# *Modular Program Report*

The following report(s) provides findings from an FDA-initiated query using its Mini-Sentinel pilot. While Mini-Sentinel queries may be undertaken to assess potential medical product safety risks, they may also be initiated for various other reasons. Some examples include determining a rate or count of an identified health outcome of interest, examining medical product use, exploring the feasibility of future, more detailed analyses within Mini-Sentinel, and seeking to better understand the capabilities of the Mini-Sentinel pilot.

Data obtained through Mini-Sentinel are intended to complement other types of evidence such as preclinical studies, clinical trials, postmarket studies, and adverse event reports, all of which are used by FDA to inform regulatory decisions regarding medical product safety. The information contained in this report is provided as part of FDA's commitment to place knowledge acquired from the Mini-Sentinel pilot in the public domain as soon as possible. Any public health actions taken by FDA regarding products involved in Mini-Sentinel queries will continue to be communicated through existing channels.

FDA wants to emphasize that the fact that FDA has initiated a query involving a medical product and is reporting findings related to that query does not mean that FDA is suggesting health care practitioners should change their prescribing practices for the medical product or that patients taking the medical product should stop using it. Patients who have questions about the use of an identified medical product should contact their health care practitioners.

**Modular Program Type**: MP 3 - Drug Use – Incident Outcomes
(See online specification for details:
http://mini-sentinel.org/data_activities/modular_programs/details.aspx?ID=111)

**Date Posted:** January 17, 2012

**Medical product exposures of interest**:

This Modular Program execution included 4 different exposure categories. Each exposure category was assessed independently.

- Varenicline – all NDCs (identified with FirstDataBank)
- Buproprion
  - All NDCs (identified with FirstDataBank)
  - NDCs classified as "smoking cessation" by FirstDataBank Enhanced Therapeutic Classification (ETC) hierarchy
  - NDCs classified as "antidepressant" by ETC hierarchy

**Exposure time at risk**:

The new user and days of exposure specifications for each exposure category are as follows:

- The first dispensing after at least 180 days of no exposure to any of the drugs of interest (i.e., new or incident users) was identified between January 1, 2006 and the most recently quality checked data at each Data Partner as of July 5, 2011. The end date across Data

Partners ranged from the end of 2009 to 1st quarter of 2011. A treatment episode was created using the number of days supplied on each consecutive dispensing; gaps of 7 days or less between dispensings were bridged, and 7 days of exposure were added to the end of the last dispensing

- Exposed time at risk began on the day after the first incident dispensing and continued for the entire treatment episode (or end of enrollment or occurrence of an outcome)

**New user inclusion/exclusion criteria and cohort definitions**:

New users for each drug of interest were further restricted by eligibility and diagnosis exclusion criteria. Separate analyses were run for 3 different new user cohorts.

- Eligibility requirements – Individuals who met the following criteria were included:
  - Continuously enrolled with both medical and drug coverage for at least 180 day before the index date (date of first incident dispensing)
  - At least 20 years or older at the time of first dispensing of varenicline or bupropion
  - Free of any dispensing of any of the drugs of interest in the 180 days before the index date
- Exclusions - Individuals with any of the following codes during the 180 days before the initial dispensing were excluded:
  - Acute myocardial infarction (ICD-9-CM 410.xx)
  - Intermediate coronary syndrome or unstable angina (ICD-9-CM 411.1)
  - Acute coronary occlusion without myocardial infarction (ICD-9-CM 411.81)
  - Coronary atherosclerosis (ICD-9-CM 414.0x)
- New user cohorts – individuals who met the inclusion/exclusion criteria were grouped into the following 3 cohorts to allow for 3 independent assessments:
  - All new users
  - Tobacco cohort: limited to individuals with a diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) during the 180 days before the index date
  - Depression cohort: limited to individuals with a diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) during the 180 days before the index date

**Outcome of interest definition**:

The outcome of interest was identified during exposure time at risk. The composite outcome was defined as any of the following diagnoses flagged as the primary diagnosis observed in the inpatient or emergency department settings during exposure time at risk:

- Acute myocardial infarction (ICD-9-CM 410.xx)
- Intermediate coronary syndrome or unstable angina (ICD-9-CM 411.1)
- Acute coronary occlusion without myocardial infarction (ICD-9-CM 411.81)

**Results**:

The results are shown in the following tables and figures.

# Table of Contents


| Table/Figure | Description |
|---|---|
| Table 1 | Table of the number of users, the number of dispensing, and the total days supplied by exposure group and cohort. |
| Figure 1a | Figure displaying the number of dispensing per user by exposure group and cohort. |
| Figure 1b | Figure displaying the number of days supplied per user by exposure group and cohort. |
| Figure 1c | Figure displaying the number of days supplied per dispensing by exposure group and cohort. |
| Table 2 | Table of the number of users, the number of dispensing, and the total days supplied by exposure group, age, and cohort. |
| Figure 2a | Figure displaying the percent of all users in each age group by exposure group. |
| Figure 2b | Figure displaying the percent of users with a pre-existing condition of depression in each age group by exposure group. |
| Figure 2c | Figure displaying the percent of users with a pre-existing condition of nondependent tobacco use in each age group by exposure group. |
| Table 3 | Table of the number of users, the number of dispensings, and the total days supplied by exposure group, sex, and cohort. |
| Figure 3a | Figure displaying the percent of all users in each sex by exposure group. |
| Figure 3b | Figure displaying the percent of users with a pre-existing condition of depression in each sex by exposure group. |
| Figure 3c | Figure displaying the percent of users with a pre-existing condition of nondependent tobacco use in each sex by exposure group. |
| Table 4 | Table of the number of users, the number of dispensings, and the total days supplied by exposure group, year, and cohort. |
| Figure 4a | Figure displaying the number of users and total days supplied of bupropion for use as an anti-depressant by cohort. |
| Figure 4b | Figure displaying the number of users and total days supplied of bupropion for smoking cessation by cohort. |
| Figure 4c | Figure displaying the number of users and total days supplied of bupropion used for any reason by cohort. |
| Figure 4d | Figure displaying the number of users and total days supplied of varenicline by cohort. |
| Table 5 | Table of the number of users, the number of days at risk, the number of cardiovascular events, the percent of users with an event, and the rate of events per 1,000 days at risk by exposure group and cohort. |
| Figure 5 | Figure displaying the rate of acute cardiovascular events per 1,000 days at risk by exposure group and cohort. |
| Table 6 | Table of the number of users, the number of days at risk, the number of cardiovascular events, the percent of users with an event, and the rate of events per 1,000 days at risk by exposure group, year, and cohort. |
| Figure 6a | Figure displaying the rate of acute cardiovascular events per 1,000 days at risk by year and cohort among users of bupropion as an anti-depressant. |
| Figure 6b | Figure displaying the rate of acute cardiovascular events per 1,000 days at risk by year and cohort among users of bupropion for smoking-cessation. |

Mini-Sentinel

# Table of Contents (Cont.)


| Table/Figure | Description |
|---|---|
| Figure 6c | Figure displaying the rate of acute cardiovascular events per 1,000 days at risk by year and cohort among users of bupropion for any reason. |
| Figure 6d | Figure displaying the rate of acute cardiovascular events per 1,000 days at risk by year and cohort among users of varenicline. |
| Table 7 | Table of the number of users, the number of days at risk, the number of cardiovascular events, the percent of users with an event, and the rate of events per 1,000 days at risk by exposure group, age group, and cohort. |
| Figure 7a | Figure displaying the rate of acute cardiovascular events per 1,000 days at risk by age group and cohort among users of bupropion as an anti-depressant. |
| Figure 7b | Figure displaying the rate of acute cardiovascular events per 1,000 days at risk by age group and cohort among users of bupropion for smoking-cessation. |
| Figure 7c | Figure displaying the rate of acute cardiovascular events per 1,000 days at risk by age group and cohort among users of bupropion for any reason. |
| Figure 7d | Figure displaying the rate of acute cardiovascular events per 1,000 days at risk by age group and cohort among users of varenicline. |
| Table 8 | Table of the number of users, the number of days at risk, the number of cardiovascular events, the percent of users with an event, and the rate of events per 1,000 days at risk by exposure group, sex, and cohort. |
| Figure 8a | Figure displaying the rate of acute cardiovascular events per 1,000 days at risk by sex and cohort among users of bupropion as an anti-depressant. |
| Figure 8b | Figure displaying the rate of acute cardiovascular events per 1,000 days at risk by sex and cohort among users of bupropion for smoking-cessation. |
| Figure 8c | Figure displaying the rate of acute cardiovascular events per 1,000 days at risk by sex and cohort among users of bupropion for any reason. |
| Figure 8d | Figure displaying the rate of acute cardiovascular events per 1,000 days at risk by sex and cohort among users of varenicline. |
| Table 9 | Table of the number of users, the number of days at risk, the number of cardiovascular events, the percent of users with an event, and the rate of events per 1,000 days at risk by exposure group, age group, sex, and cohort. |
| Figure 9a | Figure displaying the rate of acute cardiovascular events per 1,000 days at risk by age group, sex, and cohort among users of bupropion as an anti-depressant. |
| Figure 9b | Figure displaying the rate of acute cardiovascular events per 1,000 days at risk by age group, sex, and cohort among users of bupropion for smoking-cessation. |
| Figure 9c | Figure displaying the rate of acute cardiovascular events per 1,000 days at risk by age group, sex, and cohort among users of bupropion for any reason. |
| Figure 9d | Figure displaying the rate of acute cardiovascular events per 1,000 days at risk by age group, sex, and cohort among users of varenicline. |
| Table 10 | Table of the number of users, the number of days at risk, the number of cardiovascular events, the percent of users with an event, and the rate of events per 1,000 days at risk by exposure group, year, age group, and cohort. |

# Table of Contents (Cont.)


| Table/Figure | Description |
|---|---|
| Figure 10a | Figure displaying the rate of acute cardiovascular events per 1,000 days at risk by year, age group, and cohort among users of bupropion as an anti-depressant. |
| Figure 10b | Figure displaying the rate of acute cardiovascular events per 1,000 days at risk by year, age group, and cohort among users of bupropion for smoking-cessation. |
| Figure 10c | Figure displaying the rate of acute cardiovascular events per 1,000 days at risk by year, age group, and cohort among users of bupropion for any reason. |
| Figure 10d | Figure displaying the rate of acute cardiovascular events per 1,000 days at risk by year, age group, and cohort among users of varenicline. |

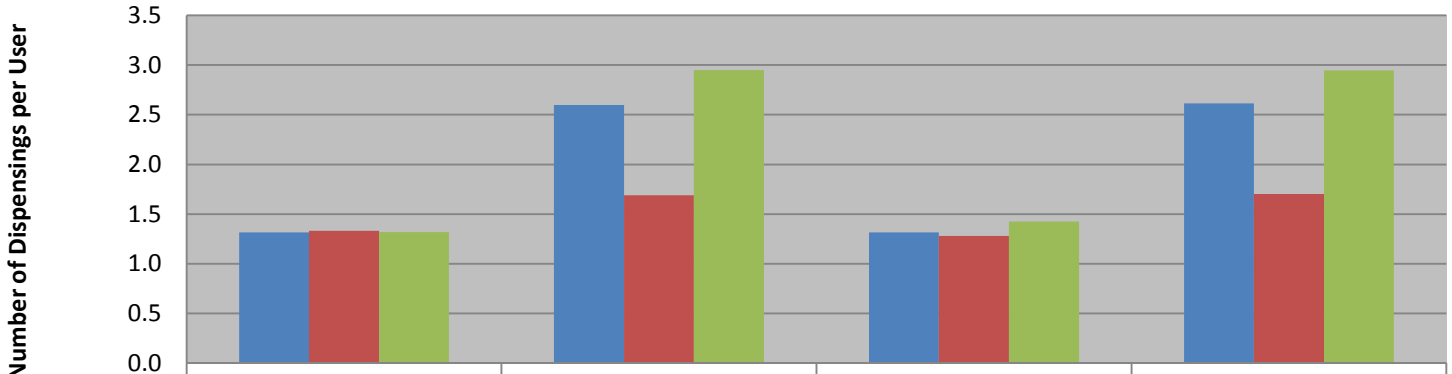
**Table 1. Number of Users, Number of Dispensings, and Total Days Supplied by Exposure Group[a] and Cohort[b]**

| | | COHORT | | |
|---|---|---|---|---|
| | | OVERALL | TOBACCO | DEPRESSION |
| Exposure Group | | | | |
| VARENICLINE | Unique Users | 260,845 | 89,573 | 22,173 |
| | Dispensings | 343,482 | 119,173 | 29,216 |
| | Total Days Supplied | 10,038,828 | 3,530,695 | 861,810 |
| BUPROPION for Any Reason | Unique Users | 745,656 | 113,427 | 298,280 |
| | Dispensings | 1,937,803 | 191,751 | 879,113 |
| | Total Days Supplied | 74,865,238 | 7,920,022 | 36,134,559 |
| BUPROPION for Smoking Cessation | Unique Users | 11,209 | 4,155 | 1,148 |
| | Dispensings | 14,729 | 5,322 | 1,636 |
| | Total Days Supplied | 462,434 | 167,999 | 50,973 |
| BUPROPION for Treatment of Depression | Unique Users | 735,932 | 109,708 | 297,474 |
| | Dispensings | 1,922,436 | 186,686 | 876,613 |
| | Total Days Supplied | 74,383,568 | 7,762,456 | 36,055,926 |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) Bupropion for Smoking Cessation: Individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

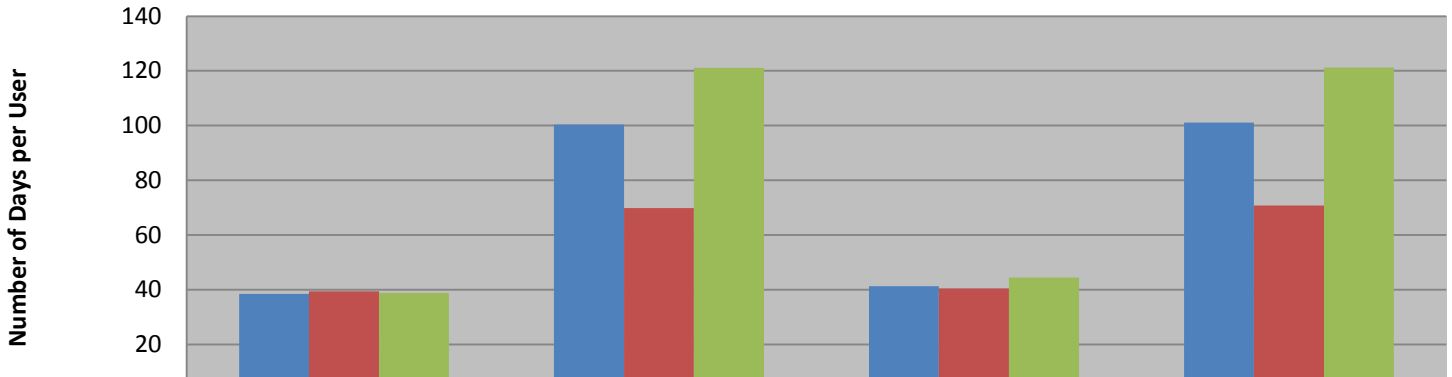
[b]Three different cohorts of users were examined in this analysis: (1) the Overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Figure 1a. Number of Dispensings per User, by Cohort[a] and Exposure Group[b]**




| | VARENICLINE | BU_ANY | BU_SMOKE | BU_ANTIDEP |
|---|---|---|---|---|
| OVERALL | 1.32 | 2.60 | 1.31 | 2.61 |
| TOBACCO | 1.33 | 1.69 | 1.28 | 1.70 |
| DEPRESSION | 1.32 | 2.95 | 1.43 | 2.95 |

**Figure 1b. Number of Days Supplied per User, by Cohort[a] and Exposure Group[b]**

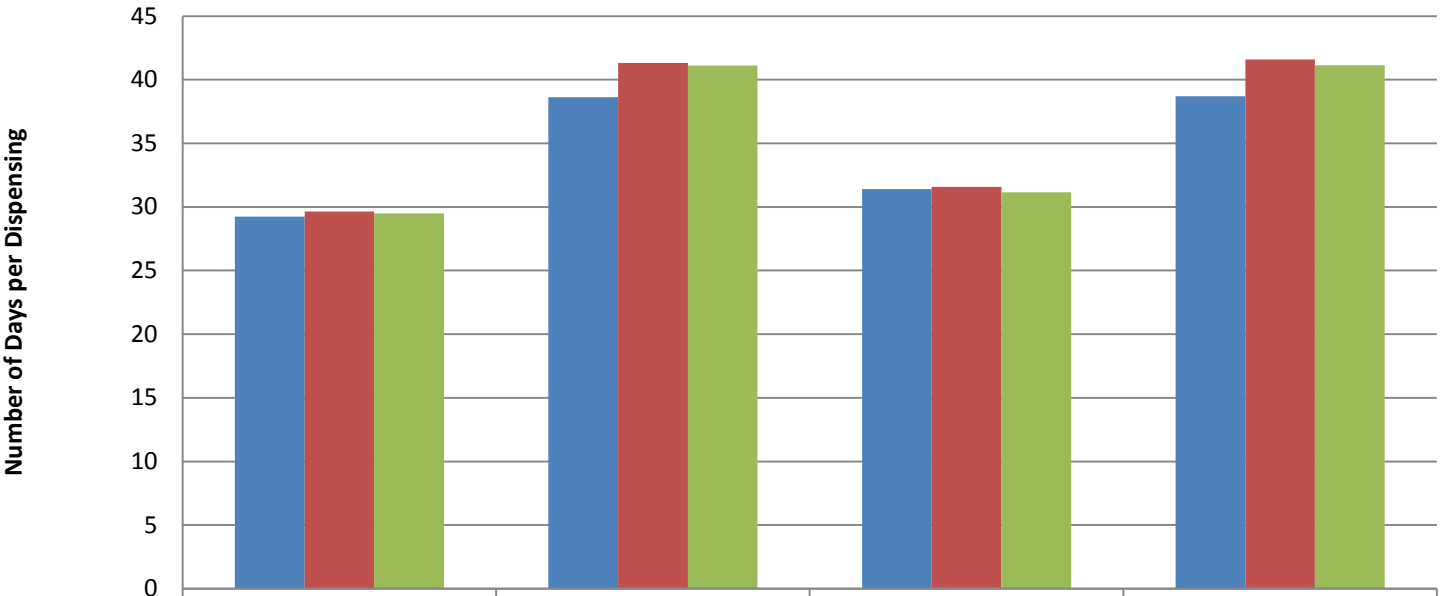



| | VARENICLINE | BU_ANY | BU_SMOKE | BU_ANTIDEP |
|---|---|---|---|---|
| OVERALL | 38.49 | 100.40 | 41.26 | 101.07 |
| TOBACCO | 39.42 | 69.82 | 40.43 | 70.76 |
| DEPRESSION | 38.87 | 121.14 | 44.40 | 121.21 |

[a]Three different cohorts of users were examined in this analysis: (1) the Overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

[b]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) BU_Any: Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) BU_SMOKE: Bupropion for Smoking Cessation includes individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) BU_ANTIDEP: Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

**Figure 1c. Number of Days Supplied per Dispensings, by Cohort[a] and Exposure Group[b]**




| | VARENICLINE | BU_ANY | BU_SMOKE | BU_ANTIDEP |
|---|---|---|---|---|
| OVERALL | 29.23 | 38.63 | 31.40 | 38.69 |
| TOBACCO | 29.63 | 41.30 | 31.57 | 41.58 |
| DEPRESSION | 29.50 | 41.10 | 31.16 | 41.13 |

[a]Three different cohorts of users were examined in this analysis: (1) the Overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

[b]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) BU_Any: Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) BU_SMOKE: Bupropion for Smoking Cessation includes individuals who initiated use of bupropion for smoking cessation (national drug code listed as “smoking cessation” as defined by First DataBank’s Enhanced Therapeutic Classification); (4) BU_ANTIDEP: Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as “antidepressant” as defined by First DataBank’s Enhanced Therapeutic Classification).

