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**Predictors of a Successful Outcome among Adult
Smokers using Smoking Cessation Medication**

By

Xin Wang

A thesis submitted in partial fulfillment of

the requirement for the degree of

Master of Science

in

Pharmacy Administration

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College of Pharmacy

Predictors of a Successful Outcome among Adult Smokers using Smoking Cessation Medication

To the faculty of the University of Houston, College of Pharmacy:

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Abstract

Title: Predictors of a Successful Outcome among Adult Smokers using Smoking Cessation Medication

Introduction: Our objectives were to assess the smoking cessation medication utilization patterns among adult smokers in 2011 and identify predictors of successful outcome among adult smokers using each type of smoking cessation medication.

Methods: A retrospective cross-sectional study and a retrospective cohort study were conducted to achieve objective I and objective II of our study using GE healthcare clinical data. Descriptive statistics were used to provide estimates of the utilization rates of each smoking cessation medication (varenicline, bupropion, NRT) in 2011. Multivariate logistic regression models were conducted to identify predictors of successful outcome among adult smokers using each type of smoking cessation medication using Andersen's health service utilization model as conceptual framework. SAS 9.3 was used in our study with a significance level of 0.05.

Results: The final cohort for objective I consisted of 886,604 current adult smokers in 2011. Among these smokers, 5.66% have been prescribed a smoking cessation medication, which included varenicline, bupropion or NRT. The use rate of varenicline in 2011 was 3.69%, followed by NRT (2.00%) and bupropion (0.18%). For objective II, we found age, gender, race, region, payment type, specialty group, baseline BMI, smoking cessation counseling, number of cigarettes smoking per day and comorbidities including hypertension, hyperlipidemia, lung cancer, diabetes and AMI were significant predictors of successful quitting for smokers who were prescribed varenicline. Age, race, baseline BMI, smoking cessation counseling, number of cigarettes smoking per day, and comorbidities including hyperlipidemia, stroke, COPD and

depression were significant predictors of successful quitting for smokers who were prescribed bupropion. Age, gender, race, region, payment type, specialty group, baseline BMI, smoking cessation counseling, number of cigarettes smoking per day, and comorbidities including lung cancer, stroke, COPD and AMI were significant predictors of successful quitting among smokers who were prescribed NRT.

Conclusions: Each different type of smoking cessation medication may be particularly beneficial to certain smoking subpopulations in real life world. NRT was more effective among patients with COPD compared to those without COPD. Bupropion could be more beneficial to smokers with depression compared to those without depression. NRT could be more beneficial to male smokers vs female smokers. Varenicline might be more beneficial to female smokers in a real world setting.

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Chapter One

Introduction and Statement of the Problem

Cigarette smoking

Cigarette smoking is a major avoidable cause of death and disability (CDC, 2006), accounting for approximately 440,000 deaths annually in the United States (CDC,2002; Mokdad et al., 2004). Cigarette smoking is the cause of many diseases including cardiovascular diseases, chronic obstructive pulmonary disease (COPD), stroke, multiple cancers, complications of pregnancy (Fiore et al., 2008). Nicotine dependence is regarded as a chronic disease since only a few of tobacco users are abstinent permanently after the first attempt to quit, while, most of them fail or relapse after first quit attempt. Cigarette smoking causes a huge economic burden to individual smokers and the whole society, which accounts for 96 billion dollars' expenditure in direct medical cost each year and 97 billion dollars in lost productivity (Fiore et al., 2008).

There are approximately 45 million current adult smokers in the US (Fiore et al., 2008). An estimated 19% of women and 23% of men are current smokers (Audrain et al., 2011). More than 70 percent of the 45 million smokers reported that they were willing to quit and almost half of those smokers had an attempt to quit. Unfortunately most of those attempting failed, only 4 to 7 percent of the 19 million adults who tried to quit in year 2005 achieved successful cessation (Fiore et al., 2008). In 2010, 68.8% of adult smokers wanted to quit smoking and 52.4% had made a quit attempt in the past year, 6.2% had recently quit. Additionally, 48.3% of those adult

smokers had been advised by a health professional to quit and 31.7% had used counseling and/or medications when they tried to quit (CDC, 2011).

Smoking Cessation

The 2008 Clinical Practice Guidelines of Treating Tobacco Use and Dependence recommended the use of pharmacotherapy for all smokers who wanted to make attempts to quit, except those having contradictions or some specific population for whom insufficient evidence of effectiveness exists (i.e., pregnant women, smokeless tobacco users, light smokers, and adolescents).

Currently there are seven first-line medications approved by the U.S. Food and Drug Administration which can help increase long-term smoking abstinence rates reliably. They are varenicline, bupropion SR, Nicotine gum, Nicotine inhaler, Nicotine lozenge, Nicotine nasal spray, and Nicotine patch. Nicotine gum, Nicotine inhaler, Nicotine lozenge, Nicotine nasal spray, and Nicotine patch were also classified as Nicotine Replacement Therapy (NRT) (Ebbert et al., 2007; Fiore et al., 2008).

Smoking Cessation Medication

Nicotine Replacement Therapy (NRT) is the most common first-line pharmacotherapy used for smoking cessation, the aim of which is to replace much of the nicotine in cigarettes in order to reduce smokers' craving for smoking and nicotine withdrawal symptoms often experienced during an attempt to quit, thus increasing the likelihood of remaining abstinent. There are five available forms of Nicotine Replacement Therapy: nicotine gum, transdermal patch, nasal spray, inhaler and sublingual tablets/lozenges (West et al., 2001).

The main results from a review which identified 132 trials indicated that the risk ratio(RR) of abstinence for any form of NRT compared to control was 1.58 (95% confidence interval[CI]: 1.50 to 1.66) and the pooled risk ratio (RR) for each type of NRT were 1.43 (95% CI: 1.33 to 1.53, 53 trials) for nicotine gum; 1.66 (95% CI: 1.53 to 1.81, 41 trials) for nicotine patch; 1.90 (95% CI: 1.36 to 2.67, 4 trials) for nicotine inhaler; 2.00 (95% CI: 1.63 to 2.45, 6 trials) for oral tablets/lozenges; and 2.02 (95% CI: 1.49 to 3.73, 4 trials) for nicotine nasal spray (Stead et al., 2008).

Another FDA-approved first line smoking cessation medication is sustained release bupropion (bupropion SR), approved for use in smoking cessation in the United States since 1997. It is an aminoketone antidepressant which aids smoking cessation by inhibiting dopamine reuptake in the mesolimbic dopamine system (Jorenby et al., 2006).

A systematic review and meta-analysis of effectiveness of smoking cessation therapies identified 12 randomized control trials which used bupropion versus placebo and yielded odds ratios (OR) ranging from 1.72–2.64 compared with placebo at 3 months and yielded ORs ranging from 1.10 to 2.21 compared with placebo at 1 year(Wu et al., 2006). In addition, another study reported that bupropion improved smoking cessation rates compared to nicotine patch (Jorenby et al., 1999). Bupropion can also delay relapse after successful abstinence for the smokers (Hays et al., 2001).

Varenicline, a partial agonist of the nicotinic acetylcholine receptor, (Chantix® in the United States) is a first-line FDA approved smoking cessation medication which has been used in the United States since August 1, 2006. Clinical studies suggest that varenicline has demonstrated clinical efficacy as a smoking cessation medication with relative risks for quitting of

approximately 2.5–3 times that of a placebo (Gonzales et al., 2006; Cahill et al., 2007; Jorenby et al., 2006).

A systematic review and meta-analysis of effectiveness of smoking cessation therapies identified 12 randomized control trials which evaluated varenicline versus placebo at 3 months and 1 year and yielded ORs ranging from 2.65–5.30 compared with placebo at 3 months and yielded ORs ranging from 2.12–4.12 compared with placebo at 1 year. Also this meta-analysis identified 3 RCTs which evaluated the effectiveness of varenicline versus bupropion, yielding ORs ranging from 1.22–2.05 at 1 year and 1.16–2.21 at 3 months (Wu et al., 2006).

Chapter Two

Literature Review and Statement of Problem

Literature on smoking cessation medication prescribing and predictors of success in smoking cessation

Langley et al. (Langley et al, 2011) conducted a study to examine the effects of introduction of varenicline on trends of other cessation medications prescribing in UK between 2000 and 2009. They found NRT was previously the most commonly prescribed smoking cessation medication and bupropion was prescribed least frequently. After being introduced in UK in December 2006, varenicline became the second most commonly prescribed cessation medication after nicotine replacement therapy.

Similarly, another study which was also conducted in UK by Kotz et al, 2011. (Kotz et al, 2011) and assessed whether varenicline affected the use of other smoking cessation medications from 2006 to 2009 in UK. They found varenicline utilization increased steadily year by year, while the utilization of bupropion remained unchanged.

A study conducted by Brian et al. which examined the utilization of smoking cessation medication from 2006 to 2008 in the United States, United Kingdom, Australia, and Canada has indicated that varenicline has become the second most widely prescribed smoking cessation medication, behind NRT and its use rate was increasing each year after being introduced into the market. In 2008, the use rate of varenicline was even comparable to that of NRT (21.7% *v.s.*

22.2%, respectively) in the US. No statistical differences were found in the use rates of NRT or bupropion during the same time period in these four countries (Brian et al., 2011). Based on previous literature, the use rate of varenicline was much higher than that of bupropion since it was approved for treating smoking cessation by FDA in 2006, despite reports of psychiatric adverse events (behaviour changes, depressed mood and self-injurious thoughts or behaviours) and many other common adverse events possibly related to varenicline treatment (Hays et al., 2010).

