

Supplementary Material

Table S1. Diagnosis Codes

| Conditions | ICD-9 Code/ Procedure Code | ICD-10 Code |
|--|---------------------------------|------------------|
| Smoking attributable conditions | | |
| Cardiovascular diseases | | |
| Coronary heart disease | 410 - 414, 429.2 | I20 - I25 |
| Pulmonary heart disease | 415 - 417 | I26 - I28 |
| Rheumatic heart disease | 390-398 | I00 - I09 |
| Other forms of heart diseases | 420 - 429.1, 429.3 - 429.9 | I30 - I52 |
| Cerebrovascular disease | 430 - 438 | I60 - I69 |
| Atherosclerosis | 440 | I70 |
| Aortic aneurysm | 441 | I71 |
| Other arterial disease | 442 - 448 | I72 - I78 |
| Diabetes mellitus | 250 | E10 - E14 |
| Pulmonary conditions | | |
| Influenza | 487 | J10 - J11 |
| Pneumonia | 480 - 486 | J12 - J18 |
| Tuberculosis | 010 - 018 | A16 - A19 |
| Chronic obstructive pulmonary disease | | |
| Bronchitis | 490 - 491 | J40 - J42 |
| Emphysema | 492 | J43 |
| Chronic airways obstruction | 496 | J44 |
| Neuropsychiatric conditions | | |
| Depression | 296.2, 296.3, 298.0, 309.0, 311 | F32, F33, F43.21 |
| Schizophrenia | 295 | F20, F21, F25 |
| Bipolar disorder | 296.0, 296.1, 296.4 - 296.8 | F31 |

| Conditions | ICD-9 Code/ Procedure Code | ICD-10 Code |
|--------------------------------|--|---|
| Suicide attempt/self-harm | E950-E959, E980-E982 | T14.91, T39.012A - T41.42A, T42.32A - T42.32A, T40.72A - T42.64A, T40.82A - T43.92A, T65.92A, T60.02A - T60.92A, T54.02A - T57.22A, T57.02A, T51.02A - T63.042A, T59.892A, T71.162A, T71.122A, X71 - X83; T39.014A - T40.44A, T42.34A, T43.014A - T43.94A, T36.04A - T44.14A, T50.904A, T54.04A - T57.24A, T60.04A - T60.94A, T57.04A, T51.04A - T63.044A, T59.894A - T59.894S, T58.04A, T58.14A - T58.94A, T53.54A - T59.94A |
| Post-traumatic stress disorder | 309.81 | F43.10 - F43.12 |
| Other psychosis | 293, 294, 297 - 299 | F05, R41.0, F06.2, F06.0, F06.30 - F06.34, F06.4, F06.1, F53, F06.8, F09; F04, F02.80, F02.81, F03.90, F06.8, F09, F06.0, F06.1, F06.8, F03.91; F22, F23, F24; F30.8, F44.89, F28, F29; F84.0, F84.3, F84.5, F84.8, F84.9 |
| Drug-induced mental disorders | 292 | F11 - F19 |
| Anxiety disorder | 300 | F40 - F41 |
| Other conditions | | |
| Tobacco dependence | 305.1 | F17.200 - F17.291 |
| Cancer (excluding skin cancer) | 196 - 199 | C77 – C80 |
| Smoking cessation counseling | 99406, 99407, G0436, G0437, G8402, G8453, 0004F, 4000F | Z716 |