Mini-Sentinel

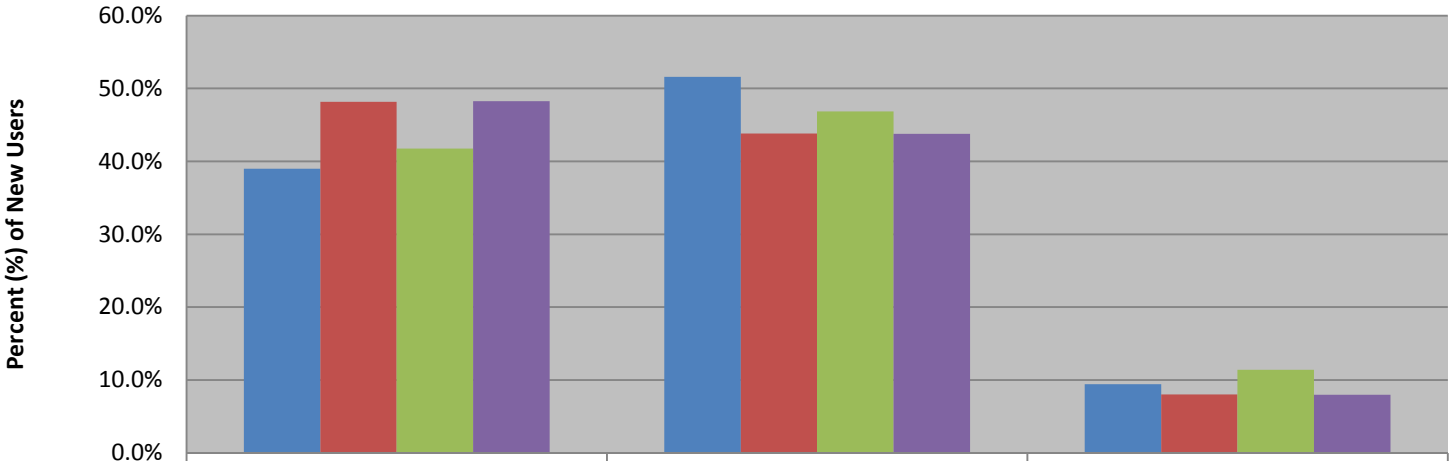
**Table 2. Number of Users, Number of Dispensings, and Total Days Supplied by Exposure Group[a], Age Group, and Cohort[b]**

| | | | COHORT | | |
|---|---|---|---|---|---|
| | | | OVERALL | TOBACCO | DEPRESSION |
| Exposure Group | AgeGroup | | | | |
| VARENICLINE | 20 to 44 | Unique Users | 101,687 | 35,317 | 8,661 |
| | | Dispensings | 128,506 | 45,179 | 10,883 |
| | | Total Days Supplied | 3,719,140 | 1,323,314 | 315,587 |
| | 45 to 64 | Unique Users | 134,589 | 44,859 | 11,537 |
| | | Dispensings | 182,588 | 61,473 | 15,676 |
| | | Total Days Supplied | 5,352,719 | 1,828,028 | 464,672 |
| | 65+ | Unique Users | 24,569 | 9,397 | 1,975 |
| | | Dispensings | 32,388 | 12,521 | 2,657 |
| | | Total Days Supplied | 966,969 | 379,353 | 81,551 |
| BUPROPION for Any Reason | 20 to 44 | Unique Users | 359,298 | 48,636 | 144,460 |
| | | Dispensings | 870,774 | 79,576 | 392,628 |
| | | Total Days Supplied | 31,283,227 | 3,087,123 | 14,857,405 |
| | 45 to 64 | Unique Users | 326,581 | 53,461 | 126,797 |
| | | Dispensings | 912,264 | 93,372 | 407,174 |
| | | Total Days Supplied | 36,641,917 | 3,984,644 | 17,483,040 |
| | 65+ | Unique Users | 59,777 | 11,330 | 27,023 |
| | | Dispensings | 154,765 | 18,803 | 79,311 |
| | | Total Days Supplied | 6,940,094 | 848,255 | 3,794,114 |
| BUPROPION for Smoking Cessation | 20 to 44 | Unique Users | 4,681 | 1,715 | 501 |
| | | Dispensings | 5,967 | 2,147 | 702 |
| | | Total Days Supplied | 181,625 | 65,895 | 21,262 |
| | 45 to 64 | Unique Users | 5,251 | 1,938 | 478 |
| | | Dispensings | 7,016 | 2,534 | 694 |
| | | Total Days Supplied | 222,903 | 80,518 | 21,790 |
| | 65+ | Unique Users | 1,277 | 502 | 169 |
| | | Dispensings | 1,746 | 641 | 240 |
| | | Total Days Supplied | 57,906 | 21,586 | 7,921 |
| BUPROPION for Treatment of Depression | 20 to 44 | Unique Users | 355,191 | 47,068 | 144,121 |
| | | Dispensings | 864,681 | 77,521 | 391,777 |
| | | Total Days Supplied | 31,097,966 | 3,024,495 | 14,831,121 |
| | 45 to 64 | Unique Users | 322,054 | 51,746 | 126,457 |
| | | Dispensings | 905,007 | 90,934 | 406,085 |
| | | Total Days Supplied | 36,412,419 | 3,908,738 | 17,449,067 |
| | 65+ | Unique Users | 58,687 | 10,894 | 26,896 |
| | | Dispensings | 152,748 | 18,231 | 78,751 |
| | | Total Days Supplied | 6,873,183 | 829,223 | 3,775,738 |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) Bupropion for Smoking Cessation: Individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

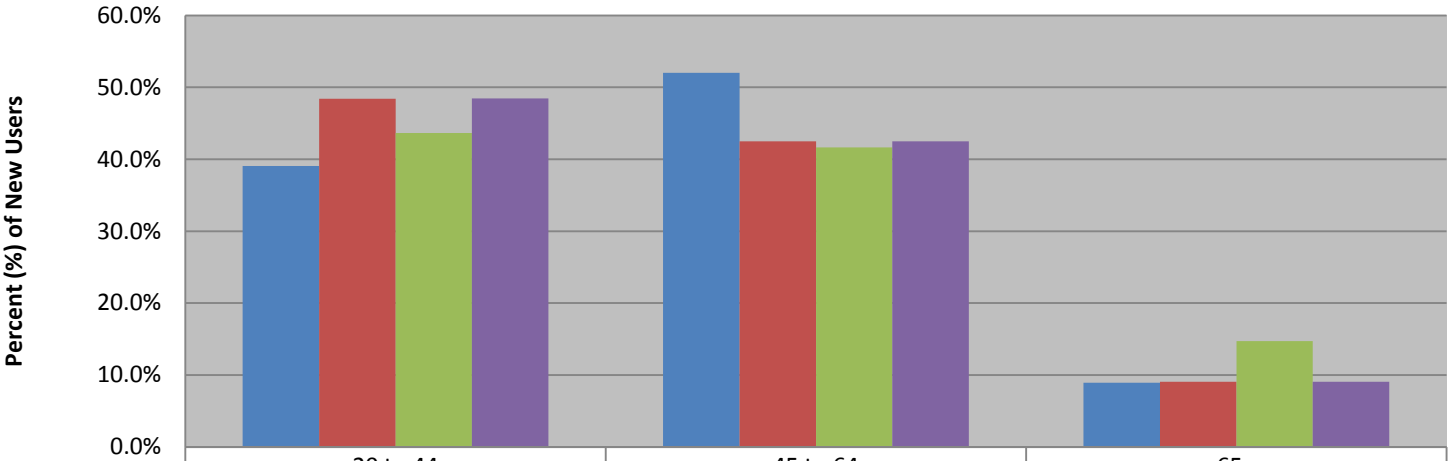
[b]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Figure 2a. Percent of All Users in each Age Group, by Exposure Group[a]**




| | 20 to 44 | 45 to 64 | 65+ |
|---|---|---|---|
| VARENICLINE | 39.0% | 51.6% | 9.4% |
| BU_ANY | 48.2% | 43.8% | 8.0% |
| BU_SMOKE | 41.8% | 46.8% | 11.4% |
| BU_ANTIDEP | 48.3% | 43.8% | 8.0% |

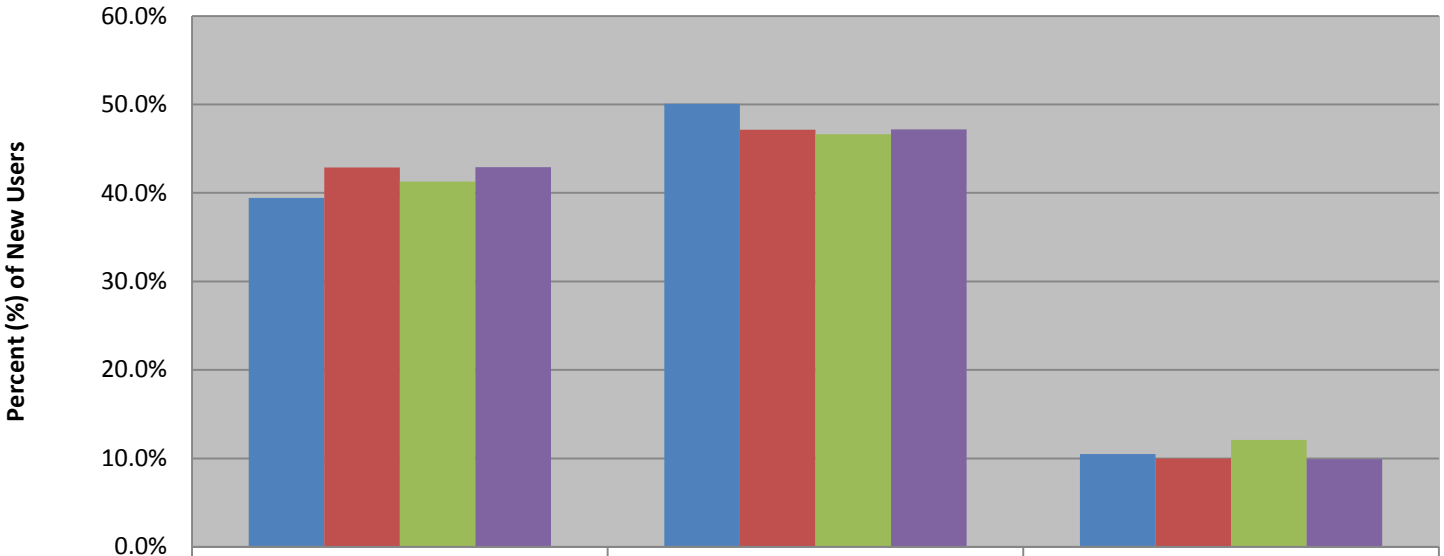
**Figure 2b. Percent of Users with a Pre-Existing Condition of Depression in each Age Group, by Exposure Group[a]**




| | 20 to 44 | 45 to 64 | 65+ |
|---|---|---|---|
| VARENICLINE | 39.1% | 52.0% | 8.9% |
| BU_ANY | 48.4% | 42.5% | 9.1% |
| BU_SMOKE | 43.6% | 41.6% | 14.7% |
| BU_ANTIDEP | 48.4% | 42.5% | 9.0% |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) BU_Any: Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) BU_SMOKE: Bupropion for Smoking Cessation includes individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) BU_ANTIDEP: Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

**Figure 2c. Percent of Users with a Pre-Existing Condition of Nondependent Tobacco Use in each Age Group, by Exposure Group[a]**




| | 20 to 44 | 45 to 64 | 65+ |
|---|---|---|---|
| VARENICLINE | 39.4% | 50.1% | 10.5% |
| BU_ANY | 42.9% | 47.1% | 10.0% |
| BU_SMOKE | 41.3% | 46.6% | 12.1% |
| BU_ANTIDEP | 42.9% | 47.2% | 9.9% |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) BU_Any: Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) BU_SMOKE: Bupropion for Smoking Cessation includes individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) BU_ANTIDEP: Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

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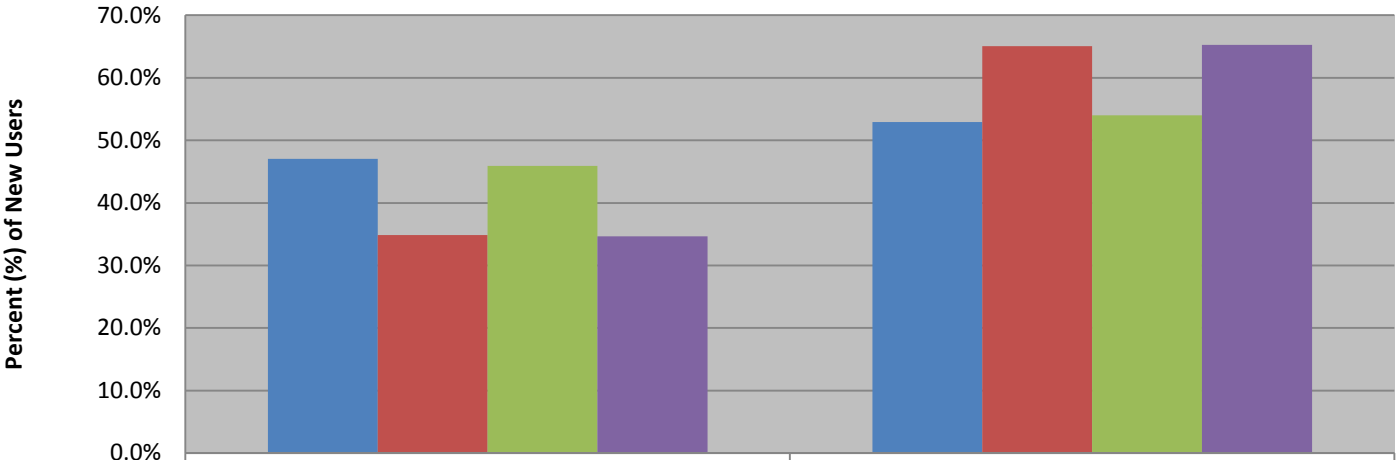
**Table 3. Number of Users, Number of Dispensings, and Total Days Supplied by Exposure Group[a], Sex, and Cohort[b]**

| | | | COHORT | | |
|---|---|---|---|---|---|
| | | | OVERALL | TOBACCO | DEPRESSION |
| Exposure Group | SEX | | | | |
| VARENICLINE | Female | Unique Users | 137,993 | 47,440 | 15,564 |
| | | Dispensings | 180,434 | 62,803 | 20,346 |
| | | Total Days Supplied | 5,277,262 | 1,863,268 | 599,469 |
| | Male | Unique Users | 122,667 | 42,079 | 6,596 |
| | | Dispensings | 162,813 | 56,304 | 8,856 |
| | | Total Days Supplied | 4,754,924 | 1,665,549 | 261,890 |
| | Unknown | Unique Users | 185 | 54 | 13 |
| | | Dispensings | 235 | 66 | 14 |
| | | Total Days Supplied | 6,642 | 1,878 | 451 |
| BUPROPION for Any Reason | Ambiguous | Unique Users | 2 | . | 2 |
| | | Dispensings | 5 | . | 5 |
| | | Total Days Supplied | 430 | . | 430 |
| | Female | Unique Users | 485,259 | 63,746 | 204,709 |
| | | Dispensings | 1,288,095 | 111,112 | 601,012 |
| | | Total Days Supplied | 49,726,933 | 4,563,865 | 24,720,529 |
| | Male | Unique Users | 259,745 | 49,632 | 93,347 |
| | | Dispensings | 647,919 | 80,560 | 277,368 |
| | | Total Days Supplied | 25,080,988 | 3,353,732 | 11,391,244 |
| | Unknown | Unique Users | 650 | 49 | 222 |
| | | Dispensings | 1,784 | 79 | 728 |
| | | Total Days Supplied | 56,887 | 2,425 | 22,356 |
| BUPROPION for Smoking Cessation | Female | Unique Users | 6,054 | 2,179 | 792 |
| | | Dispensings | 7,936 | 2,790 | 1,125 |
| | | Total Days Supplied | 248,622 | 87,213 | 35,357 |
| | Male | Unique Users | 5,149 | 1,976 | 353 |
| | | Dispensings | 6,787 | 2,532 | 508 |
| | | Total Days Supplied | 213,641 | 80,786 | 15,526 |
| | Unknown | Unique Users | 6 | - | 3 |
| | | Dispensings | 6 | - | 3 |
| | | Total Days Supplied | 171 | - | 90 |
| BUPROPION for Treatment of Depression | Ambiguous | Unique Users | 2 | . | 2 |
| | | Dispensings | 5 | . | 5 |
| | | Total Days Supplied | 430 | . | 430 |
| | Female | Unique Users | 480,167 | 61,842 | 204,165 |
| | | Dispensings | 1,279,740 | 108,509 | 599,343 |
| | | Total Days Supplied | 49,465,378 | 4,483,837 | 24,667,645 |
| | Male | Unique Users | 255,119 | 47,817 | 93,088 |
| | | Dispensings | 640,913 | 78,098 | 276,540 |
| | | Total Days Supplied | 24,861,044 | 3,276,194 | 11,365,585 |
| | Unknown | Unique Users | 644 | 49 | 219 |
| | | Dispensings | 1,778 | 79 | 725 |
| | | Total Days Supplied | 56,716 | 2,425 | 22,266 |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) Bupropion for Smoking Cessation: Individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

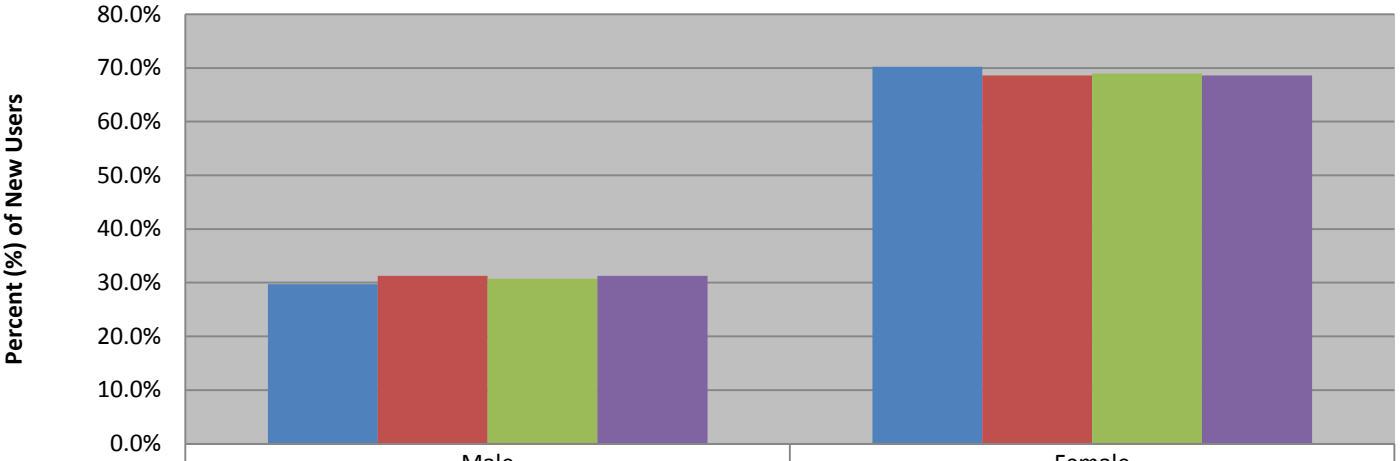
[b]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Figure 3a. Percent of All Users in each Sex, by Exposure Group[a]**




| | Male | Female |
|---|---|---|
| VARENICLINE | 47.0% | 52.9% |
| BU_ANY | 34.8% | 65.1% |
| BU_SMOKE | 45.9% | 54.0% |
| BU_ANTIDEP | 34.7% | 65.2% |

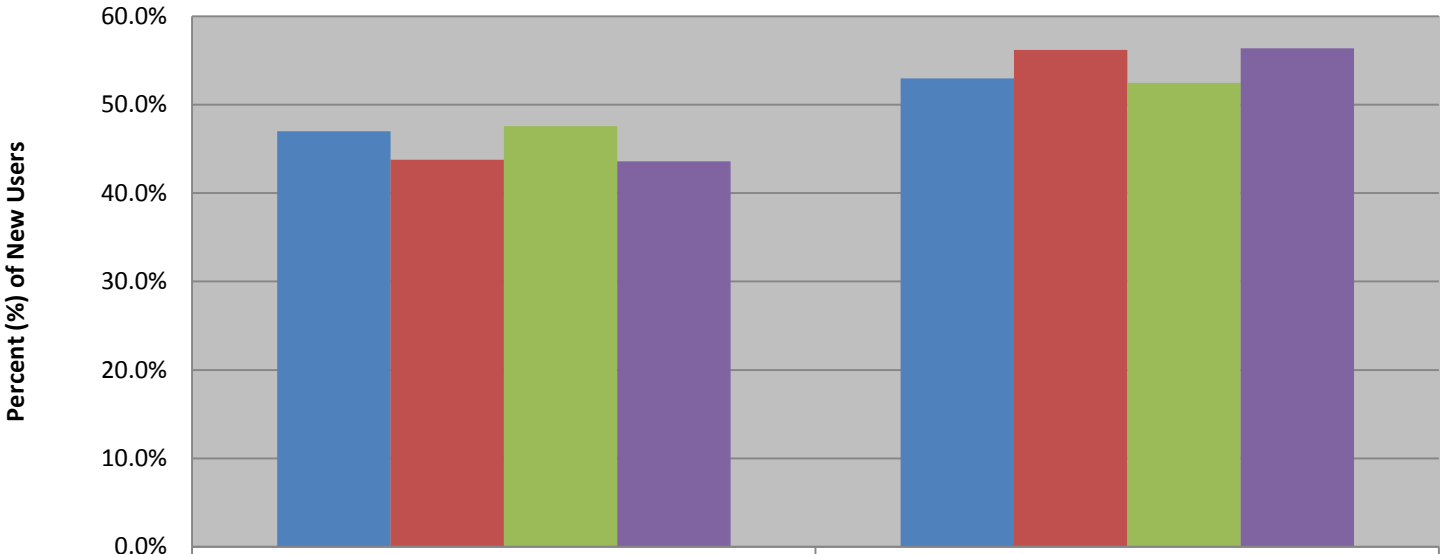
**Figure 3b. Percent of Users with a Pre-Existing Condition of Depression in each Sex, by Exposure Group[a]**




| | Male | Female |
|---|---|---|
| VARENICLINE | 29.7% | 70.2% |
| BU_ANY | 31.3% | 68.6% |
| BU_SMOKE | 30.7% | 69.0% |
| BU_ANTIDEP | 31.3% | 68.6% |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) BU_Any: Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) BU_SMOKE: Bupropion for Smoking Cessation includes individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) BU_ANTIDEP: Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

**Figure 3c. Percent of Users with a Pre-Existing Condition of Nondependent Tobacco Use in each Sex, by Exposure Group[a]**




| | Male | Female |
|---|---|---|
| VARENICLINE | 47.0% | 53.0% |
| BU_ANY | 43.8% | 56.2% |
| BU_SMOKE | 47.6% | 52.4% |
| BU_ANTIDEP | 43.6% | 56.4% |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) BU_Any: Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) BU_SMOKE: Bupropion for Smoking Cessation includes individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) BU_ANTIDEP: Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

