1.001 – 1.039), and Self-rated health (RR 1.023; 95% CI 1.011 – 1.035) – were significantly associated with the outcome measure.

Table 3 presents results of multilevel Poisson regression analysis. The empty model shows that about 4.5% of the total variance was statistically significant due to the UHF neighborhood characteristics (p-value <0.001). The crude model shows the significant unadjusted association between foreign born East Asian variable (main effect) and liver cancer incidence rate (outcome) (RR 1.018; 95% CI 1.014-1.021). The fixed effect model 1 shows the significant association between the main effect and the outcome (RR 1.012; 95% CI 1.009-1.015), adjusting covariates for age 65 and over, male population, low education attainment, working status, other than married status, and incidence rate of HCV infection. The fixed effect model 2 is the same as the previous model, except for the male population variable, and the
model shows the significant association between the main effect and the outcome (RR 1.012; 95% CI 1.009-1.016).

The mixed model 1 is the final model, which includes all significant variables and has the smallest AIC and BIC among all built models. It contains five fixed effect variables (foreign born East Asian, age 65 years and higher, working status, other than married status, and incidence rate of HCV infection), a random effect variable (low education attainment) and random effects (random intercept and random slope for Low education attainment). The result shows the significant association between the main effect and the outcome (RR 1.010; 95% CI 1.006-1.013). Interpretation for each variable is the following:

- Intercept: The estimated overall average of liver cancer incidence rate in a census tract region when all variables are equal to zero.
- Foreign born East Asian: For each one-percentage increase in the foreign born East Asian population in a census tract region, there is a significant increase in the expected incidence rate of liver cancer by 1.0%, controlling for other variables.
- Age 65 and over: For each one-percentage of increase in the percentage of population at age 65 and over in a census tract region, there is a significant increase in the expected incidence rate of liver cancer by 2.0%, controlling for other variables.
- Low education attainment: For each one-percentage increase in the population for low education attainment in a census tract region, there is a significant increase in the expected incidence rate of liver cancer by 1.5%, controlling for other variables.
• Working status: For each one-percentage increase in the population who have not been working for last 12 months, there is a significant increase in the expected incidence rate of liver cancer by 1.2%, controlling for other variables
• Other than married status: For each one-percentage increase in the population whose marital status was other than married in a census tract region, there is a significant increase in the expected incidence rate of liver cancer by 0.9%, controlling other variables
• Incidence rate of HCV infection: For each one-percentage increase in the incidence rate of HCV infection in a UHF neighborhood, there is a significant increase in the expected incidence rate of liver cancer by 747.5%, controlling other variables.

Other models also presented in table 2. The mixed model 2 was built in order to investigate whether prevalence of chronic HBV infection can substitute density of foreign born East Asian population. As a result, incidence rate of liver cancer was not explained by prevalence of chronic HBV infection, controlling for age 65 and above, low education attainment (random effect), working status, and marital status (p-value = 0.236). The full fixed effect model is presented at the end. In the model, all variables at the census tract level, except the percent below poverty level variable, significantly explains the outcome measure, while all variables at the UHF neighborhood level do not.

Table 4 presents the association between eight health indicators and liver cancer incidence rate using multilevel Poisson analysis. Each model includes variables at the census tract level that are significantly controlled. In addition to HCV variable (the model is the same
with the final model in Table 3), current smoker variable was significantly associated with liver cancer incidence rate (RR = 1.026; p-value = 0.027).

Discussion

This study demonstrates that the density of foreign born East Asian population is associated with regional incidence rate of liver cancer in NYC. We analyzed the distribution of liver cancer incidence rate and foreign born East Asian population among 34 UHF neighborhoods in NYC, and investigated characteristics of neighborhoods in terms of risk factors of liver cancer. Using multilevel Poisson regression analysis method, the significant association between the main effect and the outcome adjusting for sociodemographic characteristics (age 65 years and higher, low education attainment, working status, other than married status) at the census tract level and a health indicator (incidence rate of hepatitis C virus infection) at the UHF neighborhood level.