Table S2. Healthcare Costs in Follow-up

| Initiator Population | | | | | | | | |
|------------------------------------|----------------------------|-------------------------|----------------------------|-------------------------|----------------------------|-------------------------|----------------------------|-------------------------|
| | Quarter 1 | | Quarter 2 | | Quarter 3 | | Quarter 4 | |
| | Varenicline (n=209,284) | NRT Patch (n=34,593) | Varenicline (n=175,684) | NRT Patch (n=27,557) | Varenicline (n=153,792) | NRT Patch (n=22,606) | Varenicline (n=132,205) | NRT Patch (n=18,047) |
| Smoking-attributable Costs | | | | | | | | |
| Total Costs | \$1,185 (\$6,179) | \$2,093 (\$13,161) | \$679 (\$5,966) | \$1,374 (\$8,862) | \$619 (\$4,832) | \$1,277 (\$10,448) | \$614 (\$4,715) | \$1,107 (\$6,612) |
| Medical Costs | \$588 (\$6,090) | \$1,742 (\$13,055) | \$445 (\$5,894) | \$1,119 (\$8,749) | \$407 (\$4,742) | \$1,029 (\$10,375) | \$401 (\$4,611) | \$863 (\$6,497) |
| Outpatient Costs | \$306 (\$2,807) | \$784 (\$4,440) | \$215 (\$2,376) | \$512 (\$3,810) | \$207 (\$2,209) | \$438 (\$4,268) | \$209 (\$2,353) | \$385 (\$3,010) |
| Inpatient/ER Costs | \$282 (\$5,061) | \$957 (\$11,668) | \$230 (\$5,140) | \$606 (\$7,396) | \$199 (\$3,944) | \$591 (\$9,113) | \$192 (\$3,704) | \$478 (\$5,406) |
| Pharmacy Costs | \$597 (\$665) | \$351 (\$772) | \$234 (\$602) | \$255 (\$851) | \$212 (\$605) | \$247 (\$678) | \$212 (\$641) | \$244 (\$631) |
| Smoking Cessation Therapy Costs | \$418 (\$244) | \$71 (\$49) | \$65 (\$168) | \$7 (\$26) | \$40 (\$132) | \$4 (\$20) | \$35 (\$138) | \$4 (\$19) |
| All-cause Costs | | | | | | | | |
| Total Costs | \$4,124 (\$13,719) | \$8,602 (\$26,657) | \$3,128 (\$12,922) | \$6,152 (\$21,025) | \$2,974 (\$11,537) | \$5,543 (\$21,317) | \$2,990 (\$12,944) | \$5,136 (\$20,366) |
| Medical Costs | \$3,047 (\$13,344) | \$7,558 (\$26,102) | \$2,418 (\$12,475) | \$5,223 (\$20,270) | \$2,284 (\$11,054) | \$4,623 (\$20,701) | \$2,284 (\$11,895) | \$4,234 (\$19,790) |
| Outpatient Costs | \$1,853 (\$7,006) | \$4,137 (\$13,625) | \$1,434 (\$6,181) | \$2,817 (\$11,655) | \$1,387 (\$6,069) | \$2,518 (\$11,062) | \$1,383 (\$6,207) | \$2,310 (\$10,305) |
| Inpatient/ER Costs | \$1,194 (\$10,311) | \$3,421 (\$20,227) | \$984 (\$10,036) | \$2,406 (\$14,753) | \$897 (\$8,305) | \$2,105 (\$15,989) | \$902 (\$9,204) | \$1,924 (\$14,822) |
| Pharmacy Costs | \$1,076 (\$2,442) | \$1,044 (\$3,444) | \$710 (\$2,715) | \$929 (\$4,100) | \$689 (\$2,634) | \$920 (\$3,837) | \$706 (\$3,295) | \$902 (\$3,762) |

