Comparative Effectiveness of Varenicline and Nicotine Replacement Therapy for Smoking Cessation in Older and Younger Smokers: A Prospective Cohort in Taiwan

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Abstract

Introduction: The effectiveness of varenicline compared with nicotine replacement therapy (NRT) in achieving smoking cessation in older smokers has not been investigated. This study prospectively compared the effectiveness of varenicline relative to NRT in smokers aged 25–54 years and separately in smokers aged 55 years or older.

Methods: Among 13,397 smokers participating in the Smoking Cessation Program in Taiwan, 2012–2015, 6,336 (19.2%, aged ≥55) received varenicline and 7,061 received NRT patch or gum (23.2%, aged ≥55). Participants self-reported smoking behaviors by phone interview after 6 months. Logistic regression models estimated odds ratios (ORs) and 95% confidence intervals (CIs) for 7-day, 1-month, and 6-month point-prevalence abstinence. Age-specific models adjusted for sex, education, marital status, smoke-years, nicotine dependence, medical institution, clinic visit number, and duration of medication received.

Results: Among smokers aged 25–54 years, varenicline users had a greater point-prevalence abstinence than NRT users (e.g., 7-day point-prevalence: 34.0% vs. 23.5%), with adjusted OR ranging from 1.23 (CI: 1.09–1.39; 6-month point-prevalence) to 1.37 (CI: 1.24–1.50; 1-month point-prevalence). Among smokers aged 55 years or older, point-prevalence was similar for varenicline and NRT users (e.g., 7-day point-prevalence: 32.3% vs. 33.1%), and ORs did not suggest that varenicline has greater effectiveness than NRT. Sex and level of nicotine dependence did not modify the age-specific effectiveness of varenicline relative to NRT.

Conclusions: Varenicline did not offer greater effectiveness in achieving abstinence than NRT for smokers 55 years or older, whereas it was more effective than NRT in smokers aged 25–54 years. These findings highlighted the need for age-specific approaches for effective tobacco control.

Implications: In this prospective investigation of a national cohort, older smokers (aged ≥55 years) who received varenicline did not have a greater point-prevalence abstinence after 6 months compared with those who used NRT patch or gum. Younger smokers (aged 25–54 years) who received
varenicline had a greater likelihood of abstinence than NRT users. Sex and nicotine dependence did not modify the age-specific effectiveness of varenicline relative to NRT patch or gum. Age-appropriate approaches for effective tobacco control are needed.

Introduction

Smoking cessation greatly reduces the risk of tobacco-related morbidity and mortality at all ages, including older smokers who have relatively poor health conditions and higher nicotine addiction levels. Smokers aged 65 years or older may gain life expectancy up to 3.7 years after they quit smoking. The United States Preventive Services Task Force suggests nicotine replacement therapy (NRT) and varenicline are effective smoking cessation aids. NRT helps smokers quit smoking with a 53%–68% greater likelihood of cessation than placebo or non-NRT control groups. Compared with NRT, varenicline showed greater or similar effectiveness in achieving abstinence in two head-to-head clinical trials (the EAGLES study and an open-label trial in the United States) as well as in clinical settings.

Smoking cessation rates appear to differ by age. Older smokers have greater odds of successful quitting than younger smokers, possibly due to stronger motivation, higher participation rates, and greater health concerns in older populations. Meta-analysis of clinical trials suggested that pharmacological intervention offers a 3-fold greater chance of achieving abstinence for smokers aged 50 years or older. However, the effectiveness of varenicline relative to NRT has not been investigated in older smokers. Emerging evidence has suggested that sex and nicotine dependence level may modify the effectiveness of varenicline relative to NRT. The relative effectiveness between varenicline and NRT for older smokers by sex and nicotine dependence severity has not been studied.