Mini-Sentinel

**Table 4. Number of Users, Number of Dispensings, and Total Days Supplied by Exposure Group[a], Year, and Cohort[b]**

| | | | COHORT | | |
|---|---|---|---|---|---|
| | | | OVERALL | TOBACCO | DEPRESSION |
| Exposure Group | IndexYear | | | | |
| VARENICLINE | 2006 | Unique Users | 16,907 | 3,395 | 1,196 |
| | | Dispensings | 23,078 | 4,541 | 1,567 |
| | | Total Days Supplied | 661,000 | 129,898 | 43,661 |
| | 2007 | Unique Users | 111,412 | 30,126 | 8,411 |
| | | Dispensings | 147,962 | 40,520 | 11,160 |
| | | Total Days Supplied | 4,319,817 | 1,193,358 | 327,945 |
| | 2008 | Unique Users | 67,170 | 27,009 | 6,327 |
| | | Dispensings | 87,130 | 35,656 | 8,224 |
| | | Total Days Supplied | 2,547,133 | 1,059,807 | 243,363 |
| | 2009 | Unique Users | 39,632 | 17,702 | 3,688 |
| | | Dispensings | 51,969 | 23,530 | 4,912 |
| | | Total Days Supplied | 1,501,082 | 687,364 | 142,945 |
| | 2010 | Unique Users | 24,310 | 10,748 | 2,430 |
| | | Dispensings | 31,809 | 14,260 | 3,226 |
| | | Total Days Supplied | 961,236 | 439,239 | 99,579 |
| | 2011 | Unique Users | 1,414 | 593 | 121 |
| | | Dispensings | 1,534 | 666 | 127 |
| | | Total Days Supplied | 48,560 | 21,029 | 4,317 |
| BUPROPION for Any Reason | 2006 | Unique Users | 203,991 | 28,342 | 70,013 |
| | | Dispensings | 535,874 | 48,108 | 218,488 |
| | | Total Days Supplied | 21,634,841 | 2,035,889 | 9,573,982 |
| | 2007 | Unique Users | 150,237 | 21,671 | 59,091 |
| | | Dispensings | 426,197 | 36,933 | 191,886 |
| | | Total Days Supplied | 16,726,740 | 1,655,856 | 8,040,578 |
| | 2008 | Unique Users | 137,446 | 20,621 | 56,950 |
| | | Dispensings | 379,240 | 35,918 | 177,677 |
| | | Total Days Supplied | 14,371,905 | 1,497,082 | 7,170,710 |
| | 2009 | Unique Users | 139,309 | 23,973 | 60,837 |
| | | Dispensings | 354,056 | 41,223 | 173,392 |
| | | Total Days Supplied | 13,195,842 | 1,588,450 | 6,819,564 |
| | 2010 | Unique Users | 108,261 | 17,660 | 48,769 |
| | | Dispensings | 234,837 | 28,228 | 114,345 |
| | | Total Days Supplied | 8,676,386 | 1,093,767 | 4,416,794 |
| | 2011 | Unique Users | 6,412 | 1,160 | 2,620 |
| | | Dispensings | 7,599 | 1,341 | 3,325 |
| | | Total Days Supplied | 259,524 | 48,978 | 112,931 |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) Bupropion for Smoking Cessation: Individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

[b]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

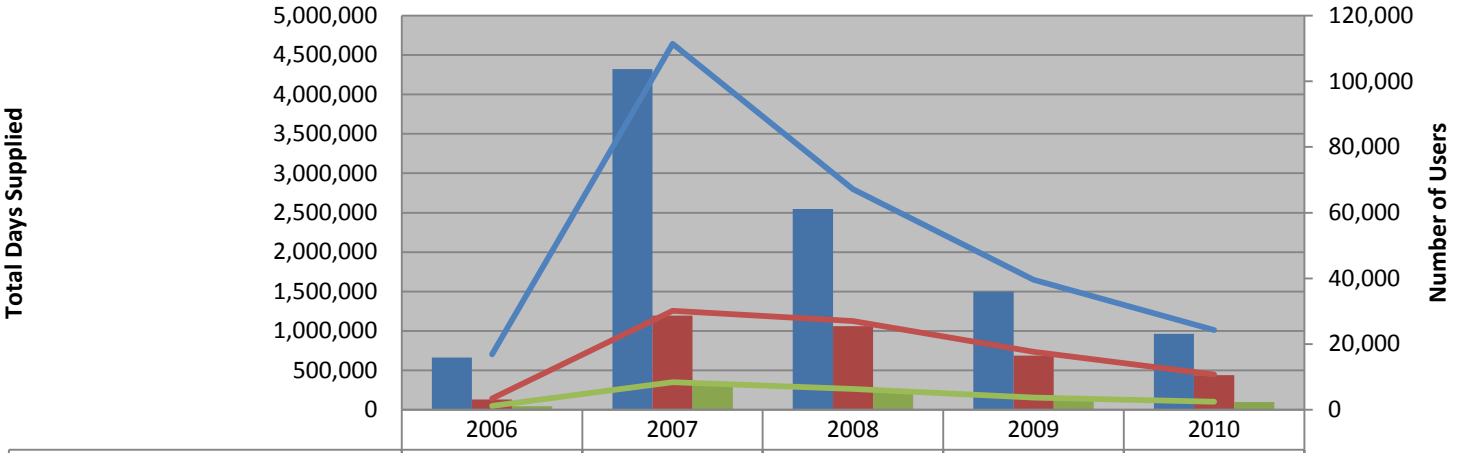
**Table 4 (Continued). Number of Users, Number of Dispensings, and Total Days Supplied by Exposure Group[a], Year, and Cohort[b]**

| | | | COHORT | | |
|---|---|---|---|---|---|
| | | | OVERALL | TOBACCO | DEPRESSION |
| Exposure Group | IndexYear | | | | |
| BUPROPION for Smoking Cessation | 2006 | Unique Users | 4,719 | 1,716 | 283 |
| | | Dispensings | 5,975 | 2,158 | 365 |
| | | Total Days Supplied | 183,503 | 65,400 | 11,246 |
| | 2007 | Unique Users | 1,939 | 701 | 193 |
| | | Dispensings | 2,530 | 894 | 296 |
| | | Total Days Supplied | 81,306 | 29,304 | 9,061 |
| | 2008 | Unique Users | 1,485 | 503 | 229 |
| | | Dispensings | 2,000 | 630 | 345 |
| | | Total Days Supplied | 62,882 | 20,582 | 10,806 |
| | 2009 | Unique Users | 1,942 | 837 | 287 |
| | | Dispensings | 2,723 | 1,105 | 419 |
| | | Total Days Supplied | 86,668 | 35,694 | 13,166 |
| | 2010 | Unique Users | 1,088 | 384 | 155 |
| | | Dispensings | 1,458 | 517 | 210 |
| | | Total Days Supplied | 46,720 | 16,419 | 6,664 |
| | 2011 | Unique Users | 36 | 14 | 1 |
| | | Dispensings | 43 | 18 | 1 |
| | | Total Days Supplied | 1,355 | 600 | 30 |
| BUPROPION for Treatment of Depression | 2006 | Unique Users | 199,377 | 26,650 | 69,757 |
| | | Dispensings | 529,291 | 45,875 | 217,827 |
| | | Total Days Supplied | 21,431,807 | 1,968,182 | 9,553,504 |
| | 2007 | Unique Users | 148,627 | 21,060 | 58,964 |
| | | Dispensings | 423,534 | 36,120 | 191,412 |
| | | Total Days Supplied | 16,642,270 | 1,630,145 | 8,026,751 |
| | 2008 | Unique Users | 136,299 | 20,204 | 56,813 |
| | | Dispensings | 376,940 | 35,346 | 177,017 |
| | | Total Days Supplied | 14,297,698 | 1,478,539 | 7,148,457 |
| | 2009 | Unique Users | 137,781 | 23,282 | 60,657 |
| | | Dispensings | 351,515 | 40,206 | 172,936 |
| | | Total Days Supplied | 13,116,449 | 1,556,525 | 6,805,504 |
| | 2010 | Unique Users | 107,455 | 17,360 | 48,661 |
| | | Dispensings | 233,581 | 27,809 | 114,094 |
| | | Total Days Supplied | 8,636,648 | 1,080,477 | 4,408,735 |
| | 2011 | Unique Users | 6,393 | 1,152 | 2,622 |
| | | Dispensings | 7,575 | 1,330 | 3,327 |
| | | Total Days Supplied | 258,696 | 48,588 | 112,975 |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) Bupropion for Smoking Cessation: Individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

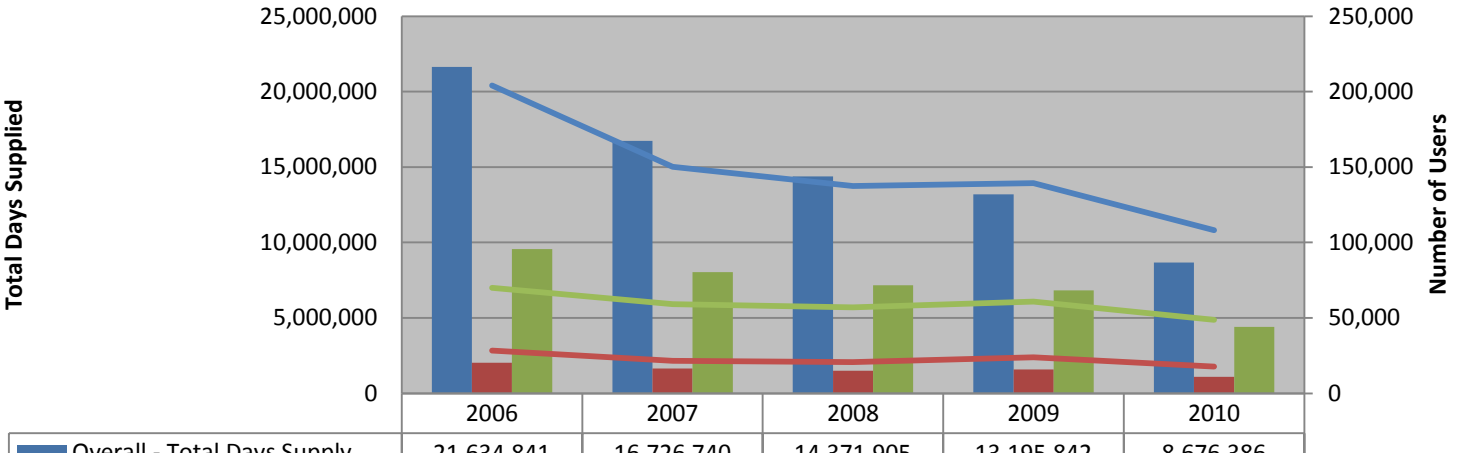
[b]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Figure 4a. Number of Users and Total Days Supplied of Varenicline, by Cohort[a] and Year**




| | 2006 | 2007 | 2008 | 2009 | 2010 |
|---|---|---|---|---|---|
| Overall - Total Days Supply | 661,000 | 4,319,817 | 2,547,133 | 1,501,082 | 961,236 |
| Tobacco - Total Days Supply | 129,898 | 1,193,358 | 1,059,807 | 687,364 | 439,239 |
| Depression - Total Days Supply | 43,661 | 327,945 | 243,363 | 142,945 | 99,579 |
| Overall - Number of Users | 16,907 | 111,412 | 67,170 | 39,632 | 24,310 |
| Tobacco - Number of Users | 3,395 | 30,126 | 27,009 | 17,702 | 10,748 |
| Depression - Number of Users | 1,196 | 8,411 | 6,327 | 3,688 | 2,430 |

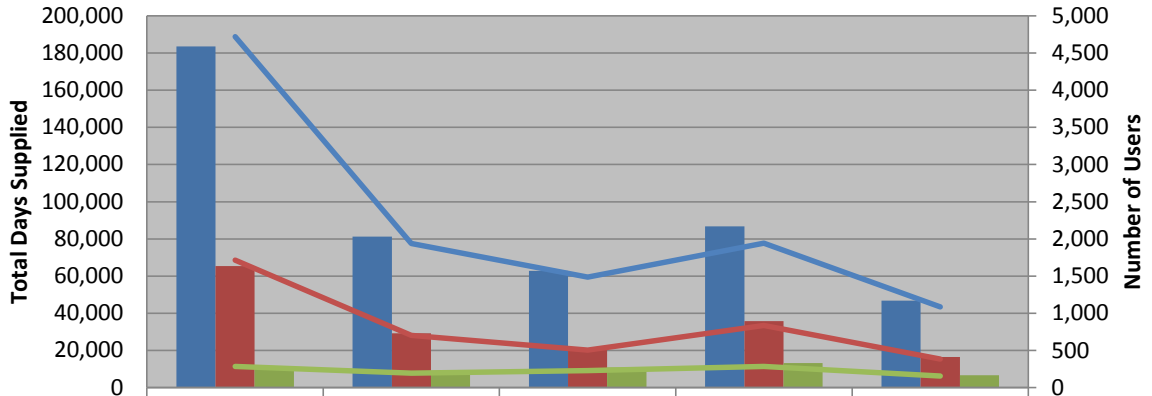
**Figure 4b. Number of Users and Total Days Supplied of Bupropion Used for Any Reason, by Cohort[a] and Year**




| | 2006 | 2007 | 2008 | 2009 | 2010 |
|---|---|---|---|---|---|
| Overall - Total Days Supply | 21,634,841 | 16,726,740 | 14,371,905 | 13,195,842 | 8,676,386 |
| Tobacco - Total Days Supply | 2,035,889 | 1,655,856 | 1,497,082 | 1,588,450 | 1,093,767 |
| Depression - Total Days Supply | 9,573,982 | 8,040,578 | 7,170,710 | 6,819,564 | 4,416,794 |
| Overall - Number of Users | 203,991 | 150,237 | 137,446 | 139,309 | 108,261 |
| Tobacco - Number of Users | 28,342 | 21,671 | 20,621 | 23,973 | 17,660 |
| Depression - Number of Users | 70,013 | 59,091 | 56,950 | 60,837 | 48,769 |

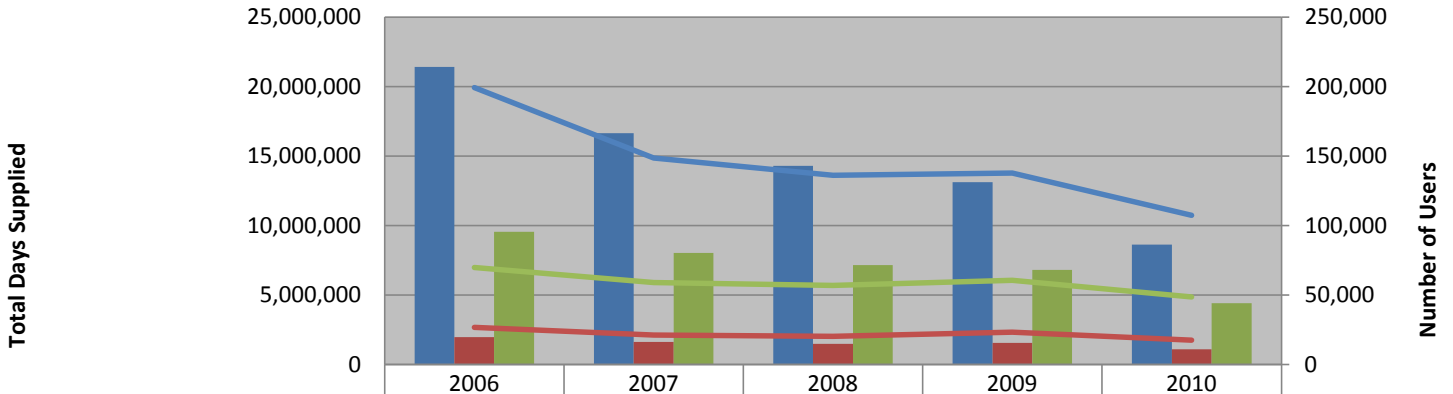
[a]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Figure 4c. Number of Users and Total Days Supplied of Bupropion for Smoking Cessation, by Cohort[a] and Year**




| | 2006 | 2007 | 2008 | 2009 | 2010 |
|---|---|---|---|---|---|
| Overall - Total Days Supply | 183,503 | 81,306 | 62,882 | 86,668 | 46,720 |
| Tobacco - Total Days Supply | 65,400 | 29,304 | 20,582 | 35,694 | 16,419 |
| Depression - Total Days Supply | 11,246 | 9,061 | 10,806 | 13,166 | 6,664 |
| Overall - Number of Users | 4,719 | 1,939 | 1,485 | 1,942 | 1,088 |
| Tobacco - Number of Users | 1,716 | 701 | 503 | 837 | 384 |
| Depression - Number of Users | 283 | 193 | 229 | 287 | 155 |

**Figure 4d. Number of Users and Total Days Supplied of Bupropion for Use as an Anti-depressant, by Cohort[a] and Year**




| | 2006 | 2007 | 2008 | 2009 | 2010 |
|---|---|---|---|---|---|
| Overall - Total Days Supply | 21,431,807 | 16,642,270 | 14,297,698 | 13,116,449 | 8,636,648 |
| Tobacco - Total Days Supply | 1,968,182 | 1,630,145 | 1,478,539 | 1,556,525 | 1,080,477 |
| Depression - Total Days Supply | 9,553,504 | 8,026,751 | 7,148,457 | 6,805,504 | 4,408,735 |
| Overall - Number of Users | 199,377 | 148,627 | 136,299 | 137,781 | 107,455 |
| Tobacco - Number of Users | 26,650 | 21,060 | 20,204 | 23,282 | 17,360 |
| Depression - Number of Users | 69,757 | 58,964 | 56,813 | 60,657 | 48,661 |

[a]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

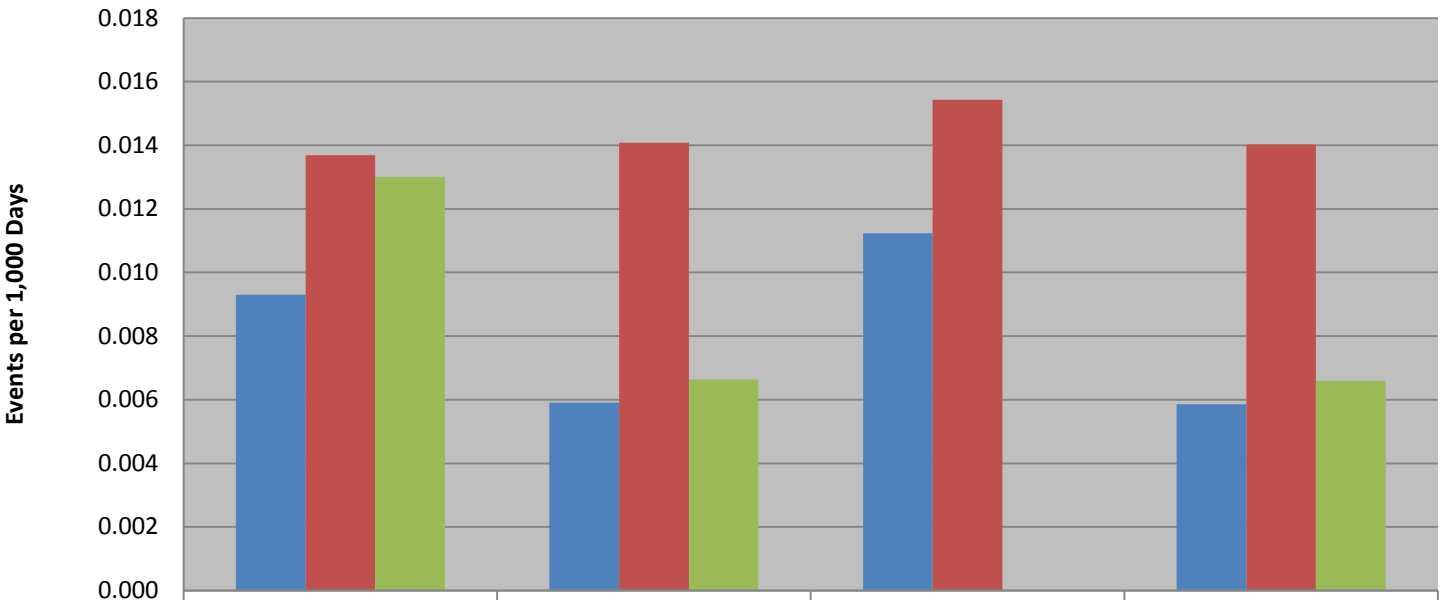
**Table 5. Number of Users, Number of Days at Risk, Number of Cardiovascular Events, Percent of Users with an Event, and Rate of Events per 1,000 Days at Risk by Exposure Group[a] and Cohort[b]**

| | | COHORT | | |
|---|---|---|---|---|
| | | OVERALL | TOBACCO | DEPRESSION |
| Exposure Group | | | | |
| VARENICLINE | Unique Users | 260,845 | 89,573 | 22,173 |
| | Days at Risk | 11,721,320 | 4,091,802 | 999,492 |
| | Number of Events | 109 | 56 | 13 |
| | Rate of Events per 1,000 Days at Risk | 0.009 | 0.014 | 0.013 |
| BUPROPION for Any Reason | Unique Users | 745,656 | 113,427 | 298,280 |
| | Days at Risk | 76,568,462 | 8,382,053 | 36,164,610 |
| | Number of Events | 452 | 118 | 240 |
| | Rate of Events per 1,000 Days at Risk | 0.006 | 0.014 | 0.007 |
| BUPROPION for Smoking Cessation | Unique Users | 11,209 | 4,155 | 1,148 |
| | Days at Risk | 534,336 | 194,408 | 57,790 |
| | Number of Events | 6 | 3 | 0 |
| | Rate of Events per 1,000 Days at Risk | 0.011 | 0.015 | 0.000 |
| BUPROPION for Treatment of Depression | Unique Users | 735,932 | 109,708 | 297,474 |
| | Days at Risk | 76,031,483 | 8,201,680 | 36,085,626 |
| | Number of Events | 445 | 115 | 238 |
| | Rate of Events per 1,000 Days at Risk | 0.006 | 0.014 | 0.007 |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) Bupropion for Smoking Cessation: Individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

