Original Research

Journal of Behavioral Health
www.scopemed.org
DOI: 10.5455/jbh.20160414103729

Comparison of abstinence rates of smoking cessation medications among obese smokers

Mo Yang, Hua Chen, Michael L. Johnson, Ekere J. Essien, Ronald J. Peters, Xin Wang, Susan Abughosh

Department of Pharmaceutical Health Outcomes and Policy, College of Pharmacy, University of Houston, Texas, USA

Address for correspondence:
Susan Abughosh, Department of Pharmaceutical Health Outcomes and Policy, College of Pharmacy, University of Houston, Texas, USA.
E-mail: smabugho@central.uh.edu

Received: April 27, 2015
Accepted: April 10, 2016
Published: April 15, 2016

ABSTRACT

Background: Despite the fact that several pharmacotherapies have been evaluated to be effective measured by continuous abstinence rate, it is not clear which smoking cessation strategy is more effective in terms of providing a higher abstinence rate following cessation among obese smokers. The objective of this study was to compare abstinence rates of different Food Drug Administration (FDA)-approved smoking cessation medication strategies among obese smokers. **Materials and Methods:** A retrospective cohort study was conducted using the General Electric, electronic medical record database (2006-2011). The cohort consisted of obese adult smokers newly initiating the use of an FDA-approved smoking cessation medication (bupropion vs. varenicline). Multivariate logistic regression models were carried out to compare the abstinence between individuals prescribed bupropion versus varenicline at 3, 6, and 12 months after the treatment initiation. Multiple imputations were used to account for the missing data on covariates. **Results:** Descriptive analysis showed a slightly higher abstinence rate for those using bupropion compared to those using varenicline among obese smokers (bupropion vs. varenicline: 19.65% vs. 17.01%) at 3 months ($P < 0.05$); 22.39% vs. 20.58% at 6 months ($P = 0.16$); 24.15% versus 22.86% at 12 months ($P = 0.28$). After adjusting for the covariates, type of medications was not associated with better abstinence among obese patients. **Conclusions:** While previous literature among adults reports better abstinence with varenicline compared to bupropion, our findings among obese smokers indicate no difference in abstinence for those using bupropion compared to those using varenicline.

KEY WORDS: Abstinence rate, bupropion, comparative effectiveness, obesity, smoking cessation, varenicline

INTRODUCTION

Tobacco use and obesity remain the primary and secondary leading cause of mortality and morbidity in the United States (US), with an estimated 480,000 annual deaths between 2005 and 2014 attributable to smoking and an annual 400,000 deaths caused by obesity [1,2]. In the US, it was estimated that approximately 9 million smokers were also obese in the 2002 US National Health Interview Survey [3].

There are several challenges to quitting smoking; in the short-term after smoking cessation, withdrawal symptoms can occur including impatience, anger, difficulty concentrating, depression, anxiety, insomnia, and restlessness. These symptoms usually peak within the first week and last 2-4 weeks [4].The greatest risk of relapse following smoking cessation is when withdrawal symptoms peak in the first few weeks. Relapse is a significant concern after smoking cessation as it leads to failure of the cessation attempt [4,5]. Those who maintain abstinence for the first 2 weeks are more likely to be abstinent 6 months later [6]. Although withdrawal symptoms may reduce and confidence in remaining abstinent may increase for those who maintain abstinence for the first few weeks, abstainers continue to relapse for months, even years following the quit attempts [5].

Abstinence rate is the primary measure for evaluating the success of smoking cessation [7]. Evidence shows that all the Food Drug Administration (FDA)-approved smoking cessation medications have higher abstinence rates compared to placebo for short-term and long-term use [8]. In addition, varenicline has a higher abstinence rate as compared to bupropion or nicotine replacement therapy (NRT) [8]. The adjusted risk ratio (RR) of continuous abstinence at 52 weeks is 1.3-2.3 times higher using varenicline than that of bupropion (RR: 1.36, 95% confidence intervals [CI]: 0.99-1.86; RR: 1.57, 95% CI: 1.14-2.17; RR: 2.27, 95% CI: 1.02-5.03) and NRT (RR: 1.31, 95% CI: 1.01-1.71) [9-12].

While varenicline is reported to have a higher abstinence rate compared to bupropion and placebo among smokers of all weight levels, several trials have demonstrated a lesser post-cessation weight gain when using bupropion compared

to varenicline or placebo [13,14].Varenicline does not seem to have a significant effect on post-cessation weight gain at the end of treatment and bupropion has been shown to attenuate post-cessation weight gain [9-11]. As a considerable concern among obese smokers, post-cessation weight gain may potentially influence the abstinence rate among such a population. Obese smokers gain most weight following quitting smoking, while obese smokers continuing smoking habits are likely to remain stable or lose weight [15]. Hence, obese quitters have the greatest need for interventions to ameliorate weight gain [15].

Despite the fact that several pharmacotherapies have been evaluated to be effective (measured by continuous abstinence rate), it is not clear which smoking cessation strategy is more effective in terms of providing a higher abstinence rate following cessation among obese smokers. Therefore, the primary objective of the study was to compare the abstinence rates of FDA-approved smoking cessation medication strategies during (a) 3-month, (b) 6-month, and (c) 12-month follow-up period among obese smokers. Knowledge gained from this study will provide additional information on the effectiveness and benefit of smoking cessation medications among obese adult smokers. That will aid both policy-makers and clinicians in optimizing drug regimens to treat this high-risk population.

MATERIALS AND METHODS

Study Design and Data Sources

This study was a retrospective cohort study using General Electric (GE) health-care clinical data, which is a real-world observational, daily-updated clinical data, rich in information of millions of patients in the ambulatory primary care setting in the US. GE health-care clinical data have the results of body mass index (BMI) and smoking status that are not commonly available in other databases. The uniqueness and the features of the GE health-care clinical data mentioned above make it the optimal clinical database to be used for conducting this study.