A number of studies have been carried out to identify the factors which are likely to lead to a successful outcome for the smokers. For example, there was a study conducted by Nerín et al., which identified the predictors of a successful outcome in a smoking cessation program at 6-month follow up. The result has indicated that individuals who fully comply with treatment and abstain from smoking during the first weeks are more likely to be successful at 6 months (Nerín et al., 2004). Hyland et al. (Hyland et al, 2004) conducted a study in US and Canada to identify predictors of smoking cessation. They followed the cohort of smokers over 13 years and found nicotine dependence is a major factor predicting long-term cessation in smokers, Other predictors included male gender, older age, higher income, and less frequent alcohol consumption.

Another study which was conducted by Swan et al. has identified the predictors of the 12-month outcome in smokers who received bupropion for smoking cessation. The study has documented a wide degree of variation in the outcome following treatment with both dosages of bupropion SR, with substantial cost consequences. Authors suggested that variation in outcome could be reduced by tailoring treatments to subgroups of individuals who are at high risk of smoking after

a quit attempt (Swan et al., 2008). Harris et al. conducted a study which identified factors that predicted successful quitting among African-Americans participating in a smoking cessation trial. The result has shown that, aside from bupropion treatment, various indicators of addiction were the strongest predictors (Harris et al., 2004). There is another study conducted by Nollen et al. which examined the predictors of successful quitting among African American (AA) light smokers who were enrolled in a smoking cessation trial. They found counseling and some other individual characteristics like older age, gender, higher BMI, higher income and treatment compliance were significant predictors of quitting (Nollen et al., 2006).

In summary, in the previous literature in terms of smoking cessation medication prescribing, it has been found that in UK, from 2000 to 2009 NRT was the most commonly prescribed smoking cessation medication, varenicline has become the second most commonly prescribed smoking cessation medication, while varenicline use increased steadily and in US, from 2006 to 2008, varenicline has become the second most widely prescribed smoking cessation medication, behind NRT and its use rate was increasing each year. In 2008, the use rate of varenicline was even comparable to that of NRT. In terms of predictors of successful quitting, it has been found multiple factors like treatment compliance, indicators of addiction, nicotine dependence and individual characteristics like older age, gender, higher BMI, higher income were significant predictors of successful quitting.

Statement of Problem

While the efficacy of various prescription smoking cessation medications has been well-demonstrated by clinical studies (Gonzales et al., 2006) and the utilization patterns of smoking cessation medications from 2006 to 2008 in US have been examined, to date, no population-

based study has investigated the use rate of varenicline in US after 2008 and whether it is displacing other smoking cessation medications. In addition, predictors of successful smoking cessation compared to placebo have been reported (Harris et al., 2004), yet, to date, no study has evaluated the factors that predict successful quitting among users of each of the available prescription cessation medications in a real world setting. This study aims to assess the utilization patterns of prescription smoking cessation medications (NRT, bupropion and varenicline) and then identify and compare the predictors of successful quitting among patients who have been prescribed each type of smoking cessation medication. Evaluating change in smoking cessation medication use over time can provide a better understanding of effective pharmacotherapy strategies to treat smoking and promote cessation. Identifying and comparing predictors of a successful outcome among patients using each type of cessation medications can help define subgroups of patients that are more likely to benefit from a specific medication and achieve a successful cessation. This knowledge will provide a better understanding of effective pharmacotherapy strategies and aid policy-makers as well as clinicians in optimizing drug regimens to treat adult smokers.

Objective

Objective1: To assess the smoking cessation medication utilization patterns among adult smokers in 2011

Hypothesis I: The use rate of varenicline is higher than that of NRT, while the use rate of bupropion remains the lowest.

Objective 2: To identify predictors of successful outcome among adult smokers using each type of smoking cessation medication.

Hypothesis II: Older age, race, fewer cigarettes smoked per day, higher BMI, comorbidities are predictors of successful outcome. There are differences in significant predictors of successful quitting among smokers using each type of cessation medication.

Chapter Three

Methods

Study design

For objective I, the study was a retrospective cross-sectional study and for objective II, the study was a retrospective cohort study.

Data Source/ Study Setting

The data source for this study was GE healthcare clinical data. GE healthcare clinical data is a real-world observational, daily-updated data, which represents national clinical data. Millions of patients' information in the ambulatory primary care setting in the United States has been recorded in GE healthcare clinical data. For example, for the year of 2011, GE healthcare clinical data had approximately 20 million unique patients. GE healthcare clinical data can provide a reliable platform for medication utilization and predictors of successful quitting with its ability to demonstrate dynamic change in health of the United States population, capture geographic variation, practice patterns, and outbreaks. Additionally, an average of 4 years of follow-up per patient, and monitoring in near real time of clinical signs and symptoms, comorbidities, labs, procedures, medication history, prescription written, make GE data appropriate for our study.

The information documented in GE data, such as documented medications and prescriptions, documented diagnoses, the records of smoking status were used in this study. In Centricity Electronic Medical Record (EMR), both ICD-9 codes as well as more granular clinical concepts were included to identify more specific problems within a patient's medical record. GE healthcare clinical data has the results of lab tests (in both numeric and test form), vital signs

such as pulse rate, blood pressure, height and weight, calculations such as BMI, and other clinical findings associated with patient care like pain scores that are not available in other databases.

Both medications and prescriptions, which are different from each other, are documented in the database. Medications may include a broader list of all medications that a patient is taking including over the counter medications, herbal remedies and medications prescribed by a provider that may be out of the EMR network. On the other hand, prescriptions are medications that have been prescribed by the responsible provider of this patient within the EMR.

Medications include: medications documented by history, medications being actively prescribed by another provider, and medications being prescribed by the documenting provider, while prescriptions include medications being prescribed by the documenting provider. The unique characteristics of the GE healthcare clinical data mentioned above and availability of smoking status information make it the ideal clinical database to be used for conducting this study. GE clinical data and other electronic medical record data (EMR) have been widely used in the previous literature to study smoking and smoking cessation (Thomas et al. 2007; Hazlehurst et al. 2005; Bentz et al. 2002; McGinnis et al. 2011). For example, there is one study conducted in the United States among the first to use EMR data to examine differences in tobacco use associated with acculturation among various population groups (Parker et al., 2010).

Research Involving Human Subjects

This study did not involve human subjects directly; patients' information already collected by physician orders was used. The patients' information in GE data is not directly identifiable; any means to identify or contact the respondents is prohibited by the Federal Law. This study was approved from the University of Houston Committees for the Protection of Human Subjects.

Study Population

Selection of patients

The inclusion criteria for identifying the cohort for objective I: 1) aged 18 years or older, 2) enrolled in the GE healthcare clinical data in the United States in 2011, 3) current smoker.

The inclusion criteria for identifying the study cohort for objective II: 1) aged 18 years or older, 2) enrolled in the GE healthcare clinical data in the United States between January 2006 and December 2011 (Bupropion was first approved by FDA as the non-nicotine medication for smoking cessation in 1997, while varenicline was first approved in 2006), 3) have been prescribed at least one of the following smoking cessation medications (varenicline, bupropion or NRT)

Exclusion criteria for our study: having missing data on smoking status.

In GE healthcare clinical data, patients' smoking status was recorded in Text Observation Data Files. Smoking status was categorized as never smoked, formerly smoked, not currently smoking, and currently smoking. Patients who had observation group name ('smoking status') and observation value of 'current' were identified as smokers.

Statistical Analyses

Objective I: Assess the smoking cessation medication utilization patterns among adult smokers in 2011

Descriptive statistics were used to provide estimates of the utilization rates of each smoking cessation medication (varenicline, bupropion, NRT) in 2011. Also, the characteristics of the smokers who have been prescribed these medications were examined and chi square tests were used to assess group differences. Variables included in the analysis were categorized as: Age:

Age group (categorized as 18 – 40; 41 – 64; ≥ 65); Gender: Female, Male; Race: White, Black and others (including Multiple races, not entered, unknown/undetermined); Region: Midwest, Northeast, South, West; Payment type: Commercial insurance, Government insurance (Medicare/Medicaid), and No insurance (self-pay); Specialty group: Primary care, Specialty care; Comorbidities: Yes/No (including hypertension, hyperlipidemia, lung cancer Stroke, COPD, diabetes, Acute Myocardial infarction and depression); Smoking Counseling: Yes/No; Number of cigarettes smoked per day: 1/>1; Alcohol consumption: Yes/No; Obesity: Normal weight, overweight, obese, extreme obese (BMI<25/25= \leq BMI<30/30= \leq BMI \leq 40/BMI>40).

Objective II: To identify predictors of a successful outcome among smokers using each type of smoking cessation medication.

An index date was defined as the first day of being prescribed a smoking cessation medication. A wash-out period was defined as not receiving any smoking cessation medication prescription during the 6 months before the index date to identify smokers who were newly prescribed smoking cessation medications. Successful outcome was defined as smokers with successful abstinence. Abstinence was defined as being reported as ‘not current’ or ‘former’ smoker at 6-month follow up time; being reported as ‘current’ smoker at 6-month follow up endpoint was categorized as non-abstinence.

All the smokers in the cohort were followed for 6 months after the index date. Smoking status of the cohort was measured at a 6 months follow up endpoint after the index date. The reason for taking a 6-month follow up time was that smoking cessation medications were usually required

for a 3-months treatment and in clinical trials 3 months follow up time was usually used to examine the efficacy of smoking cessation medication while, assessing the smoking status at 6 months after cessation treatment can help us understand the short term effect of the smoking cessation medications in a real life setting.