Effective smoking cessation therapies targeting older populations have public health and clinical relevance. The global population is aging, including in Taiwan. Up to 30% of men aged 50 years or older in Taiwan are smokers, and approximately 80% of total health care expenditures in 2010 were attributable to tobacco smoking. In the current study, we aimed to prospectively investigate (1) the age-specific effectiveness of varenicline relative to NRT in smokers aged 25–54 years and separately smokers 55 years or older and (2) whether effectiveness of varenicline compared with NRT differs by sex and level of nicotine dependence. We hypothesized that varenicline is more effective than NRT in achieving abstinence for smokers aged 25–54 years, but not so for smokers aged 55 years or older because a strong motivation to quit tobacco smoking in older smokers may override the different effectiveness of two treatments. This study could inform clinicians in selecting the appropriate medication for smokers of different age and sex.

Methods

Study Population

The Health Promotion Administration in Taiwan implemented the nation-wide Second Generation Tobacco Smoking Cessation Services Program on March 1, 2012, which subsidized copayments for smoking cessation medications. Individuals aged 18 years or older who sought to quit tobacco smoking at smoking cessation clinics were eligible to receive pharmacotherapy for smoking cessation and/or health education for up to two treatment courses. Varenicline and NRT were offered mostly as monotherapy in the treatment course. Each course consisted of up to eight prescription refills (a 90-day supply). Smoking cessation medications included NRT (patch, chewing gum, inhaler, or tablet), bupropion (tablet), and varenicline (tablet). The medications were assigned to individuals based on their preference and/or professional advice by their physicians. At the first clinic visit, participants provided information on demographics and smoking-related behaviors (years of smoking and number of cigarettes per day). They also received the Fagerström Test for Nicotine Dependence (FTND) assessment. Information on smoking status, adverse effects from medications, withdrawal symptoms of smoking cessation, and changes in prescriptions was collected approximately after 3 months and during follow-up at clinics. Each year, 1000–4000 participants were randomly selected for smoking behaviors assessment in phone interviews 6 and 12 months after initiation of the treatment.

Between March 1, 2012 and August 31, 2015, 192 703 adult smokers aged 25 years or older received a single prescription of varenicline or NRT in their first visit and 32 064 smokers were selected to receive a follow-up phone interview after 6 months. The current study included 13 397 participants who received either varenicline (n = 6336) or NRT (n = 7061 patch or gum users), excluding 17 674 non-respondents in the 6-month phone interview and 993 participants who received more than one medication in two treatment courses. This study did not include the 837 bupropion users (120 participants aged 55 years or older) who also finished the phone interview during the same period due to the limited sample size.

Medications for Cessation

The current study included participants who received a single pharmacotherapy in the first course. These medications included six NRT patch products (brand name or generic NRT with doses ranging from 10.4 to 52.5 mg/patch), six NRT gum brand-name products (dose per piece was 2 to 4 mg), and two varenicline brand-name products (0.5 and 1.0 mg/tab).

Point-Prevalence Abstinence from Cigarettes After 6 Months

In the phone interview, participants were asked, “When was the last time you smoked? Less than 1 day, 1–6 days ago, 7–29 days ago, 30–179 days ago, or more than 180 days ago?” The 7-day, 1-month, and 6-month point-prevalence abstinence indicated the percentage of participants who self-reported the last time of smoking at least 7 days ago (“7–29 days ago,” “30–179 days,” or “≥180 days ago”), 30 days ago (“30–179 days ago” or “≥180 days ago”), and 6 months ago (“≥180 days ago”), respectively.

Statistical Analysis

We conducted descriptive analyses for baseline characteristics in the overall population, smokers aged 25–54 years and those aged...
55 years or older, respectively. We examined characteristic distributions between groups using Student’s t-test for continuous variables and chi-square test for categorical variables. Participants were categorized into two nicotine dependence groups based on the total FTND score: light or moderate (scores 0–6) and severe (scores 7–10). The duration of medication received was defined as the sum of the prescription days at each clinic visit in the first treatment course and was categorized into one, two, three, or more weeks. The 7-day, 1-month, and 6-month point-prevalence abstinence rates were calculated by sex and nicotine dependence in each age group. Generalized linear-regression models were conducted to estimate 95% confidence intervals (CIs) for point-prevalence, assuming a binomial distribution for abstinence from tobacco smoking.