The G-power 3.1.4 statistical software was used for sample size calculation with a 0.05 α-level, 80% power. A medium effect size for abstinence rate of 0.30 (that is, 1.30 odds ratio [OR]), with a binominal distribution, two-tails z-test for multiple logistic regression model would need a number of 3677 observations. Based on the preliminary analysis, the differences with a small to medium effect size can be detected using GE database.

Study Population

Inclusion criteria

The study cohort was identified using the following inclusion criteria: (1) Obese, (2) aged 18 years or older, (3) patients' records being documented at least once in the GE health-care clinical data in the US between January 2006 and December 2011, and (4) were prescribed at least one smoking cessation medication (bupropion hydrochloride or varenicline tartrate).

The index date was defined as the first day of being prescribed smoking cessation medication. Wash-out period was defined as not being prescribed any smoking cessation medication 6 months before the index date [16]. New users were defined as being prescribed at least one smoking cessation medication between July 1st, 2006 and September 30th, 2011 (3-month follow-up), or June 30th, 2011 (6-month follow-up), or December 31st, 2010 (12-month follow-up), while not being prescribed any smoking cessation medication during wash-out period.

Exclusion criteria

Patients were excluded if they were: (1) Missing data on smoking status at baseline and follow-up and (2) being prescribed any of the smoking cessation medication under study during the 6 months of pre-index period.

The cohort consisted of obese smokers newly initiating the use of at least one of the FDA-approved smoking cessation medications (bupropion vs. varenicline).

Measures

The outcome variable was abstinence from smoking versus not at 3-, 6-, and 12-month follow-up time. Abstinence was defined as being reported as "not current" or "former" smoker at any point of the follow-up period; being reported as "current" smoker throughout the follow-up period was categorized as non-abstinence. Once identified as being abstinent, abstinence status was sustained until throughout the follow-up. The abstinence rate was assessed as number of abstinent smokers divided by overall obese smokers for each medication strategy.

The outcome measure – abstinence rate – was followed up by three different timelines: 3 months (end of active treatment effect), 6 months (sustained effect, short term), and 12 months (sustained effect, long-term) after the index date. The reason for taking three different follow-up time periods was that smoking cessation medications are usually required for a 3-month treatment; thus, monitoring the status of smoking 3 months after the treatment can help understand the end of the treatment effect of the smoking cessation medications. On the other hand, smoking cessation medication may also have a short-term and long-term effect on influencing the decision of smoking. 6-month and 12-month follow-up time periods are acceptable for assessing the short-term and long-term effect of smoking cessation medications on abstinence rates [17].

The BMI is a simple index of weight-for-height that is commonly used to classify underweight, overweight, and obesity in adults. It was defined as the weight in kilograms divided by the square of height in meters (kg/m^2) and was rounded to the nearest tenth.

Obesity was classified according to BMI by the World Health Organization (WHO). Individuals whose BMI is greater than

30 are classified as obese, while those whose BMI is greater than 40 are classified as morbid obese [18].

Smoking status was classified as never smoked, formerly smoked, not currently smoking, and currently smoking, which are dummy variables of smoking status in GE health-care clinical data. Never smoker was defined as an individual who has not smoked 100 or more cigarettes during his/her lifetime; former smoker or not current smoker was defined as an individual who has smoked at least 100 cigarettes during his/her lifetime but not currently smoke; current smoker was defined as an individual who has smoked at least 100 cigarettes during his/her lifetime and still regularly smokes every day or periodically.

Statistical Analyses

Descriptive analyses were conducted to assess the frequency distribution of sample demographic characteristics at baseline. Student t-tests were conducted among obese smokers for continuous variables while chi-square tests were conducted for categorical variables. Univariate analyses of participant characteristics were carried out with the three outcome variables, and results were presented as unadjusted OR with 95% CI. Three multivariate logistic regression models were carried out to assess the association between the outcome variable (abstinence vs. not) and independent variables after assessing multicollinearity and interaction. Multivariate logistic regression model results were presented as adjusted ORs with 95% CI and were reported in the results section. The major independent variable was the type of smoking cessation medication prescribed (bupropion and varenicline). Other patient characteristics identified as independent variables and potential confounders for the analysis included the following: Age (categorized as 18-40/41 - 64/≥65), sex (female/male), race (white/non-white), region (Midwest/Northeast/South/West), payment type (commercial/government/self-paid), specialty group (primary care/specialty care), BMI at baseline, comorbidities (smoking attributed diseases including hypertension, hyperlipidemia, lung cancer, stroke, chronic obstructive pulmonary disease [COPD], and acute myocardial infarction), NRT use (using NRT between index date and follow-up), weight counseling (no/yes), smoking counseling (no/yes), weight control medications (including medications which may cause weight reduction and weight gain, respectively), smoke cigarette every day (no/yes), alcohol dependence (no/yes), and alcohol consumption (no/yes). Backward elimination was used to arrive at the final models that included smoking cessation medication and any significant variable ($P < 0.20$).

Considering that missing value might have an impact on the model's fit, missing value analyses using multiple imputation method were performed after assuming that these values of covariate variables were missing at random [19]. The imputed models were then compared with the multivariate logistic regression models which missing values of covariate variables were considered as incomplete cases and deleted from the analyses.

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

RESULTS

Baseline Sample Characteristics

A total number of 4,219,784 obese individuals and 18,458,810 smokers were identified between July 2006 and December 2011 using GE health-care data, reaching out 1,765,748 obese smokers. With a total number of 281,602 smoking cessation medication users identified, the total sample consisted of 87,065 obese smokers utilizing at least one FDA-approved smoking cessation medication from July 2006 to December 2011. Based on the abstinence rate defined above, number of individuals who were considered abstinence was 18,256 at 3 months follow-up, 22,904 at 6 months follow-up, and 30,715 at 12 months follow-up. Figure 1 shows the schematic diagram for study cohort.