| Adherent Population | | | | | | | | |
|------------------------------------|---------------------------|------------------------|---------------------------|------------------------------------|---------------------------|-------------------------------------|---------------------------|-------------------------------------|
| | Quarter 1 | | Quarter 2 | | Quarter 3 | | Quarter 4 | |
| | Varenicline (n=38,744) | NRT Patch (n=2,702) | Varenicline (n=32,385) | NRT Patch (n=2,218) | Varenicline (n=28,215) | NRT Patch (n=1,840) | Varenicline (n=24,126) | NRT Patch (n=1,479) |
| Smoking-attributable Costs | | | | | | | | |
| Total Costs | \$1,730 (\$5,959) | \$2,561 (\$11,085) | \$989 (\$8,302) | \$1,571 (\$8,797) | \$782 (\$5,074) | \$1,761 (\$20,012) | \$794 (\$6,001) | \$1,101 (\$4,716) |
| Medical Costs | \$685 (\$5,846) | \$2,026 (\$10,960) | \$581 (\$8,224) | \$1,209 (\$8,709) | \$458 (\$4,949) | \$1,434 (\$19,960) | \$482 (\$5,895) | \$769 (\$4,604) |
| Outpatient Costs | \$368 (\$2,867) | \$978 (\$4,789) | \$282 (\$2,813) | \$624 (\$4,931) | \$242 (\$2,054) | \$388 (\$2,095) | \$246 (\$2,599) | \$397 (\$2,700) |
| Inpatient/ER Costs | \$318 (\$4,717) | \$1,048 (\$9,164) | \$299 (\$7,488) | \$585 (\$6,278) | \$216 (\$4,181) | \$1,046 (\$19,656) ^{NS} | \$236 (\$4,873) | \$372 (\$3,587) ^{NS} |
| Pharmacy Costs | \$1,045 (\$719) | \$534 (\$832) | \$408 (\$776) | \$362 (\$847) | \$324 (\$801) | \$326 (\$826) ^{NS} | \$312 (\$823) | \$332 (\$700) |
| Smoking Cessation Therapy Costs | \$798 (\$230) | \$176 (\$72) | \$175 (\$260) | \$30 (\$57) | \$82 (\$195) | \$14 (\$42) | \$66 (\$186) | \$10 (\$36) |
| All-cause Costs | | | | | | | | |
| Total Costs | \$4,708 (\$12,628) | \$8,398 (\$23,140) | \$3,709 (\$13,689) | \$5,935 (\$19,439) | \$3,397 (\$11,940) | \$5,550 (\$24,982) | \$3,506 (\$18,150) | \$4,209 (\$12,355) |
| Medical Costs | \$3,107 (\$12,216) | \$7,058 (\$22,614) | \$2,751 (\$13,277) | \$4,844 (\$18,736) | \$2,529 (\$11,463) | \$4,474 (\$24,624) | \$2,591 (\$15,500) | \$3,134 (\$11,396) ^{NS} |
| Outpatient Costs | \$1,955 (\$6,718) | \$4,117 (\$15,708) | \$1,596 (\$6,452) | \$2,918 (\$11,549) | \$1,516 (\$5,799) | \$2,324 (\$8,435) | \$1,555 (\$7,588) | \$2,060 (\$8,911) |
| Inpatient/ER Costs | \$1,152 (\$9,280) | \$2,941 (\$14,355) | \$1,155 (\$10,759) | \$1,926 (\$13,294) | \$1,014 (\$8,936) | \$2,150 (\$21,820) | \$1,036 (\$12,761) | \$1,075 (\$6,251) ^{NS} |
| Pharmacy Costs | \$1,601 (\$2,425) | \$1,340 (\$3,735) | \$958 (\$2,552) | \$1,091 (\$4,164) ^{NS} | \$868 (\$2,485) | \$1,077 (\$3,332) | \$915 (\$5,163) | \$1,075 (\$4,366) ^{NS} |

Mean (standard deviation) [median] were reported for continuous variables.

All differences between VAR and NRT patch cohort were statistically significant at 0.05 level, unless noted otherwise.