Three multivariate logistic regression models were constructed in order to assess the association between the outcome variable (abstinence vs. not) and independent variables.

Conceptual Framework and Variables

Andersen's health service utilization model was used as the conceptual framework (Mortensen et al., 2008). This model classifies determinants of an individual's health service utilization into predisposing, enabling, and need characteristics. Predisposing characteristics determine the baseline propensity of an individual to use health services. Enabling characteristics refer to community and personal resources an individual has, to use services. Need characteristics refer to perceived and actual need of an individual which drive the use of health services.

Model 1:

The study cohort for model 1 was comprised of smokers newly prescribed varenicline.

The dependent variable was 'abstinence or not', independent variables included predisposing, enabling and need factors.

Predisposing characteristics included Age: Age group (categorized as 18 – 40; 41 – 64; ≥ 65); Gender: Female, Male; Race: White, Black and others (including Multiple races, not entered, unknown/undetermined); Region: Midwest, Northeast, South, West.

Enabling characteristics included Payment type: Commercial insurance, Government insurance (Medicare/Medicaid), and No insurance (self-pay); Specialty group: Primary care, Specialty care.

Need characteristics included Comorbidities: Yes/No (including hypertension, hyperlipidemia, lung cancer Stroke, COPD, diabetes, Acute Myocardial infarction and depression); Smoking Counseling: Yes/No; Number of cigarettes smoked per day: 1/>1; Alcohol consumption: Yes/No; Obesity: Normal weight, overweight, obese, extreme obese (BMI<25/25=<BMI<30/30=<BMI<=40/BMI>40).

Model 2:

The study cohort for model 2 was comprised of smokers newly prescribed bupropion.

The dependent variable will be ‘abstinence or not’, independent variables include predisposing, enabling and need factors.

Predisposing characteristics include Age: Age group (categorized as 18 – 40; 41 – 64; ≥65);

Gender: Female, Male; Race: White, Black and others (including Multiple races, not entered, unknown/undetermined); Region: Midwest, Northeast, South, West.

Enabling characteristics include Payment type: Commercial insurance, Government insurance (Medicare/Medicaid), and No insurance (self-pay); Specialty group: Primary care, Specialty care.

Need characteristics included Comorbidities: Yes/No (including hypertension, hyperlipidemia, lung cancer Stroke, COPD, diabetes, Acute Myocardial infarction and depression); Smoking Counseling: Yes/No; Number of cigarettes smoked per day: 1/>1; Alcohol consumption:

Yes/No; Obesity: Normal weight, overweight, obese, extreme obese
(BMI<25/25=<BMI<30/30=<BMI<=40/BMI>40).

Model 3:

The study cohort for model 3 was comprised of smokers newly prescribed NRT.

The dependent variable were 'abstinence or not', independent variables included predisposing, enabling and need factors.

Predisposing characteristics included Age: Age group (categorized as 18 – 40; 41 – 64; ≥65);

Gender: Female, Male; Race: White and others (including Multiple races, not entered, unknown/undetermined); Region: Midwest, Northeast, South, West.

Enabling characteristics included Payment type: Commercial insurance, Government insurance (Medicare/Medicaid), and No insurance (self-pay); Specialty group: Primary care, Specialty care.

Need characteristics included Comorbidities: Yes/No (including hypertension, hyperlipidemia, lung cancer Stroke, COPD, diabetes, Acute Myocardial infarction and depression); Smoking

Counseling: Yes/No; Number of cigarettes smoked per day: 1/>1; Alcohol consumption:

Yes/No; Obesity: Normal weight, overweight, obese, extreme obese
(BMI<25/25=<BMI<30/30=<BMI<=40/BMI>40).

All the statistical analysis were performed using SAS 9.3, with a 95% confidence interval and a

prior significant level at $p < 0.05$. Univariate logistic regression models were used to estimate the unadjusted association of each independent variable with the dependent variable with cutoff of 0.20 for inclusion in the multivariate logistic regression models to control for predisposing, enabling and need factors (All those variables with p value less than 0.20 in univariate analysis were included in the multivariate model). A multi-collinearity test was carried out and variables were removed if correlation coefficients had a value greater than 0.7 and/or the variance inflation factor (VIF) was greater than 10. Backward elimination was used to arrive at the final multivariate logistic regression model. Adjusted odds ratios (OR) and 95% confidence interval (CI) were presented.

Chapter 4

Results

Result for objective I

The final cohort for objective I consisted of 886,604 current adult smokers in 2011. Among these smokers, 5.66% have been prescribed a smoking cessation medication, which included varenicline, bupropion or NRT. The use rate of varenicline in 2011 was 3.69%, followed by NRT (2.00%) and bupropion (0.18%). For the smokers who have been prescribed varenicline, 34.41% of them aged between 18 and 40, 58.03% aged between 41 and 64 and 7.56% aged more than 65. Among these smokers who were prescribed varenicline, 47.84% of them were white, 4.54% were black and 47.62% were other races which included Hispanic, Asian and other races. Based on smokers' BMI, 32.76% of them had normal weight ($BMI < 25$), 29.98% of them were overweight ($25 \leq BMI < 30$), 30.00% of them were obese ($30 \leq BMI \leq 40$) and 7.26% of them were extreme obese ($BMI > 40$). In terms of residency distribution, 27.16% of these smokers lived in the Midwest, 26.97% of them lived in the Northwest, 27.46% of them lived in South and 18.40% of them lived in the West. For the smokers who have been prescribed bupropion, 34.60% of them aged between 18 and 40, 56.13% aged between 41 and 64 and 9.26% aged more than 65. Among these smokers who have been prescribed bupropion, 44.85% of them were white, 9.33% were black and 45.83% were other races which included Hispanic, Asian and other races. Based on smokers' BMI, 33.37% of them had normal weight ($BMI < 25$), 29.94% of them were overweight ($25 \leq BMI < 30$), 29.45% of them were obese ($30 \leq BMI \leq 40$) and 7.24% of them were extreme obese ($BMI > 40$). In terms of residency distribution, 30.31% of these smokers

lived in the Midwest, 19.88% of them lived in the Northwest, 31.90% of them lived in South and 17.91% of them lived in the West. For the smokers who have been prescribed NRT, 32.51% of them aged between 18 and 40, 58.69% aged between 41 and 64 and 8.80% aged more than 65. Among these smokers who have been prescribed NRT, 47.16% of them were white, 13.47% were black and 39.37% were other races which included Hispanic, Asian and other races. Based on smokers' BMI, 34.87% of them had normal weight ($BMI < 25$), 27.18% of them were overweight ($25 \leq BMI < 30$), 29.31% of them were obese ($30 \leq BMI \leq 40$) and 8.64% of them were extreme obese ($BMI > 40$). In terms of residency distribution, 29.38% of these smokers lived in the Midwest, 39.88% of them lived in the Northwest, 15.85% of them lived in South and 14.89% of them lived in the West. Chi-square tests showed that there were group differences between those who have been prescribed varenicline and those who haven't been prescribed varenicline. Age, gender, race, region, payment, specialty group, obesity, number of cigarette smoking per day and alcohol consumption, comorbidities including hypertension, hyperlipidemia, lung cancer, stroke, COPD, diabetes, AMI and depression were found to be statistically significant variables which were associated with varenicline prescribing. Also, there were group differences between those who have been prescribed bupropion and those haven't. Age, gender, race, region, payment, specialty group, obesity, number of cigarette smoking per day and alcohol consumption, comorbidities including hypertension, hyperlipidemia, lung cancer, COPD and depression were found to be statistically significant variables which were associated with bupropion prescribing. Similarly, there were group differences between those who have been prescribed NRT and those who haven't been prescribed NRT. Age, gender, race, region, payment, specialty group, obesity, number of cigarette smoking per day and alcohol consumption, comorbidities including hypertension, hyperlipidemia, lung cancer, stroke, COPD,

diabetes, AMI and depression were found to be statistically significant variables which were associated with NRT prescribing. Complete results of socio-demographic characteristics of the smokers who were prescribed each medication and group differences are shown in Table 1.