Descriptive Analysis

In our study, crude incidence rate of liver cancer was 12 per 100,000 in NYC during 2009 – 2013. Cancer incidence rate is usually adjusted by age, but we decided not to adjust the incidence rate by age since the rates at the census tract level would be too small for meaningful statistical analysis. Instead, we decided to include a variable for the population of age 65 years or higher, which is close to the median age of liver cancer diagnosis age at 647, in the model. We also found that neighborhoods with either a high incidence rate of liver cancer or a high density of foreign born East Asian population are likely to be adjacent to each other. For instance, UHF neighborhoods located in upper New York county and Bronx county were categorized as the class with a high age-adjusted liver cancer incidence rate; it involves two of three class 5 neighborhoods (105/106/107, 303) and two of three class 4 neighborhoods (103 and 104).
Likewise, neighborhoods with a relatively high density of foreign born East Asian population are likely to cluster as well.

**Statistical Analysis**

As a result of statistical analyses, our findings confirmed the disparity of liver cancer by socioeconomic status and the density of foreign born East Asian population among UHF neighborhoods in NYC. Selected sociodemographic characteristics – such as age 65 years and higher, low education attainment, unemployment status, other than married status – were significantly positively associated with incidence rate of liver cancer at census tract level, consistent with previous studies. Foreign born Asians are usually at higher level of SES than US born Asians, but they are less likely to receive health care services. In addition, health disparity is more likely to be occurred in low SES neighborhoods. Therefore, clustered foreign born Asians living in low SES community may be more likely to be at higher risk of liver cancer.

We found that the chronic HCV prevalence at UHF neighborhood level was a strong indicator of liver cancer incidence. Our finding shows that a UHF neighborhood with high prevalence of chronic HCV infection is significantly associated with high liver cancer incidence rate in a census tract region within the neighborhood. Previous studies support the plausibility of the result. A study found that chronic HCV cases are significantly associated with death due to liver diseases such as alcoholic liver disease, alcoholic cirrhosis, cirrhosis/fibrosis, and liver failure in NYC during 2001 – 2012. The risk of HCC largely increases when a HCV case develops cirrhosis or advanced fibrosis, and multiple steps for inducing cancer can be skipped developing HCC for a HCV case. Meanwhile, HCV infection is not strongly related to Asian patients with HCC in NYC. Percentage of HCV infection among Asian/Pacific Islander non-
Hispanic individuals with HCC (5.3%) was the second lowest among five race/ethnicities, which includes Hispanic (35%), Black non-Hispanic (30%), White non-Hispanic (29.1%), and other/unknown race (0.5%) in NYC during 2001 – 2012\(^5\). This is because Asian population are less likely to be exposed to the risk factor of HCV infection such as intravenous drug abuse, which is a minor contributor to overall disease burden for Asian Americans with chronic HCV\(^5\).

In addition, percentage of current smokers at UHF neighborhood level was significantly associated with liver cancer incidence rate in our data. Smoking is a well-established risk factor of liver cancer. Previous studies found not only a direct association between smoking and HCC risk but also the increase of HCC risk when smokers are infected with HBV or HCV\(^5\). Our finding shows analogous results. Percentage of current smokers among UHF neighborhoods not only statistically significantly explained liver cancer incidence rate, but most of the neighborhoods classified as a high liver cancer incidence rate were also classified as neighborhoods with a high percentage of current smokers (figure 2 and figure 11). Therefore, health practitioners should recommend current smokers, who are at risk of developing liver cancer as well as all other types of cancer, quite smoking.