The mean age of the cohort was 45.41 years (±standard deviation [SD]: 12.19), while the mean BMI was 35.36 (±SD: 5.43). An overall abstinence rate at each follow-up was 17.01% ($n = 3106$), 20.58% ($n = 4714$), and 22.86% ($n = 7021$), respectively. In terms of follow-up at 3 months, the abstinence rate was 16.90% ($n = 2958$) for obese smokers who were prescribed varenicline, while 19.65% ($n = 148$) for those who were prescribed bupropion ($P < 0.05$); in terms of follow-up at 6 months, the abstinence rate was 20.51% ($n = 4506$) for those who were prescribed varenicline, while 22.39% ($n = 208$) for those who were prescribed bupropion ($P = 0.16$); in terms of follow-up at 12 months, the abstinence rate was 22.86% ($n = 6,730$) for those who were prescribed varenicline, while 22.86% ($n = 291$) for those who were prescribed bupropion ($P = 0.28$). There was a statistically significant difference of age group, region, NRT use for abstinence at all three follow-up times ($P < 0.05$). There was a statistically significant difference of specialty group for abstinence at 6 months; and payment type, alcohol dependence, and smoking counseling for abstinence at 12 months ($P < 0.05$). Table 1 summarizes the results of patients' characteristics and chi-square tests with the three outcome variables. Smoking cessation medication type and BMI value at baseline were multi-imputed. Results from multiple imputation missing value analyses showed consistent results compared to the baseline models (data not shown).

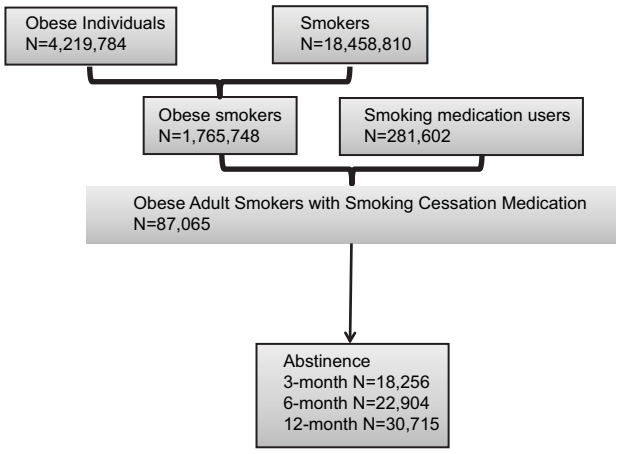

Figure 1: Schematic diagram for study cohort

Table 1: Baseline characteristics for abstinence among obese adult smokers who were prescribed any smoking cessation medication at 3-, 6-, and 12-month follow-up period

Variables	Abstinence at 3 months (17.01%, *n*=3106)		*P* value	Abstinence at 6 months (20.58%, *n*=4714)		*P* value	Abstinence at 12 months (22.86%, *n*=7021)		*P* value
	Varenicline (16.90%, *n*=2958)	Bupropion (19.65%, *n*=148)		Varenicline (20.51%, *n*=4506)	Bupropion (22.39%, *n*=208)		Varenicline (22.86%, *n*=6730)	Bupropion (24.15%, *n*=291)	
Age (±SD)	43.50 (11.96)	44.35 (12.88)	0.00**	43.93 (12.10)	44.56 (13.09)	0.00**	44.30 (12.17)	44.89 (13.19)	0.00***
Baseline BMI (±SD)	35.45 (5.41)	35.75 (5.55)	0.37	35.51 (5.48)	35.67 (5.48)	0.98	35.51 (5.52)	35.74 (5.57)	0.73
Weight change (±SD)	1.18 (16.75)	0.23 (25.90)	0.00***	2.14 (18.14)	0.22 (25.32)	0.00***	3.12 (20.89)	1.47 (17.50)	0.00***
Gender									
Female	49.67	59.76	0.00***	50.63	59.10	0.00***	51.90	59.17	0.00***
Male	50.33	40.24		49.37	40.90		48.10	40.83	
Age group									
18-39	39.16	37.72	0.04*	37.92	37.57	0.02*	36.82	36.27	0.00**
40-64	56.48	56.04		57.22	55.54		58.03	56.18	
≥65	4.35	6.24		4.86	6.89		5.14	7.55	
Race									
White	39.92	39.97	0.98	40.90	40.80	0.95	42.30	41.58	0.62
Non-white	60.08	60.03		59.10	59.20		57.70	58.42	
Region									
Midwest	26.38	27.79	0.03*	25.91	27.69	0.04*	25.97	29.40	0.00**
Northeast	21.51	16.89		22.35	18.32		23.00	18.27	
South	31.69	34.04		31.41	32.87		31.19	32.39	
West	20.41	21.28		20.33	21.12		19.85	19.93	
Payment type									
Commercial	71.54	68.60	0.40	70.03	66.95	0.35	69.21	63.59	0.01**
Medicare/paid	21.86	23.48		23.40	25.73		24.33	27.66	
Self-paid	6.61	7.92		6.58	7.32		6.46	8.75	
Specialty group									
Primary care	89.37	87.71	0.25	90.45	87.80	0.03*	91.44	90.03	0.17
Specialty care	10.63	12.29		9.55	12.20		8.56	9.97	
Hypertension									
No	87.16	85.39	0.16	87.04	84.50	0.02*	87.27	85.64	0.10
Yes	12.84	14.61		12.96	15.50		12.73	14.36	
Depression									
No	93.81	92.30	0.09	93.58	92.25	0.11	93.44	92.03	0.05
Yes	6.19	7.70		6.42	7.75		6.56	7.97	
Weight-reduction drug									
No	92.17	90.70	0.14	91.82	90.53	0.16	91.44	90.54	0.27
Yes	7.83	9.30		8.18	9.47		8.56	9.46	
Alcohol dependence									
No	51.82	54.45	0.16	53.54	56.19	0.11	55.52	44.48	0.04*
Yes	48.18	45.55		46.46	43.81		58.51	41.49	
Smoking counseling									
No	52.89	55.78	0.12	54.00	57.16	0.06	55.68	59.00	0.02*
Yes	47.11	44.22		46.00	42.84		44.32	41.00	
Smoke cigarette every day									
No	46.64	46.75	0.95	48.72	49.41	0.68	51.32	51.95	0.67
Yes	53.36	53.25		51.28	50.59		48.68	48.05	
NRT									
No	98.20	92.03	0.00***	97.48	90.96	0.00***	96.51	89.05	0.00***
Yes	1.80	7.97		2.52	9.04		3.49	10.95	
Abstinence at follow-up months (i.e., 3/6/12)									
No	83.10	80.35	0.05*	79.49	77.61	0.16	77.19	75.85	0.28
Yes	16.90	19.65		20.51	22.39		22.81	24.15	