Table 1. Baseline characteristics for smokers that were prescribed each cessation medication in 2011

	Total, N=886604 (100%)	With Varenicline N=32688 (3.69%)	Without Varenicline	p-value	With Bupropion N=1630 (0.18%)	Without Bupropion	p-value	With NRT N=17716 (2.00%)	Without NRT	p-value	With any cessation medication N=50157 (5.66%)	Without any cessation medication	p-value
<i>Predisposing characteristics</i>													
Age (±SD)	46.01 (15.95)	46.10 (12.74)	46.01 (16.05)		46.40 (13.37)	46.01 (15.95)		46.53 (13.45)	46.00 (15.99)		46.25 (13.02)	45.99 (16.10)	
Age group				<0.0001*			<0.0001*			<0.0001*			<0.0001*
18-40	38.36	34.41	37.09		34.60	38.36		32.51	38.48		33.86	38.63	
41-64	47.97	58.03	45.83		56.13	47.95		58.69	47.75		58.10	47.36	
≥65	13.67	7.56	13.39		9.26	13.68		8.80	13.77		8.04	14.01	
Gender				0.0110*			0.0105*			<0.0001*			0.3552
Female	55.48	54.79	55.50		58.62	55.47		57.49	55.44		55.68	55.47	
Male	44.52	45.21	44.50		41.38	44.53		42.51	44.56		44.32	44.53	
Race				<0.0001*			0.0128*			<0.0001*			<0.0001*
Black	7.47	4.54	7.58		9.33	7.46		13.47	7.34		7.69	7.45	
White	44.85	47.84	44.74		44.85	44.85		47.16	44.81		47.40	44.70	
Others	47.68	47.62	47.68		45.83	47.68		39.37	47.85		44.92	47.84	
Region				<0.0001*			<0.0001*			<0.0001*			<0.0001*

Midwest	27.71	27.16	27.73	30.31	27.71	29.38	27.68	27.92	27.70
Northeast	24.88	26.97	24.80	19.88	24.89	39.88	24.58	30.96	24.52
South	30.80	27.46	30.93	31.90	30.80	15.85	31.11	23.83	31.22
West	16.60	18.40	16.53	17.91	16.60	14.89	16.64	17.29	16.56
<i>Enabling characteristics</i>									
Payment type				<0.0001*		<0.0001*		<0.0001*	<0.0001*
Commercial	32.14	38.55	30.71	32.12	38.59	29.75	32.18	35.72	31.92
Medi-care/caid	16.57	12.89	16.10	16.58	14.85	23.80	16.42	16.39	16.58
Self-paid	4.49	2.80	4.39	4.50	2.88	2.75	4.53	2.82	4.59
Unknown	46.80	45.76	45.11	46.81	43.68	43.69	46.86	45.06	46.90
Specialty group				<0.0001*		<0.0001*		<0.0001*	<0.0001*
Primary Care	49.12	65.36	46.71	61.35	49.10	63.94	48.82	64.63	48.19
Specialty care	11.29	4.13	11.14	5.83	11.30	3.34	11.45	3.96	11.73
Unknown	39.59	30.51	38.46	32.82	39.60	32.72	39.73	31.41	40.08
<i>Need characteristics</i>									
Hypertension				<0.0001*		<0.0001*		<0.0001*	<0.0001*
Yes	7.10	7.89	7.07	10.86	7.10	9.20	7.06	8.39	7.03
No	92.90	92.11	92.93	89.14	92.90	90.80	92.94	91.61	92.97
Hyperlipidemia				<0.0001*		<0.0001*		<0.0001*	<0.0001*
Yes	7.04	10.31	6.91	12.39	7.03	9.80	6.98	10.17	6.85

No	92.96	89.69	93.09		87.61	92.97		90.20	93.02		89.83	93.15
Lung cancer				<0.0001*			<0.0001*			<0.0001*		<0.0001*
Yes	0.63	1.28	0.60		2.02	0.62		1.82	0.60		1.42	0.58
No	99.37	98.72	99.40		97.98	99.38		98.18	99.40		98.58	99.42
Stroke				0.0020*			0.7276*			<0.0001*		<0.0001*
Yes	0.90	1.06	0.89		0.98	0.90		1.55	0.89		1.21	0.88
No	99.10	98.94	99.11		99.02	99.10		98.45	99.11		98.79	99.12
COPD				<0.0001*			<0.0001*			<0.0001*		<0.0001*
Yes	3.64	7.16	3.51		7.48	3.63		9.39	3.52		7.70	3.40
No	96.36	92.84	96.49		92.52	96.37		90.61	96.48		92.30	96.60
Diabetes				0.5145			0.1409			<0.0001*		<0.0001*
Yes	3.28	3.34	3.28		3.93	3.28		4.44	3.25		3.68	3.25
No	96.72	96.66	96.72		96.07	96.72		95.56	96.75		96.32	96.75
AMI				<0.0001*			0.7695			<0.0001*		<0.0001*
Yes	0.21	0.34	0.21		0.25	0.21		0.76	0.20		0.48	0.20
No	99.79	99.66	99.79		99.75	99.79		99.24	99.80		99.52	99.80
Depression				<0.0001*			<0.0001*			<0.0001*		<0.0001*
Yes	5.31	6.34	5.27		8.90	5.30		9.38	5.22		7.37	5.18
No	94.69	93.66	94.73		91.10	94.70		90.62	94.78		92.63	94.82
Obesity				<0.0001*			<0.0001*			<0.0001*		<0.0001*
Normal weight	39.67	32.76	39.93		33.37	39.68		34.87	39.77		33.61	40.03
Overweight	27.03	29.98	26.92		29.94	27.03		27.18	27.03		29.06	26.91

Obese	26.65	30.00	26.52	29.45	26.64	29.31	26.59	29.71	26.46
Extreme obese	6.65	7.26	6.63	7.24	6.65	8.64	6.61	7.62	6.59
Smoking counseling				<0.0001*		<0.0001*		<0.0001*	<0.0001*
Yes	46.28	59.68	45.77	55.15	46.27	61.13	45.98	59.99	45.46
No	53.72	40.32	54.23	44.85	53.73	38.87	54.02	40.01	54.54
# of cigarettes/day				<0.0001*		<0.0001*		<0.0001*	<0.0001*
1	49.84	41.23	50.17	37.30	49.86	31.66	50.21	38.16	50.54
>1	50.16	58.77	49.83	62.70	50.14	68.34	49.79	61.84	49.46
Alcohol consumption				<0.0001*		0.0160*		<0.0001*	<0.0001*
Yes	2.08	1.31	2.11	1.23	2.08	1.07	2.10	1.22	2.13
No	97.92	98.69	97.89	98.77	97.92	98.93	97.90	98.78	97.87

Result for objective II

Baseline sample characteristics for smokers who were prescribed varenicline (Model 1)

The total sample for model I consisted of 132,885 adult smokers who were newly prescribed varenicline between 2006 and 2011. Among the cohort, 18.28% of them were abstinent successfully at 6-month follow up time. The cohort had a mean age of 45.41(\pm 12.81), 56.78% of them aged between 41 and 64, 36.05% of them aged between 18 and 40 and 7.17% of them were older than 65. Among the analytical cohort, 53.44% were female smokers and 46.56% were male smokers. In terms of race, 40.89% of them were white smokers, 3.57% of them were black smokers and 55.54% of them were other races which included Hispanic, Asian and other races. Among these smokers, 28.06% of them lived in the Midwest, 26.06% of them lived in the Northeast, 28.63% of them lived in the South and 17.25% of them lived in the West. Based on smokers' BMI, 29.53% of them had normal weight, 32.92% of them were overweight, 30.69% of them were obese and 6.87% of them were extreme obese. In terms of quitting successfully, 18.28% of them were abstinent at 6-month follow up time. Complete descriptive statistics of the analytical cohort in model 1 were shown in table 2.

Table 2. Descriptive statistics of analytic cohort that has been prescribed varenicline

	Total, N=132885 (100%)	Abstinent at 6 months N=24294 (18.28%)	Not abstinent at 6 month N=108591 (81.72%)	p-value
<i>Predisposing characteristics</i>				
Age (±SD)	45.41(12.81)	46.91(13.28)	45.08(12.67)	
Age group				<0.0001*
18-40	36.05	33.14	36.70	
41-64	56.78	56.88	56.76	
>=65	7.17	9.98	6.54	
Gender				<0.0001*
Female	53.44	55.93	52.89	
Male	46.56	44.07	47.11	
Race				<0.0001*
Black	3.57	3.06	3.68	
White	40.89	42.11	40.62	
Others	55.54	54.83	55.70	
Region				<0.0001*
Midwest	28.06	27.41	28.21	
Northeast	26.06	25.25	26.24	
South	28.63	27.90	28.79	
West	17.25	19.44	16.76	

<i>Enabling characteristics</i>			
Payment type			<0.0001*
Commercial	41.63	41.75	41.60
Medi-care/caid	13.31	14.51	13.04
Self-paid	2.95	2.38	3.07
Unknown	42.12	41.37	42.29
Specialty group			<0.0001*
Primary Care	64.29	64.68	64.16
Specialty care	4.29	5.72	3.97
Unknown	31.42	29.42	31.86
<i>Need characteristics</i>			
Hypertension			<0.0001*
Yes	7.12	7.99	6.93
No	92.88	92.01	93.07
Hyperlipidemia			<0.0001*
Yes	10.38	11.37	10.16
No	89.62	88.63	89.84
Lung cancer			<0.0001*
Yes	0.86	1.45	0.73
No	99.14	98.55	99.27
Stroke			<0.0001*
Yes	0.80	1.02	0.74
No	99.20	98.98	99.26

COPD				0.0386*
Yes	5.49	5.77	5.43	
No	94.51	94.23	94.57	
Diabetes				<0.0001*
Yes	2.63	3.28	2.48	
No	97.37	96.72	97.52	
AMI				<0.0001*
Yes	0.23	0.40	0.19	
No	99.77	99.60	99.81	
Depression				0.0257*
Yes	5.22	5.50	5.15	
No	94.78	94.50	94.85	
Obesity				<0.0001*
Normal weight	29.53	26.57	30.20	
Overweight	32.92	32.08	33.11	
Obese	30.69	33.09	30.14	
Extreme obese	6.87	8.26	6.55	
Smoking counseling				<0.0001*
Yes	50.69	28.24	55.71	
No	49.31	71.76	44.29	
# of cigarettes/day				<0.0001*
1	44.69	50.79	43.33	
>1	55.31	49.21	56.67	

Alcohol consumption				0.2847
Yes	1.18	1.24	1.16	
No	98.82	98.76	98.84	

Logistic regression results for smokers that have been prescribed varenicline (Model 1)