In the analysis, the HBV variable was excluded from the final model. The HBV variable is unlikely to statistically explain the outcome in most of the built models, which means that the prevalence of chronic HBV infection does not appropriately capture liver cancer incidence rate in each census tract. The HBV variable was insignificantly associated with the liver cancer incidence rate in the final model, controlling for foreign born East Asian, Age 65 years and higher, low education attainment, other than married status, incidence rate of chronic HCV infection (the result is not presented).
The prevalence of HBV at the community level may be on the causal pathway between the density of foreign born East Asian population and liver cancer incidence rate at the census tract level. The HBV variable significantly explained the outcome in the crude model (p-value = 0.0075). We also found a statistically significant association between density of foreign born East Asian population and prevalence of chronic HBV infection controlling for variables such as age 65 and older, low educational attainment, and income below the poverty level (the result is not presented). In addition, previous studies have found the highest prevalence of chronic HBV infection among Asian population, and that foreign born Asians are significantly more likely to have HBV infection in NYC as well as national wide. Accordingly, high density of foreign born East Asian population in a community may imply high prevalence of chronic HBV infection, and the high prevalence of chronic HBV infection, thus, cause the high incidence rate of liver cancer. However, the prevalence of chronic HBV infection could not substitute the density of foreign born East Asian population for explaining regional liver cancer incidence rate in our data.

Male population at census tract level was excluded in the final model because we assumed that the male variable does not appropriately explain the dependent variable. Male population had a significant negative association with the outcome, which is opposed to the result in previous studies. The inconsistent result may relate to the distribution of the percentage of male population in NYC. The percentage of male population among census tracts in NYC was likely to be uniformly distributed (Median = 47.715%; 95% CI 47.500% - 47.900%; IQR = 3.7%). Thus, we concluded that it is not statistically meaningful to include the male population variable in the model. However, since gender is a strong predictor of liver cancer, it should generally be included when evaluating liver cancer rates.
Implementation

Our findings suggest characteristics of communities in NYC that should be targeted for implementing liver cancer prevention. We generated maps for the distribution of the density of foreign born East Asian population and the regional incidence rate of liver cancer among the UHF neighborhoods, which can be useful for visually highlighting neighborhoods that should be targeted in order to cost-effectively implement interventions for liver cancer\textsuperscript{59}. We can preemptively target people in neighborhoods where both the density of foreign born East Asian population and liver cancer incidence rate are high, and initiate the intervention program for preventing liver cancer. HBV infection is the most common cause of HCC, and the attributable risk estimates for combined effects of hepatitis B and C infection account for over 80\% of liver cancer cases worldwide\textsuperscript{60}. Since the prevalence of chronic HBV infection among Asian population is the highest, public health action for preventing HBV targeting region with high density of foreign born East Asian population would efficiently prevent the liver cancer. In addition, many studies have found that the liver cancer can be effectively prevented with the vaccination of HBV\textsuperscript{24–27,61}.

UHF 205, for instance, has both a high age-adjusted incidence rate of liver cancer (class 5) and a high density of foreign-born East Asian population (class 4). Since this neighborhood also has high prevalence of chronic HBV (class 5), we can tentatively conclude that the intervention for preventing HBV should be carried out in this neighborhood, especially targeting communities within the neighborhood where East Asian immigrants are likely to reside. In addition, the accessibility of health care services among those residents should be investigated. Our findings show that the neighborhood was classified as low socioeconomic status such as low educational attainment (class 4), working status (class 4), and income below the poverty level (class 4).
Therefore, health practitioners should figure out what social barriers potentially interrupt residents taking benefits from healthcare services, and in turn contrive strategies for liver cancer prevention.

The education program for hepatitis B virus infection is a critical public health implement for preventing liver cancer incidence. As demonstrated above, the HBV infection is highly associated with developing HCC, and 1 in 10 foreign born Asian Americans are infected with chronic HBV\textsuperscript{20,62}. Mostly, the low awareness of HBV attributes to the high incidence rate of HBV among Asian Americans\textsuperscript{22,28,29}. Studies have found that the community-based education program for liver cancer intervention considering individuals’ cultural beliefs and barriers of assessing health care services significantly increased the HBV screening rate among Asian Americans\textsuperscript{59,62}. Therefore, we expect that the community-based intervention of HBV infection targeting UHF neighborhoods with high liver cancer incidence rate and high density of foreign born East Asian population would cost-effectively increase the awareness and screening test rate of HBV so as to prevent the incidence of liver cancer among Asian Americans.