Separate logistic regression models were conducted to estimate adjusted odds ratios (ORs) and 95% CIs for 7-day, 1-month, and 6-month point-prevalence rates comparing varenicline with NRT (reference group) for smokers aged 25–54 years and those 55 years or older, respectively. Age-specific models adjusted for sex, education level (junior high school, senior high school, college or above, and other), marital status (single, married, or other), continuous smoke-years (per 1-year change), nicotine dependence severity (light/moderate vs. severe), medical institution (community clinics or hospital outpatient clinics), categorical number of clinic visits, and categorical duration of medication received. Age and smoke-years were highly correlated ($r = 0.81$), which led us to exclude continuous age as a covariate in age-specific regression models to avoid potential multicollinearity.

In secondary analyses, we aimed to address the question of whether effectiveness of varenicline versus NRT differs by sex and level of nicotine dependence. We performed age-specific adjusted modeling separately for men, women, smokers with light/moderate dependence, and smokers with severe dependence.

In sensitivity analyses, we included 993 participants who received more than one medication in two treatment courses and 17 674 non-respondents. These participants were conservatively treated as being smokers (failed to quit smoking) in age-specific models to compare effectiveness of varenicline versus NRT.

All $p$-values were two-sided, with $p < .05$ considered statistically significant. Statistical analyses were performed using SAS software (version 9.4; Cary, NC, USA).

Results

Cohort Characteristics

Among the 13 397 participants, the mean age was 45.4 ($\pm$11.9) years with 22% aged 55 years or older. The majority of the participants (85%) were male (Table 1). Participants tended to have severe nicotine dependence (53%, FTND ≥ 7) and to have had smoked at least 20 years (67%). Smokers aged 25–54 years were more likely than smokers aged 55 years or older to receive varenicline (49% vs. 43%, $p < .001$) and smokers in either age group had similar nicotine dependence. Regardless of age, varenicline users were more likely than NRT users to have a severe nicotine dependence, have a college education, receive medication in hospital outpatient clinics, visit the clinics two times or more, and use the smoking cessation medication for at least 3 weeks (all $p$-values < .001).

Point-Prevalence Abstinence Rate

Among smokers aged 25–54 years, the 7-day, 1-month, and 6-month point-prevalence abstinence was greater in varenicline users than NRT users: Approximately, one in three varenicline users and one in four NRT users self-reported that they smoked cigarettes at least 30 days prior to the interview (1-month point-prevalence: 32.5 [95% CI: 31.3–33.7] vs. 21.9 [95% CI: 20.8–23.0], Table 2). Greater abstinence rates among varenicline users were observed across different sex and nicotine dependence subgroups. Among smokers aged 55 years or older, the point-prevalence abstinence was similar between varenicline and NRT users.

The point-prevalence abstinence for NRT users was lower in those aged 25–54 years than those aged 55 years or older, regardless of sex and nicotine dependence. For varenicline users, the point-prevalence abstinence was similar between smokers of the two age groups.

Effectiveness of Varenicline Relative to NRT

Varenicline was more effective than NRT in achieving abstinence for younger smokers, but not so for older smokers (all $p$-values for medication × age < .001, Table 3). For smokers aged 25–54 years, varenicline users had a 23% (95% CI: 9%–39%) to 37% (95% CI: 24%–50%) greater odd of reporting abstinence after 6 months. For smokers aged 55 years or older, varenicline was less effective than NRT, with adjusted OR ranging from 0.75 (95% CI: 0.60–0.94) for 6-month point-prevalence to 0.82 (95% CI: 0.39–0.98) for 1-month point-prevalence.

Age-specific Comparative Effectiveness by Sex and Nicotine Dependence

Sex and nicotine dependence severity did not modify the effectiveness of varenicline relative to NRT (Table 4). For example, in smokers aged 25–54 years, varenicline users reported abstinence at higher rates than NRT users, regardless of sex or dependence severity, except that the OR for 6-month point-prevalence was not statistically significant for women. Among smokers aged 55 years or older, varenicline was less effective than NRT patch or gum for men and smokers with severe dependence, and the two medications had similar effectiveness for women and smokers with light/moderate dependence.

