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Predictors of a successful outcome among adult smokers using smoking cessation medication

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ABSTRACT

Objective: To evaluate the prescribing rate of each type of smoking cessation medication and to identify predictors of a successful cessation outcome among adult smokers newly prescribed each type of smoking cessation medication. **Methods:** A retrospective cohort study was conducted using general electric health-care clinical data. Andersen's health service utilization model was used as conceptual framework. An index date was assigned as the 1st day of being prescribed smoking cessation medication. A successful outcome was defined as smokers being successfully abstinent. All the smokers in the cohort were followed up to 6 months after the index date. Smoking status of the cohort was measured at 6-month after the index date. The independent variables were categorized into predisposing, enabling, and need characteristics. Three multivariate logistic regression models were conducted to identify the predictors of successful outcome among adult smokers prescribed each type of smoking cessation medication. All statistical analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC, USA) statistical package at a priori significant level of 0.05. **Results:** For the year of 2011, there were 886,604 current adult smokers. Among these smokers, varenicline was the most commonly prescribed (n = 32,688, 3.69%), followed by nicotine replacement therapy (NRT) (n = 17,716, 2.00%) and bupropion (n = 1,630, 0.18%). In total, we identified 132,885 adult smokers who were newly prescribed varenicline, 4045 adult smokers newly prescribed bupropion, and 38,001 adult smokers newly prescribed nicotine NRT between 2006 and 2011. Among smokers who were newly prescribed varenicline, male smokers were less likely to be abstinent compared with female smokers (odds ratios [ORs]: 0.88, 95% confidence interval [CI]: 0.85-0.91). Among smokers using bupropion, smokers with depression (OR: 1.55, 95% CI: 1.11-2.16) were more likely to quit compared to those without depression. **Conclusions:** Findings of this real world study indicate that in 2011, varenicline was the most commonly prescribed smoking cessation medication followed by NRT than bupropion. The different types of cessation medication may be particularly beneficial to certain sub-populations in the real world.

KEY WORDS: Predictors, smoking cessation medication, smoking cessation

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INTRODUCTION

Cigarette smoking is a leading preventable cause of death and disability, accounting for approximately 480,000 annual deaths in the United States (US) [1,2]. Cigarette smoking is the cause of many diseases including cardiovascular diseases, chronic obstructive pulmonary disease (COPD), stroke, multiple cancers, and complications of pregnancy [3]. There are approximately 42.1 million current adult smokers in the US [4]. An estimated 15.3% of women and 20.5% of men are current smokers [4]. Annual smoking-attributable economic costs in the US were estimated to be over $289 billion for years 2009-2012, with approximately $133 billion for direct medical care of adults and over $156 billion in lost productivity [2].

The 2008 Clinical Practice Guidelines of Treating Tobacco Use and Dependence recommended the use of pharmacotherapy for all adult smokers who attempted to quit, except those with contraindications or some specific population (e.g., pregnant women) [3]. Currently, there are seven first-line medications approved by the US Food and Drug Administration (FDA) for smoking cessation. They are varenicline, bupropion hydrochloride sustained-release (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) [3,5,6]. NRT is the most common first-line pharmacotherapy used for smoking cessation by replacing much of the nicotine in cigarettes to reduce smokers' craving for smoking and increasing the likelihood of remaining

abstinent. Another FDA-approved first-line smoking cessation medication is bupropion SR, which was approved for smoking cessation in the US since 1997. It is a noncompetitive nicotinic receptor antagonist, which aids smoking cessation by inhibiting dopamine reuptake in the mesolimbic dopamine system [7]. Varenicline, a partial agonist of the nicotinic acetylcholine receptor, (Chantix® in the US) is an FDA-approved first-line smoking cessation medication, which has been used in the US 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 [7-9].

While the efficacy of various prescription smoking cessation medications has been well-demonstrated by clinical studies and the utilization patterns of smoking cessation medications from 2006 to 2008 in the US have been examined, to date, no population-based study has investigated the use rate of varenicline in the US after 2008 compared to other available smoking cessation medications [8].