Furthermore, the prevention of chronic HCV infection should be considered to reduce liver cancer incidence rate in NYC. If only communities with a high density of foreign born East Asian population were targeted for implementing program for liver cancer prevention, most of communities with a high liver cancer incidence rate and potentially at risk of high incidence rate of liver cancer would be ignored. The distribution of foreign born East Asian population among UHF neighborhoods does not exactly match up with the distribution of regional incidence rate of liver cancer; only UHF 205 neighborhood has both high density of East Asian population and high liver cancer incidence rate. In addition, our study showed that the magnitude of the association between the density of East Asian population and the incidence rate of liver cancer
was marginal. Rather, prevalence of chronic HCV infection was a stronger indicator for explaining liver cancer incidence rate than any other covariates in our statistic models. A previous study indicated that the development of liver cancer is more likely to be caused by chronic HCV infection than chronic HBV infection in NYC. Our study also shows that the overall prevalence of chronic HCV infection was slightly higher than the overall prevalence of chronic HBV infection in NYC. These findings imply that the effective prevention of liver cancer can be accomplished by preventing both chronic HCV infection and chronic HBV infection. Therefore, the prevention for chronic HCV infection should be contrived along with the prevention for chronic HBV infection in order to reduce the incidence rate of liver cancer.

Neighborhoods with high age-adjusted incidence rate of liver cancer, such as UHF 103, 104, 105/106/107 and 303, may be associated with density of Latino population and non-Latino Black population. In 2014, New York City Department of Health and Mental Hygiene reported that the percentage of both HCV infection alone (35%) and with HBV (28%) among Latinos with HCC was higher than any other race/ethnicity groups such as non-Latino White, non-Latino Black, Asian/Pacific Islander, and other/unknown during 2001 - 2012. Furthermore, the percentage of HCV infection alone among non-Latino Black with HCC was the second highest (30.1%)\textsuperscript{63}. Our findings show that neighborhoods classified as a high age-adjusted incidence rate of liver cancer are likely to overlap neighborhoods with high prevalence of chronic HCV where the density of Hispanic and non-Black population is seemingly high\textsuperscript{13}. In order to successfully prevent liver cancer through preventing HCV infection, further study should be conducted for investigating the association between liver cancer incidence rate and density of Latino and non-Latino Black population among NYC neighborhoods.
Strengths and limitations

Our study has three major strengths. First, we retrieved data from credible sources such as the NYSCR, the United States Census Bureau, the New York City Health Community Survey (NYC HCS), and the Communicable Disease Surveillance (CDS) data. Every cases of cancer or other malignant disease is required to be reported to the Department of Health since cancer is a reportable disease in every state in the U.S.; all reported cancer cases are collected and processed though the cancer registry\textsuperscript{64}. Thus, our data, which are retrieved from the cancer registry data, contains nearly every reported liver cancer case that occurred in NYS during 2009 – 2013. The United States Census Bureau carries out the American Community Survey (ACS), which is a nationwide survey to collect information such as age, race, income, occupations, and other important population-based data\textsuperscript{65}. They contact over 3.5 million householders across the country to participate in the survey every year\textsuperscript{65}. Based on the collected data, they create and publish ACS period estimates (1-year, 3-year, and 5-year)\textsuperscript{65}. The NYC HCS is an annual telephone survey with an annual sample of approximately 8,500 randomly selected adults aged 18 and older from all five boroughs of NYC (Manhattan, Brooklyn, Queens, Bronx, and Staten Island)\textsuperscript{66}. The CDS collects information regarding demographic, geographic, diseases and specific health conditions from reported cases of communicable diseases for monitoring and disease control\textsuperscript{67}. The NYC Department of Health and Mental Hygiene files the reported communicable disease cases with CDS in order to clean, analyze, and report the data for public health surveillance\textsuperscript{67}. Second, the strength of our study includes the advantage of hierarchical multilevel modeling. The modeling allows us to comprehensively include covariates at the different geographical levels, which potentially affect the association between the exposure and the outcome. Lastly, the significant heterogeneity of incidence rate of liver cancer at census tract
level across UHF neighborhoods supports the rationale for selectively targeting neighborhoods where the intervention of liver cancer should be preemptively implemented.