Sensitivity Analysis

Overall, the comparative effectiveness from the sensitivity analyses was consistent with that from the original analyses. In sensitivity analyses, the distributions for type of medical institution, number of clinic visits, and duration of medication received in 17 674 non-respondents were similar to those in respondents who failed to remain abstinent (Supplementary Table 1). The point-prevalence abstinence was lower in sensitivity analyses than the original analyses (Supplementary Table 2). For smokers aged 25–54 years, varenicline was more effective than NRT patch or gum; for smokers aged 55 years or older, varenicline was not superior to NRT patch or gum (Supplementary Tables S2 and S3).

Discussion

In this cohort of 13 397 adult smokers, varenicline was more effective than NRT patch or gum for improving the rates of tobacco cessation in smokers aged 25–54 years. In contrast, for smokers aged 55 years or older, varenicline did not provide a greater effectiveness in achieving abstinence than NRT patch or gum, regardless of sex or nicotine dependence. To our knowledge, the current study is the first of its kind to compare effectiveness of varenicline versus NRT in
Table 1. Baseline characteristics of smokers who used varenicline or NRT (patch or gum) in the Tobacco Smoking Cessation Services Program in Taiwan, 2012 to 2015

| Covariate                          | Mean ± SD or N (%) | Varenicline (n = 5117) | NRT patch or gum (n = 5419) | p-value* | Varenicline (n = 1219) | NRT patch or gum (n = 1642) | p-value*
|------------------------------------|--------------------|------------------------|-----------------------------|----------|------------------------|-----------------------------|----------
| Age, years                         | 45.4 ± 11.9        | 40.5 ± 7.8             | 40.8 ± 8.0                  | 0.057    | 62.3 ± 5.9             | 63.6 ± 6.9                  | <0.001   |
| 25–34                              | 2996 (22)          | 1467 (29)              | 1529 (28)                  | 0.030    | N/A                    | N/A                          | N/A      |
| 35–44                              | 4011 (30)          | 1998 (39)              | 2013 (37)                  |          | N/A                    | N/A                          | N/A      |
| 45–54                              | 3529 (26)          | 1652 (32)              | 1877 (35)                  |          | N/A                    | N/A                          | N/A      |
| 55–64                              | 1974 (15)          | N/A                   | N/A                        |          | 909 (75)               | 1065 (65)                   | <0.001   |
| 65+                                | 887 (7)            | N/A                   | N/A                        |          | 310 (25)               | 577 (35)                    |          |
| Male                               | 11 344 (85)        | 4281 (84)              | 4483 (83)                  | 0.199    | 1090 (89)              | 1490 (91)                   | 0.239    |
| Education                          |                    |                       |                             |          |                       |                             |          |
| Elementary or less                 | 1361 (10)          | 105 (2)                | 185 (3)                    |          | 403 (33)               | 668 (41)                    |          |
| Junior high school                 | 1829 (14)          | 578 (11)               | 791 (15)                   |          | 193 (16)               | 267 (16)                    |          |
| Senior high school                 | 5080 (38)          | 1976 (39)              | 2374 (44)                  |          | 313 (26)               | 417 (25)                    |          |
| College or more                    | 5127 (38)          | 2458 (48)              | 2069 (38)                  | 0.068    | 310 (25)               | 290 (18)                    |          |
| Marital status                     |                    |                       |                             |          |                       |                             |          |
| Single                             | 2866 (21)          | 1374 (27)              | 1395 (26)                  |          | 47 (4)                 | 50 (3)                      |          |
| Married                            | 8781 (66)          | 3208 (63)              | 3374 (62)                  |          | 945 (78)               | 1254 (76)                   |          |
| Other                              | 1430 (11)          | 535 (10)               | 523 (10)                   |          | 227 (19)               | 291 (18)                    |          |