[b]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Figure 5. Rate of Acute Cardiovascular Events per 1,000 Days at Risk, by Cohort[a] and Exposure Group[b]**




| | VARENICLINE | BU_ANY | BU_SMOKE | BU_ANTIDEP |
|---|---|---|---|---|
| OVERALL | 0.009 | 0.006 | 0.011 | 0.006 |
| TOBACCO | 0.014 | 0.014 | 0.015 | 0.014 |
| DEPRESSION | 0.013 | 0.007 | 0.000 | 0.007 |

[a]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

[b]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) BU_Any: Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) BU_SMOKE: Bupropion for Smoking Cessation includes individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) BU_ANTIDEP: Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

**Table 6. Number of Users, Number of Days at Risk, Number of Cardiovascular Events, Percent of Users with an Event, and Rate of Events per 1,000 Days at Risk by Exposure Group[a], Year, and Cohort[b]**

| | | | COHORT | | |
|---|---|---|---|---|---|
| | | | OVERALL | TOBACCO | DEPRESSION |
| Exposure Group | IndexYear | | | | |
| VARENICLINE | 2006 | Unique Users | 16,907 | 3,395 | 1,196 |
| | | Days at Risk | 776,092 | 152,063 | 51,744 |
| | | Number of Events | 7 | 3 | 2 |
| | | Rate of Events per 1,000 Days at Risk | 0.009 | 0.020 | 0.039 |
| | 2007 | Unique Users | 111,412 | 30,126 | 8,411 |
| | | Days at Risk | 5,081,043 | 1,395,551 | 383,814 |
| | | Number of Events | 42 | 22 | 8 |
| | | Rate of Events per 1,000 Days at Risk | 0.008 | 0.016 | 0.021 |
| | 2008 | Unique Users | 67,170 | 27,009 | 6,327 |
| | | Days at Risk | 3,002,006 | 1,240,904 | 285,821 |
| | | Number of Events | 36 | 21 | 2 |
| | | Rate of Events per 1,000 Days at Risk | 0.012 | 0.017 | 0.007 |
| | 2009 | Unique Users | 39,632 | 17,702 | 3,688 |
| | | Days at Risk | 1,762,166 | 802,915 | 166,796 |
| | | Number of Events | 16 | 6 | 1 |
| | | Rate of Events per 1,000 Days at Risk | 0.009 | 0.007 | 0.006 |
| | 2010 | Unique Users | 24,310 | 10,748 | 2,430 |
| | | Days at Risk | 1,072,732 | 487,900 | 109,006 |
| | | Number of Events | 8 | 4 | 0 |
| | | Rate of Events per 1,000 Days at Risk | 0.007 | 0.008 | 0.000 |
| | 2011 | Unique Users | 1,414 | 593 | 121 |
| | | Days at Risk | 27,281 | 12,469 | 2,311 |
| | | Number of Events | 0 | 0 | 0 |
| | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) Bupropion for Smoking Cessation: Individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

[b]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Table 6 (Continued). Number of Users, Number of Days at Risk, Number of Cardiovascular Events, Percent of Users with an Event, and Rate of Events per 1,000 Days at Risk by Exposure Group[a], Year, and Cohort[b]**

| | | | COHORT | | |
|---|---|---|---|---|---|
| | | | OVERALL | TOBACCO | DEPRESSION |
| Exposure Group | IndexYear | | | | |
| BUPROPION for Any Reason | 2006 | Unique Users | 203,991 | 28,342 | 70,013 |
| | | Days at Risk | 22,535,024 | 2,191,358 | 9,754,571 |
| | | Number of Events | 136 | 28 | 70 |
| | | Rate of Events per 1,000 Days at Risk | 0.006 | 0.013 | 0.007 |
| | 2007 | Unique Users | 150,237 | 21,671 | 59,091 |
| | | Days at Risk | 17,344,047 | 1,768,961 | 8,197,298 |
| | | Number of Events | 109 | 34 | 59 |
| | | Rate of Events per 1,000 Days at Risk | 0.006 | 0.019 | 0.007 |
| | 2008 | Unique Users | 137,446 | 20,621 | 56,950 |
| | | Days at Risk | 14,842,438 | 1,597,905 | 7,265,347 |
| | | Number of Events | 86 | 25 | 43 |
| | | Rate of Events per 1,000 Days at Risk | 0.006 | 0.016 | 0.006 |
| | 2009 | Unique Users | 139,309 | 23,973 | 60,837 |
| | | Days at Risk | 13,491,812 | 1,694,424 | 6,825,519 |
| | | Number of Events | 88 | 24 | 48 |
| | | Rate of Events per 1,000 Days at Risk | 0.007 | 0.014 | 0.007 |
| | 2010 | Unique Users | 108,261 | 17,660 | 48,769 |
| | | Days at Risk | 8,198,813 | 1,093,920 | 4,052,335 |
| | | Number of Events | 33 | 7 | 20 |
| | | Rate of Events per 1,000 Days at Risk | 0.004 | 0.006 | 0.005 |
| | 2011 | Unique Users | 6,412 | 1,160 | 2,620 |
| | | Days at Risk | 156,328 | 35,485 | 69,540 |
| | | Number of Events | 0 | 0 | 0 |
| | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) Bupropion for Smoking Cessation: Individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

[b]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Table 6 (Continued). Number of Users, Number of Days at Risk, Number of Cardiovascular Events, Percent of Users with an Event, and Rate of Events per 1,000 Days at Risk by Exposure Group[a], Year, and Cohort[b]**

| | | | COHORT | | |
|---|---|---|---|---|---|
| | | | OVERALL | TOBACCO | DEPRESSION |
| Exposure Group | IndexYear | | | | |
| BUPROPION for Smoking Cessation | 2006 | Unique Users | 4,719 | 1,716 | 283 |
| | | Days at Risk | 216,003 | 77,277 | 13,141 |
| | | Number of Events | 4 | 1 | 0 |
| | | Rate of Events per 1,000 Days at Risk | 0.019 | 0.013 | 0.000 |
| | 2007 | Unique Users | 1,939 | 701 | 193 |
| | | Days at Risk | 94,618 | 34,020 | 10,239 |
| | | Number of Events | 0 | 0 | 0 |
| | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | 2008 | Unique Users | 1,485 | 503 | 229 |
| | | Days at Risk | 73,112 | 23,858 | 12,252 |
| | | Number of Events | 0 | 0 | 0 |
| | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | 2009 | Unique Users | 1,942 | 837 | 287 |
| | | Days at Risk | 99,138 | 40,948 | 14,905 |
| | | Number of Events | 2 | 2 | 0 |
| | | Rate of Events per 1,000 Days at Risk | 0.020 | 0.049 | 0.000 |
| | 2010 | Unique Users | 1,088 | 384 | 155 |
| | | Days at Risk | 50,702 | 17,928 | 7,226 |
| | | Number of Events | 0 | 0 | 0 |
| | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | 2011 | Unique Users | 36 | 14 | 1 |
| | | Days at Risk | 763 | 377 | 27 |
| | | Number of Events | 0 | 0 | 0 |
| | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) Bupropion for Smoking Cessation: Individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

[b]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

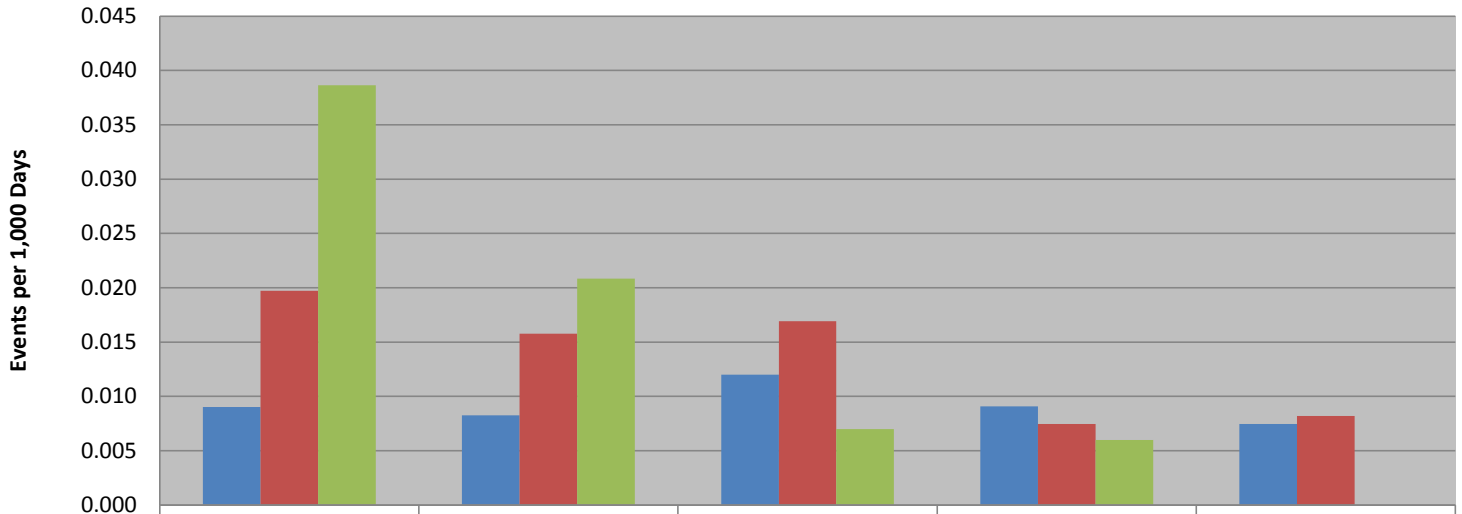
**Table 6 (Continued). Number of Users, Number of Days at Risk, Number of Cardiovascular Events, Percent of Users with an Event, and Rate of Events per 1,000 Days at Risk by Exposure Group[a], Year, and Cohort[b]**

| | | | COHORT | | |
|---|---|---|---|---|---|
| | | | OVERALL | TOBACCO | DEPRESSION |
| Exposure Group | IndexYear | | | | |
| BUPROPION for Treatment of Depression | 2006 | Unique Users | 199,377 | 26,650 | 69,757 |
| | | Days at Risk | 22,301,240 | 2,112,067 | 9,732,560 |
| | | Number of Events | 131 | 27 | 69 |
| | | Rate of Events per 1,000 Days at Risk | 0.006 | 0.013 | 0.007 |
| | 2007 | Unique Users | 148,627 | 21,060 | 58,964 |
| | | Days at Risk | 17,249,104 | 1,739,240 | 8,183,087 |
| | | Number of Events | 109 | 34 | 59 |
| | | Rate of Events per 1,000 Days at Risk | 0.006 | 0.020 | 0.007 |
| | 2008 | Unique Users | 136,299 | 20,204 | 56,813 |
| | | Days at Risk | 14,764,044 | 1,576,648 | 7,244,640 |
| | | Number of Events | 87 | 26 | 43 |
| | | Rate of Events per 1,000 Days at Risk | 0.006 | 0.016 | 0.006 |
| | 2009 | Unique Users | 137,781 | 23,282 | 60,657 |
| | | Days at Risk | 13,404,283 | 1,658,981 | 6,811,172 |
| | | Number of Events | 85 | 21 | 47 |
| | | Rate of Events per 1,000 Days at Risk | 0.006 | 0.013 | 0.007 |
| | 2010 | Unique Users | 107,455 | 17,360 | 48,661 |
| | | Days at Risk | 8,156,870 | 1,079,473 | 4,044,601 |
| | | Number of Events | 33 | 7 | 20 |
| | | Rate of Events per 1,000 Days at Risk | 0.004 | 0.006 | 0.005 |
| | 2011 | Unique Users | 6,393 | 1,152 | 2,622 |
| | | Days at Risk | 155,942 | 35,271 | 69,566 |
| | | Number of Events | 0 | 0 | 0 |
| | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) Bupropion for Smoking Cessation: Individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

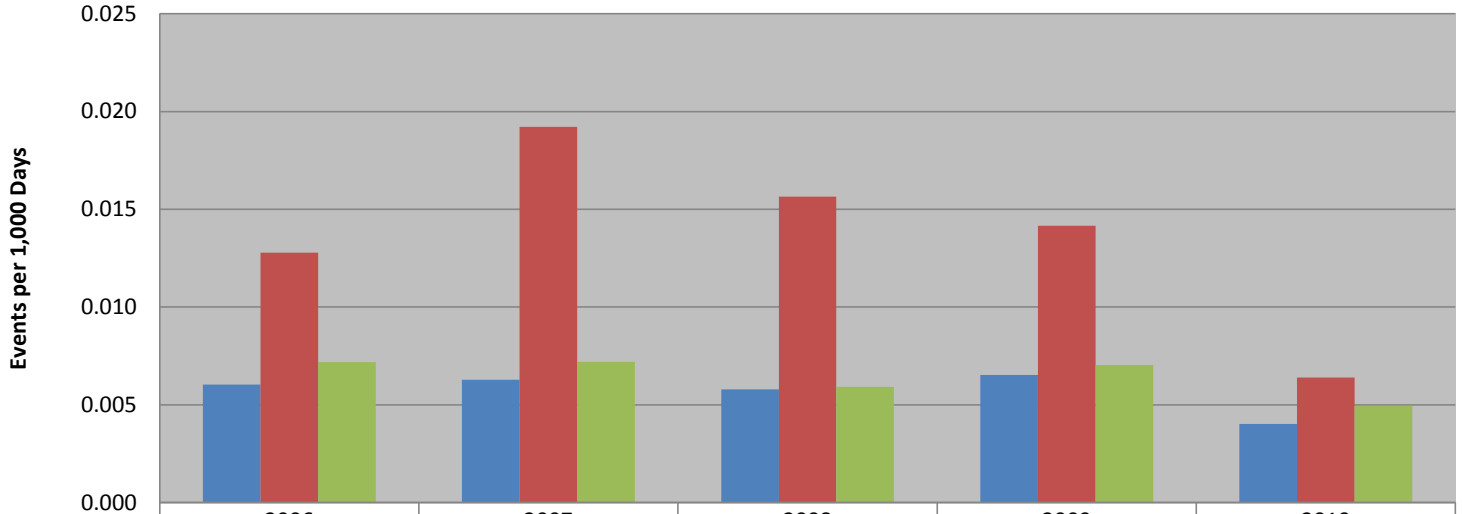
[b]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Figure 6a. Rate of Acute Cardiovascular Events per 1,000 Days at Risk, by Cohort[a] and Year among Users of Varenicline**




| | 2006 | 2007 | 2008 | 2009 | 2010 |
|---|---|---|---|---|---|
| Overall | 0.009 | 0.008 | 0.012 | 0.009 | 0.007 |
| Tobacco | 0.020 | 0.016 | 0.017 | 0.007 | 0.008 |
| Depression | 0.039 | 0.021 | 0.007 | 0.006 | 0.000 |

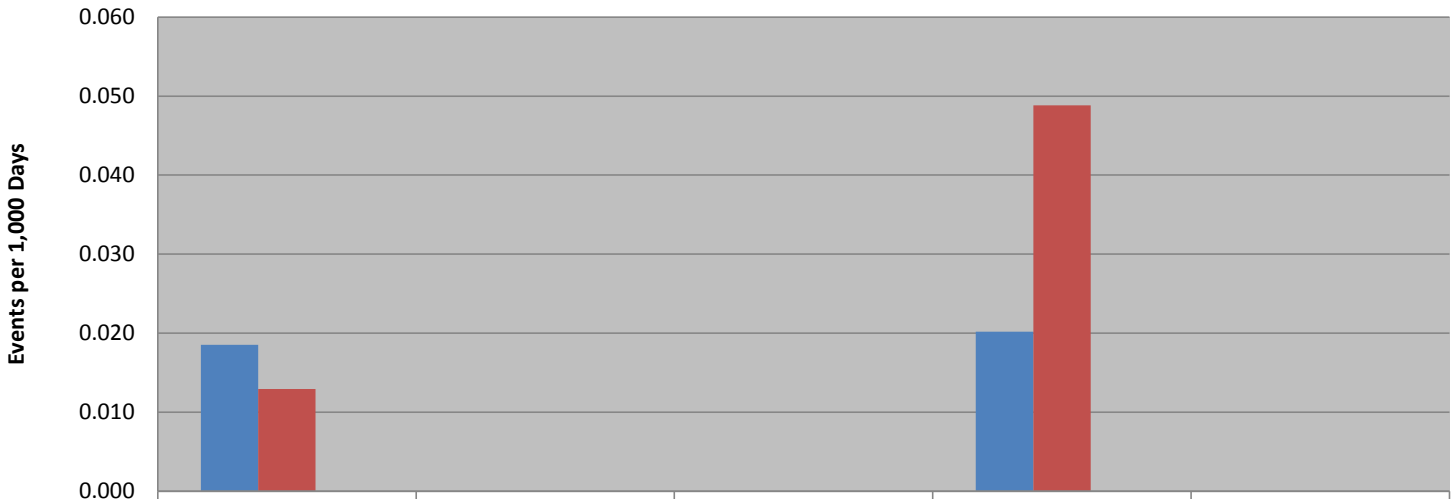
**Figure 6b. Rate of Acute Cardiovascular Events per 1,000 Days at Risk, by Cohort[a] and Year among Users of Bupropion for Any Reason**




| | 2006 | 2007 | 2008 | 2009 | 2010 |
|---|---|---|---|---|---|
| Overall | 0.006 | 0.006 | 0.006 | 0.007 | 0.004 |
| Tobacco | 0.013 | 0.019 | 0.016 | 0.014 | 0.006 |
| Depression | 0.007 | 0.007 | 0.006 | 0.007 | 0.005 |

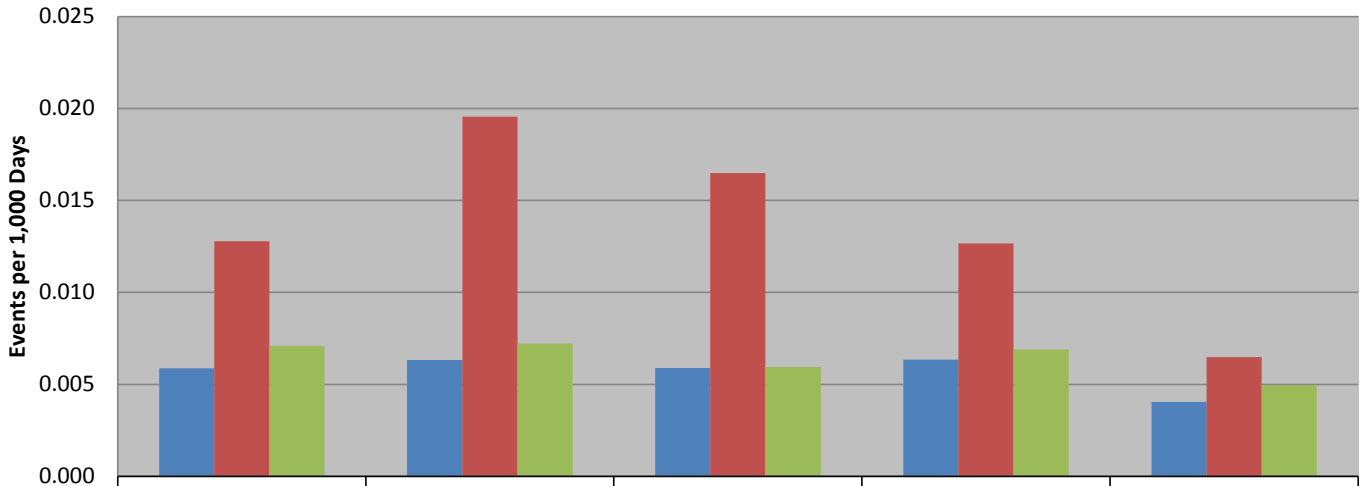
[a]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Figure 6c. Rate of Acute Cardiovascular Events per 1,000 Days at Risk, by Cohort[a] and Year among Users of Bupropion for Smoking Cessation**




| | 2006 | 2007 | 2008 | 2009 | 2010 |
|---|---|---|---|---|---|
| Overall | 0.019 | 0.000 | 0.000 | 0.020 | 0.000 |
| Tobacco | 0.013 | 0.000 | 0.000 | 0.049 | 0.000 |
| Depression | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |

**Figure 6d. Rate of Acute Cardiovascular Events per 1,000 Days at Risk, by Cohort[a] and Year among Users of Bupropion for Treatment of Depression**




| | 2006 | 2007 | 2008 | 2009 | 2010 |
|---|---|---|---|---|---|
| Overall | 0.006 | 0.006 | 0.006 | 0.006 | 0.004 |
| Tobacco | 0.013 | 0.020 | 0.016 | 0.013 | 0.006 |
| Depression | 0.007 | 0.007 | 0.006 | 0.007 | 0.005 |

[a]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Table 7. Number of Users, Number of Days at Risk, Number of Cardiovascular Events, Percent of Users with an Event, and Rate of Events per 1,000 Days at Risk, by Exposure Group[a], Age Group, and Cohort[b]**

| | | | COHORT | | |
|---|---|---|---|---|---|
| | | | OVERALL | TOBACCO | DEPRESSION |
| Exposure Group | AgeGroup | | | | |
| VARENICLINE | 20 to 44 | Unique Users | 101,687 | 35,317 | 8,661 |
| | | Days at Risk | 4,359,002 | 1,538,381 | 368,233 |
| | | Number of Events | 12 | 4 | 0 |
| | | Rate of Events per 1,000 Days at Risk | 0.003 | 0.003 | 0.000 |
| | 45 to 64 | Unique Users | 134,589 | 44,859 | 11,537 |
| | | Days at Risk | 6,237,841 | 2,115,455 | 537,624 |
| | | Number of Events | 71 | 38 | 11 |
| | | Rate of Events per 1,000 Days at Risk | 0.011 | 0.018 | 0.020 |
| | 65+ | Unique Users | 24,569 | 9,397 | 1,975 |
| | | Days at Risk | 1,124,477 | 437,966 | 93,635 |
| | | Number of Events | 26 | 14 | 2 |
| | | Rate of Events per 1,000 Days at Risk | 0.023 | 0.032 | 0.021 |
| BUPROPION for Any Reason | 20 to 44 | Unique Users | 359,298 | 48,636 | 144,460 |
| | | Days at Risk | 32,394,207 | 3,289,347 | 15,063,344 |
| | | Number of Events | 36 | 12 | 17 |
| | | Rate of Events per 1,000 Days at Risk | 0.001 | 0.004 | 0.001 |
| | 45 to 64 | Unique Users | 326,581 | 53,461 | 126,797 |
| | | Days at Risk | 37,207,454 | 4,199,380 | 17,366,676 |
| | | Number of Events | 239 | 66 | 125 |
| | | Rate of Events per 1,000 Days at Risk | 0.006 | 0.016 | 0.007 |
| | 65+ | Unique Users | 59,777 | 11,330 | 27,023 |
| | | Days at Risk | 6,966,801 | 893,326 | 3,734,590 |
| | | Number of Events | 177 | 40 | 98 |
| | | Rate of Events per 1,000 Days at Risk | 0.025 | 0.045 | 0.026 |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) Bupropion for Smoking Cessation: Individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