NS = p value \geq 0.05

Table S3. Propensity Score Regressions and Summary Statistics

| Covariates | Initiator Population | | Adherent Population | |
|--|----------------------|---------------|---------------------|---------------|
| | Odds Ratio | 95% CI | Odds Ratio | 95% CI |
| Age groups | | | | |
| 45-54 vs 18-44 | 1.01 | (0.95 - 1.07) | 1.20 | (1.01 - 1.43) |
| 55-64 vs 18-44 | 0.91 | (0.86 - 0.96) | 1.06 | (0.90 - 1.25) |
| 65+ vs 18-44 | 0.89 | (0.84 - 0.94) | 1.05 | (0.89 - 1.23) |
| Gender | | | | |
| Male vs female | 0.91 | (0.89 - 0.93) | 1.01 | (0.93 - 1.09) |
| Health plan out-of-network coverage | | | | |
| Covered vs not covered | 0.49 | (0.47 - 0.51) | 0.61 | (0.53 - 0.70) |
| Other/missing vs not covered | 0.92 | (0.89 - 0.95) | 0.91 | (0.83 - 1.01) |
| Region | | | | |
| North Central vs West | 0.54 | (0.48 - 0.61) | 0.58 | (0.38 - 0.88) |
| Northeast vs West | 0.77 | (0.68 - 0.86) | 0.83 | (0.55 - 1.26) |
| South vs West | 1.26 | (1.12 - 1.42) | 1.45 | (0.95 - 2.21) |
| Unknown/missing vs West | 0.81 | (0.72 - 0.92) | 0.90 | (0.59 - 1.39) |
| Residence type | | | | |
| Urban vs Rural | 0.86 | (0.83 - 0.89) | 0.83 | (0.74 - 0.92) |
| Index year | | | | |
| 2012 vs 2016 | 3.13 | (2.97 - 3.29) | 2.70 | (2.27 - 3.20) |
| 2013 vs 2016 | 2.29 | (2.19 - 2.39) | 2.18 | (1.88 - 2.52) |
| 2014 vs 2016 | 1.48 | (1.43 - 1.54) | 1.37 | (1.20 - 1.56) |
| 2015 vs 2016 | 0.92 | (0.88 - 0.96) | 0.89 | (0.78 - 1.01) |
| Baseline characteristics | | | | |
| Diagnosis of specific conditions (Yes vs No) | | | | |
| Cardiovascular diseases | 0.87 | (0.83 - 0.90) | 0.86 | (0.76 - 0.98) |
| Diabetes | 1.24 | (1.19 - 1.30) | 1.23 | (1.07 - 1.42) |
| Pulmonary conditions | 0.98 | (0.95 - 1.02) | 0.89 | (0.79 - 1.01) |
| Neuropsychiatric conditions | 0.60 | (0.58 - 0.61) | 0.62 | (0.56 - 0.68) |

| Covariates | Initiator Population | | Adherent Population | |
|--|----------------------------------|---------------|----------------------------------|---------------|
| | Odds Ratio | 95% CI | Odds Ratio | 95% CI |
| Cancer (excluding skin cancer) | 0.98 | (0.91 - 1.04) | 0.84 | (0.68 - 1.03) |
| Charlson Comorbidity Index | | | | |
| 0 vs 3+ | 2.48 | (2.35 - 2.61) | 1.73 | (1.45 - 2.06) |
| 1 vs 3+ | 1.69 | (1.61 - 1.77) | 1.32 | (1.13 - 1.54) |
| 2 vs 3+ | 1.37 | (1.30 - 1.43) | 1.11 | (0.96 - 1.29) |
| Any smoking cessation counseling (Yes vs No) | 1.09 | (1.03 - 1.15) | 1.03 | (0.87 - 1.22) |
| Any smoking attributable hospitalization (Yes vs No) | 0.23 | (0.22 - 0.25) | 0.25 | (0.21 - 0.30) |
| Total smoking attributable healthcare costs (\$) | 0.99 | (0.99 - 1.00) | 0.98 | (0.97 - 1.00) |
| Number of quarters in follow-up | 1.08 | (1.07 - 1.09) | 1.02 | (0.98 - 1.06) |
| Summary Statistics of Propensity Score | Mean (Standard Deviation) | | Mean (Standard Deviation) | |
| Varenicline cohort | 0.87 (0.10) | | 0.94 (0.05) | |
| NRT patch cohort | 0.77 (0.17) | | 0.89 (0.11) | |

Logistic regression was conducted on the indicator of being in varenicline cohort (vs. in NRT patch cohort).