In addition, several studies have examined factors associated with successful smoking cessation compared to placebo including older age, male gender, higher income, better compliance, low nicotine dependence, less frequent alcohol consumption, and receiving counseling [10-12]. Predictors of successful cessation with the available prescription cessation medications in a real-world setting have not been adequately explored. This study has 2 objectives: (1) To assess the utilization patterns of prescription smoking cessation medications (i.e., varenicline, bupropion, and NRT) in 2011 and (2) to identify and compare the predictors of successful quitting among patients who have been prescribed each type of smoking cessation medication in a real-world setting. Evaluating change in smoking cessation medication use over time can provide a better understanding of the most commonly used 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 to achieve a successful cessation.

METHODS

Study Design

For objective 1, the study was a retrospective cross-sectional study. For objective 2, the study was a retrospective cohort study.

Data Source/Study Setting

The data source for this study was general electric (GE) Centricity Electronic Medical Record (EMR) data (2006-2011). GE healthcare clinical database is a large commercial EMR system, used by more than 20,000 clinicians for the management of medical records of more than 30 million patients throughout the US [13]. Data include patient vital signs, clinical outcomes, payment plans, prescription and over-the-counter drugs, and laboratory test results [14]. All data were de-identified. The unique characteristics of the GE data mentioned above and availability of smoking status information make it the ideal clinical database to be used for conducting this study.

Research Involving Human Subjects

This study was approved by the University of Houston Committees for the protection of human subjects.

Study Population

Current smokers aged 18 years or older enrolled in the GE healthcare clinical data in 2011 were selected for objective 1. Those aged 18 years or older, enrolled in the GE data through January 2006 to December 2011, having at least one new prescription of the smoking cessation medications (i.e., varenicline, bupropion, or NRT) were included in the study for objective 2. Those having missing data on smoking status were excluded.

In GE data, patients' smoking status was categorized as never smoked, formerly smoked, not currently smoking, and currently smoking. Patients whose smoking status was recorded as "current," "formerly smoked," and "not currently smoking" were identified as smokers.

Statistical Analyses

For objective 1

Descriptive statistics were used to estimate the utilization rates of each smoking cessation medication (i.e., varenicline, bupropion, and NRT) in 2011. The sample characteristics of the identified cohort were examined, and Chi-square tests were performed to assess group differences for each cessation medication used. Variables included in the analysis were: Age, gender, race, region, payment type, specialty group, comorbidities (including hypertension, hyperlipidemia, lung cancer, stroke, COPD, diabetes, acute myocardial infarction [AMI], and depression), smoking counseling, number of cigarettes smoked per day, alcohol consumption, and obesity.

For objective 2

An index date was assigned as the 1st day of being prescribed smoking cessation medication. A washout period was defined as not being on any smoking cessation medication during the 6 months before the index date to identify smokers who were newly prescribed cessation medications. A successful outcome was defined as smokers being successfully abstinent. Those who were reported as "not current" or "former" smoker at 6-month follow-up time were defined as being successful abstinent; being reported as "current" smoker at 6-month follow-up endpoint was categorized as not-abstinent. All the smokers in the cohort were followed up to 6 months after the index date. Smoking status of the cohort was measured at 6-month after the index date.

Three multivariate logistic regression models (i.e., model I, II, and III) were constructed to assess the association between the

outcome variable (abstinent vs. not) and independent variables for each smoking cessation medication.

Outcomes and Measurement Variables

Andersen's health service utilization model was used as the conceptual framework [15]. 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 service.

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

Predisposing characteristics included age group (categorized as 18-40; 41-64; ≥65), gender (female, male), race (white, non-white (including multiple races, not entered, unknown/undetermined), and region (Midwest, Northeast, South, West).

Enabling characteristics included payment type (commercial insurance, government insurance [Medicare/Medicaid], no insurance) and specialty group (primary care, specialty care).

Need characteristics included comorbidities (yes, no [including hypertension, hyperlipidemia, lung cancer, stroke, COPD, diabetes, AMI, and depression], smoking counseling [yes and no], number of cigarettes smoked per day [1, ≥2], alcohol consumption [yes and no], obesity [normal weight, overweight, obese, and extreme obese]).

Univariate logistic regression models were used to estimate the unadjusted association between each independent variable and the dependent variable with cutoff of 0.20 for inclusion in the multivariate logistic regression models (i.e., all those variables with $P < 0.20$ in the univariate logistic regression were included in the multivariate logistic regression model). A multicollinearity test was carried out, and variables were removed if correlation coefficients had a value of >0.7 and/or the variance inflation factor (VIF) was >10. Backward elimination was used to arrive at the final multivariate logistic regression model. Adjusted odds ratios (ORs) and 95% confidence interval (CI) were presented.