[b]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

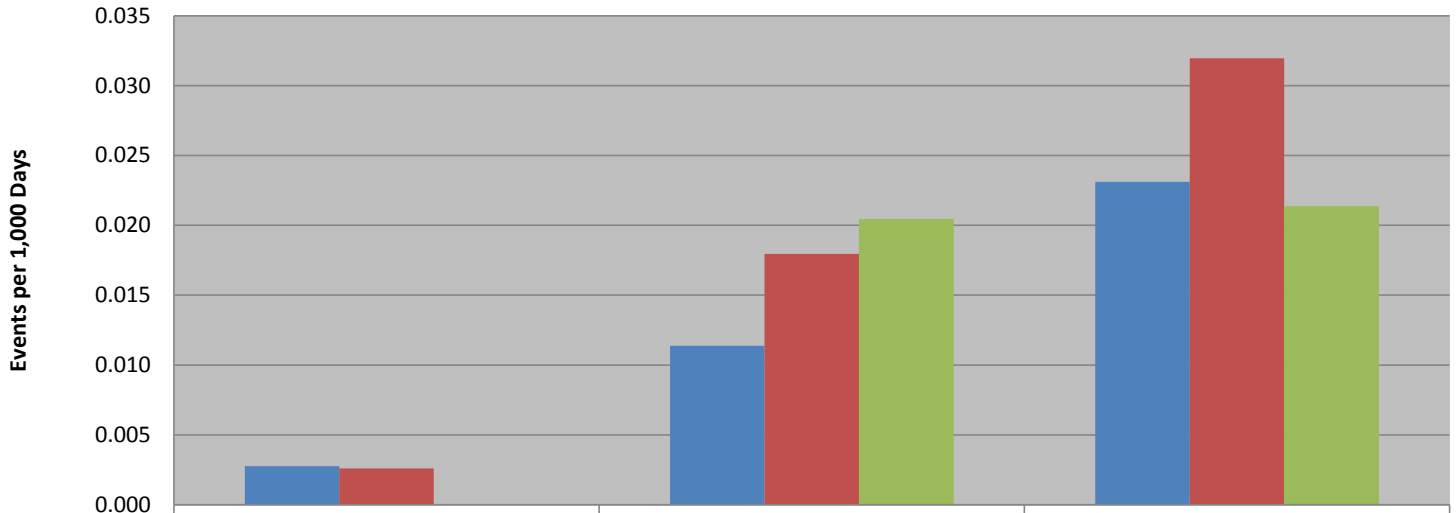
**Table 7 (Continued). Number of Users, Number of Days at Risk, Number of Cardiovascular Events, Percent of Users with an Event, and Rate of Events per 1,000 Days at Risk, by Exposure Group[a], Age Group, and Cohort[b]**

| | | | COHORT | | |
|---|---|---|---|---|---|
| | | | OVERALL | TOBACCO | DEPRESSION |
| Exposure Group | AgeGroup | | | | |
| BUPROPION for Smoking Cessation | 20 to 44 | Unique Users | 4,681 | 1,715 | 501 |
| | | Days at Risk | 211,864 | 76,794 | 24,108 |
| | | Number of Events | 0 | 0 | 0 |
| | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | 45 to 64 | Unique Users | 5,251 | 1,938 | 478 |
| | | Days at Risk | 256,191 | 92,946 | 24,723 |
| | | Number of Events | 5 | 2 | 0 |
| | | Rate of Events per 1,000 Days at Risk | 0.020 | 0.022 | 0.000 |
| | 65+ | Unique Users | 1,277 | 502 | 169 |
| | | Days at Risk | 66,281 | 24,668 | 8,959 |
| | | Number of Events | 1 | 1 | 0 |
| | | Rate of Events per 1,000 Days at Risk | 0.015 | 0.041 | 0.000 |
| BUPROPION for Treatment of Depression | 20 to 44 | Unique Users | 355,191 | 47,068 | 144,121 |
| | | Days at Risk | 32,183,785 | 3,216,965 | 15,035,842 |
| | | Number of Events | 35 | 12 | 16 |
| | | Rate of Events per 1,000 Days at Risk | 0.001 | 0.004 | 0.001 |
| | 45 to 64 | Unique Users | 322,054 | 51,746 | 126,457 |
| | | Days at Risk | 36,951,861 | 4,112,811 | 17,331,877 |
| | | Number of Events | 234 | 64 | 124 |
| | | Rate of Events per 1,000 Days at Risk | 0.006 | 0.016 | 0.007 |
| | 65+ | Unique Users | 58,687 | 10,894 | 26,896 |
| | | Days at Risk | 6,895,837 | 871,904 | 3,717,907 |
| | | Number of Events | 176 | 39 | 98 |
| | | Rate of Events per 1,000 Days at Risk | 0.026 | 0.045 | 0.026 |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) Bupropion for Smoking Cessation: Individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

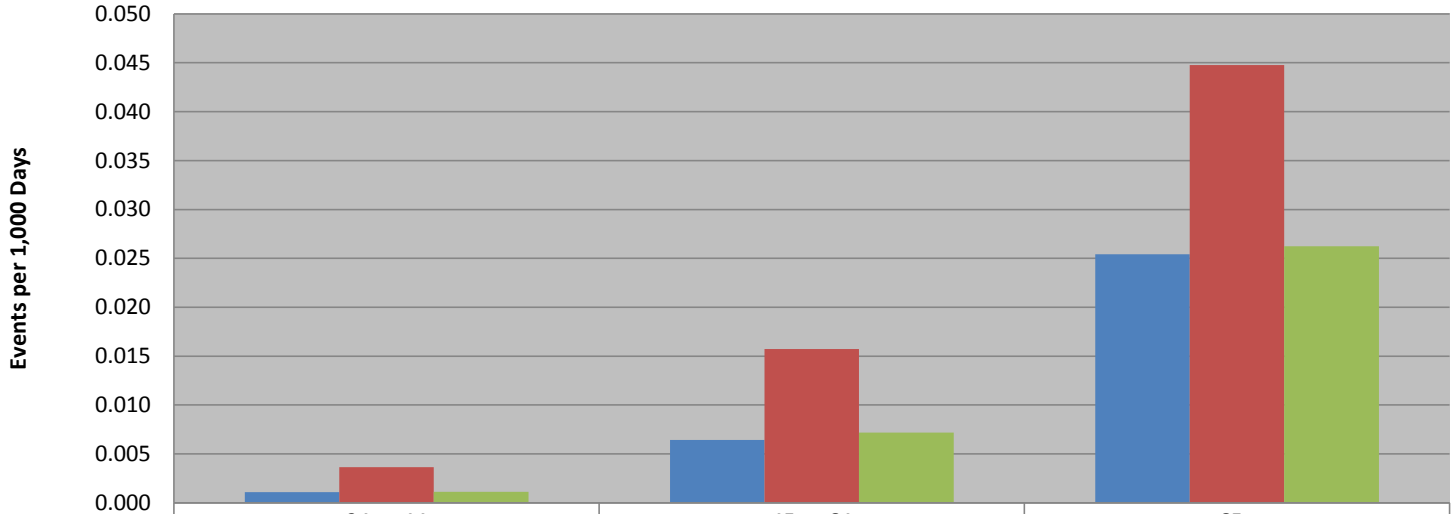
[b]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Figure 7a. Rate of Acute Cardiovascular Events per 1,000 Days at Risk, by Cohort[a] and Age Group among Users of Varenicline**




| | 24 to 44 | 45 to 64 | 65+ |
|---|---|---|---|
| OVERALL | 0.003 | 0.011 | 0.023 |
| TOBACCO | 0.003 | 0.018 | 0.032 |
| DEPRESSION | 0.000 | 0.020 | 0.021 |

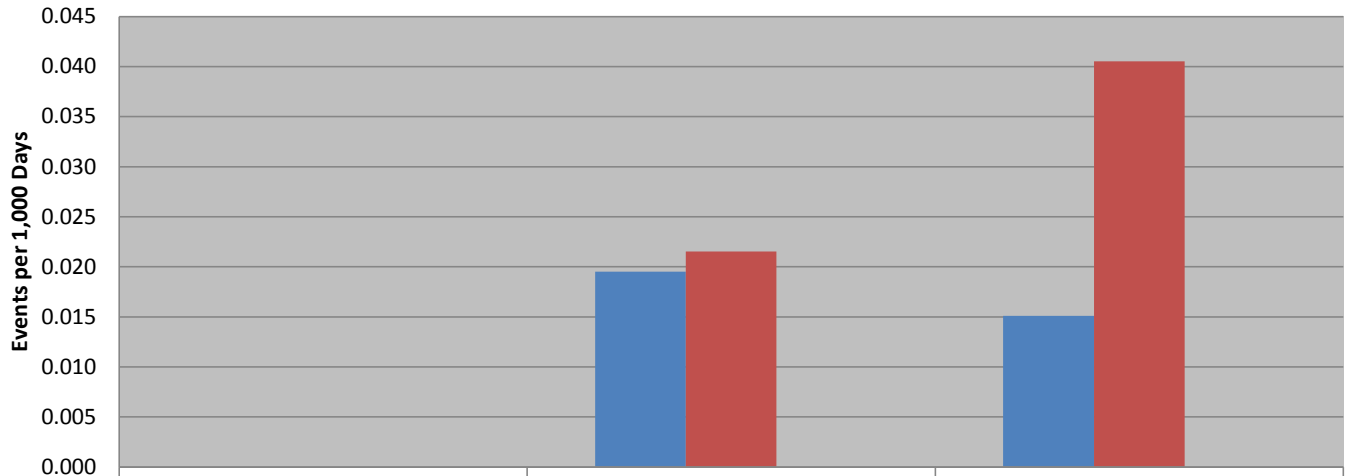
**Figure 7b. Rate of Acute Cardiovascular Events per 1,000 Days at Risk, by Cohort[a] and Age Group among Users of Bupropion for Any Reason**




| | 24 to 44 | 45 to 64 | 65+ |
|---|---|---|---|
| OVERALL | 0.001 | 0.006 | 0.025 |
| TOBACCO | 0.004 | 0.016 | 0.045 |
| DEPRESSION | 0.001 | 0.007 | 0.026 |

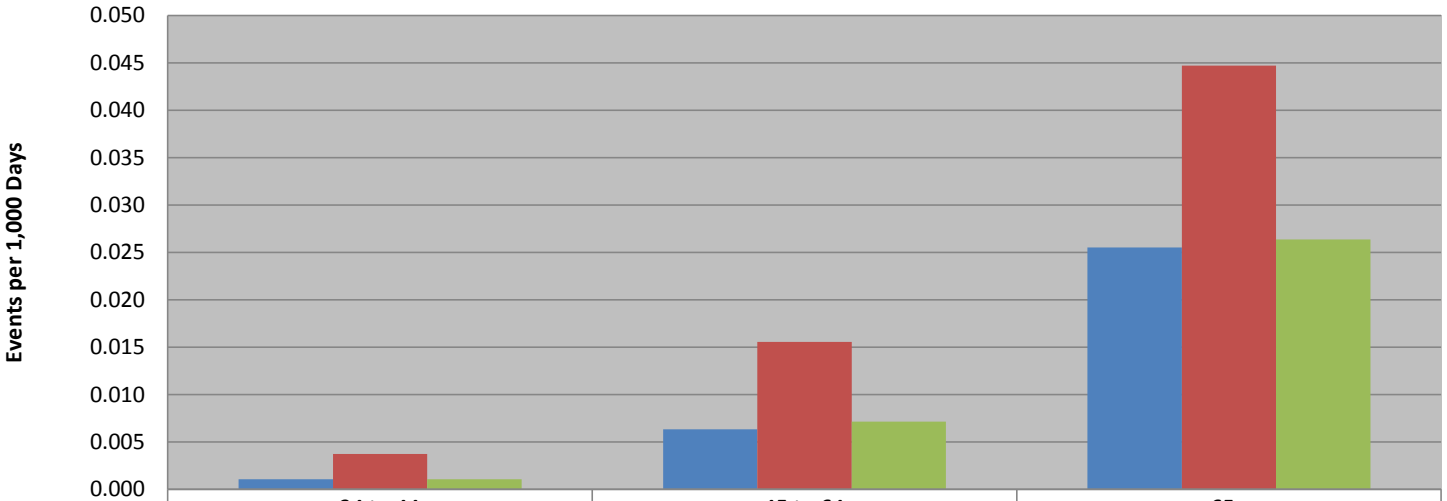
[a]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Figure 7c. Rate of Acute Cardiovascular Events per 1,000 Days at Risk, by Cohort[a] and Age Group among Users of Bupropion for Smoking Cessation**




| | 24 to 44 | 45 to 64 | 65+ |
|---|---|---|---|
| OVERALL | 0.000 | 0.020 | 0.015 |
| TOBACCO | 0.000 | 0.022 | 0.041 |
| DEPRESSION | 0.000 | 0.000 | 0.000 |

**Figure 7d. Rate of Acute Cardiovascular Events per 1,000 Days at Risk, by Cohort[a] and Age Group among Users of Bupropion for Treatment of Depression**




| | 24 to 44 | 45 to 64 | 65+ |
|---|---|---|---|
| OVERALL | 0.001 | 0.006 | 0.026 |
| TOBACCO | 0.004 | 0.016 | 0.045 |
| DEPRESSION | 0.001 | 0.007 | 0.026 |

[a]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Table 8. Number of Users, Number of Days at Risk, Number of Cardiovascular Events, Percent of Users with an Event, and Rate of Events per 1,000 Days at Risk by Exposure Group[a], Sex, and Cohort[b]**

| | | | COHORT | | |
|---|---|---|---|---|---|
| | | | OVERALL | TOBACCO | DEPRESSION |
| Exposure Group | SEX | | | | |
| VARENICLINE | Female | Unique Users | 137,993 | 47,440 | 15,564 |
| | | Days at Risk | 6,168,474 | 2,160,400 | 696,390 |
| | | Number of Events | 40 | 24 | 5 |
| | | Rate of Events per 1,000 Days at Risk | 0.006 | 0.011 | 0.007 |
| | Male | Unique Users | 122,667 | 42,079 | 6,596 |
| | | Days at Risk | 5,545,001 | 1,929,221 | 302,614 |
| | | Number of Events | 69 | 32 | 8 |
| | | Rate of Events per 1,000 Days at Risk | 0.012 | 0.017 | 0.026 |
| | Unknown | Unique Users | 185 | 54 | 13 |
| | | Days at Risk | 7,845 | 2,181 | 488 |
| | | Number of Events | 0 | 0 | 0 |
| | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| BUPROPION for Any Reason | Ambiguous | Unique Users | 2 | . | 2 |
| | | Days at Risk | 293 | . | 293 |
| | | Number of Events | 0 | . | 0 |
| | | Rate of Events per 1,000 Days at Risk | 0.000 | . | 0.000 |
| | Female | Unique Users | 485,259 | 63,746 | 204,709 |
| | | Days at Risk | 50,796,120 | 4,812,964 | 24,754,085 |
| | | Number of Events | 216 | 46 | 128 |
| | | Rate of Events per 1,000 Days at Risk | 0.004 | 0.010 | 0.005 |
| | Male | Unique Users | 259,745 | 49,632 | 93,347 |
| | | Days at Risk | 25,713,974 | 3,566,479 | 11,387,863 |
| | | Number of Events | 236 | 72 | 112 |
| | | Rate of Events per 1,000 Days at Risk | 0.009 | 0.020 | 0.010 |
| | Unknown | Unique Users | 650 | 49 | 222 |
| | | Days at Risk | 58,075 | 2,610 | 22,369 |
| | | Number of Events | 0 | 0 | 0 |
| | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) Bupropion for Smoking Cessation: Individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

[b]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

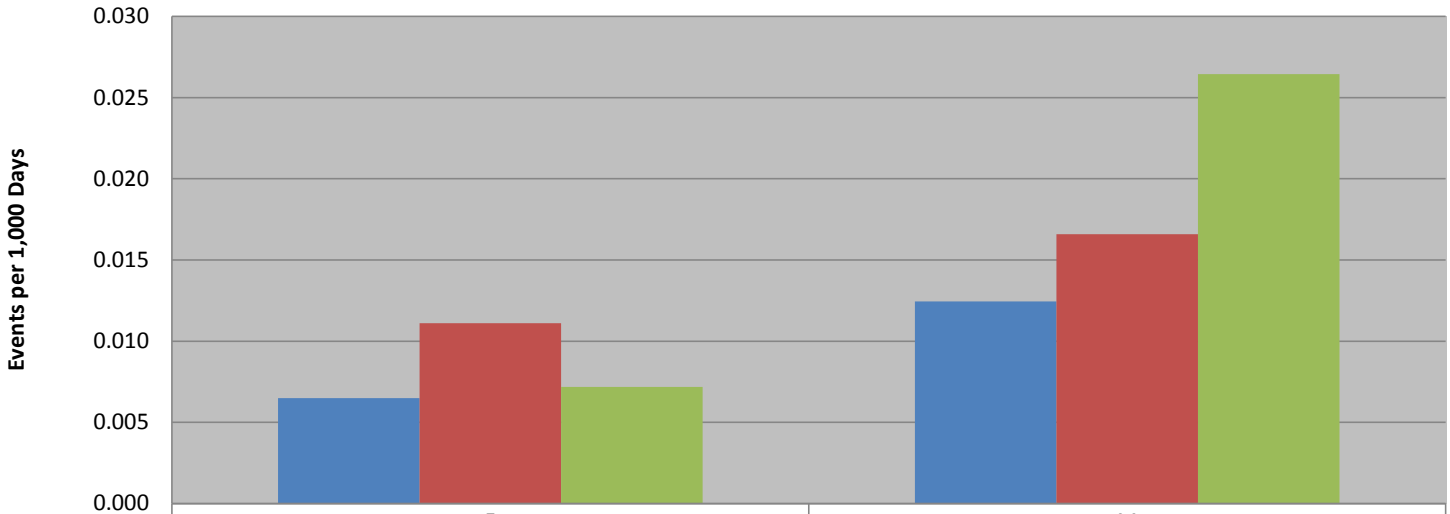
**Table 8 (Continued). Number of Users, Number of Days at Risk, Number of Cardiovascular Events, Percent of Users with an Event, and Rate of Events per 1,000 Days at Risk by Exposure Group[a], Sex, and Cohort[b]**

| | | | COHORT | | |
|---|---|---|---|---|---|
| | | | OVERALL | TOBACCO | DEPRESSION |
| Exposure Group | SEX | | | | |
| BUPROPION for Smoking Cessation | Female | Unique Users | 6,054 | 2,179 | 792 |
| | | Days at Risk | 287,109 | 100,928 | 40,082 |
| | | Number of Events | 1 | 0 | 0 |
| | | Rate of Events per 1,000 Days at Risk | 0.003 | 0.000 | 0.000 |
| | Male | Unique Users | 5,149 | 1,976 | 353 |
| | | Days at Risk | 247,014 | 93,480 | 17,597 |
| | | Number of Events | 5 | 3 | 0 |
| | | Rate of Events per 1,000 Days at Risk | 0.020 | 0.032 | 0.000 |
| | Unknown | Unique Users | 6 | 0 | 3 |
| | | Days at Risk | 213 | 0 | 111 |
| | | Number of Events | 0 | 0 | 0 |
| | | Rate of Events per 1,000 Days at Risk | 0.000 | . | 0.000 |
| BUPROPION for Treatment of Depression | Ambiguous | Unique Users | 2 | . | 2 |
| | | Days at Risk | 293 | . | 293 |
| | | Number of Events | 0 | . | 0 |
| | | Rate of Events per 1,000 Days at Risk | 0.000 | . | 0.000 |
| | Female | Unique Users | 480,167 | 61,842 | 204,165 |
| | | Days at Risk | 50,507,670 | 4,721,918 | 24,701,811 |
| | | Number of Events | 214 | 45 | 127 |
| | | Rate of Events per 1,000 Days at Risk | 0.004 | 0.010 | 0.005 |
| | Male | Unique Users | 255,119 | 47,817 | 93,088 |
| | | Days at Risk | 25,465,658 | 3,477,152 | 11,361,264 |
| | | Number of Events | 231 | 70 | 111 |
| | | Rate of Events per 1,000 Days at Risk | 0.009 | 0.020 | 0.010 |
| | Unknown | Unique Users | 644 | 49 | 219 |
| | | Days at Risk | 57,862 | 2,610 | 22,258 |
| | | Number of Events | 0 | 0 | 0 |
| | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) Bupropion for Smoking Cessation: Individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