Abbreviations: NRT = nicotine replacement therapy

Table S4. Regressions Results on Healthcare Costs

| Coefficients on treatment cohort in different regressions | Total Costs | | Medical Costs | | Pharmacy Costs | | Outpatient Costs | | Inpatient & ER Costs | |
|--|------------------------|--------------------|------------------------|--------------------|------------------------|--------------------|------------------------|--------------------|------------------------|--------------------|
| | Any costs [†] | Costs [‡] | Any costs [†] | Costs [‡] | Any costs [†] | Costs [‡] | Any costs [†] | Costs [‡] | Any costs [†] | Costs [‡] |
| | Odds Ratio | Cost Ratio | Odds Ratio | Cost Ratio | Odds Ratio | Cost Ratio | Odds Ratio | Cost Ratio | Odds Ratio | Cost Ratio |
| Smoking-attributable costs among initiator population | | | | | | | | | | |
| Treatment cohort (varenicline vs NRT patch) by quarter | | | | | | | | | | |
| Quarter 1 | 96.14* | 1.30* | 1.34* | 0.79* | 104.46* | 3.04* | 1.31* | 0.87* | 0.78* | 1.02 |
| Quarter 2 | 0.36* | 1.08* | 0.70* | 0.87* | 0.40* | 1.62* | 0.68* | 0.91* | 0.70* | 1.00 |
| Quarter 3 | 0.30* | 1.01 | 0.72* | 0.80* | 0.34* | 1.53* | 0.70* | 0.91* | 0.70* | 0.77* |
| Quarter 4 | 0.30* | 1.01 | 0.73* | 0.80* | 0.34* | 1.55* | 0.71* | 0.92 | 0.68* | 0.86* |
| All-cause costs among initiator population | | | | | | | | | | |
| Treatment cohort (varenicline vs NRT patch) by quarter | | | | | | | | | | |
| Quarter 1 | 107.07* | 0.99 | 2.11* | 0.81* | 29.66* | 1.82* | 2.1* | 0.85* | 0.8* | 1.03 |
| Quarter 2 | 0.57* | 0.83* | 0.7* | 0.8* | 0.48* | 1.09* | 0.69* | 0.8* | 0.74* | 0.91* |
| Quarter 3 | 0.50* | 0.82* | 0.69* | 0.79* | 0.42* | 1.07* | 0.68* | 0.8* | 0.72* | 0.9* |
| Quarter 4 | 0.50* | 0.84* | 0.69* | 0.81* | 0.41* | 1.14* | 0.69* | 0.83* | 0.72* | 0.91* |
| Smoking-attributable costs among adherent population | | | | | | | | | | |
| Treatment cohort (varenicline vs NRT patch) by quarter | | | | | | | | | | |
| Quarter 1 | 61.61* | 1.59* | 1.3* | 0.79* | 60.46* | 3.12* | 1.27* | 0.88 | 0.78* | 0.99 |
| Quarter 2 | 0.65* | 0.98 | 0.73* | 0.87 | 0.72* | 1.46* | 0.71* | 0.95 | 0.72* | 0.93 |
| Quarter 3 | 0.37* | 0.86 | 0.72* | 0.73* | 0.42* | 1.22* | 0.69* | 0.84 | 0.71* | 0.76 |
| Quarter 4 | 0.33* | 0.86 | 0.74* | 0.76* | 0.38* | 1.21* | 0.71* | 0.85 | 0.7* | 0.79 |
| All-cause costs among adherent population | | | | | | | | | | |
| Treatment cohort (varenicline vs NRT patch) by quarter | | | | | | | | | | |
| Quarter 1 | 65.86* | 1.14* | 2.11* | 0.85* | 17.13* | 2.11* | 2.09* | 0.90* | 0.82* | 1.04 |
| Quarter 2 | 0.69* | 0.92 | 0.72* | 0.91 | 0.71* | 1.11 | 0.71* | 0.87* | 0.84* | 0.99 |
| Quarter 3 | 0.46* | 0.88* | 0.7* | 0.87* | 0.48* | 1.02 | 0.68* | 0.87* | 0.8* | 0.93 |

| Coefficients on treatment cohort in different regressions | Total Costs | | Medical Costs | | Pharmacy Costs | | Outpatient Costs | | Inpatient & ER Costs | |
|---|------------------------|--------------------|------------------------|--------------------|------------------------|--------------------|------------------------|--------------------|------------------------|--------------------|
| | Any costs [†] | Costs [‡] | Any costs [†] | Costs [‡] | Any costs [†] | Costs [‡] | Any costs [†] | Costs [‡] | Any costs [†] | Costs [‡] |
| | Odds Ratio | Cost Ratio | Odds Ratio | Cost Ratio | Odds Ratio | Cost Ratio | Odds Ratio | Cost Ratio | Odds Ratio | Cost Ratio |
| Quarter 4 | 0.44* | 0.92 | 0.7* | 0.93 | 0.44* | 1.07 | 0.68* | 0.92 | 0.81* | 0.96 |

† Logistic regression on probability of any costs; other covariates included baseline characteristics — demographics , Charlson Comorbidity Index, diagnosis of specific conditions (cardiovascular diseases, diabetes mellitus, pulmonary conditions, neuropsychiatric conditions, malignancy [excluding skin cancer], and tobacco dependence), use of smoking cessation counseling, occurrence of hospitalization (SA or all cause, corresponding to study outcomes), healthcare costs (corresponding to study outcomes) — and propensity scores