Univariate logistic regression results showed that for adult smokers who were newly prescribed varenicline, those who were aged between 41 and 64 (odds ratio [OR]: 1.110, 95% confidence interval [CI]: 1.077-1.144) and those who were more than 65 years old (OR: 1.691, 95% CI: 1.606-1.782) were more likely to be abstinent compared to those aged between 18 and 40. White smokers were more likely to quit compared to black smokers (OR: 1.248, 95% CI: 1.151-1.354). Smokers who had no insurance were less likely to be abstinent than those who were covered by commercial insurance (OR: 0.770, 95% CI: 0.703-0.843). Smokers with specialty care were more likely to successfully quit compared to those who received primary care (OR: 1.425, 95% CI: 1.338-1.518). Smokers who were overweight (OR: 1.101, 95% CI: 1.059-1.145), obese (OR: 1.248, 95% CI: 1.200-1.297) and extreme obese smokers (OR: 1.434, 95% CI: 1.350-1.524) were more likely to successfully quit than those with normal weight. Smokers with hypertension (OR: 1.168, 95% CI: 1.108-1.230), hyperlipidemia (OR: 1.135, 95% CI: 1.086-1.186), lung cancer (OR: 1.997, 95% CI: 1.760-2.265), diabetes (OR: 1.334, 95% CI: 1.231-1.445) and acute myocardial infarction (OR: 2.109, 95% CI: 1.656-2.686) were more likely to quit compared to those without these comorbidities. Complete univariate logistic regression results are shown in Table 5. Multivariate logistic regression results showed that for adult smokers who were newly prescribed varenicline, those who were aged between 41 and 64 (OR: 1.089, 95% [CI]: 1.053-1.127) and those who were more than 65 years old (OR: 1.666, 95% CI: 1.564-1.775) were more likely to be abstinent compared to those aged between 18 and 40. White smokers were more likely to quit compared to black smokers (OR: 1.232, 95% CI: 1.127-1.346). Male smokers were less likely to be abstinent compared with female smokers (OR: 0.878, 95% CI: 0.851-0.907). Smokers who lived in the Northeast (OR: 1.196, 95% CI: 1.144-1.249), Southern United States

(OR: 1.662, 95% CI: 1.113-1.214) and those who lived in the Western United States (OR: 1.321, 95% CI: 1.259-1.386) were more likely to be abstinent than those who lived in Midwest. Smokers who had no insurance were less likely to be abstinent than those who were covered by commercial insurance (OR: 0.785, 95% CI: 0.711-0.868). Smokers with unknown care were less likely to successfully quit compared to those who received primary care (OR: 0.872, 95% CI: 0.843-0.903). Smokers who were overweight (OR: 1.126, 95% CI: 1.081-1.173), obese (OR: 1.277, 95% CI: 1.226-1.330) and extreme obese smokers (OR: 1.487, 95% CI: 1.396-1.585) were more likely to successfully quit than those with normal weight. Smokers who have received smoking counseling were less likely to be abstinent than those without smoking counseling (OR: 0.288, 95% CI: 0.278-0.297). Smokers who reported smoking at least one cigarettes every day were less likely to be abstinent than those who didn't (OR: 0.701, 95% CI: 0.680-0.724). Smokers with hypertension (OR: 1.072, 95% CI: 1.008-1.140), hyperlipidemia (OR: 1.075, 95% CI: 1.021-1.133), lung cancer (OR: 2.043, 95% CI: 1.774-2.353), diabetes (OR: 1.187, 95% CI: 1.083-1.301) and acute myocardial infarction (OR: 1.798, 95% CI: 1.379-2.344) were more likely to quit compared to those without these comorbidities. However, comorbidities like depression, stroke, COPD were not found to be significant predictors. Similarly, alcohol consumption was not a significant predictor which would affect quitting successfully. The complete results of multivariate logistic regression were shown in Table 3.

Table3. Logistic regression models for successful outcome among smokers who have been prescribed varenicline

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
<i>Predisposing characteristics</i>		
Age group		
18-40	1	1
41-64	1.110(1.077-1.144)	1.089(1.053-1.127)
>=65	1.691(1.606-1.782)	1.666(1.564-1.775)
Gender		
Female	1	1
Male	0.885(0.860-0.910)	0.878(0.851-0.907)
Race		
Black	1	1
White	1.248(1.151-1.354)	1.232(1.127-1.346)
Others	1.185(1.093-1.284)	1.091(0.998-1.192)
Region		
Midwest	1	1
Northeast	0.990(0.953-1.029)	1.196(1.144-1.249)
South	0.997(0.961-1.035)	1.162(1.113-1.214)
West	1.194(1.145-1.245)	1.321(1.259-1.386)
<i>Enabling characteristics</i>		
Payment type		
Commercial	1	1

Medi-care/caid	1.109(1.062-1.157)	0.967(0.918-1.018)
Self-paid	0.770(0.703-0.843)	0.785(0.711-0.868)
Unknown	0.975(0.945-1.005)	1.008(0.974-1.044)
Specialty group		
Primary Care	1	1
Specialty care	1.425(1.338-1.518)	1.019(0.949-1.094)
Unknown	0.914(0.886-0.942)	0.872(0.843-0.903)
<i>Need characteristics</i>		
Hypertension		
No	1	1
Yes	1.168(1.108-1.230)	1.072(1.008-1.140)
Hyperlipidemia		
No	1	1
Yes	1.135(1.086-1.186)	1.075(1.021-1.133)
Lung cancer		
No	1	1
Yes	1.997(1.760-2.265)	2.043(1.774-2.353)
Stroke		
No	1	
Yes	1.374(1.191-1.586)	
COPD		
No	1	
Yes	1.065(1.003-1.131)	
Diabetes		

No	1	1
Yes	1.334(1.231-1.445)	1.187(1.083-1.301)
AMI		
No	1	1
Yes	2.109(1.656-2.686)	1.798(1.379-2.344)
Depression		
No	1	
Yes	1.072(1.008-1.140)	
Obesity		
Normal weight	1	1
Overweight	1.101(1.059-1.145)	1.126(1.081-1.173)
Obese	1.248(1.200-1.297)	1.277(1.226-1.330)
Extreme obese	1.434(1.350-1.524)	1.487(1.396-1.585)
Smoking counseling		
No	1	1
Yes	0.313(0.303-0.322)	0.288(0.278-0.297)
# of cigarettes/day		
1	1	1
> 1	0.741(0.721-0.762)	0.701(0.680-0.724)
Alcohol consumption		
No	1	
Yes	1.073(0.946-1.217)	

Baseline sample characteristics for smokers who were prescribed bupropion (Model 2)

The total sample for model 2 consisted of 4,045 adult smokers newly prescribed bupropion between 2006 and 2011. Among the cohort, 20.15% of them were abstinent successfully at 6-month follow up. The cohort had a mean age of 44.95(\pm 13.52), most of them aged between 41 and 64 (52.76%), followed by those aged between 18 and 40 (38.94%) and those older than 65(8.31%). Among the analytical cohort, 56.87% were female smokers and 43.13% were male smokers. Among these smokers, 37.55% of them were white, 8.18% were black and 54.26% were other races which included Hispanic, Asian and other races. In terms of residency distribution, 30.58% of them lived in the Midwest, 20.52% of them lived in the Northeast, 27.93% of them lived in the South and 20.97% of them lived in the West. Based on smokers' baseline BMI, 31.75 % of them had normal weight, 31.09% of them were overweight, 30.13% of them were obese and 7.03% of them were extreme obese. In terms of quitting successfully, 20.15% of them were abstinent at 6-month follow up time. Complete descriptive statistics of the analytical cohort in model 2 were shown in table 4.

Table 4.Descriptive statistics of analytic cohort who have been prescribed bupropion

	Total, N=4045 (100%)	Abstinent at 6 months N=815 (20.15%)	Not abstinent at 6 month N=3230 (79.85%)	p-value
<i>Predisposing characteristics</i>				
Age (±SD)	44.95(13.52)	48.82(14.61)	43.96(13.05)	
Age group				<0.0001*
18-40	38.94	30.55	41.05	
41-64	52.76	54.60	52.29	
>=65	8.31	14.85	6.66	
Gender				<0.6618
Female	56.87	56.20	57.05	
Male	43.13	43.80	42.95	
Race				<0.0001*
Black	8.18	4.42	9.13	
White	37.55	35.95	37.96	
Others	54.26	59.63	52.91	
Region				<0.0001*
Midwest	30.58	31.94	30.23	
Northeast	20.52	19.53	20.78	
South	27.93	22.24	29.36	
West	20.97	26.29	19.63	

<i>Enabling characteristics</i>				
Payment type				0.0169*
Commercial	41.06	42.09	40.80	
Medi-care/caid	13.42	16.32	12.69	
Self-paid	4.13	3.56	4.27	
Unknown	41.38	38.04	42.23	
Specialty group				<0.0002*
Primary Care	61.61	58.28	62.45	
Specialty care	5.71	8.59	4.98	
Unknown	32.68	33.13	32.57	
<i>Need characteristics</i>				
Hypertension				<0.0322*
Yes	8.33	10.18	7.86	
No	91.67	89.82	92.14	
Hyperlipidemia				<0.0001*
Yes	10.73	15.09	9.63	
No	89.27	84.91	90.37	
Lung cancer				<0.0186*
Yes	0.99	1.72	0.80	
No	99.01	98.28	99.20	
Stroke				<0.0005*
Yes	0.62	1.47	0.40	
No	99.38	98.53	99.60	