*Significance level α is<0.05; **Significance level α is<0.01; ***Significance level α is<0.001. SD: Standard deviation, BMI: Body mass index, NRT: Nicotine replacement treatment

Logistic Regression Analyses

Table 2 summarizes the results of univariate logistic regression and multivariate logistic regression of abstinence rate at each follow-up period. Multicollinearity analysis and interaction assessment showed that there was no multicollinearity or interaction among the independent variables.

Table 2: Logistic regression models for abstinence among obese adult smokers who were prescribed any smoking cessation medication at 3-, 6-, and 12-month follow-up period

Variables	Model 1: Abstinence at 3 months		Model 2: Abstinence at 6 months		Model 3: Abstinence at 12 months	
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Smoking cessation medication						
Varenicline	1		1		1	
Bupropion	1.20 (1.00-1.45)		1.12 (0.96-1.31)		1.08 (0.94-1.23)	
Age group						
18-39	1	1	1	1	1	1
40-64	1.25 (1.15-1.36)	1.03 (0.91-1.17)	1.26 (1.18-1.35)	1.10 (1.01-1.20)	1.27 (1.20-1.34)	1.16 (1.05-1.28)
≥65	2.28 (1.93-2.69)	1.58 (1.21-2.06)	2.48 (2.17-2.84)	2.02 (1.70-2.39)	2.35 (2.11-2.63)	1.79 (1.46-2.20)
Race						
White	1	1	1	1	1	1
Non-white	0.87 (0.81-0. 94)	0.86 (0.76-0.96)	0.87 (0.81-0.92)	0.88 (0.81-0.95)	0.87 (0.83-0.92)	0.86 (0.78-0.94)
Region						
Midwest	1	1	1	1	1	1
Northeast	1.10 (0.98-1.24)	1.21 (1.01-1.45)	1.26 (1.15-1.39)	1.37 (1.22-1.54)	1.23 (1.14-1.33)	1.30 (1.15-1.48)
South	1.07 (0.97-1.19)	1.07 (0.91-1.25)	1.15 (1.05-1.26)	1.20 (1.07-1.33)	1.13 (1.05-1.21)	1.11 (0.98-1.26)
West	1.40 (1.25-1.56)	1.34 (1.12-1.60)	1.49 (1.35-1.63)	1.56 (1.39-1.75)	1.39 (1.28-1.50)	1.44 (1.24-1.66)
Payment type						
Commercial	1		1		1	1
Medicare/paid	1.22 (1.07-1.39)		1.26 (1.13-1.39)		1.14 (1.05-1.24)	0.97 (0.86-1.08)
Self-paid	0.80 (0.63-1.02)		0.75 (0.62-0.92)		0.72 (0.61-0.85)	0.71 (0.58-0.86)
Specialty group						
Primary care	1	1	1		1	
Specialty care	1.78 (1.55-2.04)	1.36 (1.15-1.61)	1.38 (1.22-1.56)		1.34 (1.20-1.50)	
Hypertension						
No	1	1	1	1	1	
Yes	1.14 (1.02-1.28)	1.25 (1.06-1.47)	1.12 (1.02-1.23)	1.14 (1.02-1.28)	1.06 (0.98-1.15)	
Alcohol dependence						
No	1	1	1	1	1	1
Yes	0.57 (0.53-0. 62)	0.64 (0.57-0.72)	0.65 (0.61-0.69)	0.68 (0.63-0.74)	0.72 (0.68-0.76)	0.77 (0.70-0.85)
Weight-reduction drug						
No	1	1	1	1	1	1
Yes	1.50 (1.32-1.71)	1.51 (1.25-1.83)	1.33 (1.20-1.49)	1.36 (1.20-1.55)	1.20 (1.10-1.32)	1.50 (1.30-1.73)
Smoking counseling						
No	1	1	1	1	1	1
Yes	0.43 (0.39-0.46)	0.50 (0.45-0.57)	0.48 (0.45-0.52)	0.52 (0.48-0.57)	0.55 (0.52-0.58)	0.59 (0.54-0.65)
Smoke cigarette every day						
No	1	1	1	1	1	1
Yes	0.68 (0.63-0.73)	0.83 (0.74-0.93)	0.70 (0.65-0.74)	0.81 (0.75-0.87)	0.74 (0.70-0.78)	0.89 (0.81-0.97)
Base BMI value	1.02 (1.01-1.02)	1.02 (1.01-1.03)	1.02 (1.01-1.02)	1.02 (1.01-1.02)	1.01 (1.00-1.02)	1.02 (1.01-1.02)