‡ Generalized linear model with gamma distribution and log link, among patients with any costs; other covariates included baseline characteristics — demographics , Charlson Comorbidity Index, diagnosis of specific conditions (cardiovascular diseases, diabetes mellitus, pulmonary conditions, neuropsychiatric conditions, malignancy [excluding skin cancer], and tobacco dependence), use of smoking cessation counseling, occurrence of hospitalization (SA or all cause, corresponding to study outcomes), healthcare costs (corresponding to study outcomes) — and propensity scores

* p <0.05

Abbreviations: NRT = nicotine replacement therapy

Table S5. Sensitivity Analysis: Patient Characteristics in Follow-up after Propensity Score Matching

| | Initiator Population | | | | Adherent Population | | | |
|-------------------------------------|--|----------------------|--|----------------------|--|---------------------|--|---------------------|
| | Study Sample in Main Analysis after Matching | | Subgroup with ≥12 Months of Follow-up after Matching | | Study Sample in Main Analysis after Matching | | Subgroup with ≥12 Months of Follow-up after Matching | |
| | Varenicline (n=53,100) | NRT Patch (n=26,550) | Varenicline (n=29,408) | NRT Patch (n=14,704) | Varenicline (n=5,048) | NRT Patch (n=2,524) | Varenicline (n=2,104) | NRT Patch (n=1,052) |
| Age | 48.6 (11.8) | 47.8 (12.7)* | 48.7 (11.7) | 48.4 (12.6)* | 50.9 (10.8) | 51.0 (12.1) | 50 (11) | 50 (12) |
| Male | 24,232 (45.6%) | 12,405 (46.7%)* | 13,734 (46.7%) | 6,878 (46.8%) | 2,575 (51.0%) | 1,287 (51.0%) | 1,022 (49%) | 532 (51%) |
| Health plan out-of-network coverage | | * | | | | | | |
| Covered | 8,152 (15.4%) | 4,475 (16.9%) | 5,067 (17.2%) | 2,495 (17.0%) | 697 (13.8%) | 339 (13.4%) | 274 (13%) | 142 (13%) |
| Not covered | 34,545 (65.1%) | 16,861 (63.5%) | 19,534 (66.4%) | 9,772 (66.5%) | 3,286 (65.1%) | 1,642 (65.1%) | 1,432 (68%) | 698 (66%) |
| Other/missing | 10,403 (19.6%) | 5,214 (19.6%) | 4,807 (16.3%) | 2,437 (16.6%) | 1,065 (21.1%) | 543 (21.5%) | 398 (19%) | 212 (20%) |
| Region | | * | | * | | | | |
| Northeast | 13,093 (24.7%) | 6,967 (26.2%) | 7,820 (26.6%) | 3,761 (25.6%) | 1,368 (27.1%) | 674 (26.7%) | 524 (25%) | 229 (22%) |
| North Central | 15,627 (29.4%) | 8,083 (30.4%) | 9,162 (31.2%) | 4,665 (31.7%) | 1,565 (31.0%) | 774 (30.7%) | 655 (31%) | 360 (34%) |
| South | 16,319 (30.7%) | 7,623 (28.7%) | 8,256 (28.1%) | 4,238 (28.8%) | 1,368 (27.1%) | 700 (27.7%) | 602 (29%) | 315 (30%) |
| West | 7,377 (13.9%) | 3,617 (13.6%) | 4,001 (13.6%) | 1,915 (13.0%) | 702 (13.9%) | 352 (13.9%) | 305 (14%) | 145 (14%) |
| Unknown/missing | 684 (1.3%) | 260 (1.0%) | 169 (0.6%) | 125 (0.9%) | 45 (0.9%) | 24 (1.0%) | 18 (1%) | 3 (0%) |
| Residence type, Urban | 43,465 (81.9%) | 21,658 (81.6%) | 24,068 (81.8%) | 12,012 (81.7%) | 4,082 (80.9%) | 2,060 (81.6%) | 1,717 (82%) | 860 (82%) |
| Index year | | * | | | | | | |
| 2012 | 5,127 (9.7%) | 2,342 (8.8%) | 3,407 (11.6%) | 1,720 (11.7%) | 425 (8.4%) | 214 (8.5%) | 234 (11%) | 125 (12%) |
| 2013 | 10,279 (19.4%) | 4,897 (18.4%) | 7,375 (25.1%) | 3,786 (25.7%) | 828 (16.4%) | 418 (16.6%) | 532 (25%) | 266 (25%) |
| 2014 | 12,212 (23.0%) | 6,066 (22.8%) | 7,570 (25.7%) | 3,786 (25.7%) | 1,179 (23.4%) | 604 (23.9%) | 619 (29%) | 288 (27%) |
| 2015 | 13,594 (25.6%) | 6,946 (26.2%) | 11,035 (37.5%) | 5,399 (36.7%) | 1,397 (27.7%) | 695 (27.5%) | 718 (34%) | 372 (35%) |
| 2016 | 11,888 (22.4%) | 6,299 (23.7%) | 21 (0.1%) | 13 (0.1%) | 1,219 (24.1%) | 593 (23.5%) | 1 (0%) | 1 (0%) |