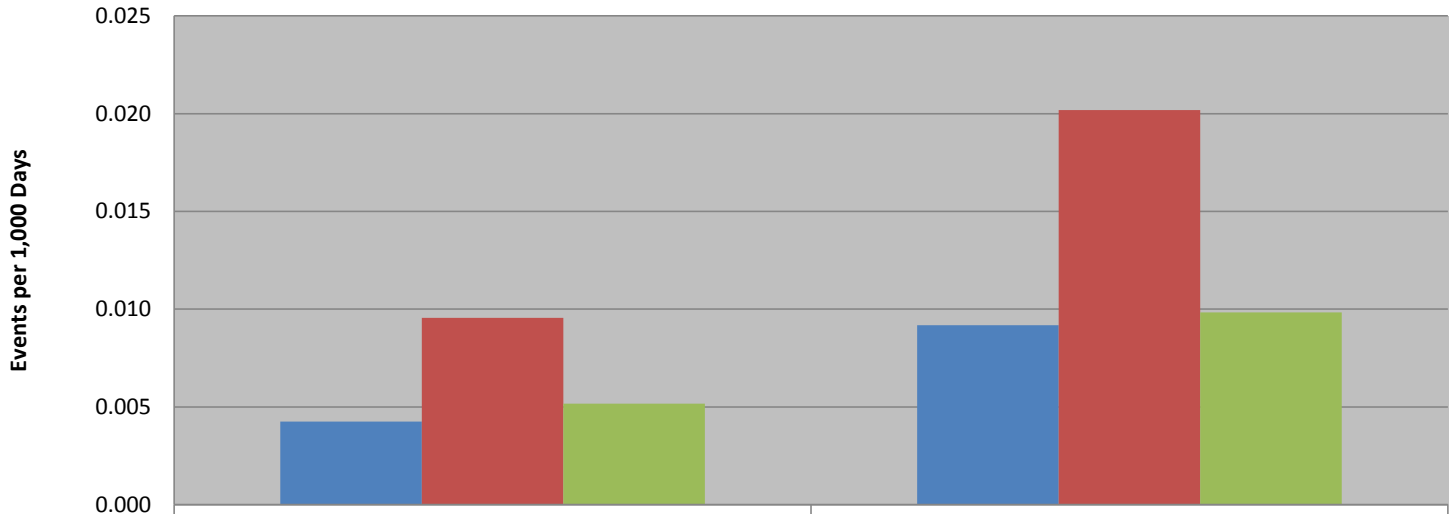
[b]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Figure 8a. Rate of Acute Cardiovascular Events per 1,000 Days at Risk, by Cohort[a] and Sex among Users of Varenicline**




| | F | M |
|---|---|---|
| OVERALL | 0.006 | 0.012 |
| TOBACCO | 0.011 | 0.017 |
| DEPRESSION | 0.007 | 0.026 |

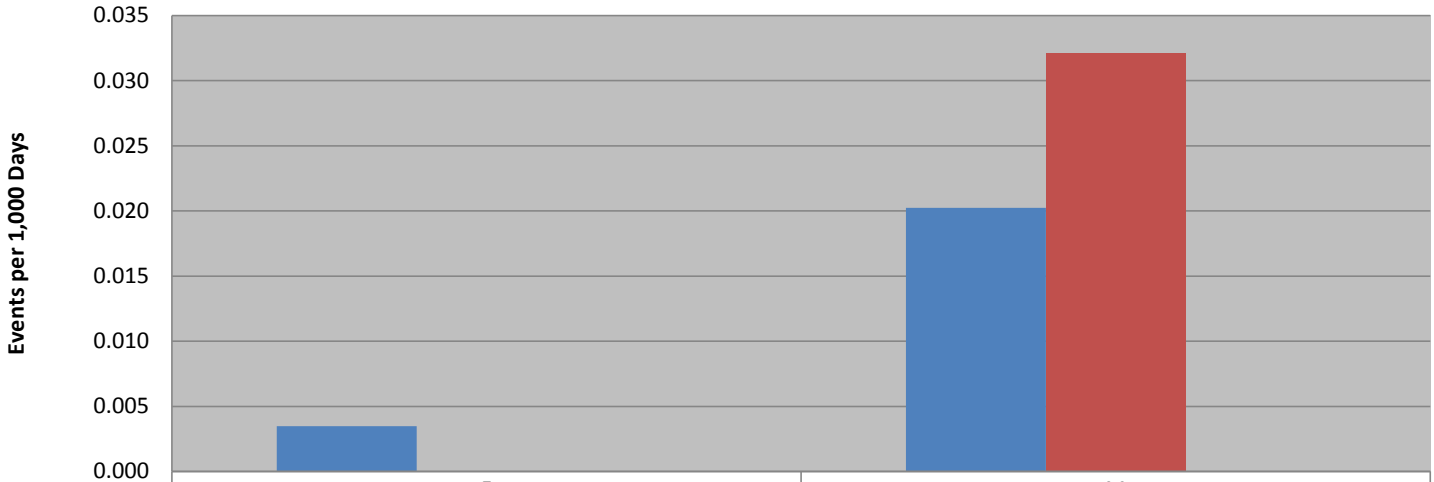
**Figure 8b. Rate of Acute Cardiovascular Events per 1,000 Days at Risk, by Cohort[a] and Sex among Users of Bupropion for Any Reason**




| | F | M |
|---|---|---|
| OVERALL | 0.004 | 0.009 |
| TOBACCO | 0.010 | 0.020 |
| DEPRESSION | 0.005 | 0.010 |

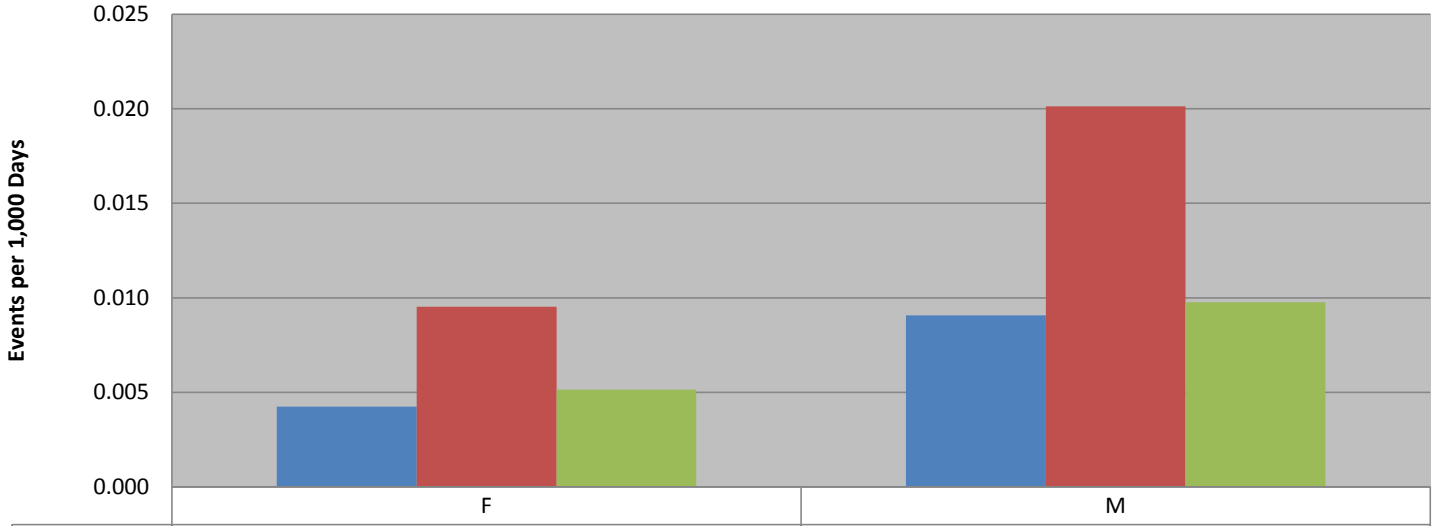
[a]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Figure 8c. Rate of Acute Cardiovascular Events per 1,000 Days at Risk, by Cohort[a] and Sex among Users of Bupropion for Smoking Cessation**




| | F | M |
|---|---|---|
| OVERALL | 0.003 | 0.020 |
| TOBACCO | 0.000 | 0.032 |
| DEPRESSION | 0.000 | 0.000 |

**Figure 8d. Rate of Acute Cardiovascular Events per 1,000 Days at Risk, by Cohort[a] and Sex among Users of Bupropion for Treatment of Depression**




| | F | M |
|---|---|---|
| OVERALL | 0.004 | 0.009 |
| TOBACCO | 0.010 | 0.020 |
| DEPRESSION | 0.005 | 0.010 |

[a]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Table 9. Number of Users, Number of Days at Risk, Number of Cardiovascular Events, Percent of Users with an Event, and Rate of Events per 1,000 Days at Risk by Exposure Group[a], Sex, Age Group, and Cohort[b]**

| | | | | COHORT | | |
|---|---|---|---|---|---|---|
| | | | | OVERALL | TOBACCO | DEPRESSION |
| Exposure Group | SEX | AgeGroup | | | | |
| VARENICLINE | Female | 20 to 44 | Unique Users | 53,518 | 18,459 | 6,091 |
| | | | Days at Risk | 2,273,462 | 799,872 | 258,815 |
| | | | Number of Events | 2 | 2 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.001 | 0.003 | 0.000 |
| | | 45 to 64 | Unique Users | 71,362 | 23,881 | 8,086 |
| | | | Days at Risk | 3,300,209 | 1,124,259 | 373,246 |
| | | | Number of Events | 24 | 13 | 3 |
| | | | Rate of Events per 1,000 Days at Risk | 0.007 | 0.012 | 0.008 |
| | | 65+ | Unique Users | 13,113 | 5,100 | 1,387 |
| | | | Days at Risk | 594,803 | 236,269 | 64,329 |
| | | | Number of Events | 14 | 9 | 2 |
| | | | Rate of Events per 1,000 Days at Risk | 0.024 | 0.038 | 0.031 |
| | Male | 20 to 44 | Unique Users | 48,069 | 16,826 | 2,561 |
| | | | Days at Risk | 2,081,673 | 737,367 | 109,159 |
| | | | Number of Events | 10 | 2 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.005 | 0.003 | 0.000 |
| | | 45 to 64 | Unique Users | 63,156 | 20,961 | 3,447 |
| | | | Days at Risk | 2,934,240 | 990,368 | 164,149 |
| | | | Number of Events | 47 | 25 | 8 |
| | | | Rate of Events per 1,000 Days at Risk | 0.016 | 0.025 | 0.049 |
| | | 65+ | Unique Users | 11,442 | 4,292 | 588 |
| | | | Days at Risk | 529,088 | 201,486 | 29,306 |
| | | | Number of Events | 12 | 5 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.023 | 0.025 | 0.000 |
| | Unknown | 20 to 44 | Unique Users | 100 | 32 | 9 |
| | | | Days at Risk | 3,867 | 1,142 | 259 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | | 45 to 64 | Unique Users | 71 | 17 | 4 |
| | | | Days at Risk | 3,392 | 828 | 229 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | | 65+ | Unique Users | 14 | 5 | 0 |
| | | | Days at Risk | 586 | 211 | 0 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | . |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) Bupropion for Smoking Cessation: Individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

[b]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Table 9 (Continued). Number of Users, Number of Days at Risk, Number of Cardiovascular Events, Percent of Users with an Event, and Rate of Events per 1,000 Days at Risk by Exposure Group[a], Sex, Age Group, and Cohort[b]**

| | | | | COHORT | | |
|---|---|---|---|---|---|---|
| | | | | OVERALL | TOBACCO | DEPRESSION |
| Exposure Group | SEX | AgeGroup | | | | |
| BUPROPION for Any Reason | Ambiguous | 20 to 44 | Unique Users | 2 | . | 2 |
| | | | Days at Risk | 293 | . | 293 |
| | | | Number of Events | 0 | . | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | . | 0.000 |
| | Female | 20 to 44 | Unique Users | 241,540 | 27,783 | 101,829 |
| | | | Days at Risk | 22,375,503 | 1,926,012 | 10,728,728 |
| | | | Number of Events | 19 | 6 | 10 |
| | | | Rate of Events per 1,000 Days at Risk | 0.001 | 0.003 | 0.001 |
| | | 45 to 64 | Unique Users | 207,219 | 29,586 | 85,100 |
| | | | Days at Risk | 24,174,893 | 2,388,234 | 11,634,369 |
| | | | Number of Events | 111 | 25 | 66 |
| | | | Rate of Events per 1,000 Days at Risk | 0.005 | 0.010 | 0.006 |
| | | 65+ | Unique Users | 36,500 | 6,377 | 17,780 |
| | | | Days at Risk | 4,245,724 | 498,718 | 2,390,988 |
| | | | Number of Events | 86 | 15 | 52 |
| | | | Rate of Events per 1,000 Days at Risk | 0.020 | 0.030 | 0.022 |
| | Male | 20 to 44 | Unique Users | 117,351 | 20,826 | 42,486 |
| | | | Days at Risk | 9,986,486 | 1,361,912 | 4,322,983 |
| | | | Number of Events | 17 | 6 | 7 |
| | | | Rate of Events per 1,000 Days at Risk | 0.002 | 0.004 | 0.002 |
| | | 45 to 64 | Unique Users | 119,158 | 23,856 | 41,632 |
| | | | Days at Risk | 13,010,614 | 1,810,110 | 5,723,937 |
| | | | Number of Events | 128 | 41 | 59 |
| | | | Rate of Events per 1,000 Days at Risk | 0.010 | 0.023 | 0.010 |
| | | 65+ | Unique Users | 23,236 | 4,950 | 9,229 |
| | | | Days at Risk | 2,716,874 | 394,457 | 1,340,943 |
| | | | Number of Events | 91 | 25 | 46 |
| | | | Rate of Events per 1,000 Days at Risk | 0.033 | 0.063 | 0.034 |
| | Unknown | 20 to 44 | Unique Users | 405 | 27 | 143 |
| | | | Days at Risk | 31,925 | 1,423 | 11,340 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | | 45 to 64 | Unique Users | 204 | 19 | 65 |
| | | | Days at Risk | 21,947 | 1,036 | 8,370 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | | 65+ | Unique Users | 41 | 3 | 14 |
| | | | Days at Risk | 4,203 | 151 | 2,659 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) Bupropion for Smoking Cessation: Individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

[b]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Table 9 (Continued). Number of Users, Number of Days at Risk, Number of Cardiovascular Events, Percent of Users with an Event, and Rate of Events per 1,000 Days at Risk by Exposure Group[a], Sex, Age Group, and Cohort[b]**

| | | | | COHORT | | |
|---|---|---|---|---|---|---|
| | | | | OVERALL | TOBACCO | DEPRESSION |
| Exposure Group | SEX | AgeGroup | | | | |
| BUPROPION for Smoking Cessation | Female | 20 to 44 | Unique Users | 2,611 | 893 | 345 |
| | | | Days at Risk | 117,644 | 39,761 | 16,921 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | | 45 to 64 | Unique Users | 2,723 | 995 | 330 |
| | | | Days at Risk | 131,563 | 47,005 | 17,328 |
| | | | Number of Events | 1 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.008 | 0.000 | 0.000 |
| | | 65+ | Unique Users | 720 | 291 | 117 |
| | | | Days at Risk | 37,902 | 14,162 | 5,833 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | Male | 20 to 44 | Unique Users | 2,068 | 822 | 155 |
| | | | Days at Risk | 94,146 | 37,033 | 7,150 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | | 45 to 64 | Unique Users | 2,525 | 943 | 147 |
| | | | Days at Risk | 124,526 | 45,941 | 7,358 |
| | | | Number of Events | 4 | 2 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.032 | 0.044 | 0.000 |
| | | 65+ | Unique Users | 556 | 211 | 51 |
| | | | Days at Risk | 28,342 | 10,506 | 3,089 |
| | | | Number of Events | 1 | 1 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.035 | 0.095 | 0.000 |
| | Unknown | 20 to 44 | Unique Users | 2 | 0 | 1 |
| | | | Days at Risk | 74 | 0 | 37 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | . | 0.000 |
| | | 45 to 64 | Unique Users | 3 | 0 | 1 |
| | | | Days at Risk | 102 | 0 | 37 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | . | 0.000 |
| | | 65+ | Unique Users | 1 | 0 | 1 |
| | | | Days at Risk | 37 | 0 | 37 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | . | 0.000 |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) Bupropion for Smoking Cessation: Individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

[b]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

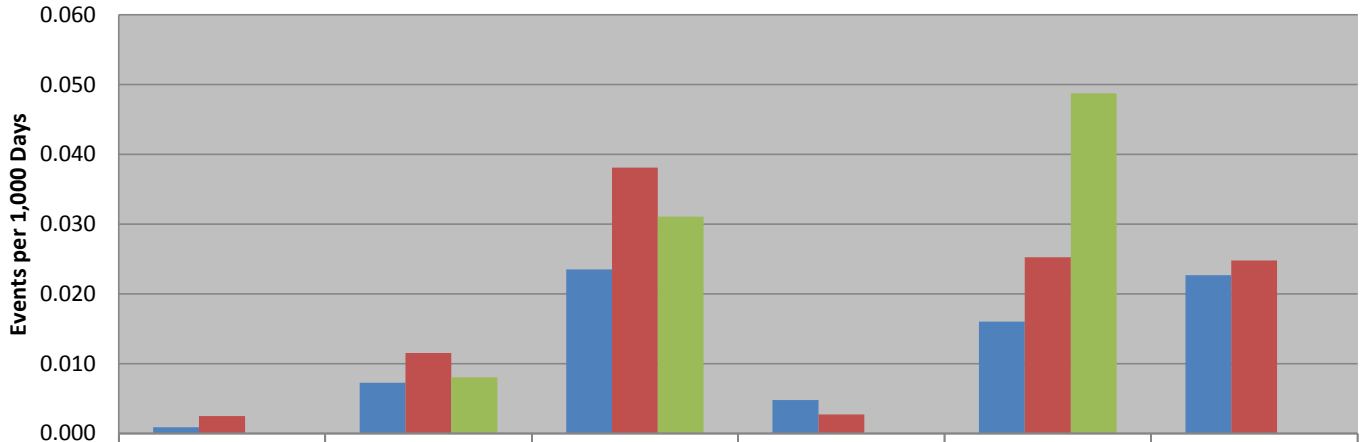
**Table 9 (Continued). Number of Users, Number of Days at Risk, Number of Cardiovascular Events, Percent of Users with an Event, and Rate of Events per 1,000 Days at Risk by Exposure Group[a], Sex, Age Group, and Cohort[b]**

| | | | | COHORT | | |
|---|---|---|---|---|---|---|
| | | | | OVERALL | TOBACCO | DEPRESSION |
| Exposure Group | SEX | AgeGroup | | | | |
| BUPROPION for Treatment of Depression | Ambiguous | 20 to 44 | Unique Users | 2 | . | 2 |
| | | | Days at Risk | 293 | . | 293 |
| | | | Number of Events | 0 | . | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | . | 0.000 |
| | Female | 20 to 44 | Unique Users | 239,326 | 26,989 | 101,606 |
| | | | Days at Risk | 22,257,929 | 1,889,884 | 10,709,017 |
| | | | Number of Events | 19 | 6 | 10 |
| | | | Rate of Events per 1,000 Days at Risk | 0.001 | 0.003 | 0.001 |
| | | 45 to 64 | Unique Users | 204,938 | 28,723 | 84,866 |
| | | | Days at Risk | 24,043,401 | 2,344,341 | 11,611,891 |
| | | | Number of Events | 109 | 24 | 65 |
| | | | Rate of Events per 1,000 Days at Risk | 0.005 | 0.010 | 0.006 |
| | | 65+ | Unique Users | 35,903 | 6,130 | 17,693 |
| | | | Days at Risk | 4,206,340 | 487,693 | 2,380,903 |
| | | | Number of Events | 86 | 15 | 52 |
| | | | Rate of Events per 1,000 Days at Risk | 0.020 | 0.031 | 0.022 |
| | Male | 20 to 44 | Unique Users | 115,460 | 20,052 | 42,371 |
| | | | Days at Risk | 9,893,712 | 1,325,658 | 4,315,229 |
| | | | Number of Events | 16 | 6 | 6 |
| | | | Rate of Events per 1,000 Days at Risk | 0.002 | 0.005 | 0.001 |
| | | 45 to 64 | Unique Users | 116,915 | 23,004 | 41,527 |
| | | | Days at Risk | 12,886,615 | 1,767,434 | 5,711,653 |
| | | | Number of Events | 125 | 40 | 59 |
| | | | Rate of Events per 1,000 Days at Risk | 0.010 | 0.023 | 0.010 |
| | | 65+ | Unique Users | 22,744 | 4,761 | 9,190 |
| | | | Days at Risk | 2,685,331 | 384,060 | 1,334,382 |
| | | | Number of Events | 90 | 24 | 46 |
| | | | Rate of Events per 1,000 Days at Risk | 0.034 | 0.062 | 0.034 |
| | Unknown | 20 to 44 | Unique Users | 403 | 27 | 142 |
| | | | Days at Risk | 31,851 | 1,423 | 11,303 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | | 45 to 64 | Unique Users | 201 | 19 | 64 |
| | | | Days at Risk | 21,845 | 1,036 | 8,333 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | | 65+ | Unique Users | 40 | 3 | 13 |
| | | | Days at Risk | 4,166 | 151 | 2,622 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) Bupropion for Smoking Cessation: Individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