OR: Odds ratio, 95% CI: 95% Confidence interval, AMI: Acute myocardial infarction, BMI: Body mass index. Some adjusted ORs in multivariate logistic regression models were missing due to the use of backward elimination, which removed those covariates that were not statistically significant

Obese smokers aged between 40 and 64 years (OR: 1.10, 95% CI: 1.01-1.20 in model 2; OR: 1.16, 95% CI: 1.05-1.28 in model 3) and 65 years or older (OR: 1.58, 95% CI: 1.21-2.06 in model 1; OR: 2.02, 95% CI: 1.70-2.39 in model 2; OR: 1.79, 95% CI: 1.46-2.20 in model 3) were more likely to be abstinent than those who were aged between 18 and 39 years old. Non-white (OR: 0.86, 95% CI: 0.76-0.96 in model 1; OR: 0.88, 95% CI: 0.81-0.95 in model 2; OR: 0.86, 95% CI: 0.78-0.94 in model 3) were less likely to be abstinent than white. Obese smokers who were from the Northeast (OR: 1.21, 95% CI: 1.01-1.45 in model 1; OR: 1.37, 95% CI: 1.22-1.54 in model 2; OR: 1.30, 95% CI: 1.15-1.48 in model 3), Southern (OR: 1.20, 95% CI: 1.07-1.33 in model 2), and Western US (OR: 1.34, 95% CI: 1.12-1.60 in model 1; OR: 1.56, 95% CI: 1.39-1.75 in model 2; OR: 1.44, 95% CI: 1.24-1.66 in model 3) were more likely to be abstinent than those who were from Midwest. Obese smokers who were diagnosed with hypertension (OR: 1.25, 95% CI: 1.06-1.47 in model 1; OR: 1.14, 95% CI: 1.02-1.28 in model 2) were more likely to be abstinent than those who were not. In contrast, obese smokers who were diagnosed with alcohol dependence were less likely to be abstinent than those who did not (OR: 0.64, 95% CI: 0.57-0.72 in model 1; OR: 0.68, 95% CI: 0.63-0.74 in model 2; OR: 0.77, 95% CI: 0.70-0.85 in model 3). Obese smokers who were prescribed weight influencing medications which may cause weight reduction were more likely to be abstinent than those who did not (OR: 1.51, 95% CI: 1.25-1.83 in model 1; OR: 1.36, 95% CI: 1.20-1.55 in model 2; OR: 1.50, 95% CI: 1.30-1.73 in model 3). Obese smokers who were offered smoking counseling were less likely to be abstinent than those who were not (OR: 0.50, 95% CI: 0.45-0.57 in model 1; OR: 0.52, 95% CI: 0.48-0.57 in model 2; OR: 0.59, 95% CI: 0.54-0.65 in model 3). Obese smokers who were identified to smoke at least one cigarette per day were less likely to be abstinent than those who were not (OR: 0.83, 95% CI: 0.74-0.93 in model 1; OR: 0.81, 95% CI: 0.75-0.87 in model 2; OR: 0.89 95% CI: 0.81-0.97 in model 3). In addition, each unit increase of BMI at baseline

resulted in 2% more likelihood to be abstinent (OR: 1.02, 95% CI: 1.01-1.03 in model 1; OR: 1.02, 95% CI: 1.01-1.02 in model 2; OR: 1.02, 95% CI: 1.01-1.02 in model 3).

Some associations were found only in one model out of the three models: Obese smokers who received a specialty care were more likely to be abstinent than those who received a primary care (OR: 1.36, 95% CI: 1.15-1.61 in model 1). Obese smokers who paid insurance out of pocket were less likely to be abstinent than those who had a commercial insurance (OR: 0.71, 95% CI: 0.58-0.86 in model 3).

DISCUSSION

An overall abstinence rate between approximately 18% and 23% from 3- to 12-month follow-up following smoking cessation medication intervention was documented among obese smokers in this study. For obese smokers who were prescribed varenicline, abstinence rate increased from nearly 17% at 3-month follow-up to nearly 23% at 12-month follow-up, whereas for those who were prescribed bupropion, abstinence rates increased from nearly 21% at 3-month follow-up to 25% at 12-month follow-up. Our finding is consistent with the study conducted by Chatkin *et al*. (2004), which found an estimated continuous abstinence rate of 23.2% at 12-month follow-up among a Brazilian cohort of non-obese smokers [20]. As compared to the clinical trial conducted by Jorenby *et al*. (2006), the 12-month follow-up abstinence rate of our study is similar for varenicline while 10% more for bupropion [10].To be noted, however, a study conducted by Jorenby *et al*. (2006) was a clinical study with small sample size, general population of obese and non-obese participants.