All statistical analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC, USA) statistical package at a priori significant level of 0.05.

RESULTS

Results for Objective 1

The final cohort for objective 1 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 among total smokers in 2011 was 3.69%, followed by NRT (2.00%) and bupropion (0.18%). Chi-square tests showed that there were group differences between those who have been prescribed each cessation medication and those who were not. Age, gender, race, region, payment, specialty group, obesity, number of cigarettes smoked per day, alcohol consumption, and comorbidities including hypertension, hyperlipidemia, lung cancer, COPD, and depression were found to be statistically significant predictors which were associated with varenicline, bupropion, and NRT prescribing, respectively. In addition, stroke, diabetes, and AMI were also found to be statistically significantly associated with varenicline and NRT prescribing, while not associated with bupropion prescribing. Complete results of sociodemographic characteristics of the smokers who were prescribed each medication and group differences are shown in Table 1.

Results for Objective 2

In total, 132,885 adult smokers were identified as newly prescribed varenicline, 4045 adult smokers newly prescribed bupropion, and 38,001 adult smokers newly prescribed NRT between 2006 and 2011. The abstinence rates at 6-month follow-up time were 18.28%, 20.15%, and 20.03% for varenicline, bupropion, and NRT, respectively. Those on varenicline had a mean age of 45.41 (±12.81), with 56.78% aged between 41 and 64, and 53.44% were female. Complete descriptive statistics of the analytical cohort in model 1 are shown in Table 2.

Those on bupropion had a mean age of 44.95 (±13.52), with most aged between 41 and 64 (52.76%), 56.87% were female, and 37.55% were white. Complete descriptive statistics of the analytical cohort in model 2 are shown in Table 3.

Those on NRT had a mean age of 45.40 (±14.01), with most aged between 41 and 64 (54.75%), 56.87% were female smokers, and 44.08% were white. Complete descriptive statistics of the analytical cohort in model 3 are shown in Table 4.

Multicollinearity test results showed that none of the VIF was larger than 10, which indicated that there was no multicollinearity in the model.

Results of multivariate logistic regression models for a successful outcome among smokers who have been prescribed varenicline, bupropion and NRT are presented in Table 5. Multivariate logistic regression model showed that those who aged between 41 and 64 as well as those who were 65 years old or more were more likely to be abstinent compared to those aged between 18 and 40 for those who were newly prescribed varenicline (OR: 1.08, 95% CI: 1.05-1.12) (OR: 1.66, 95% CI: 1.56-1.77), bupropion (OR: 1.37, 95% CI: 1.12-1.67) (OR: 2.67, 95% CI: 1.94-3.65) and NRT (OR: 1.19, 95% CI: 1.12-1.27) (OR: 2.33, 95% CI: 2.10-2.58).

White smokers were more likely to quit compared to nonwhite smokers for those on varenicline (OR: 1.23, 95% CI: 1.12-1.34),

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

Variables	Total *n*=886,604 (%)	With varenicline *n*=32,688 (3.69%)	Without varenicline (%)	*P*	With bupropion *n*=1630 (0.18%)	Without bupropion (%)	*P*	With NRT *n*=17,716 (2.00%)	Without NRT %	*P*	With any cessation medication *n*=50,157 (5.66%)	Without any cessation medication (%)	*P*
Predisposing characteristics													
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 (female)	55.48	54.79	55.50	0.0110*	58.62	55.47	0.0105*	57.49	55.44	<0.0001*	55.68	55.47	0.3552
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	
Enabling characteristics													
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	
Need characteristics													
Hypertension (yes)	7.10	7.89	7.07	<0.0001*	10.86	7.10	<0.0001*	9.20	7.06	<0.0001*	8.39	7.03	<0.0001*
Hyperlipidemia (yes)	7.04	10.31	6.91	<0.0001*	12.39	7.03	<0.0001*	9.80	6.98	<0.0001*	10.17	6.85	<0.0001*
Lung cancer (yes)	0.63	1.28	0.60	<0.0001*	2.02	0.62	<0.0001*	1.82	0.60	<0.0001*	1.42	0.58	<0.0001*
Stroke (yes)	0.90	1.06	0.89	0.0020*	0.98	0.90	0.7276*	1.55	0.89	<0.0001*	1.21	0.88	<0.0001*
COPD (yes)	3.64	7.16	3.51	<0.0001*	7.48	3.63	<0.0001*	9.39	3.52	<0.0001*	7.70	3.40	<0.0001*

(Contd...)