There are several major limitations in our study. The first limitation includes disadvantages of cross sectional design; this study lacks temporality, which means that the result would scarcely contribute to the temporal relationship between the change in density of East Asian population and the change in regional incidence rate of liver cancer in neighborhoods. The second limitation comes from disadvantages of ecological study. Our study design would bring about the ecological fallacy since the minimum level of unit is the census tract level, which implies that the result of the study is not essentially applied to individuals. For instance, the percentage of marital status was significantly associated with the percentage of liver cancer incidence, but it also cannot be directly applied to the individuals with liver cancer.
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Appendix - 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Definition</th>
<th>% (or count)</th>
<th>Median (or mean)</th>
<th>95% Confidence Interval of Median</th>
<th>Quantile</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lower</td>
<td>Upper</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Q1 (25%)</td>
<td>Q3 (75%)</td>
</tr>
<tr>
<td>Population</td>
<td>Estimated population in NYC</td>
<td>R282725.18</td>
<td>3906.9</td>
<td>3815.2</td>
<td>3998.7</td>
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<tr>
<td>Incidence rate of liver cancer</td>
<td>Percentage of liver cancer cases in NYC</td>
<td>0.012%</td>
<td>0.010%</td>
<td>0.010%</td>
<td>0.011%</td>
</tr>
<tr>
<td>Foreign born east Asian</td>
<td>Estimated percentage of foreign born population from South east Asia and East Asian (China, Japan, Korea, Cambodia, Indonesia, Laos, Malaysia, Burma, Philippines, Singapore, Thailand, Vietnam, other South Eastern Asia)</td>
<td>6.642%</td>
<td>2.425%</td>
<td>2.138%</td>
<td>2.625%</td>
</tr>
<tr>
<td>Age at 65 and above</td>
<td>Estimated percentage of average population over age 65</td>
<td>12.455%</td>
<td>11.000%</td>
<td>10.000%</td>
<td>10.000%</td>
</tr>
<tr>
<td>Male population</td>
<td>Estimated percentage of average of male population</td>
<td>47.557%</td>
<td>47.155%</td>
<td>47.500%</td>
<td>47.900%</td>
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<tr>
<td>Low educational attainment</td>
<td>Estimated percent of Education attainment for over 25 year-old - less than high school diploma (less than 9th and 9th - 12th)</td>
<td>13.841%</td>
<td>12.361%</td>
<td>11.950%</td>
<td>12.735%</td>
</tr>
<tr>
<td>Below poverty level</td>
<td>Estimated percent of population below poverty line</td>
<td>20.008%</td>
<td>15.771%</td>
<td>15.008%</td>
<td>16.510%</td>
</tr>
<tr>
<td>Unemployed status</td>
<td>Estimated percent of population who did not work for last 12 months</td>
<td>20.066%</td>
<td>19.754%</td>
<td>19.380%</td>
<td>20.070%</td>
</tr>
<tr>
<td>Other than married Status</td>
<td>Estimated percentage of population who did not said &quot;yes&quot; for the marital status question</td>
<td>50.154%</td>
<td>49.512%</td>
<td>48.700%</td>
<td>50.200%</td>
</tr>
<tr>
<td>Population</td>
<td>Average of estimated population in NYC during 2010 Census Tract (N = 2120)</td>
<td>R282725.18</td>
<td>243609.6</td>
<td>210512</td>
<td>276707</td>
</tr>
<tr>
<td>Prevalence of Chronic HBV infection</td>
<td>Percentage of chronic HBV infection in 2011</td>
<td>0.094%</td>
<td>0.056%</td>
<td>0.040%</td>
<td>0.072%</td>
</tr>
<tr>
<td>Prevalence of Chronic HCV infection</td>
<td>Percentage of chronic HCV infection in 2011</td>
<td>0.094%</td>
<td>0.078%</td>
<td>0.072%</td>
<td>0.116%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Estimated count who have been told by a doctor, nurse or other health professional that they have diabetes</td>
<td>10.569%</td>
<td>13.505%</td>
<td>11.436%</td>
<td>15.514%</td>
</tr>
<tr>
<td>Obesity</td>
<td>Estimated count whose Body Mass Index (BMI) is calculated based on respondents self-reported weight and height. A BMI between 25.0 and 29.9 is classified as overweight, and a BMI of 30 or greater is classified as obese.</td>
<td>25.416%</td>
<td>25.979%</td>
<td>22.434%</td>
<td>30.532%</td>
</tr>
<tr>
<td>Heavy drinker</td>
<td>An average of more than 2 drinks per day for men and more than 1 drink per day for women</td>
<td>4.615%</td>
<td>3.939%</td>
<td>3.820%</td>
<td>4.654%</td>
</tr>
<tr>
<td>Self-reported health</td>
<td>Estimated count of people who say that their health is poor</td>
<td>24.549%</td>
<td>23.956%</td>
<td>21.976%</td>
<td>27.045%</td>
</tr>
<tr>
<td>Current smoker</td>
<td>Estimated count of people that are current or former smoker or have smoked less than 100 cigarettes ever.</td>
<td>14.048%</td>
<td>14.054%</td>
<td>13.109%</td>
<td>16.152%</td>
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<tr>
<td>Physical inactivity</td>
<td>Estimated count of people participate in any physical activities or exercises - such as running, calisthenics, golf, gardening, or walking for exercise - other than their regular job during the past 30 days</td>
<td>25.674%</td>
<td>26.828%</td>
<td>25.164%</td>
<td>27.657%</td>
</tr>
</tbody>
</table>