Previous literature has consistently reported that varenicline had a higher abstinence rate as compared to bupropion with an adjusted RR ranged between 1.3 and 2.3 at 1-year follow-up [9-11,21-23]. This study found that obese smokers who were prescribed bupropion had a statistically significant higher abstinence rate than those who were prescribed varenicline at 3-month follow-up while there is no statistically significant difference at 6-month and 12-month follow-up. This finding is expected; a possible explanation for this improved abstinence with bupropion at 3 months follow-up could be related to less post-cessation weight gain for bupropion users compared to varenicline or placebo users [13,14].Meanwhile, long-term (e.g., 12 months) weight gain following smoking cessation intervention was not well documented [24]. Varenicline is not reported to decrease post-cessation weight gain, although a higher abstinence rate was reported by clinical trials conducted with participants of all weight levels [9-11]. Weight gain has been recognized as a distinguishing feature of nicotine withdrawal [4]. Weight gain is one of the major cited reasons for continuity of smoking and relapse after smoking cessation, especially among women [25,26]. As bupropion is reported to significantly attenuate post-cessation weight gain, it might be a better choice among obese smokers and might affect the abstinence rate among such population. Our finding is consistent with the study conducted by Jiménez Ruiz *et al*. (2012), which found no statistically significant differences on continuous abstinence rate up to 6 months between COPD smokers who were prescribed varenicline and who were prescribed bupropion [27]. Our study results varied from the latest Cochrane meta-analyses, which have found that both varenicline and bupropion improved smoking cessation rate; the pooled relative risk for continuous abstinence at 12-month follow-up for varenicline versus bupropion was 1.52 (95% CI: 1.22-1.88), analyzing from 3 clinical trials with a total of 1622 participants [8].This, however, was based on participants of all weight levels, while our study included only obese smokers expected to gain most weight gain following cessation [15].

In this study, we found that there was no significant difference of abstinence from smoking at any of the follow-up times between bupropion and varenicline after adjusting for covariates. This finding was unexpected. Previous studies indicated that both varenicline and bupropion were effective in helping quitting smoking up to 1-year follow-up [8]; however, the adjusted results showed in this study indicated that there is no statistically significant difference of using varenicline and bupropion for smoking cessation at different follow-up times. It is important to note that studies included in the previous systematic review were all clinical trials, and independent cohort observational studies in smokers with varying comorbidities are needed. In addition, the cohorts of all the selected studies included individuals with various weights; hence, different populations may result in different abstinence rates. Our study suggests an improved abstinence with bupropion among obese smokers and the significant advantage of varenicline disappeared when only obese smokers were examined. In addition, we found the following demographic characteristics of the cohort were significant predictors of successful abstinence from smoking: age, race, region, payment type, and specialty group.

Our finding that age was a predictor of abstinence is consistent with the study conducted by Dale *et al.* (1997), which found that older age was more likely to be abstinent than smokers at younger age [28]. Older aged smokers tend to be concerned more about their health than younger aged smokers [29], particularly among obese smokers, who might have more health problems due to cigarette smoking and obesity.

We found that both race and region were significant predictors of abstinence from smoking. Non-whites were less likely to be abstinence than whites among obese smokers who were prescribed smoking cessation medications. Cokkinides *et al.* (2008) concluded that there were racial and ethnic disparities in receiving smoking-cessation interventions [30]. Our study shows that minorities receiving smoking cessation medications also showed lower abstinence. Both the geographic variation and racial disparity affecting simultaneously the abstinence rate among obese smokers, highlight the importance of exploring and understanding the underlying causes of disparities within and across regions [31].

In terms of insurance status, only obese smokers who were self-payers had less likelihood of being abstinent than those who had commercial insurance for the 12 months outcome. This finding might be because self-pay patients may not want to continue

to pay for the medication. Our finding is consistent with the study conducted by Bouvy *et al.* (2003), who found that having health insurance was associated with tobacco abstinence at 3 months follow-up [32]; furthermore, private insurance status was associated with a higher successful abstinence rate [33].

Those who were offered specialty care were more likely to be abstinent than those who were offered a primary care for the 3 months outcome. Specialists may be more influential in convincing patients. This finding was similar with the study conducted by Brose *et al.* (2011), which found that specialist clinics settings were more successful in terms of effective smoking cessation intervention than primary care [34]. Obese smokers who were diagnosed with hypertension were more likely to be abstinent than those who were not. This finding is reasonable as hypertension is related to cigarette smoking; therefore, stopping smoking maybe necessary to improve the health status of obese smokers. In addition, the higher the BMI of the obese smokers, the more they were likely to be abstinent from smoking. This is possibly related to the concern that the health condition tends to worsen with a higher BMI.

Obese smokers who were also alcohol dependent were less likely to be abstinent from smoking; consistent with previous reports showing that smoking cessation failure is highly correlated with alcohol consumption [35]. The co-occurrence of cigarette smoking and alcohol consumption has been well documented and was well known among the public [36,37]. Individuals who are smokers are more likely to be alcoholics at the same time than non-smokers; moreover, smokers tend to consume alcohol more frequently and heavily than non-smokers [36-38]. On the other hand, more than 60% of alcohol dependents are also cigarette smokers [37], and approximately 80% of these alcohol dependents are heavy smokers [39].

Obese smokers who were prescribed weight influencing medications which may cause weight reduction were more likely to be abstinent than those who did not. An obese smoker's health is expected to be of high concern to physicians, and patients are usually advised to stop smoking and lose weight. Weight-concerned smokers may prefer taking weight control drugs along with quitting smoking. By taking weight control drugs along with cessation, obese smokers might be able to have more control of post-cessation weight gain. Thus, they might be more inclined to continue with cessation, as the increased weight might cause relapse after smoking cessation [25,26].

Obese smokers who were offered smoking counseling were less likely to be abstinent from smoking than those who were not. This result was not expected. Possible explanation could be that obese smokers who were offered smoking counseling were more addicted to nicotine. Although smoking counseling was offered, it is not easy to stop smoking by counseling only. Previous studies showed that smoking cessation interventions with both pharmacological and behavioral intervention are more effective than pharmacological or behavioral interventions only [40]. However, our finding is not consistent with most of the studies which stated that smoking cessation is more likely to be successful when smoking counseling is offered. Another plausible explanation is that discussing potential weight gain in counseling might have deterred patients from a successful cessation.

Obese smokers who smoked at least one cigarette per day were less likely to be abstinent from smoking compared to those who did not. As one of the factors associated with nicotine dependence, the group of obese smokers who smoked at least one cigarette per day were more likely to be smokers with high-level nicotine dependence, thus had more difficulty stopping smoking. Our study was consistent with the finding from another study, which found that smokers who had smoking history were less likely to be abstinence in a long-term period [41].