Table 1: *(Continued)*

Variables	Total n=886, 604 (%)	With varenicline n=32,688 (3.69%)	Without varenicline (%)	*P*	With bupropion n=1630 (0.18%)	Without bupropion (%)	*P*	With NRT n=17, 716 (2.00%)	Without NRT %	*P*	With any cessation medication n=50, 157 (5.66%)	Without any cessation medication (%)	*P*
Diabetes (yes)	3.28	3.34	3.28	0.5145	3.93	3.28	0.1409	4.44	3.25	<0.0001*	3.68	3.25	<0.0001*
AMI (yes)	0.21	0.34	0.21	<0.0001*	0.25	0.21	0.7695	0.76	0.20	<0.0001*	0.48	0.20	<0.0001*
Depression (yes)	5.31	6.34	5.27	<0.0001*	8.90	5.30	<0.0001*	9.38	5.22	<0.0001*	7.37	5.18	<0.0001*
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 (yes)	46.28	59.68	45.77	<0.0001*	55.15	46.27	<0.0001*	61.13	45.98	<0.0001*	59.99	45.46	<0.0001*
Number of cigarettes/ day (1)	49.84	41.23	50.17	<0.0001*	37.30	49.86	<0.0001*	31.66	50.21	<0.0001*	38.16	50.54	<0.0001*
Alcohol consumption (yes)	2.08	1.31	2.11	<0.0001*	1.23	2.08	0.0160*	1.07	2.10	<0.0001*	1.22	2.13	<0.0001*

*Significance level α is<0.05. NRT: Nicotine replacement therapy, COPD: Chronic obstructive pulmonary disease, AMI: Acute myocardial infarction, SD: Standard deviation, NRT: Nicotine replacement treatment, SD: Standard deviation

Table 2: Descriptive statistics of analytical cohort that has been prescribed varenicline *n*=132,885

Variables	Total *n*=132,885 (100%)	Abstinent months *n*=24,294 (18.28%)	Not abstinent at 6 month *n*=108,591 (81.72%)	*P*
Predisposing characteristics				
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	
Enabling characteristics				
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	
Need characteristics				
Hypertension				<0.0001*
Yes	7.12	7.99	6.93	
Hyperlipidemia				<0.0001*
Yes	10.38	11.37	10.16	
Lung cancer				<0.0001*
Yes	0.86	1.45	0.73	
Stroke				<0.0001*
Yes	0.80	1.02	0.74	
COPD				0.0386*
Yes	5.49	5.77	5.43	
Diabetes				<0.0001*
Yes	2.63	3.28	2.48	
AMI				<0.0001*
Yes	0.23	0.40	0.19	
Depression				0.0257*
Yes	5.22	5.50	5.15	
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	
Number of cigarettes/day				<0.0001*
1	44.69	50.79	43.33	
Alcohol consumption				0.2847
Yes	1.18	1.24	1.16	

*Significance level α is<0.05. SD: Standard deviation, COPD: Chronic obstructive pulmonary disease, AMI: Acute myocardial infarction

bupropion (OR: 1.79, 95% CI: 1.19-2.69), and NRT (OR: 1.59, 95% CI: 1.44-1.76).

Furthermore, smokers of other races were more likely to quit compared to nonwhite smokers for those on bupropion (OR: 2.10, 95% CI: 1.41-3.13) and NRT (OR: 1.53, 95% CI: 1.38-1.69). Male smokers were less likely to be abstinent compared to female smokers (OR: 0.87, 95% CI: 0.85-0.90) for those on varenicline; however, they were more likely to be abstinent compared to female smokers (OR: 1.07, 95% CI: 1.01-1.13) for those on NRT. Smokers who lived in the Northeast (OR: 1.19, 95% CI: 1.14-1.24), the South (OR: 1.66, 95% CI: 1.11-1.21)

Table 3: Descriptive statistics of analytic cohort who have been prescribed bupropion (n=4045)