Table 1 Univariate Analysis
Figure 1 Distribution of age-adjusted incidence rate of liver cancer
Figure 2: Distribution of density of foreign born East Asian population
<table>
<thead>
<tr>
<th>Variable</th>
<th>RR</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Censustract level</strong></td>
<td></td>
<td></td>
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<tr>
<td>Age at 65 and above</td>
<td>1.021</td>
<td>1.016</td>
<td>1.026</td>
</tr>
<tr>
<td>Male population</td>
<td>0.988</td>
<td>0.979</td>
<td>0.998</td>
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<tr>
<td>Low educational attainment</td>
<td>1.031</td>
<td>1.026</td>
<td>1.035</td>
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<td>Unemployed status</td>
<td>1.021</td>
<td>1.017</td>
<td>1.026</td>
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<tr>
<td>Other than married Status</td>
<td>1.008</td>
<td>1.005</td>
<td>1.012</td>
</tr>
<tr>
<td>Below poverty level</td>
<td>1.011</td>
<td>1.008</td>
<td>1.014</td>
</tr>
<tr>
<td><strong>UHF neighborhood level</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Prevalence of Chronic HBV infection</td>
<td>2.335</td>
<td>1.274</td>
<td>4.278</td>
</tr>
<tr>
<td>Prevalence of Chronic HCV infection</td>
<td>46.899</td>
<td>5.940</td>
<td>370.295</td>
</tr>
<tr>
<td>Current smoker</td>
<td>1.038</td>
<td>1.005</td>
<td>1.072</td>
</tr>
<tr>
<td>Physical inactivity</td>
<td>1.019</td>
<td>1.001</td>
<td>1.039</td>
</tr>
<tr>
<td>Self-rated health</td>
<td>1.023</td>
<td>1.011</td>
<td>1.035</td>
</tr>
<tr>
<td>Obesity</td>
<td>1.008</td>
<td>0.995</td>
<td>1.021</td>
</tr>
<tr>
<td>Heavy drinker</td>
<td>0.972</td>
<td>0.933</td>
<td>1.013</td>
</tr>
<tr>
<td>Diabetes ever</td>
<td>1.021</td>
<td>0.994</td>
<td>1.048</td>
</tr>
</tbody>
</table>