Strengths and Limitations

There are certain limitations in this study. This observational cohort study limits us from drawing a causal relationship of identified predictors of successful abstinence at different follow-up times. Other limitations in this study are mainly related to using electronic medical record (EMR) data. Data for smoking and obesity may not be completely recorded, and the diagnosis codes in the EMR data may not match those in the administrative claims data. Furthermore, prescription data were identified by physician orders, which did not guarantee that the patients actually filled the prescription and persistence cannot be accounted for. Some confounders such as eating habits and education cannot be controlled for in the analysis as this information is lacking.

Although these foregoing deficiencies may belie the precision of the finding, 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. Our study has other strengths: the follow-up times was from 3 to 12 months. It was suggested that for longitudinal studies, 3-month follow-up may be a reasonable period to assess the intermediate success of smoking cessation while the optimal estimate of success smoking cessation rate is the 12-month continuous abstinence rate, for 12-month data are available for many interventions [17].

Future Study

The study compared the effectiveness of the available prescription cessation medications among a high-risk population of obese smokers. Future research should take the findings into consideration to help obese smokers achieve successful cessation and provide an improvement to the future health of the American society.

CONCLUSIONS

An overall abstinence rate of 17-23% from 3- to 12-month follow-up was found among obese smokers. While many studies reported better abstinence with varenicline compared

to bupropion, we found no such difference among obese smokers after adjusting for other covariates. This might be related to the antiobesity effects of bupropion. Predictors identified in this study included: age, race, region, payment type, specialty group, morbidities including hypertension, alcohol dependence, weight influencing medications, which may cause weight reduction, smoking counseling, smoke cigarette every day, and BMI value at baseline, whereas smoking cessation medications were not found to be a significant predictor of abstinence from smoking at any follow-up time. Predictors identified in this study should be considered when designing smoking cessation interventions among the high-risk population of obese smokers.