Variables	Total, n=4045 (100%)	Abstinent at 6 months n=815 (20.15%)	Not abstinent at 6 month n=3230 (79.85%)	P
Predisposing characteristics				
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	
Enabling characteristics				
Payment type				0.0169*
Commercial	41.06	42.09	40.80	
Medicare/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	
Need characteristics				
Hypertension				<0.0322*
Yes	8.33	10.18	7.86	
Hyperlipidemia				<0.0001*
Yes	10.73	15.09	9.63	
Lung cancer				<0.0186*
Yes	0.99	1.72	0.80	
Stroke				<0.0005*
Yes	0.62	1.47	0.40	
COPD				0.1822
Yes	4.82	3.93	5.05	
Diabetes				<0.0008*
Yes	3.09	4.91	2.63	
AMI				<0.4312
Yes	0.35	0.49	0.31	
Depression				0.0154*
Yes	6.48	8.34	6.01	
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	
Number of cigarettes/day				<0.0001*
1	44.28	55.34	41.49	
Alcohol consumption				0.3758
Yes	1.43	1.10	1.52	

*Significance level α is<0.05. SD: Standard deviation, COPD: Chronic obstructive pulmonary disease, AMI: Acute myocardial infarction

and those who lived in the West (OR: 1.32, 95% CI: 1.25-1.38) were more likely to be abstinent than those who lived in the Midwest for those on varenicline. Similarly, smokers who lived in the Northeast (OR: 1.083, 95% CI: 1.005-1.167) and those who lived in the West (OR: 1.33, 95% CI: 1.21-1.45) were more likely to be abstinent than those who lived in the Midwest for those on NRT. However, this association was not found among those on bupropion. Smokers who had no insurance were less likely to be abstinent than those who were covered by commercial insurance for those on varenicline (OR: 0.78,

Table 4: Descriptive statistics of analytic cohort who have been prescribed NRT (*n*=38001)

Variables	Total, *n*=38,001 (100%)	Abstinent at 6 months *n*=7612 (20.03%)	Not abstinent at 6 month *n*=30,389 (79.97%)	*P*
Predisposing characteristics				
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	
Enabling characteristics				
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	
Need characteristics				
Hypertension				<0.0001*
Yes	8.05	9.33	7.73	
Hyperlipidemia				<0.0001*
Yes	8.88	10.22	8.54	
Lung cancer				<0.0001*
Yes	1.41	2.68	1.09	
Stroke				<0.0001*
Yes	1.47	2.92	1.11	
COPD				<0.0001*
Yes	7.03	8.99	6.54	
Diabetes				<0.0003*
Yes	3.63	4.32	3.46	
AMI				<0.0001*
Yes	0.50	1.01	0.37	
Depression				0.1098
Yes	7.62	7.19	7.73	
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	
Number of cigarettes/day				<0.0001*
1	40.04	51.47	37.18	
Alcohol consumption				<0.0001*
Yes	1.05	1.28	0.92	

*Significance level α is<0.05. SD: Standard deviation, NRT: Nicotine replacement therapy, COPD: Chronic obstructive pulmonary disease, AMI: Acute myocardial infarction

95% CI: 0.71-0.86) and NRT (OR: 0.81, 95% CI: 0.68-0.97). Smokers with unknown care were less likely to successfully quit compared to those who received primary care for those on varenicline (OR: 0.87, 95% CI: 0.84-0.90) and NRT (OR: 0.86, 95% CI: 0.81-0.92). However, smokers who received specialty care were more likely to be abstinent than those who received primary care (OR: 1.27, 95% CI: 1.11-1.46) for NRT users. Obese smokers and extreme obese smokers were more likely to successfully quit than those with normal weight for varenicline users (OR: 1.27, 95% CI: 1.22-1.33) (OR: 1.48, 95% CI: 1.39-

Table 5: Logistic regression models for successful outcome among smokers who have been prescribed varenicline, bupropion and NRT