*Table 2 Crude association between covariates and the outcome variable*
<table>
<thead>
<tr>
<th>Effect</th>
<th>Empty model</th>
<th>Crude Association Model</th>
<th>Fixed effect model 1</th>
<th>Mixed model 1 (Final model)</th>
<th>Full Fixed effect model</th>
<th>Mixed model 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR</td>
<td>95% CI</td>
<td>P-value</td>
<td>RR</td>
<td>95% CI</td>
<td>P-value</td>
</tr>
<tr>
<td>Intercept</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>&lt;.0001</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>Foreign born east Asian</td>
<td>1.018</td>
<td>1.014</td>
<td>1.021</td>
<td>&lt;.0001</td>
<td>1.012</td>
<td>1.009</td>
</tr>
<tr>
<td>Age at 65 and above</td>
<td>1.021</td>
<td>1.016</td>
<td>1.027</td>
<td>&lt;.0001</td>
<td>1.020</td>
<td>1.014</td>
</tr>
<tr>
<td>Male population</td>
<td>0.988</td>
<td>0.980</td>
<td>0.996</td>
<td>0.005</td>
<td>0.989</td>
<td>0.980</td>
</tr>
<tr>
<td>Low educational attainment</td>
<td>1.017</td>
<td>1.012</td>
<td>1.022</td>
<td>&lt;.0001</td>
<td>1.015</td>
<td>1.007</td>
</tr>
<tr>
<td>Unemployed status</td>
<td>1.016</td>
<td>1.010</td>
<td>1.022</td>
<td>&lt;.0001</td>
<td>1.012</td>
<td>1.006</td>
</tr>
<tr>
<td>Other than married Status</td>
<td>1.006</td>
<td>1.003</td>
<td>1.010</td>
<td>0.002</td>
<td>1.009</td>
<td>1.005</td>
</tr>
<tr>
<td>Below poverty level</td>
<td>1.001</td>
<td>0.997</td>
<td>1.004</td>
<td>0.676</td>
<td>1.007</td>
<td>0.998</td>
</tr>
</tbody>
</table>

**Census tract level**

**UHF neighborhood level**

Table 3 Multilevel Poisson regression modeling for association between density of foreign born East Asian population and regional incidence rate of liver cancer.
Table 4 Association between health indicators and liver cancer incidence rate

<table>
<thead>
<tr>
<th>Variable</th>
<th>RR</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence of Chronic HBV infection</td>
<td>1.095</td>
<td>0.628</td>
<td>1.909</td>
</tr>
<tr>
<td>Prevalence of Chronic HCV infection</td>
<td>7.475</td>
<td>1.644</td>
<td>33.981</td>
</tr>
<tr>
<td>Current smoker</td>
<td>1.026</td>
<td>1.003</td>
<td>1.049</td>
</tr>
<tr>
<td>Physical inactivity</td>
<td>1.005</td>
<td>0.990</td>
<td>1.021</td>
</tr>
<tr>
<td>Self-rated health</td>
<td>1.007</td>
<td>0.997</td>
<td>1.017</td>
</tr>
<tr>
<td>Obesity</td>
<td>1.006</td>
<td>0.997</td>
<td>1.015</td>
</tr>
<tr>
<td>Heavy drinker</td>
<td>0.997</td>
<td>0.967</td>
<td>1.029</td>
</tr>
<tr>
<td>Diabetes ever</td>
<td>1.005</td>
<td>0.986</td>
<td>1.024</td>
</tr>
</tbody>
</table>

* Each model includes significantly controlled variables: East Asian population, age at 65 and over, low education attainment, working status, and marital status
Appendix – 2

Age at 65 and Over
per 100,000 [35]
- 8115 - 10410 [8]
- 10410 - 12705 [12]
- 12705 - 15000 [7]
- 15000 - 17295 [5]
- 17295 - 19590 [2]

Figure 3 Age at 65 and over
Figure 4 Male population
Figure 5 Low education attainment
Figure 6 Working status
Figure 7 Other than married status
Figure 8 Below poverty level
Figure 9 Prevalence of Chronic HBV
Figure 10 Prevalence of chronic HCV
Figure 11 Current Smoker
Figure 12 Physical inactivity
Figure 13 Self-reported health status
Figure 14 Obesity
Figure 15 Heavy drinker
Figure 16: Diabetes ever