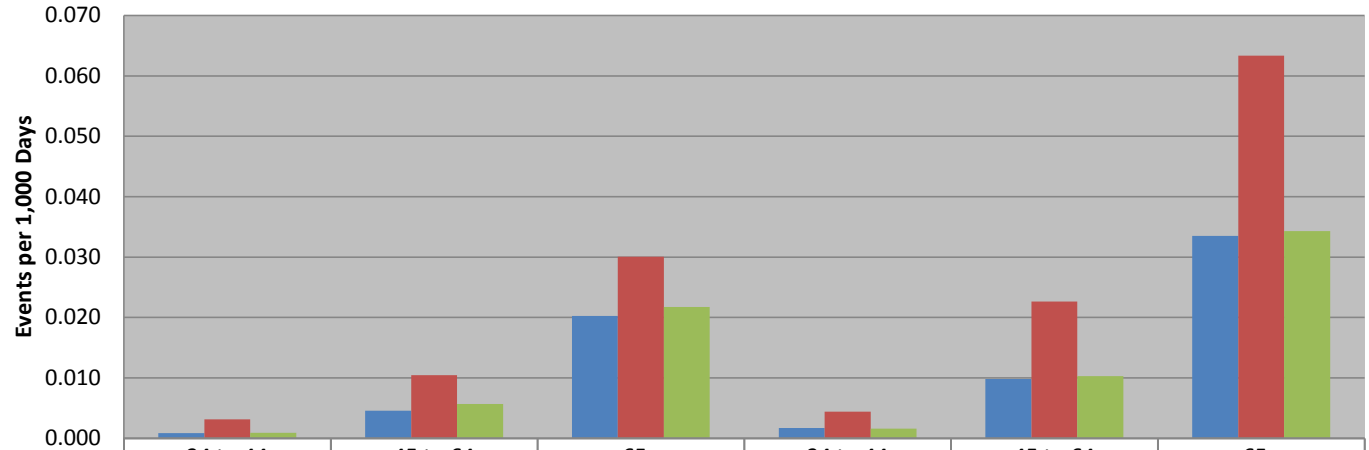
[b]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Figure 9a. Rate of Acute Cardiovascular Events per 1,000 Days at Risk, by Cohort[a], Age Group, and Sex among Users of Varenicline**




| | Female | | | Male | | |
|---|---|---|---|---|---|---|
| | 24 to 44 | 45 to 64 | 65+ | 24 to 44 | 45 to 64 | 65+ |
| OVERALL | 0.001 | 0.007 | 0.024 | 0.005 | 0.016 | 0.023 |
| TOBACCO | 0.003 | 0.012 | 0.038 | 0.003 | 0.025 | 0.025 |
| DEPRESSION | 0.000 | 0.008 | 0.031 | 0.000 | 0.049 | 0.000 |

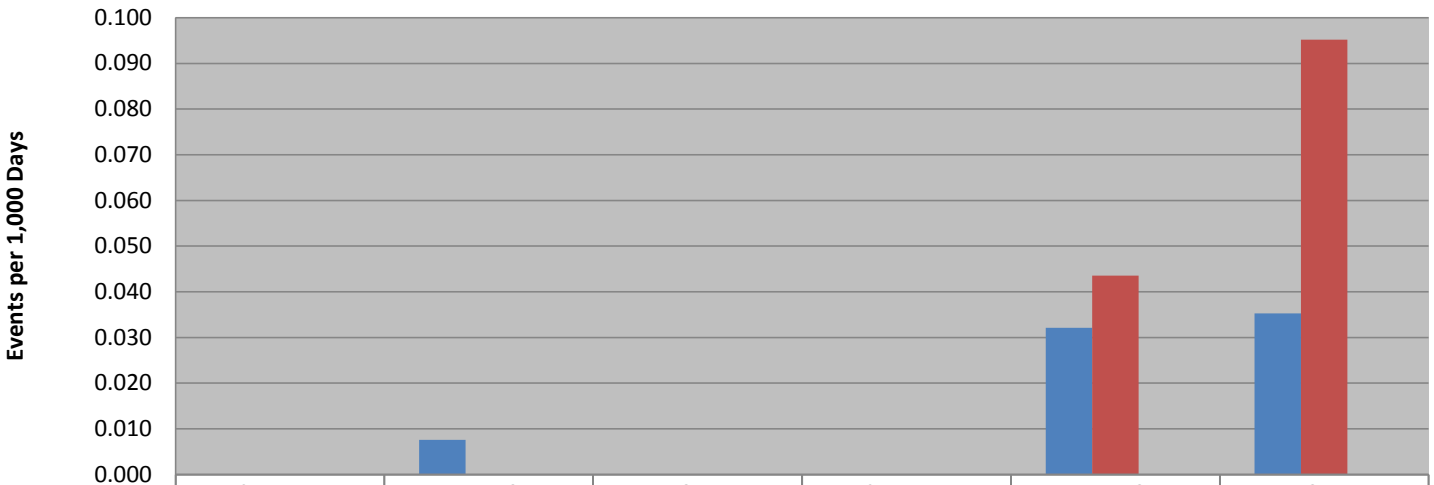
**Figure 9b. Rate of Acute Cardiovascular Events per 1,000 Days at Risk, by Cohort[a], Age Group, and Sex among Users of Bupropion for Any Reason**




| | Female | | | Male | | |
|---|---|---|---|---|---|---|
| | 24 to 44 | 45 to 64 | 65+ | 24 to 44 | 45 to 64 | 65+ |
| OVERALL | 0.001 | 0.005 | 0.020 | 0.002 | 0.010 | 0.033 |
| TOBACCO | 0.003 | 0.010 | 0.030 | 0.004 | 0.023 | 0.063 |
| DEPRESSION | 0.001 | 0.006 | 0.022 | 0.002 | 0.010 | 0.034 |

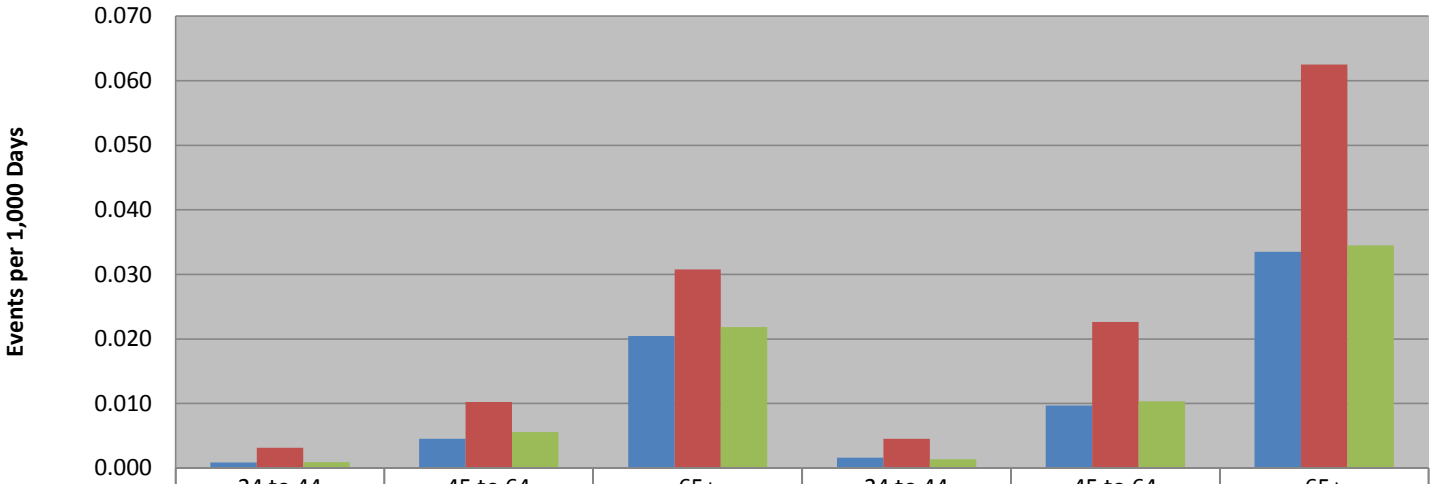
[a]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Figure 9c. Rate of Acute Cardiovascular Events per 1,000 Days at Risk, by Cohort[a], Age Group, and Sex among Users of Bupropion for Smoking Cessation**




| | Female | | | Male | | |
|---|---|---|---|---|---|---|
| | 24 to 44 | 45 to 64 | 65+ | 24 to 44 | 45 to 64 | 65+ |
| OVERALL | 0.000 | 0.008 | 0.000 | 0.000 | 0.032 | 0.035 |
| TOBACCO | 0.000 | 0.000 | 0.000 | 0.000 | 0.044 | 0.095 |
| DEPRESSION | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |

**Figure 9d. Rate of Acute Cardiovascular Events per 1,000 Days at Risk, by Cohort[a], Age Group, and Sex among Users of Bupropion for Treatment of Depression**




| | Female | | | Male | | |
|---|---|---|---|---|---|---|
| | 24 to 44 | 45 to 64 | 65+ | 24 to 44 | 45 to 64 | 65+ |
| OVERALL | 0.001 | 0.005 | 0.020 | 0.002 | 0.010 | 0.034 |
| TOBACCO | 0.003 | 0.010 | 0.031 | 0.005 | 0.023 | 0.062 |
| DEPRESSION | 0.001 | 0.006 | 0.022 | 0.001 | 0.010 | 0.034 |

[a]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Table 10. Number of Users, Number of Days at Risk, Number of Cardiovascular Events, Percent of Users with an Event, and Rate of Events per 1,000 Days at Risk by Exposure Group[a], Year, Age Group, and Cohort[b]**

| | | | | COHORT | | |
|---|---|---|---|---|---|---|
| | | | | OVERALL | TOBACCO | DEPRESSION |
| Exposure Group | IndexYear | AgeGroup | | | | |
| VARENICLINE | 2006 | 20 to 44 | Unique Users | 5,766 | 1,298 | 472 |
| | | | Days at Risk | 252,945 | 55,578 | 20,162 |
| | | | Number of Events | 2 | 1 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.008 | 0.018 | 0.000 |
| | | 45 to 64 | Unique Users | 9,771 | 1,879 | 677 |
| | | | Days at Risk | 459,643 | 86,417 | 29,494 |
| | | | Number of Events | 4 | 2 | 2 |
| | | | Rate of Events per 1,000 Days at Risk | 0.009 | 0.023 | 0.068 |
| | | 65+ | Unique Users | 1,370 | 218 | 47 |
| | | | Days at Risk | 63,504 | 10,068 | 2,088 |
| | | | Number of Events | 1 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.016 | 0.000 | 0.000 |
| | 2007 | 20 to 44 | Unique Users | 42,014 | 11,862 | 3,429 |
| | | | Days at Risk | 1,819,784 | 520,318 | 146,516 |
| | | | Number of Events | 4 | 1 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.002 | 0.002 | 0.000 |
| | | 45 to 64 | Unique Users | 60,566 | 15,857 | 4,453 |
| | | | Days at Risk | 2,843,208 | 756,764 | 210,422 |
| | | | Number of Events | 28 | 16 | 7 |
| | | | Rate of Events per 1,000 Days at Risk | 0.010 | 0.021 | 0.033 |
| | | 65+ | Unique Users | 8,832 | 2,407 | 529 |
| | | | Days at Risk | 418,051 | 118,469 | 26,876 |
| | | | Number of Events | 10 | 5 | 1 |
| | | | Rate of Events per 1,000 Days at Risk | 0.024 | 0.042 | 0.037 |
| | 2008 | 20 to 44 | Unique Users | 26,927 | 10,419 | 2,371 |
| | | | Days at Risk | 1,151,626 | 456,188 | 99,912 |
| | | | Number of Events | 5 | 1 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.004 | 0.002 | 0.000 |
| | | 45 to 64 | Unique Users | 32,395 | 13,040 | 3,232 |
| | | | Days at Risk | 1,495,954 | 619,247 | 150,976 |
| | | | Number of Events | 19 | 14 | 1 |
| | | | Rate of Events per 1,000 Days at Risk | 0.013 | 0.023 | 0.007 |
| | | 65+ | Unique Users | 7,848 | 3,550 | 724 |
| | | | Days at Risk | 354,426 | 165,469 | 34,933 |
| | | | Number of Events | 12 | 6 | 1 |
| | | | Rate of Events per 1,000 Days at Risk | 0.034 | 0.036 | 0.029 |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) Bupropion for Smoking Cessation: Individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

[b]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Table 10 (Continued). Number of Users, Number of Days at Risk, Number of Cardiovascular Events, Percent of Users with an Event, and Rate of Events per 1,000 Days at Risk by Exposure Group[a], Year, Age Group, and Cohort[b]**

| | | | | COHORT | | |
|---|---|---|---|---|---|---|
| | | | | OVERALL | TOBACCO | DEPRESSION |
| Exposure Group | IndexYear | AgeGroup | | | | |
| VARENICLINE | 2009 | 20 to 44 | Unique Users | 17,327 | 7,672 | 1,547 |
| | | | Days at Risk | 734,352 | 331,837 | 66,561 |
| | | | Number of Events | 1 | 1 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.001 | 0.003 | 0.000 |
| | | 45 to 64 | Unique Users | 19,377 | 8,595 | 1,847 |
| | | | Days at Risk | 890,110 | 402,667 | 86,290 |
| | | | Number of Events | 15 | 5 | 1 |
| | | | Rate of Events per 1,000 Days at Risk | 0.017 | 0.012 | 0.012 |
| | | 65+ | Unique Users | 2,928 | 1,435 | 294 |
| | | | Days at Risk | 137,704 | 68,411 | 13,945 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | 2010 | 20 to 44 | Unique Users | 9,023 | 3,787 | 791 |
| | | | Days at Risk | 388,634 | 168,966 | 34,202 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | | 45 to 64 | Unique Users | 11,792 | 5,218 | 1,269 |
| | | | Days at Risk | 535,211 | 244,249 | 59,208 |
| | | | Number of Events | 5 | 1 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.009 | 0.004 | 0.000 |
| | | 65+ | Unique Users | 3,495 | 1,743 | 370 |
| | | | Days at Risk | 148,887 | 74,685 | 15,596 |
| | | | Number of Events | 3 | 3 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.020 | 0.040 | 0.000 |
| | 2011 | 20 to 44 | Unique Users | 630 | 279 | 51 |
| | | | Days at Risk | 11,661 | 5,494 | 880 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | | 45 to 64 | Unique Users | 688 | 270 | 59 |
| | | | Days at Risk | 13,715 | 6,111 | 1,234 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | | 65+ | Unique Users | 96 | 44 | 11 |
| | | | Days at Risk | 1,905 | 864 | 197 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) Bupropion for Smoking Cessation: Individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

[b]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Table 10 (Continued). Number of Users, Number of Days at Risk, Number of Cardiovascular Events, Percent of Users with an Event, and Rate of Events per 1,000 Days at Risk by Exposure Group[a], Year, Age Group, and Cohort[b]**

| | | | | COHORT | | |
|---|---|---|---|---|---|---|
| | | | | OVERALL | TOBACCO | DEPRESSION |
| Exposure Group | IndexYear | AgeGroup | | | | |
| BUPROPION for Any Reason | 2006 | 20 to 44 | Unique Users | 97,661 | 12,639 | 34,118 |
| | | | Days at Risk | 9,115,039 | 870,854 | 3,885,430 |
| | | | Number of Events | 13 | 3 | 4 |
| | | | Rate of Events per 1,000 Days at Risk | 0.001 | 0.003 | 0.001 |
| | | 45 to 64 | Unique Users | 93,390 | 13,511 | 30,897 |
| | | | Days at Risk | 11,650,699 | 1,143,419 | 5,015,442 |
| | | | Number of Events | 85 | 17 | 45 |
| | | | Rate of Events per 1,000 Days at Risk | 0.007 | 0.015 | 0.009 |
| | | 65+ | Unique Users | 12,940 | 2,192 | 4,998 |
| | | | Days at Risk | 1,769,286 | 177,085 | 853,699 |
| | | | Number of Events | 38 | 8 | 21 |
| | | | Rate of Events per 1,000 Days at Risk | 0.021 | 0.045 | 0.025 |
| | 2007 | 20 to 44 | Unique Users | 73,580 | 9,377 | 29,594 |
| | | | Days at Risk | 7,280,137 | 692,654 | 3,422,580 |
| | | | Number of Events | 11 | 4 | 8 |
| | | | Rate of Events per 1,000 Days at Risk | 0.002 | 0.006 | 0.002 |
| | | 45 to 64 | Unique Users | 66,080 | 10,328 | 25,159 |
| | | | Days at Risk | 8,593,563 | 891,544 | 3,999,302 |
| | | | Number of Events | 58 | 18 | 34 |
| | | | Rate of Events per 1,000 Days at Risk | 0.007 | 0.020 | 0.009 |
| | | 65+ | Unique Users | 10,577 | 1,966 | 4,338 |
| | | | Days at Risk | 1,470,347 | 184,763 | 775,416 |
| | | | Number of Events | 40 | 12 | 17 |
| | | | Rate of Events per 1,000 Days at Risk | 0.027 | 0.065 | 0.022 |
| | 2008 | 20 to 44 | Unique Users | 66,880 | 8,790 | 27,552 |
| | | | Days at Risk | 6,379,215 | 620,188 | 3,035,185 |
| | | | Number of Events | 8 | 3 | 3 |
| | | | Rate of Events per 1,000 Days at Risk | 0.001 | 0.005 | 0.001 |
| | | 45 to 64 | Unique Users | 58,466 | 9,570 | 23,772 |
| | | | Days at Risk | 6,980,738 | 791,719 | 3,396,322 |
| | | | Number of Events | 40 | 12 | 19 |
| | | | Rate of Events per 1,000 Days at Risk | 0.006 | 0.015 | 0.006 |
| | | 65+ | Unique Users | 12,100 | 2,261 | 5,626 |
| | | | Days at Risk | 1,482,485 | 185,998 | 833,840 |
| | | | Number of Events | 38 | 10 | 21 |
| | | | Rate of Events per 1,000 Days at Risk | 0.026 | 0.054 | 0.025 |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) Bupropion for Smoking Cessation: Individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

[b]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Table 10 (Continued). Number of Users, Number of Days at Risk, Number of Cardiovascular Events, Percent of Users with an Event, and Rate of Events per 1,000 Days at Risk by Exposure Group[a], Year, Age Group, and Cohort[b]**

| | | | | COHORT | | |
|---|---|---|---|---|---|---|
| | | | | OVERALL | TOBACCO | DEPRESSION |
| Exposure Group | IndexYear | AgeGroup | | | | |
| BUPROPION for Any Reason | 2009 | 20 to 44 | Unique Users | 67,064 | 10,097 | 28,985 |
| | | | Days at Risk | 5,839,438 | 656,988 | 2,866,939 |
| | | | Number of Events | 3 | 2 | 1 |
| | | | Rate of Events per 1,000 Days at Risk | 0.001 | 0.003 | 0.000 |
| | | 45 to 64 | Unique Users | 59,326 | 11,144 | 25,512 |
| | | | Days at Risk | 6,235,128 | 825,629 | 3,146,731 |
| | | | Number of Events | 43 | 15 | 20 |
| | | | Rate of Events per 1,000 Days at Risk | 0.007 | 0.018 | 0.006 |
| | | 65+ | Unique Users | 12,919 | 2,732 | 6,340 |
| | | | Days at Risk | 1,417,246 | 211,807 | 811,849 |
| | | | Number of Events | 42 | 7 | 27 |
| | | | Rate of Events per 1,000 Days at Risk | 0.030 | 0.033 | 0.033 |
| | 2010 | 20 to 44 | Unique Users | 50,899 | 7,178 | 22,853 |
| | | | Days at Risk | 3,703,736 | 432,302 | 1,819,219 |
| | | | Number of Events | 1 | 0 | 1 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.001 |
| | | 45 to 64 | Unique Users | 46,563 | 8,396 | 20,373 |
| | | | Days at Risk | 3,681,081 | 531,547 | 1,779,565 |
| | | | Number of Events | 13 | 4 | 7 |
| | | | Rate of Events per 1,000 Days at Risk | 0.004 | 0.008 | 0.004 |
| | | 65+ | Unique Users | 10,799 | 2,086 | 5,543 |
| | | | Days at Risk | 813,996 | 130,071 | 453,551 |
| | | | Number of Events | 19 | 3 | 12 |
| | | | Rate of Events per 1,000 Days at Risk | 0.023 | 0.023 | 0.026 |
| | 2011 | 20 to 44 | Unique Users | 3,214 | 555 | 1,358 |
| | | | Days at Risk | 76,642 | 16,361 | 33,991 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | | 45 to 64 | Unique Users | 2,756 | 512 | 1,084 |
| | | | Days at Risk | 66,245 | 15,522 | 29,314 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | | 65+ | Unique Users | 442 | 93 | 178 |
| | | | Days at Risk | 13,441 | 3,602 | 6,235 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) Bupropion for Smoking Cessation: Individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

[b]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Table 10 (Continued). Number of Users, Number of Days at Risk, Number of Cardiovascular Events, Percent of Users with an Event, and Rate of Events per 1,000 Days at Risk by Exposure Group[a], Year, Age Group, and Cohort[b]**

| | | | | COHORT | | |
|---|---|---|---|---|---|---|
| | | | | OVERALL | TOBACCO | DEPRESSION |
| Exposure Group | IndexYear | AgeGroup | | | | |
| BUPROPION for Smoking Cessation | 2006 | 20 to 44 | Unique Users | 2,135 | 812 | 159 |
| | | | Days at Risk | 93,880 | 35,729 | 7,188 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | | 45 to 64 | Unique Users | 2,264 | 800 | 111 |
| | | | Days at Risk | 106,408 | 36,584 | 5,364 |
| | | | Number of Events | 3 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.028 | 0.000 | 0.000 |
| | | 65+ | Unique Users | 320 | 104 | 13 |
| | | | Days at Risk | 15,715 | 4,964 | 589 |
| | | | Number of Events | 1 | 1 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.064 | 0.201 | 0.000 |
| | 2007 | 20 to 44 | Unique Users | 852 | 311 | 101 |
| | | | Days at Risk | 39,177 | 13,770 | 5,132 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | | 45 to 64 | Unique Users | 904 | 328 | 78 |
| | | | Days at Risk | 45,572 | 17,139 | 4,375 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | | 65+ | Unique Users | 183 | 62 | 14 |
| | | | Days at Risk | 9,869 | 3,111 | 732 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | 2008 | 20 to 44 | Unique Users | 612 | 199 | 87 |
| | | | Days at Risk | 29,365 | 9,471 | 4,449 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | | 45 to 64 | Unique Users | 633 | 216 | 91 |
| | | | Days at Risk | 31,371 | 10,133 | 4,959 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | | 65+ | Unique Users | 240 | 88 | 51 |
| | | | Days at Risk | 12,376 | 4,254 | 2,844 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) Bupropion for Smoking Cessation: Individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