Variables	Model 1 with varenicline *n*=132,885		Model 2 with bupropion *n*=4045		Model 3 with NRT *n*=38,001	
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Predisposing characteristics						
Age group						
18-40	1	1	1	1	1	1
41-64	1.11 (1.07-1.14)	1.08 (1.05-1.12)*	1.40 (1.18-1.66)	1.37 (1.12-1.67)*	1.30 (1.23-1.38)	1.19 (1.12-1.27)*
≥65	1.69 (1.60-1.78)	1.66 (1.56-1.77)*	2.99 (2.30-3.88)	2.67 (1.94-3.65)*	2.99 (2.75-3.25)	2.33 (2.10-2.58)*
Gender						
Female	1	1	1		1	1
Male	0.88 (0.86-0.91)	0.87 (0.85-0.90)*	1.03 (0.88-1.20)		1.10 (1.04-1.15)	1.07 (1.01-1.13)*
Race						
Black	1	1	1	1	1	1
White	1.24 (1.15-1.35)	1.23 (1.12-1.34)*	1.95 (1.35-2.83)	1.79 (1.19-2.69)*	1.62 (1.48-1.77)	1.59 (1.44-1.76)*
Others	1.18 (1.09-1.28)	1.09 (0.99-1.19)*	2.33 (1.62-3.34)	2.10 (1.41-3.13)*	1.93 (1.77-2.11)	1.53 (1.38-1.69)*
Region						
Midwest	1	1	1	1	1	1
Northeast	0.99 (0.95-1.02)	1.19 (1.14-1.24)*	0.89 (0.71-1.10)	1.025 (0.79-1.32)	0.83 (0.78-0.89)	1.08 (1.01-1.16)*
South	0.99 (0.96-1.03)	1.16 (1.11-1.21)*	0.71 (0.58-0.88)	0.806 (0.63-1.02)	0.95 (0.88-1.02)	1.05 (0.96-1.15)
West	1.19 (1.14-1.24)	1.32 (1.25-1.38)*	1.26 (1.03-1.55)	1.175 (0.92-1.49)	1.28 (1.18-1.38)	1.33 (1.21-1.45)*
Enabling characteristics						
Payment type						
Commercial	1	1	1		1	1
Medicare/caid	1.10 (1.06-1.15)	0.96 (0.91-1.01)	1.24 (0.99-1.56)		1.02 (0.95-1.09)	0.85 (0.78-0.92)*
Self-paid	0.77 (0.70-0.84)	0.78 (0.71-0.86)*	0.80 (0.53-1.22)		0.59 (0.50-0.69)	0.81 (0.68-0.97)*
Unknown	0.97 (0.94-1.00)	1.00 (0.97-1.04)	0.87 (0.73-1.03)		0.93 (0.88-0.99)	0.91 (0.84-0.97)*
Specialty group						
Primary care	1	1	1		1	1
Specialty care	1.42 (1.33-1.51)	1.01 (0.94-1.09)	1.84 (1.37-2.48)		1.78 (1.58-2.00)	1.27 (1.11-1.46)*
Unknown	0.91 (0.88-0.94)	0.87 (0.84-0.90)*	1.09 (0.92-1.28)		0.92 (0.88-0.98)	0.86 (0.81-0.92)*
Need characteristics						
Hypertension						
No	1	1	1		1	
Yes	1.16 (1.10-1.23)	1.07 (1.00-1.14)	1.32 (1.02-1.72)		1.22 (1.12-1.34)	
Hyperlipidemia						
No	1	1	1	1	1	
Yes	1.13 (1.08-1.18)	1.07 (1.02-1.13)*	1.66 (1.33-2.08)	1.50 (1.15-1.96)*	1.21 (1.12-1.32)	
Lung cancer						
No	1	1	1		1	1
Yes	1.99 (1.76-2.26)	2.04 (1.77-2.35)*	2.15 (1.12-4.14)		2.50 (2.10-2.99)	1.99 (1.62-2.45)*
Stroke						
No	1		1	1	1	1
Yes	1.37 (1.19-1.58)		3.69 (1.68-8.13)	3.42 (1.35-8.65)*	2.68 (2.26-3.18)	1.91 (1.55-2.35)*
COPD						
No	1		1	1	1	1
Yes	1.06 (1.01-1.13)		0.76 (0.52-1.13)	0.60 (0.37-0.97)*	1.41 (1.29-1.54)	1.24 (1.12-1.39)*
Diabetes						
No	1	1	1		1	
Yes	1.33 (1.23-1.44)	1.18 (1.08-1.30)*	1.91 (1.30-2.80)		1.26 (1.11-1.43)	
AMI						
No	1	1	1		1	1
Yes	2.10 (1.65-2.68)	1.79 (1.37-2.34)*	1.58 (0.49-5.08)		2.73 (2.04-3.66)	2.15 (1.52-3.04)*
Depression						
No	1		1	1	1	
Yes	1.07 (1.01-1.14)		1.42 (1.06-1.90)	1.55 (1.11-2.16)*	0.92 (0.83-1.01)	
Obesity						
Normal weight	1	1	1	1	1	1
Overweight	1.10 (1.05-1.14)	1.126 (1.08-1.17)*	1.20 (0.96-1.49)	1.15 (0.91-1.44)	1.04 (0.97-1.12)	1.08 (1.01-1.16)*
Obese	1.24 (1.20-1.29)	1.277 (1.22-1.33)*	1.32 (1.06-1.63)	1.27 (1.01-1.60)*	1.02 (0.95-1.09)	1.13 (1.05-1.22)*
Extreme obese	1.43 (1.35-1.52)	1.487 (1.39-1.58)*	1.76 (1.28-2.44)	1.84 (1.30-2.61)*	0.97 (0.88-1.08)	1.21 (1.09-1.36)*
Smoking counseling						
No	1	1	1	1	1	1
Yes	0.31 (0.30-0.32)	0.28 (0.27-0.29)*	0.28 (0.23-0.33)	0.28 (0.23-0.34)*	0.22 (0.20-0.23)	0.22 (0.20-0.23)*