COPD				0.1822
Yes	4.82	3.93	5.05	
No	95.18	96.07	94.95	
Diabetes				<0.0008*
Yes	3.09	4.91	2.63	
No	96.91	95.09	97.37	
AMI				<0.4312
Yes	0.35	0.49	0.31	
No	99.65	99.51	99.69	
Depression				0.0154*
Yes	6.48	8.34	6.01	
No	93.52	91.66	93.99	
Obesity				0.0026*
Normal weight	31.75	27.25	32.90	
Overweight	31.09	30.96	31.12	
Obese	30.13	32.38	29.56	
Extreme obese	7.03	9.42	6.43	
Smoking counseling				<0.0001*
Yes	47.66	24.54	53.50	
No	52.34	75.46	46.50	
# of cigarettes/day				<0.0001*
1	44.28	55.34	41.49	
>1	55.72	44.66	58.51	

Alcohol consumption				0.3758
Yes	1.43	1.10	1.52	
No	98.57	98.90	98.48	

Logistic Regression Results for Smokers Who Have Been Prescribed Bupropion (Model 2)

Univariate logistic regression showed that for adult smokers who were newly prescribed bupropion, those who aged between 41 and 64 (OR: 1.403, 95% CI: 1.183-1.665) and those who were more than 65 years old (OR: 2.997, 95% CI: 2.309-3.889) were more likely to be abstinent compared to those aged between 18 and 40. White smokers (OR: 1.958, 95% CI: 1.354-2.832) and smokers with other races (OR: 2.330, 95% CI: 1.625-3.341) were more likely to quit compared to black smokers. Obese smokers (OR: 1.323, 95% CI: 1.067-1.639) and extreme obese smokers (OR: 1.769, 95% CI: 1.281-2.444) were more likely to quit than those with normal weight. Smokers who have received smoking counseling were less likely to be abstinent than those without smoking counseling (OR: 0.283, 95% CI: 0.238-0.336). Smokers who reported smoking at least one cigarettes every day were less likely to be abstinent than those who didn't (OR: 0.572, 95% CI: 0.490-0.668). Comorbidities like hypertension, hyperlipidemia, stroke, lung cancer were also statistically significant. Complete univariate logistic regression results are shown in Table 5. Multivariate logistic regression results showed that for adult smokers who were newly prescribed bupropion, those who aged between 41 and 64 (OR: 1.372, 95% CI: 1.128-1.670) and those who were more than 65 years old (OR: 2.670, 95% CI: 1.949-3.657) were more likely to be abstinent compared to those aged between 18 and 40. White smokers (OR: 1.797, 95% CI: 1.197-2.698) and smokers with other races (OR: 2.103, 95% CI: 1.410-3.138) were more likely to quit compared to black smokers. Obese smokers (OR: 1.279, 95% CI: 1.018-1.606) and extreme obese smokers (OR: 1.849, 95% CI: 1.308-2.615) were more likely to quit than those with normal weight. Smokers who have received smoking counseling were less likely to be abstinent than those without smoking counseling (OR: 0.289, 95% CI: 0.238-0.349). Smokers who reported smoking at least one cigarettes every day were less likely to

be abstinent than those who didn't (OR: 0.514, 95% CI: 0.429-0.617). Smokers with hyperlipidemia (OR: 1.508, 95% CI: 1.158-1.964), stroke (OR: 3.424, 95% CI: 1.355-8.653) and depression (OR: 1.551, 95% CI: 1.111-2.164) were more likely to quit compared to those without these comorbidities. Smokers with COPD were less likely to be abstinent than those without COPD (OR: 0.605, 95% CI: 0.376-0.973). However, comorbidities like hypertension, lung cancer, diabetes and acute myocardial infarction were found to be not significant predictors. Similarly, alcohol consumption, gender, payment type and specialty group were not a significant predictor of quitting successfully. The complete results of multivariate logistic regression are shown in Table 5.

Table 5. Logistic regression models for successful outcome among smokers who have been prescribed bupropion

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
<i>Predisposing characteristics</i>		
<i>Age group</i>		
18-40	1	1
41-64	1.403(1.183-1.665)	1.372(1.128-1.670)
>=65	2.997(2.309-3.889)	2.670(1.949-3.657)
Gender		
Female	1	
Male	1.035(0.887-1.209)	
Race		
Black	1	1
White	1.958(1.354-2.832)	1.797(1.197-2.698)
Others	2.330(1.625-3.341)	2.103(1.410-3.138)
Region		
Midwest	1	1
Northeast	0.890(0.714-1.109)	1.025(0.791-1.328)
South	0.717(0.581-0.884)	0.806(0.631-1.029)
West	1.268(1.031-1.559)	1.175(0.922-1.499)
<i>Enabling characteristics</i>		
Payment type		
Commercial	1	

Medi-care/caid 1.247(0.992-1.567)

Self-paid 0.808(0.532-1.226)

Unknown 0.873(0.736-1.036)

Specialty group

Primary Care 1

Specialty care 1.846(1.371-2.487)

Unknown 1.090(0.922-1.288)

Need characteristics

Hypertension

No 1

Yes 1.329(1.024-1.724)

Hyperlipidemia

No 1 1

Yes 1.668(1.333-2.088) **1.508(1.158-1.964)**

Lung cancer

No 1

Yes 2.154(1.120-4.144)

Stroke

No 1 1

Yes 3.698(1.681-8.135) **3.424(1.355-8.653)**

COPD

No 1 1

Yes 0.769(0.522-1.132) **0.605(0.376-0.973)**

Diabetes

No	1
Yes	1.910(1.301-2.804)

AMI

No	1
Yes	1.589(0.497-5.080)

Depression

No	1	1
Yes	1.425(1.069-1.900)	1.551(1.111-2.164)

Obesity

Normal weight	1	1
Overweight	1.201(0.968-1.490)	1.150(0.916-1.445)
Obese	1.323(1.067-1.639)	1.279(1.018-1.606)
Extreme obese	1.769(1.281-2.444)	1.849(1.308-2.615)

Smoking counseling

No	1	1
Yes	0.283(0.238-0.336)	0.289(0.238-0.349)

of cigarettes/day

1	1	1
>1	0.572(0.490-0.668)	0.514(0.429-0.617)

Alcohol consumption

No	1
Yes	0.725(0.355-1.482)

Baseline sample characteristics for smokers who were prescribed NRT (Model 3)

The total sample for model 3 consisted of 38,001 adult newly prescribed NRT between 2006 and 2011. Among the cohort, 20.03% of them were abstinent successfully at 6-month follow up. The cohort had a mean age of 45.40(\pm 14.01), most of them aged between 41 and 64 (54.75%), followed by those aged between 18 and 40 (36.17%) and those older than 65 (9.08%). Among the analytical cohort, 56.87% were female smokers and 43.13% were male smokers. Among these smokers, 44.08% of them were white, 13.82% were black and 42.10% were other races which included Hispanic, Asian and other races. In terms of residency distribution, 30.62% of them lived in the Midwest, 37.39% of them lived in the Northeast, 18.36% of them lived in the South and 13.63% of them lived in the West. Based on smokers' baseline BMI, 31.54 % of them had normal weight, 29.24% of them were overweight, 30.53% of them were obese and 8.68% of them were extreme obese. In terms of quitting successfully, 20.03% of them were abstinent at 6-month follow up time. Complete descriptive statistics of the analytical cohort in model 2 were shown in table 6.

Table 6.Descriptive statistics of analytic cohort who have been prescribed NRT

	Total, N=38001 (100%)	Abstinent at 6 months N=7612 (20.03%)	Not abstinent at 6 month N=30389 (79.97%)	p-value
<i>Predisposing characteristics</i>				
Age (±SD)	45.40 (14.01)	49.26 (14.91)	44.44(13.61)	
Age group				<0.0001*
18-40	36.17	28.93	37.99	
41-64	54.75	54.58	54.79	
>=65	9.08	16.49	7.22	
Gender				0.0002
Female	55.52	53.61	56.00	
Male	44.48	46.39	44.00	
Race				<0.0001*
Black	13.82	9.05	15.02	
White	44.08	43.35	44.27	
Others	42.10	47.60	40.72	
Region				<0.0001*
Midwest	30.62	31.54	30.39	
Northeast	37.39	33.32	38.41	
South	18.36	18.15	18.41	
West	13.63	16.98	12.79	
<i>Enabling characteristics</i>				
Payment type				0.0001*
Commercial	30.90	31.91	30.65	
Medi-care/caid	24.84	26.06	24.53	
Self-paid	4.04	2.69	4.37	
Unknown	40.22	39.33	40.45	
Specialty group				<0.0001*
Primary Care	58.97	59.00	58.97	
Specialty care	3.88	5.98	3.35	
Unknown	37.15	35.02	37.68	
<i>Need characteristics</i>				
Hypertension				<0.0001*
Yes	8.05	9.33	7.73	
No	91.95	90.67	92.27	
Hyperlipidemia				<0.0001*
Yes	8.88	10.22	8.54	
No	91.12	89.78	91.46	
Lung cancer				<0.0001*