REFERENCES

1. National Center for Chronic Disease Prevention and Health Promotion (US) Office on Smoking and Health. The Health Consequences of Smoking: 50 years of Progress: A Report of the Surgeon General. Atlanta, GA: Centers for Disease Control and Prevention (US); 2014. p. 11.
2. Hurt RT, Frazier TH, McClave SA, Kaplan LM. Obesity epidemic: Overview, pathophysiology, and the intensive care unit conundrum. JPEN J Parenter Enteral Nutr 2011;35:4S-13.
3. Healton CG, Vallone D, McCausland KL, Xiao H, Green MP. Smoking, obesity, and their co-occurrence in the United States: Cross sectional analysis. BMJ 2006;333:25-6.
4. Hughes JR, Higgins ST, Bickel WK. Nicotine withdrawal versus other drug withdrawal syndromes: similarities and dissimilarities. Addiction 1994;89:1461-70.
5. Coleman T, Agboola S, Leonardi-Bee J, Taylor M, McEwen A, McNeill A. Relapse prevention in UK stop smoking services: Current practice, systematic reviews of effectiveness and cost-effectiveness analysis. Health Technol Assess 2010;14:1-152.
6. Kenford SL, Fiore MC, Jorenby DE, Smith SS, Wetter D, Baker TB. Predicting smoking cessation. Who will quit with and without the nicotine patch. JAMA 1994;271:589-94.
7. North American Quit Line Consortium Issue Paper, 2009. Measuring Quit Rates. Available from: http://www.c.ymcdn.com/sites/www.naquitline.org/resource/resmgr/docs/naqc_issuepaper_measuringqui.pdf. [Last accessed on 2013 Dec 07].
8. Cahill K, Stevens S, Perera R, Lancaster T. Pharmacological interventions for smoking cessation: An overview and network meta-analysis. Cochrane Database Syst Rev 2013;5:CD009329.
9. Gonzales D, Rennard SI, Nides M, Oncken C, Azoulay S, Billing CB, *et al*. Varenicline, an alpha4beta2 nicotinic acetylcholine receptor partial agonist, vs. sustained-release bupropion and placebo for smoking cessation: A randomized controlled trial. JAMA 2006;296:47-55.
10. Jorenby DE, Hays JT, Rigotti NA, Azoulay S, Watsky EJ, Williams KE, *et al.* Efficacy of varenicline, an alpha4beta2 nicotinic acetylcholine receptor partial agonist, vs. placebo or sustained-release bupropion for smoking cessation: A randomized controlled trial. JAMA 2006;296:56-63.
11. Nides M, Oncken C, Gonzales D, Rennard S, Watsky EJ, Anziano R, *et al.* Smoking cessation with varenicline, a selective alpha4beta2 nicotinic receptor partial agonist: Results from a 7-week, randomized, placebo- and bupropion-controlled trial with 1-year follow-up. Arch Intern Med 2006;166:1561-8.
12. Aubin HJ, Bobak A, Britton JR, Oncken C, Billing CB Jr, Gong J, *et al.* Varenicline versus transdermal nicotine patch for smoking cessation: Results from a randomised open-label trial. Thorax 2008;63:717-24.
13. Parsons AC, Shraim M, Inglis J, Aveyard P, Hajek P. Interventions for preventing weight gain after smoking cessation. Cochrane Database Syst Rev 2009:CD006219.
14. Gadde KM, Xiong GL. Bupropion for weight reduction. Expert Rev Neurother 2007;7:17-24.
15. Lycett D, Munafò M, Johnstone E, Murphy M, Aveyard P. Associations between weight change over 8 years and baseline body mass index in a cohort of continuing and quitting smokers. Addiction 2011;106:188-96.
16. Chatterjee S, Chen H, Johnson ML, Aparasu RR. Comparative risk of cerebrovascular adverse events in community-dwelling older adults using risperidone, olanzapine and quetiapine: A multiple propensity score-adjusted retrospective cohort study. Drugs Aging 2012;29:807-17.
17. Gilpin EA, Pierce JP, Farkas AJ. Duration of smoking abstinence and success in quitting. J Natl Cancer Inst 1997;89:572-6.
18. Seidell JC. Epidemiology - Definition and classification of obesity. In: Kopelman PG, Caterson ID, Dietz WH, editors. Clinical Obesity in Adults and Children. 2nd ed. Oxford, UK: Blackwell Publishing Ltd.; 2007.
19. Sterne JA, White IR, Carlin JB, Spratt M, Royston P, Kenward MG, *et al.* Multiple imputation for missing data in epidemiological and clinical research: Potential and pitfalls. BMJ 2009;338:b2393.
20. Chatkin JM, Mariante de Abreu C, Haggsträm FM, Wagner MB, Fritscher CC. Abstinence rates and predictors of outcome for smoking cessation: Do Brazilian smokers need special strategies? Addiction 2004;99:778-84.
21. Rankin KV, Jones DL. Treatment of nicotine dependence with Chantix (varenicline). Tex Dent J 2011;128:457-61.
22. Xenakis JG, Kinter ET, Ishak KJ, Ward AJ, Marton JP, Willke RJ, *et al.* A discrete-event simulation of smoking-cessation strategies based on varenicline pivotal trial data. Pharmacoeconomics 2011;29:497-510.
23. Casella G, Caponnetto P, Polosa R. Therapeutic advances in the treatment of nicotine addiction: Present and future. Ther Adv Chronic Dis 2010;1:95-106.
24. Yang M, Bhowmik D, Wang X, Abughosh S. Does combination pharmacological intervention for smoking cessation prevent post-cessation weight gain? A systemic review. Addict Behav 2013;38:1865-75.
25. Klesges RC, Meyers AW, Klesges LM, La Vasque ME. Smoking, body weight, and their effects on smoking behavior: A comprehensive review of the literature. Psychol Bull 1989;106:204-30.
26. Klesges RC, Shumaker SA. Understanding the relations between smoking and body weight and their importance to smoking cessation and relapse. Health Psychol 1992;11 Suppl:1-3.
27. Jiménez Ruiz CA, Ramos Pinedo A, Cicero Guerrero A, Mayayo Ulibarri M, Cristobal Fernández M, Lopez Gonzalez G. Characteristics of COPD smokers and effectiveness and safety of smoking cessation medications. Nicotine Tob Res 2012;14:1035-9.
28. Dale LC, Olsen DA, Patten CA, Schroeder DR, Croghan IT, Hurt RD, *et al.* Predictors of smoking cessation among elderly smokers treated for nicotine dependence. Tob Control 1997;6:181-7.
29. Yang M, Essien EJ, Sansgiry SS, Wu IH, Peter RJ, Abughosh S. Predictors of intention to quit cigarette smoking among Chinese adults. J Behav Health 2012;1:93-101.
30. Cokkinides VE, Halpern MT, Barbeau EM, Ward E, Thun MJ. Racial and ethnic disparities in smoking-cessation interventions: Analysis of the 2005 National Health interview survey. Am J Prev Med 2008;34:404-12.
31. McClure LA, Murphy HL, Roseman J, Howard G, Malarcher A. Regional and racial differences in smoking and exposure to secondhand smoke: The reasons for geographic and racial differences in stroke (REGARDS) study. Prev Chronic Dis 2011;8:A108.
32. Biazzo LL, Froshaug DB, Harwell TS, Beck HN, Haugland C, Campbell SL, *et al.* Characteristics and abstinence outcomes among tobacco quitline enrollees using varenicline or nicotine replacement therapy. Nicotine Tob Res 2010;12:567-73.
33. Bouvy ML, Buurma H, Egberts AC. Determinants for successful smoking cessation with bupropion in daily practice. Pharm World Sci 2003;25:207-11.
34. Brose LS, West R, McDermott MS, Fidler JA, Croghan E, McEwen A. What makes for an effective stop-smoking service? Thorax 2011;66:924-6.
35. Cook JW, Fucito LM, Piasecki TM, Piper ME, Schlam TR, Berg KM, *et al.* Relations of alcohol consumption with smoking cessation milestones and tobacco dependence. J Consult Clin Psychol 2012;80:1075-85.
36. Dawson DA. Drinking as a risk factor for sustained smoking. Drug Alcohol Depend 2000;59:235-49.
37. Falk DE, Yi HY, Hiller-Sturmhöfel S. An epidemiologic analysis of co-occurring alcohol and tobacco use and disorders: Findings from the national epidemiologic survey on alcohol and related conditions. Alcohol Res Health 2006;29:162-71.

38. Piasecki TM, Jahng S, Wood PK, Robertson BM, Epler AJ, Cronk NJ, *et al*. The subjective effects of alcohol-tobacco co-use: An ecological momentary assessment investigation. J Abnorm Psychol 2011;120:557-71.
39. Dierker L, Donny E. The role of psychiatric disorders in the relationship between cigarette smoking and DSM-IV nicotine dependence among young adults. Nicotine Tob Res 2008;10:439-46.
40. Stead LF, Koilpillai P, Fanshawe TR, Lancaster T. Combined pharmacotherapy and behavioural interventions for smoking cessation. Cochrane Database Syst Rev 2016;3:CD008286.
41. Curry S, Thompson B, Sexton M, Omenn GS. Psychosocial predictors of outcome in a worksite smoking cessation program. Am J Prev Med 1989;5:2-7.

Source of Support: Nil, Conflict of Interest: None declared.