(Contd...)

Table 5: *(Continued)*

Variables	Model 1 with varenicline *n*=132,885		Model 2 with bupropion *n*=4045		Model 3 with NRT *n*=38,001	
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Number of cigarettes/day						
1	1	1	1	1	1	1
>1	0.74 (0.72-0.76)	0.70 (0.68-0.72)*	0.57 (0.49-0.66)	0.51 (0.42-0.61)*	0.558 (0.53-0.58)	0.56 (0.53-0.60)*
Alcohol consumption						
No	1		1		1	
Yes	1.07 (0.94-1.21)		0.72 (0.35-1.48)		1.13 (1.09-1.14)	

*Significance level α is<0.05. OR: Odds ratio, COPD: Chronic obstructive pulmonary disease, AMI: Acute myocardial infarction, CI: Confidence interval, NRT: Nicotine replacement therapy

1.58), bupropion users (OR: 1.27, 95% CI: 1.01-1.60) (OR: 1.84, 95% CI: 1.30-2.61), and NRT users (OR: 1.13, 95% CI: 1.05-1.22) (OR: 1.21, 95% CI: 1.09-1.36). Smokers who have received smoking counseling were less likely to be abstinent than those without smoking counseling for varenicline users (OR: 0.28, 95% CI: 0.27-0.29), bupropion users (OR: 0.28, 95% CI: 0.23-0.34), and NRT users (OR: 0.22, 95% CI: 0.20-0.23). Smokers who reported smoking at least one cigarette every day were less likely to be abstinent than those who did not smoke one cigarette for varenicline users (OR: 0.70, 95% CI: 0.68-0.72), bupropion users (OR: 0.51, 95% CI: 0.42-0.61), and NRT users (OR: 0.56, 95% CI: 0.53-0.60). Smokers with hypertension (OR: 1.07, 95% CI: 1.00-1.14), hyperlipidemia (OR: 1.07, 95% CI: 1.02-1.13), lung cancer (OR: 2.04, 95% CI: 1.77-2.35), diabetes (OR: 1.18, 95% CI: 1.08-1.30), and AMI (OR: 1.79, 95% CI: 1.37-2.34) were more likely to quit compared to those without these comorbidities. However, comorbidities such as depression, stroke, and COPD were not found to be significant predictors. Similarly, alcohol consumption was not a significant predictor that would affect quitting successfully. The complete results of multivariate logistic regression were shown in Table 5. For bupropion users, smokers with hyperlipidemia (OR: 1.50, 95% CI: 1.15-1.96), stroke (OR: 3.42, 95% CI: 1.35-8.65), and depression (OR: 1.55, 95% CI: 1.11-2.16) 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: 0.60, 95% CI: 0.37-0.97). However, comorbidities such as hypertension, lung cancer, diabetes, and AMI were not found to be significant predictors. Similarly, alcohol consumption, gender, payment type, and specialty group were not a significant predictor of quitting successfully. For NRT users, smokers with lung cancer (OR: 1.99, 95% CI: 1.62-2.45), stroke (OR: 1.91, 95% CI: 1.55-2.35), COPD (OR: 1.24, 95% CI: 1.12-1.39), and AMI (OR: 2.15, 95% CI: 1.52-3.04) were more likely to quit compared to those without these comorbidities. Comorbidities such as depression, diabetes, hypertension, and hyperlipidemia were not found to be significant predictors. Alcohol consumption was not a significant predictor of quitting successfully.