| | Initiator Population | | | | Adherent Population | | | |
|----------------------------------|--|----------------------|--|----------------------|--|---------------------|--|---------------------|
| | Study Sample in Main Analysis after Matching | | Subgroup with ≥12 Months of Follow-up after Matching | | Study Sample in Main Analysis after Matching | | Subgroup with ≥12 Months of Follow-up after Matching | |
| | Varenicline (n=53,100) | NRT Patch (n=26,550) | Varenicline (n=29,408) | NRT Patch (n=14,704) | Varenicline (n=5,048) | NRT Patch (n=2,524) | Varenicline (n=2,104) | NRT Patch (n=1,052) |
| Diagnosis of specific conditions | | | | | | | | |
| Cardiovascular diseases | 8,740 (16.5%) | 3,791 (14.3%)* | 4,638 (15.8%) | 2,373 (16.1%) | 1,076 (21.3%) | 551 (21.8%) | 286 (14%) | 152 (14%) |
| Diabetes mellitus | 6,448 (12.1%) | 2,991 (11.3%)* | 3,282 (11.2%) | 1,684 (11.5%) | 656 (13.0%) | 342 (13.5%) | 247 (12%) | 125 (12%) |
| Pulmonary conditions | 7,912 (14.9%) | 3,678 (13.9%)* | 4,040 (13.7%) | 2,063 (14.0%) | 898 (17.8%) | 450 (17.8%) | 281 (13%) | 130 (12%) |
| Neuropsychiatric conditions | 13,483 (25.4%) | 6,673 (25.1%) | 5,366 (18.2%) | 2,803 (19.1%)* | 1,361 (27.0%) | 673 (26.7%) | 351 (17%) | 177 (17%) |
| Tobacco dependence | 17,761 (33.4%) | 8,414 (31.7%)* | 8,958 (30.5%) | 4,650 (31.6%)* | 1,774 (35.1%) | 891 (35.3%) | 636 (30%) | 303 (29%) |
| Charlson Comorbidity Index | 1.2 (1.5) | 1.0 (1.5) * | 1.1 (1.5) | 1.1 (1.6) | 1.4 (1.8) | 1.4 (1.8) | 1 (2) | 1 (2) |
| Any smoking cessation counseling | 3,288 (6.2%) | 1,639 (6.2%) | 1,701 (5.8%) | 892 (6.1%) | 341 (6.8%) | 164 (6.5%) | 126 (6%) | 54 (5%) |
| Any all-cause hospitalization | 1,848 (3.5%) | 1,235 (4.7%)* | 2,246 (7.6%) | 1,180 (8.0%) | 855 (16.9%) | 437 (17.3%) | 73 (3%) | 47 (4%) |
| All-cause total healthcare cost | \$6,084 (\$11,255) | \$6,068 (\$10,228) | \$7,844 (\$18,032) | \$8,563 (\$20,317)* | \$12,684 (\$26,272) | \$15,372 (\$45,055) | \$6,091 (\$13,029) | \$7,676 (\$33,289) |

N (%) were reported for categorical/binary variables, and mean (standard deviation) were reported for continuous variables.

All standard differences were <10%.

* p <0.05

Abbreviations: NRT = nicotine replacement therapy; VAR = varenicline