[b]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Table 10 (Continued). Number of Users, Number of Days at Risk, Number of Cardiovascular Events, Percent of Users with an Event, and Rate of Events per 1,000 Days at Risk by Exposure Group[a], Year, Age Group, and Cohort[b]**

| | | | | COHORT | | |
|---|---|---|---|---|---|---|
| | | | | OVERALL | TOBACCO | DEPRESSION |
| Exposure Group | IndexYear | AgeGroup | | | | |
| BUPROPION for Smoking Cessation | 2009 | 20 to 44 | Unique Users | 689 | 273 | 107 |
| | | | Days at Risk | 32,574 | 12,739 | 5,217 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | | 45 to 64 | Unique Users | 920 | 407 | 128 |
| | | | Days at Risk | 47,430 | 19,927 | 6,423 |
| | | | Number of Events | 2 | 2 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.042 | 0.100 | 0.000 |
| | | 65+ | Unique Users | 333 | 157 | 52 |
| | | | Days at Risk | 19,134 | 8,282 | 3,265 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | 2010 | 20 to 44 | Unique Users | 385 | 117 | 47 |
| | | | Days at Risk | 16,681 | 4,967 | 2,122 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | | 45 to 64 | Unique Users | 505 | 177 | 69 |
| | | | Days at Risk | 24,967 | 8,928 | 3,575 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | | 65+ | Unique Users | 198 | 90 | 39 |
| | | | Days at Risk | 9,054 | 4,033 | 1,529 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | 2011 | 20 to 44 | Unique Users | 8 | 3 | 0 |
| | | | Days at Risk | 187 | 118 | 0 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | . |
| | | 45 to 64 | Unique Users | 25 | 10 | 1 |
| | | | Days at Risk | 443 | 235 | 27 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | | 65+ | Unique Users | 3 | 1 | 0 |
| | | | Days at Risk | 133 | 24 | 0 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | . |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) Bupropion for Smoking Cessation: Individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

[b]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Table 10 (Continued). Number of Users, Number of Days at Risk, Number of Cardiovascular Events, Percent of Users with an Event, and Rate of Events per 1,000 Days at Risk by Exposure Group[a], Year, Age Group, and Cohort[b]**

| | | | | COHORT | | |
|---|---|---|---|---|---|---|
| Exposure Group | IndexYear | AgeGroup | | OVERALL | TOBACCO | DEPRESSION |
| BUPROPION for Treatment of Depression | 2006 | 20 to 44 | Unique Users | 95,586 | 11,842 | 33,979 |
| | | | Days at Risk | 9,017,223 | 834,755 | 3,875,870 |
| | | | Number of Events | 12 | 3 | 3 |
| | | | Rate of Events per 1,000 Days at Risk | 0.001 | 0.004 | 0.001 |
| | | 45 to 64 | Unique Users | 91,169 | 12,720 | 30,792 |
| | | | Days at Risk | 11,533,162 | 1,105,255 | 5,005,150 |
| | | | Number of Events | 82 | 17 | 45 |
| | | | Rate of Events per 1,000 Days at Risk | 0.007 | 0.015 | 0.009 |
| | | 65+ | Unique Users | 12,622 | 2,088 | 4,986 |
| | | | Days at Risk | 1,750,855 | 172,057 | 851,540 |
| | | | Number of Events | 37 | 7 | 21 |
| | | | Rate of Events per 1,000 Days at Risk | 0.021 | 0.041 | 0.025 |
| | 2007 | 20 to 44 | Unique Users | 72,878 | 9,102 | 29,532 |
| | | | Days at Risk | 7,240,096 | 680,309 | 3,416,367 |
| | | | Number of Events | 11 | 4 | 8 |
| | | | Rate of Events per 1,000 Days at Risk | 0.002 | 0.006 | 0.002 |
| | | 45 to 64 | Unique Users | 65,333 | 10,046 | 25,106 |
| | | | Days at Risk | 8,549,226 | 876,645 | 3,992,981 |
| | | | Number of Events | 58 | 18 | 34 |
| | | | Rate of Events per 1,000 Days at Risk | 0.007 | 0.021 | 0.009 |
| | | 65+ | Unique Users | 10,416 | 1,912 | 4,326 |
| | | | Days at Risk | 1,459,782 | 182,286 | 773,739 |
| | | | Number of Events | 40 | 12 | 17 |
| | | | Rate of Events per 1,000 Days at Risk | 0.027 | 0.066 | 0.022 |
| | 2008 | 20 to 44 | Unique Users | 66,405 | 8,621 | 27,509 |
| | | | Days at Risk | 6,349,720 | 611,357 | 3,029,922 |
| | | | Number of Events | 8 | 3 | 3 |
| | | | Rate of Events per 1,000 Days at Risk | 0.001 | 0.005 | 0.001 |
| | | 45 to 64 | Unique Users | 57,991 | 9,395 | 23,715 |
| | | | Days at Risk | 6,947,160 | 782,288 | 3,386,683 |
| | | | Number of Events | 41 | 13 | 19 |
| | | | Rate of Events per 1,000 Days at Risk | 0.006 | 0.017 | 0.006 |
| | | 65+ | Unique Users | 11,903 | 2,188 | 5,589 |
| | | | Days at Risk | 1,467,164 | 183,003 | 828,035 |
| | | | Number of Events | 38 | 10 | 21 |
| | | | Rate of Events per 1,000 Days at Risk | 0.026 | 0.055 | 0.025 |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) Bupropion for Smoking Cessation: Individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

[b]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

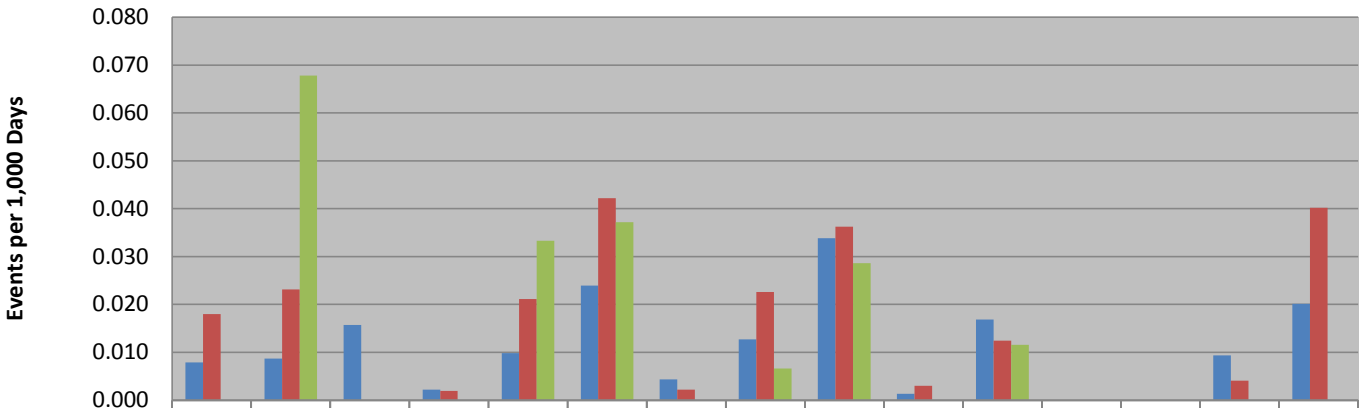
**Table 10 (Continued). Number of Users, Number of Days at Risk, Number of Cardiovascular Events, Percent of Users with an Event, and Rate of Events per 1,000 Days at Risk by Exposure Group[a], Year, Age Group, and Cohort[b]**

| | | | | COHORT | | |
|---|---|---|---|---|---|---|
| | | | | OVERALL | TOBACCO | DEPRESSION |
| Exposure Group | IndexYear | AgeGroup | | | | |
| BUPROPION for Treatment of Depression | 2009 | 20 to 44 | Unique Users | 66,517 | 9,867 | 28,925 |
| | | | Days at Risk | 5,810,671 | 645,925 | 2,862,586 |
| | | | Number of Events | 3 | 2 | 1 |
| | | | Rate of Events per 1,000 Days at Risk | 0.001 | 0.003 | 0.000 |
| | | 45 to 64 | Unique Users | 58,618 | 10,822 | 25,434 |
| | | | Days at Risk | 6,195,612 | 809,168 | 3,142,206 |
| | | | Number of Events | 40 | 12 | 19 |
| | | | Rate of Events per 1,000 Days at Risk | 0.006 | 0.015 | 0.006 |
| | | 65+ | Unique Users | 12,646 | 2,593 | 6,298 |
| | | | Days at Risk | 1,398,000 | 203,888 | 806,380 |
| | | | Number of Events | 42 | 7 | 27 |
| | | | Rate of Events per 1,000 Days at Risk | 0.030 | 0.034 | 0.033 |
| | 2010 | 20 to 44 | Unique Users | 50,595 | 7,084 | 22,816 |
| | | | Days at Risk | 3,689,543 | 428,376 | 1,817,080 |
| | | | Number of Events | 1 | 0 | 1 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.001 |
| | | 45 to 64 | Unique Users | 46,201 | 8,255 | 20,326 |
| | | | Days at Risk | 3,660,651 | 524,005 | 1,775,543 |
| | | | Number of Events | 13 | 4 | 7 |
| | | | Rate of Events per 1,000 Days at Risk | 0.004 | 0.008 | 0.004 |
| | | 65+ | Unique Users | 10,659 | 2,021 | 5,519 |
| | | | Days at Risk | 806,676 | 127,092 | 451,978 |
| | | | Number of Events | 19 | 3 | 12 |
| | | | Rate of Events per 1,000 Days at Risk | 0.024 | 0.024 | 0.027 |
| | 2011 | 20 to 44 | Unique Users | 3,210 | 552 | 1,360 |
| | | | Days at Risk | 76,532 | 16,243 | 34,017 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | | 45 to 64 | Unique Users | 2,742 | 508 | 1,084 |
| | | | Days at Risk | 66,050 | 15,450 | 29,314 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |
| | | 65+ | Unique Users | 441 | 92 | 178 |
| | | | Days at Risk | 13,360 | 3,578 | 6,235 |
| | | | Number of Events | 0 | 0 | 0 |
| | | | Rate of Events per 1,000 Days at Risk | 0.000 | 0.000 | 0.000 |

[a]Four different exposure groups were examined in this analysis: (1) Varenicline includes individuals who initiated use of varenlicine; (2) Bupropion for Any Reason includes individuals who initiated use of bupropion for any reason; (3) Bupropion for Smoking Cessation: Individuals who initiated use of bupropion for smoking cessation (national drug code listed as "smoking cessation" as defined by First DataBank's Enhanced Therapeutic Classification); (4) Bupropion for Treatment of Depression includes individuals who initiated use of bupropion as an anti-depressant (national drug code listed as "antidepressant" as defined by First DataBank's Enhanced Therapeutic Classification).

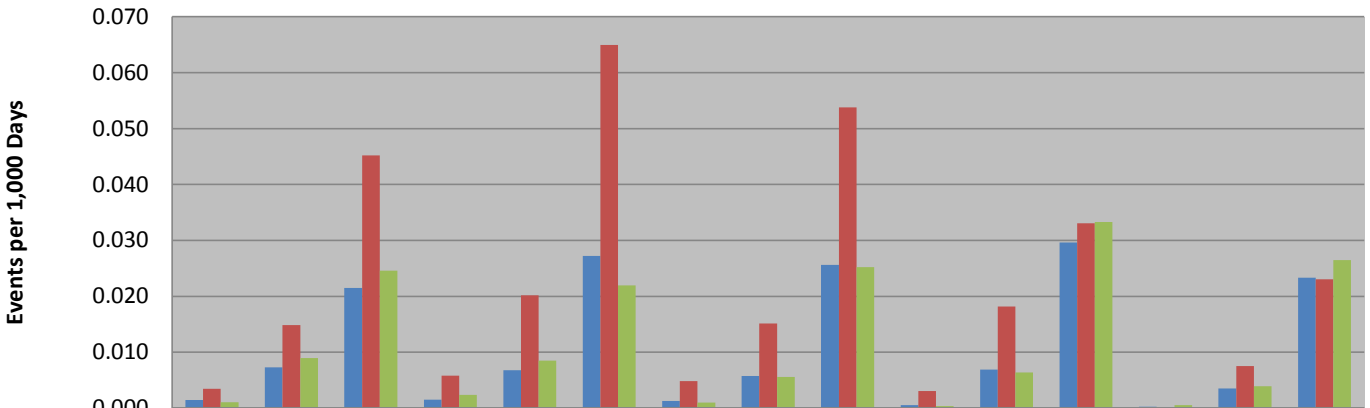
[b]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Figure 10a. Rate of Acute Cardiovascular Events per 1,000 Days at Risk, by Cohort[a], Age Group, and Year among Users of Varenicline**




| | 2006 | | | 2007 | | | 2008 | | | 2009 | | | 2010 | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 24 to 44 | 45 to 64 | 65+ | 24 to 44 | 45 to 64 | 65+ | 24 to 44 | 45 to 64 | 65+ | 24 to 44 | 45 to 64 | 65+ | 24 to 44 | 45 to 64 | 65+ |
| OVERALL | 0.008 | 0.009 | 0.016 | 0.002 | 0.010 | 0.024 | 0.004 | 0.013 | 0.034 | 0.001 | 0.017 | 0.000 | 0.000 | 0.009 | 0.020 |
| TOBACCO | 0.018 | 0.023 | 0.000 | 0.002 | 0.021 | 0.042 | 0.002 | 0.023 | 0.036 | 0.003 | 0.012 | 0.000 | 0.000 | 0.004 | 0.040 |
| DEPRESSION | 0.000 | 0.068 | 0.000 | 0.000 | 0.033 | 0.037 | 0.000 | 0.007 | 0.029 | 0.000 | 0.012 | 0.000 | 0.000 | 0.000 | 0.000 |

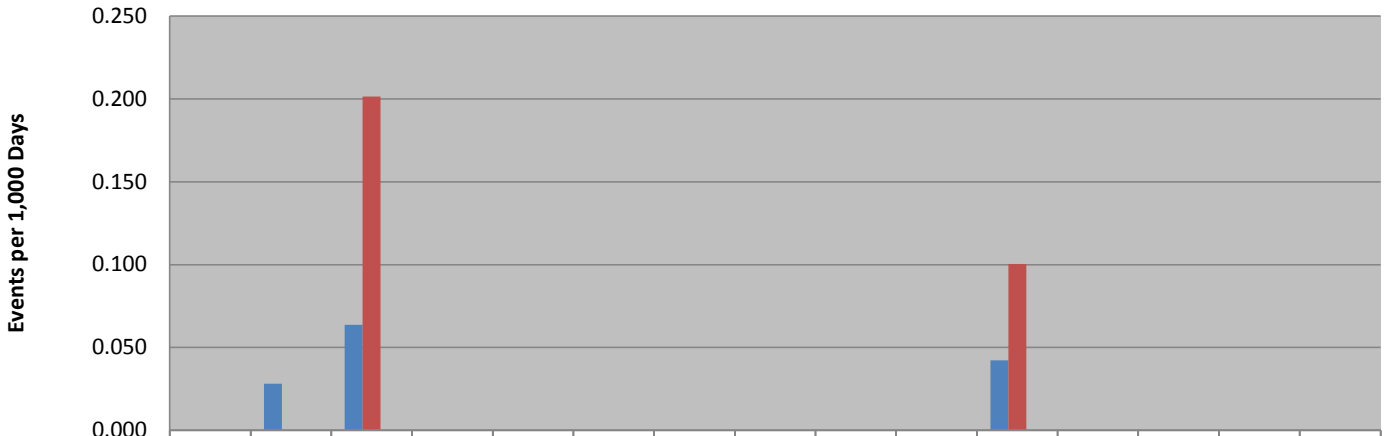
**Figure 10b. Rate of Acute Cardiovascular Events per 1,000 Days at Risk, by Cohort[a], Age Group, and Year among Users of Bupropion for any Reason**




| | 2006 | | | 2007 | | | 2008 | | | 2009 | | | 2010 | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 24 to 44 | 45 to 64 | 65+ | 24 to 44 | 45 to 64 | 65+ | 24 to 44 | 49 to 64 | 65+ | 24 to 44 | 45 to 64 | 65+ | 24 to 44 | 45 to 64 | 65+ |
| OVERALL | 0.001 | 0.007 | 0.021 | 0.002 | 0.007 | 0.027 | 0.001 | 0.006 | 0.026 | 0.001 | 0.007 | 0.030 | 0.000 | 0.004 | 0.023 |
| TOBACCO | 0.003 | 0.015 | 0.045 | 0.006 | 0.020 | 0.065 | 0.005 | 0.015 | 0.054 | 0.003 | 0.018 | 0.033 | 0.000 | 0.008 | 0.023 |
| DEPRESSION | 0.001 | 0.009 | 0.025 | 0.002 | 0.009 | 0.022 | 0.001 | 0.006 | 0.025 | 0.000 | 0.006 | 0.033 | 0.001 | 0.004 | 0.026 |

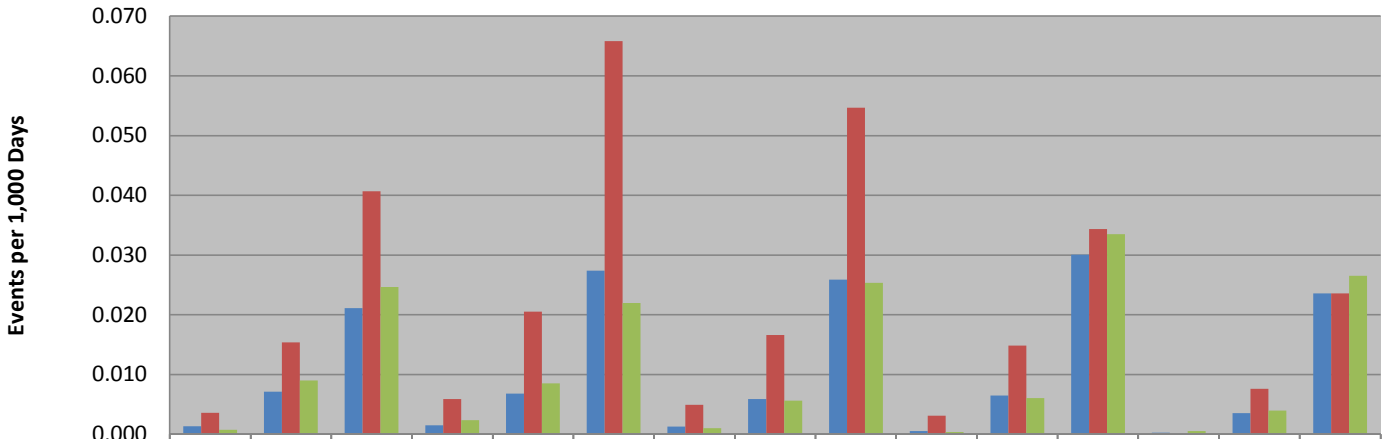
[a]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.

**Figure 10c. Rate of Acute Cardiovascular Events per 1,000 Days at Risk, by Cohort[a], Age Group, and Year among Users of Bupropion for Smoking Cessation**




| | 2006 | | | 2007 | | | 2008 | | | 2009 | | | 2010 | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 24 to 44 | 45 to 64 | 65+ | 24 to 44 | 45 to 64 | 65+ | 24 to 44 | 45 to 64 | 65+ | 24 to 44 | 45 to 64 | 65+ | 24 to 44 | 45 to 64 | 65+ |
| OVERALL | 0.000 | 0.028 | 0.064 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.042 | 0.000 | 0.000 | 0.000 | 0.000 |
| TOBACCO | 0.000 | 0.000 | 0.201 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.100 | 0.000 | 0.000 | 0.000 | 0.000 |
| DEPRESSION | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |

**Figure 10d. Rate of Acute Cardiovascular Events per 1,000 Days at Risk, by Cohort[a], Age Group, and Year among Users of Bupropion for Treatment of Depression**




| | 2006 | | | 2007 | | | 2008 | | | 2009 | | | 2010 | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 24 to 44 | 45 to 64 | 65+ | 24 to 44 | 45 to 64 | 65+ | 24 to 44 | 45 to 64 | 65+ | 24 to 44 | 45 to 64 | 65+ | 24 to 44 | 49 to 64 | 65+ |
| OVERALL | 0.001 | 0.007 | 0.021 | 0.002 | 0.007 | 0.027 | 0.001 | 0.006 | 0.026 | 0.001 | 0.006 | 0.030 | 0.000 | 0.004 | 0.024 |
| TOBACCO | 0.004 | 0.015 | 0.041 | 0.006 | 0.021 | 0.066 | 0.005 | 0.017 | 0.055 | 0.003 | 0.015 | 0.034 | 0.000 | 0.008 | 0.024 |
| DEPRESSION | 0.001 | 0.009 | 0.025 | 0.002 | 0.009 | 0.022 | 0.001 | 0.006 | 0.025 | 0.000 | 0.006 | 0.033 | 0.001 | 0.004 | 0.027 |

[a]Three different cohorts of users were examined in this analysis: (1) the overall Cohort includes all new users of drug product group of interest without respect to pre-existing conditions; (2) the Tobacco Cohort includes new users of drug product of interest with a prior diagnosis of nondependent tobacco use disorder (ICD-9-CM Code 305.1) in the 180 days before drug product initiation; (3) the Depression Cohort includes new users of drug product of interest with a prior diagnosis of depression (ICD-9-CM Codes 296.2, 296.3, 300.4, 311) in the 180 days before drug product initiation.