DISCUSSION

Findings from this real-world data indicated that in 2011, varenicline was the most commonly used smoking cessation medication followed by NRT and bupropion. One previous study that examined utilization patterns of smoking cessation medication in four countries including the US, the United Kingdom, Australia, and Canada from 2006 to 2008 found that the use rate of varenicline increased year by year in the US [16]. In 2008, the use rate of varenicline was comparable to that of NRT, which was the most commonly used cessation medication in prior years, while the use rate of bupropion remained the lowest [16]. Since the use rate of varenicline was increasing each year, it was quite reasonable that varenicline became the most commonly used cessation medication in 2011. The rates of smoking cessation medication use documented in this study are generally lower than what has been found in the reported study Fix *et al*., possibly due to the definition of use rate [16]. In this study, the denominator was defined as patients who reported they were current smokers to physicians in 2011 in GE clinical data, whereas in Brian's study, the denominator was defined as overall smokers who had attempted to quit. In GE data, the information of attempt to quit was not available. For successful outcome, we found that the abstinence rate of varenicline was slightly lower than that of bupropion and NRT. The abstinence rate of bupropion and NRT were close. This finding was not consistent with finding from clinical trials that the abstinence rate of varenicline was higher than that of bupropion [8,17].

In terms of predictors of successful outcomes among smokers who were newly prescribed each smoking cessation medication, we found age, obesity, race, smoking cessation counseling, number of cigarettes smoked per day, and comorbidities were significant predictors of quitting successfully for the smokers who were newly prescribed varenicline, bupropion, and NRT, respectively. In our study, we found that the higher baseline body mass index (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 [18]. Similarly, older smokers were more likely to be abstinent than younger smokers, since older people also would be concerned about their health status, and comorbidities also increase with age adding to this concern [18]. We found that white smokers were more likely to be abstinent compared to nonwhite smokers; this result was consistent among varenicline, bupropion, and NRT users. Furthermore, smokers with other races were also found to be more likely to be abstinent compared to nonwhite

smokers among those who were prescribed bupropion and NRT. This finding of racial differences was consistent with what had been found in Cokkinides *et al.*'s study, which indicated that racial disparity to receive smoking cessation treatment existed for white, black, and Hispanic smokers [19]. This study adds that the racial differences also exist in achieving a successful outcome among those that were prescribed smoking cessation medication. In our study, we found that smokers who had received smoking cessation counseling were less likely to be abstinent compared to those who did not receive cessation counseling. This finding was against what one would expect, as smoking cessation counseling should help improve outcome of smoking cessation intervention [3]. 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, and the more heavy smokers smoked, the more likely they were to get smoking cessation counseling [20]. In our study, we also found that 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 [20]. Several comorbidities were also found to be significant predictors of successful quitting as comorbidities may increase the health concerns of these patients [18], even though there are some variations in the types of comorbidities which affect successful quitting for different cessation medication users. Overall, it showed that smokers with certain diseases were more likely to quit with certain cessation medications, which could be related to suggestions from their physicians or different side effects of each type of cessation medication that affects successful quitting for patients with different comorbidities. There are missing value and some unmeasured confounders such as education level, family income, physician preference, and intention to quit, which were not available in GE data that might have contributed to our findings. To be noted, depression was found 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 [21]. In our study, there were variable results regarding gender differences in successful quitting among smokers who took varenicline and NRT, which showed that 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. One 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 [22]. The finding in this study is consistent with Bohadana's study. Although a randomized control trial which examined the efficacy of varenicline found no sex difference in the efficacy of varenicline [8], 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 to differences in other factors such as education level, income level, and marital status that are reported to affect successful outcomes and may differ in people living in different regions [23]. However, information about these factors was not reported in GE data, and we could not control for them in the data analysis.

For need factors, payment type and specialty group were significant predictors that 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 [3] 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 influence the achievement of a successful outcome of smoking cessation [24]. For 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.

CONCLUSION

In summary, 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 world. 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. Furthermore, smoking information in GE data was available. However, our study has the general limitations of EMR data. GE data can only capture information of smokers who have reported their smoking status; those smokers who have not reported their smoking status to physicians were missing. Some independent variables that 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, and 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. In addition, physician order information does not guarantee that the patients actually filled the prescription. Since EMR data are not recorded as weighted-level nationally representative, there might be some selection bias in our study that can affect generalizability. 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 important strengths.

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