Yes	1.41	2.68	1.09	
No	98.59	97.32	98.91	
Stroke				<0.0001*
Yes	1.47	2.92	1.11	
No	98.53	97.08	98.89	
COPD				<0.0001*
Yes	7.03	8.99	6.54	
No	92.97	91.01	93.46	
Diabetes				<0.0003*
Yes	3.63	4.32	3.46	
No	96.37	95.68	96.54	
AMI				<0.0001*
Yes	0.50	1.01	0.37	
No	99.50	98.99	99.63	
Depression		7.19	7.73	0.1098
Yes	7.62	92.81	92.27	
No	92.38			
Obesity				0.4527
Normal weight	31.54	31.08	31.66	
Overweight	29.24	29.92	29.08	
Obese	30.53	30.61	30.52	
Extreme obese	8.68	8.93	8.75	
Smoking counseling				<0.0001*
Yes	51.13	23.45	58.07	
No	48.87	76.55	41.93	
# of cigarettes/day				<0.0001*
1	40.04	51.47	37.18	
>1	59.96	48.53	62.82	
Alcohol consumption				<0.0001*
Yes	1.05	1.28	0.92	
No	98.95	98.72	99.08	

Logistic Regression Results for Smokers Who Were Prescribed NRT (Model 3)

Univariate logistic regression result showed that for the smokers who were prescribed NRT, those who aged between 41 and 64 (OR: 1.308, 95% CI: 1.236-1.385) and those who were more than 65 years old (OR: 2.997, 95% CI: 2.759-3.257) were more likely to be abstinent compared to those aged between 18 and 40. White smokers (OR: 1.625, 95% CI: 1.487-1.775) and smokers with other races (OR: 1.939, 95% CI: 1.775-2.118) were more likely to quit compared to black smokers. Male smokers were more likely to be abstinent compared with female smokers (OR: 1.102, 95% CI: 1.047-1.159). Smokers without insurance (OR: 0.591, 95% CI: 0.507-0.690) and those with unknown insurance (OR: 0.934, 95% CI: 0.880-0.992) were less likely to be abstinent than those who were covered by commercial insurance. Smokers with lung cancer (OR: 2.508, 95% CI: 2.103-2.992), stroke (OR: 2.687, 95% CI: 2.264-3.189), COPD (OR: 1.412, 95% CI: 1.290-1.547) and acute myocardial infarction (OR: 2.738, 95% CI: 2.047-3.662) were more likely to quit compared to those without these comorbidities. Complete univariate logistic regression results are shown in Table 7. Multivariate logistic regression results showed that for adult smokers who were newly prescribed NRT, those who aged between 41 and 64 (OR: 1.195, 95% CI: 1.120-1.276) and those who were more than 65 years old (OR: 2.332, 95% CI: 2.103-2.587) were more likely to be abstinent compared to those aged between 18 and 40. White smokers (OR: 1.596, 95% CI: 1.443-1.765) and smokers with other races (OR: 1.533, 95% CI: 1.386-1.697) were more likely to quit compared to black smokers. Male smokers were more likely to be abstinent compared with female smokers (OR: 1.072, 95% CI: 1.011-1.136). Smokers who lived in the Northeast (OR: 1.083, 95% CI: 1.005-1.167) and those who lived in the Western United States (OR: 1.330, 95% CI: 1.213-1.458) were more likely to be abstinent than those who lived in the Midwest. Smokers covered by Medicare or Medicaid (OR: 0.852,

95% CI: 0.787-0.923) and those without insurance (OR: 0.818, 95% CI: 0.689-0.973) and those with unknown insurance (OR: 0.910, 95% CI: 0.849-0.976) were less likely to be abstinent than those who were covered by commercial insurance. Smokers with unknown care were less likely to quit compared to those who received primary care (OR: 0.869, 95% CI: 0.817-0.925). However, smokers who received specialty care were more likely to be abstinent than those who received primary care (OR: 1.279, 95% CI: 1.114-1.468). Smokers who were overweight (OR: 1.082, 95% CI: 1.005-1.165), obese (OR: 1.138, 95% CI: 1.057-1.224) and extreme obese smokers (OR: 1.219, 95% CI: 1.090-1.364) were more likely to quit than those with normal weight. Smokers who have received smoking counseling were less likely to be abstinent than those without smoking counseling (OR: 0.223, 95% CI: 0.209-0.238). Smokers who reported smoking at least one cigarettes every day were less likely to be abstinent than those who didn't (OR: 0.569, 95% CI: 0.537-0.604). Smokers with lung cancer (OR: 1.996, 95% CI: 1.620-2.459), stroke (OR: 1.914, 95% CI: 1.553-2.359), COPD (OR: 1.249, 95% CI: 1.121-1.392) and acute myocardial infarction (OR: 2.154, 95% CI: 1.524-3.044) were more likely to quit compared to those without these comorbidities. However, comorbidities like depression, diabetes, hypertension and hyperlipidemia were not found to be significant predictors. Similarly, alcohol consumption was not a significant predictor of quitting successfully. The complete results of multivariate logistic regression are shown in Table 7.

Table 7. Logistic Regression Models for successful outcome among smokers who have been prescribed NRT

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
<i>Predisposing characteristics</i>		
<i>Age group</i>		
18-40	1	1
41-64	1.308(1.236-1.385)	1.195(1.120-1.276)
>=65	2.997(2.759-3.257)	2.332(2.103-2.587)
Gender		
Female	1	1
Male	1.102(1.047-1.159)	1.072(1.011-1.136)
Race		
Black	1	1
White	1.625(1.487-1.775)	1.596(1.443-1.765)
Others	1.939(1.775-2.118)	1.533(1.386-1.697)
Region		
Midwest	1	1
Northeast	0.836(0.786-0.890)	1.083(1.005-1.167)
South	0.950(0.882-1.023)	1.059(0.969-1.158)
West	1.280(1.185-1.383)	1.330(1.213-1.458)
<i>Enabling characteristics</i>		
Payment type		
Commercial	1	1

Medi-care/caid	1.020(0.955-1.091)	0.852(0.787-0.923)
Self-paid	0.591(0.507-0.690)	0.818(0.689-0.973)
Unknown	0.934(0.880-0.992)	0.910(0.849-0.976)

Specialty group

Primary Care	1	1
Specialty care	1.783(1.589-2.001)	1.279(1.114-1.468)
Unknown	0.929(0.881-0.980)	0.869(0.817-0.925)

Need characteristics

Hypertension

No	1	
Yes	1.227(1.124-1.340)	

Hyperlipidemia

No	1	
Yes	1.219(1.120-1.326)	

Lung cancer

No	1	1
Yes	2.508(2.103-2.992)	1.996(1.620-2.459)

Stroke

No	1	1
Yes	2.687(2.264-3.189)	1.914(1.553-2.359)

COPD

No	1	1
Yes	1.412(1.290-1.547)	1.249(1.121-1.392)

Diabetes

No	1	
Yes	1.261(1.111-1.431)	
AMI		
No	1	1
Yes	2.738(2.047-3.662)	2.154(1.524-3.044)
Depression		
No	1	
Yes	0.924(0.839-1.018)	
Obesity		
Normal weight	1	1
Overweight	1.048(0.978-1.123)	1.082(1.005-1.165)
Obese	1.022(0.954-1.094)	1.138(1.057-1.224)
Extreme obese	0.978(0.881-1.085)	1.219(1.090-1.364)
Smoking counseling		
No	1	1
Yes	0.221(0.209-0.234)	0.223(0.209-0.238)
# of cigarettes/day		
1	1	1
> 1	0.558(0.530-0.587)	0.569(0.537-0.604)
Alcohol consumption		
No	1	
Yes	1.131(1.096-1.147)	

Multicollinearity Analysis

We also conducted correlation coefficient analysis to assess the collinearity within independent variables. No Pearson Correlation Coefficients were found to be greater than 0.70 between each two independent variables. Multicollinearity test results showed that none of the Variance Inflation Factor (VIF) were larger than 10, which indicated that there was no multicollinearity in the model.

Chapter 5

Discussion and Conclusion

Discussion

Findings of this real world study indicated that the utilization rate of varenicline in 2011 was much higher than that of NRT, the use rate of bupropion was the lowest, varenicline was the most commonly prescribed smoking cessation medication followed by NRT and bupropion. A previous study which examined utilization patterns of smoking cessation medication in four countries including the United States, United Kingdom, Australia and Canada from 2006 to 2008 found that the use rate of varenicline increased year by year in the United States and in 2008, the use rate of varenicline was even comparable to that of NRT which was most commonly use cessation medication originally, while the use rate of bupropion remained the lowest (Brian et al., 2011). Since the use rate of varenicline was increasing each year, it was quite reasonable that varenicline became the most commonly used cessation medication. The rates of smoking cessation medication use documented in this study are generally lower than what has been found in the reported study by Brian et al. possibly due to the definition of use rate. In this study, we had a different denominator defined as patients who reported they were current smokers to physicians in 2011 in GE healthcare clinical data, while in previous study, the definition used was overall smokers who had attempted to quit as denominator. In the GE healthcare clinical data, the information of attempt to quit was not available. Also, we found all those predisposing, enabling and need factors were statistically significant factors which were associated with

varenicline, bupropion and NRT prescribing. However, in our study, we only did univariate analysis, as a result, the association was unadjusted. In the previous study where multivariate analysis was conducted, they also found these factors were associated with smoking cessation medication prescribing (Yu YP, et al., to be submitted).