| Region                             |                    |                       |                             |          |                       |                             |          |
| Northern area                      | 6501 (49)          | 2785 (54)              | 2384 (44)                  | <0.001   | 659 (54)               | 673 (41)                    | <0.001   |
| Middle area                        | 3084 (23)          | 968 (19)               | 1422 (26)                  |          | 235 (19)               | 459 (28)                    |          |
| Southern area                      | 3812 (28)          | 1364 (27)              | 1613 (30)                  |          | 325 (27)               | 510 (31)                    |          |
| Medical institution                |                    |                       |                             | <0.001   |                       |                             | <0.001   |
| Community clinics                  | 8743 (65)          | 2784 (54)              | 4232 (78)                  |          | 543 (45)               | 1184 (72)                   |          |
| Hospital outpatient               | 4654 (35)          | 2333 (46)              | 1187 (22)                  |          | 676 (55)               | 458 (28)                    |          |
| FTND score‡                        | 6.6 ± 2.1          | 6.7 ± 2.1              | 6.5 ± 2.1                  | <0.001   | 6.7 ± 2.1              | 6.4 ± 2.0                   | <0.001   |
| Nicotine dependency                |                    |                       |                             | <0.001   |                       |                             | <0.001   |
| Light/moderate‡                    | 6299 (47)          | 2289 (45)              | 2647 (49)                  |          | 536 (44)               | 827 (50)                    |          |
| Severe‡                            | 7098 (53)          | 2828 (55)              | 2772 (51)                  |          | 683 (56)               | 815 (50)                    |          |
| Smoking years                      | 23.8 ± 11.2        | 20.5 ± 8.0             | 19.9 ± 8.4                 | <0.01    | 37.5 ± 10.0            | 36.8 ± 11.5                 | 0.078    |
| <20                                | 4349 (32)          | 2013 (39)              | 2221 (41)                  | 0.219    | 34 (3)                 | 81 (5)                      | 0.004    |
| 20–39                              | 7402 (55)          | 3049 (60)              | 3144 (58)                  |          | 501 (41)               | 708 (43)                    |          |
| ≥40                                | 1646 (12)          | 55 (1)                 | 54 (1)                     |          | 684 (56)               | 853 (52)                    |          |
| Clinic visit number                | 2.3 ± 1.8          | 2.6 ± 1.8              | 2.1 ± 1.8                  | <0.001   | 2.5 ± 1.7              | 2.0 ± 1.7                   | <0.001   |
| Once                               | 6280 (47)          | 1771 (35)              | 3072 (57)                  | <0.001   | 475 (39)               | 962 (59)                    | <0.001   |
| Twice or more                      | 7117 (53)          | 3346 (65)              | 2347 (43)                  |          | 744 (61)               | 680 (41)                    |          |
| Duration of medication received    |                    |                       |                             |          |                       |                             |          |
| (week)                            | 3.5 ± 2.5          | 4.1 ± 2.6              | 3.0 ± 2.3                  | <0.001   | 4.1 ± 2.7              | 3.0 ± 2.4                   | <0.001   |
| 1 week                             | 3783 (28)          | 1037 (20)              | 1871 (35)                  | <0.001   | 300 (25)               | 575 (35)                    | <0.001   |
| 2 weeks                            | 2818 (21)          | 876 (17)               | 1341 (25)                  |          | 191 (16)               | 410 (25)                    |          |
| ≥3 weeks                           | 6796 (51)          | 3204 (63)              | 2207 (41)                  |          | 728 (60)               | 657 (40)                    |          |

NRT = nicotine replacement therapy; SD = standard deviation.

*P-value for χ² test or Student’s t-test.

‡Nicotine dependence level defined by the Fagerström Test for Nicotine Dependence (FTND) score (19): 0–3, light; 4–6, moderate; 7–10, severe.

an older population. Our study findings highlight the need for age-specific approaches for effective tobacco control.