In our study, we found among those smokers who were newly prescribed varenicline, 18.28% of them were successfully abstinent at 6-month, among those smokers who were newly prescribed bupropion, 20.15% of them were successfully abstinent at 6-month and among those smokers who were newly prescribed NRT, 20.03% of them were successfully abstinent at 6-month. The abstinence rate of varenicline was a little lower than that of bupropion and NRT. The abstinence rate of bupropion and NRT were quite similar. In clinical trials, the abstinence rate of varenicline was higher than that of bupropion (Tonstad et al., 2006; Gonzales et al., 2006). However, the abstinence rate of varenicline compared with bupropion was not higher in this real world setting. In terms of predictors of successful outcome among smokers who were newly prescribed each smoking cessation medication, we found age, obesity, race, smoking cessation counseling, number of cigarettes smoking per day and comorbidities were significant predictors of quitting successfully for the smokers who were newly prescribed varenicline, bupropion and NRT. In our study, we found the higher baseline BMI value the smokers had, the higher likelihood of being abstinent. A potential reason could be that those who are overweight, especially obese and extreme obese smokers may have more concern about their health status (Yu YP, et al., to be submitted). Similarly, older smokers were more likely to be abstinent than younger smokers, since older people also would be concerned about their health status, and co morbidities also increase with age adding to this concern (Yu YP, et al., to be submitted). We found white smokers were more likely to be abstinent compared to black smokers, this result was consistent

among each analytical cohort, that is, smokers who took varenicline, bupropion or NRT. Also, smokers with other races were also found to be more likely to be abstinent compared with black smokers among those who were prescribed bupropion and those who were prescribed NRT, but not among those who took varenicline. This finding of racial differences was consistent with what had been found in Cokkinides et al.'s study, which indicated racial disparity to receive smoking cessation treatment existed for white, black and Hispanic smokers (Cokkinides et al., 2008). This study adds that the racial differences also exist in achieving a successful outcome among those that are prescribed smoking cessation medication. In our study, we found smokers who had received smoking cessation counseling were less likely to be abstinent compared to those who didn't receive cessation counseling in each model. This finding was opposite to what one would expect, as smoking cessation counseling should help improve outcome of smoking cessation intervention (Fiore MC et al., 2008). A potential reason could be that the smokers who received cessation counseling were heavy smokers who had a higher nicotine dependence level, which was a barrier to successful quitting (John U et al., 2004), and the more heavily smokers smoked, the more likely they were to get smoking cessation counseling. In our study, we also found the smokers who reported a higher number of cigarettes smoked per day were less likely to be abstinent. Similarly, this could also be due to a higher level of nicotine dependence, which is a reported barrier for quitting smoking successfully (John U et al., 2004). Several comorbidities were also found to be significant predictors of successful quitting as comorbidities may increase the health concerns of these patients (Yu YP, et al., to be submitted); however, in our study comorbidities which were identified to be significant among smokers who were prescribed varenicline, bupropion and NRT respectively were different. For those who took varenicline, smokers with hypertension, hyperlipidemia, lung cancer, diabetes and AMI were more likely to

be abstinent than those without these comorbidities. For those who took bupropion, smokers with hyperlipidemia, stroke or depression were more likely to be abstinent compared to those without these comorbidities. Among those who took bupropion, smokers with COPD were less likely to be abstinent compared to those without COPD, this result was inconsistent with previous literature in which bupropion has been found to be efficacious in treating smokers with COPD (E. J. Wagena et al., 2005). There are missing value and some unmeasured confounders like education level, family income, physician preference, intention to quit which were not available in GE data that might have contributed to this finding. For those who took NRT, smokers with lung cancer, stroke and AMI were more likely to be abstinent than those without these comorbidities. Additionally, among those who were prescribed took NRT, we found smokers with COPD were more likely to be abstinent than those without COPD. This finding is consistent with a previous meta-analysis of randomized trials, which indicated NRT combined with smoking cessation counseling was more effective than any other combined or single cessation interventions among patients with COPD (Strassmann et al., 2009). To be noted, depression was found in our study to be a significant predictor of successful quitting for smokers who were prescribed bupropion, while not a significant predictor among those who took varenicline or NRT. A potential reason could be that bupropion is used as an antidepressant to treat depression (John A et al., 1995). As a result, bupropion could be more beneficial to smokers with depression compared to those without depression. AMI in our study has been found to be a significant predictor of successful quitting for those who took varenicline or NRT, while to be not significant predictor of successful quitting for smokers who took bupropion. This is consistent with the randomized trial study conducted by Eisenberg et al. which found bupropion was not effective for smoking cessation in patients with AMI (Eisenberg et al., 2013). In our

study, there were variable results regarding gender differences in successful quitting among smokers who took varenicline and NRT, which showed female smokers were more likely to be abstinent among those who were prescribed varenicline, while male smokers were more likely to be abstinent among those who were prescribed NRT. Thus varenicline might be more beneficial for female smokers. A study conducted by Bohadana et al. which examined gender difference in successful quitting among participants who used NRT indicated that for the participants who used NRT, female smokers were less successful in quitting than male smokers (Bohadana et al). The findings in this study are consistent. Although a randomized control trial which examined the efficacy of varenicline found no sex difference in the efficacy of varenicline (Gonzales D et al., 2006), the results of this study indicate a gender difference in achieving a successful outcome among those prescribed varenicline. This study is the first real world study to examine differences in successful outcomes among smoking cessation medication users. In our study, region was also a significant predictor of successful quitting for smokers who had been prescribed varenicline and NRT, this may partially be due differences in other factors like education level, income level, marital status that are reported to affect successful outcomes that may differ in people living in different regions (Broms U et al., 2004), however, the information of these factors were not reported in GE healthcare clinical data and we could not control for them.

In terms of need factors, payment type and specialty group were significant predictors which affected successful quitting among smokers who were prescribed varenicline or NRT, however they were not significant among those who were prescribed bupropion. Among those who were prescribed NRT, smokers with self-paid insurance or unknown insurance or those who were covered by Medicare/Medicaid were less likely to be abstinent compared with those with

commercial insurance. Among those who were prescribed varenicline, smokers with self-paid insurance were less likely to be abstinent compared with those having commercial insurance. In the Clinical Practice Guideline for Treating Tobacco Use and Dependence, it has been noted that covering smoking cessation by insurance plans will increase the likelihood of receiving cessation treatment and having a successful outcome of quitting (Fiore MC et al., 2008). Results of this study show that different insurance plans can influence successful quitting and information regarding reimbursement policies on each smoking cessation medication need to be further investigated, as it can also affect achievement of a successful outcome of smoking cessation (Kaper et al., 2005). In terms of specialty group, among those who were prescribed NRT, smokers who received specialty care were more likely to quit successfully than those who received primary care. However, this association has not been found among those who were prescribed varenicline or bupropion. Among those who were prescribed varenicline, smokers who received care from providers with unknown specialty were less likely to be abstinent compared with those who received primary care. Unknown specialty means the specialty of providers was not available in GE data since this information was not documented. However, this association has not been found among those who were prescribed NRT or bupropion. Since the specialty of some providers was not documented in GE data, we cannot provide an explanation of this finding and further research with more completely recorded datasets is needed. Physician and patient preferences of a specific smoking cessation medication may affect the type of smoking cessation medication prescribed. How these preferences affect achieving a successful outcome of cessation needs to be addressed in future research.

In summary, in our study, we found the predictors of successful quitting for smokers who were newly prescribed varenicline were age, gender, race, region, payment type, specialty group, baseline BMI value, smoking cessation counseling, number of cigarettes smoking per day and comorbidities including hypertension, hyperlipidemia, lung cancer, diabetes and AMI. The predictors of successful quitting for smokers who were newly prescribed bupropion were age, race, baseline BMI value, smoking cessation counseling, number of cigarettes smoking per day, and comorbidities including hyperlipidemia, stroke, COPD and depression. The predictors of successful quitting for smokers who were newly prescribed NRT were age, gender, race, region, payment type, specialty group, baseline BMI value, smoking cessation counseling, number of cigarettes smoking per day, and comorbidities including lung cancer, stroke, COPD and AMI. There were some differences in the predictors of successful outcome of smoking cessation among smokers who took varenicline, bupropion and NRT, respectively, which indicated that each different type of smoking cessation medication may be particularly beneficial to certain smoking subpopulations in the real life world. In our study, we found NRT was more effective among patients with COPD compared with those without COPD, bupropion could be more beneficial to smokers with depression compared to those without depression, NRT was more beneficial to male smokers. Varenicline might be more beneficial to female smokers in real life world, and further investigation is needed. Future research is needed to examine the effectiveness of each smoking cessation medication on these specific subpopulations in real world settings.

Strength and Limitation

Our study has several strengths. Our study has a large sample size and represents the outpatient practice. Also, smoking information in GE healthcare clinical data was quite rich. However, our

study has the general limitations of EMR data. In this study, GE healthcare clinical was used and data can only capture information of smokers who have reported their smoking status, those smokers who haven't reported their smoking status to physicians were missed. Additionally, physician order information does not guarantee that the patients actually filled the prescription. Since EMR data is not recorded in a weighted level like NAMCS, MEPS or NHANES which can be nationally representative, there might be some selection bias in our study that can affect generalizability. Some independent variables which were found to be predictive of smoking cessation in previous literature were not available in the data, such as education level, marital status, intention to quit, previous quit attempts, smokers in the household, and thus were not controlled for. Missing data in GE database regarding smoking information and other diagnosis information may slightly bias results. Although these limitations may affect the precision of the findings, the overall research perspective provided by the database, due to its sample size and representativeness of outpatient practice, and availability of BMI and smoking information, serves as an important strength.

Conclusions

Each different type of smoking cessation medication may be particularly beneficial to certain smoking subpopulations in real life world. NRT was more effective among patients with COPD compared to those without COPD. Bupropion could be more beneficial to smokers with depression compared to those without depression. NRT could be more beneficial to male smokers vs female smokers. Varenicline might be more beneficial to female smokers in a real world setting.

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