Older smokers may have a stronger motivation to quit smoking than young or middle-aged smokers, likely due to health concerns. Health-related factors, such as taking a greater number of medications or having chronic conditions,14,15 were positively associated with smoking cessation in smokers aged 60 years or older. A newly diagnosed chronic health condition appeared to motivate older smokers to quit smoking but did not motivate middle-aged smokers. Indeed, the participation rates increased exponentially from 2.4% in young smokers (aged 20–29 years) to 47.5% in older smokers (aged ≥60 years) who attended free smoking cessation clinics in Korea.15 It is plausible that the strong health-related motivations to quit smoking make the superior effectiveness of varenicline compared with NRT, less relevant for older smokers. In the current study, the abstinence rates in younger smokers were higher than varenicline than NRT users, whereas in older smokers, the abstinence rates were similar between two groups. A similar age-dependent pattern in abstinence rates for NRT users was also observed in a Brazilian cohort.21

Concerns regarding medication-related adverse events may influence physicians’ practice or discourage adherence in the elderly,22 which may affect the effectiveness of varenicline relative to NRT.
Physicians may be more willing to prescribe varenicline to younger smokers. In our study population, only 35% of smokers aged 65 years or older received varenicline (65% received NRT), and smokers aged 25–54 years had a greater likelihood of receiving varenicline than those 55 years or older. Unfortunately, we did not have access to information on adverse events and adherence. We cannot rule out the possibility that adherence to varenicline was poorer in older smokers although the duration of receiving varenicline appeared to be similar between the two age groups. The EAGLES trial and a future prospective investigation reported the age-specific comparative effectiveness in a large, population-based sample in clinical settings. We performed regression modeling to adjust for important confounding factors (including smoke-years, nicotine dependence) and factors influencing abstinence (including duration of medication received and clinic visit numbers). Results from the original sample were accordant to those from sensitivity analyses, which conservatively assumed all non-respondents failed to quit.

The present study has several limitations. First, smoking abstinence was not chemically confirmed, and the abstinence rates were likely overestimated. Respondents may have misreported the last

Table 2. Point-prevalence abstinence among smokers who received varenicline or NRT patch/gum after 6 months

|                      | Age 25–54 years |                      | Age 55 or older |                      |
|----------------------|----------------|----------------------|-----------------|----------------------|
|                      | N              | 7-day (% 95% CI)     | 1-month (%)     | 6-month (%)          |
|                      | 5117           | 34.0 (32.7, 35.3)    | 32.5 (31.3, 33.7)| 16.4 (15.4, 17.4)   |
| Varenicline          | 5419           | 23.5 (22.4, 24.7)    | 21.9 (20.8, 23.0)| 11.6 (10.7, 12.4)   |
|                      | 1219           | 32.3 (29.7, 34.9)    | 30.9 (28.3, 33.5)| 15.5 (13.5, 17.5)   |
| NRT patch or gum     | 1440           | 31.3 (30.4, 32.3)    | 31.2 (28.9, 33.4)| 16.8 (15.0, 18.6)   |
| Men                  | 4281           | 34.3 (32.9, 35.7)    | 32.8 (31.4, 34.2)| 16.8 (15.7, 17.9)   |
| Varenicline          | 4483           | 23.4 (22.2, 24.6)    | 21.7 (20.5, 23.0)| 11.9 (10.9, 12.8)   |
|                      | 1090           | 32.9 (30.1, 35.7)    | 31.7 (28.9, 34.4)| 16.2 (14.0, 18.4)   |
| NRT patch or gum     | 1490           | 33.8 (31.3, 36.2)    | 31.7 (29.3, 34.0)| 17.4 (15.5, 19.3)   |
| Women                | 836            | 32.5 (29.4, 35.7)    | 30.9 (27.7, 34.0)| 14.1 (11.8, 16.5)   |
| Varenicline          | 936            | 24.3 (21.5, 27.0)    | 22.5 (19.9, 25.2)| 10.0 (8.11, 11.7)   |
|                      | 129            | 27.1 (19.5, 34.8)    | 24.8 (17.4, 32.3)| 9.3 (4.3, 14.3)     |
| NRT patch or gum     | 152            | 26.3 (19.3, 33.3)    | 26.3 (19.3, 33.3)| 10.5 (5.6, 15.4)    |
| Light/moderate nicotine dependence |    |                      |                  |                      |
| Varenicline          | 2289           | 39.3 (37.3, 41.3)    | 37.4 (35.5, 39.4)| 18.5 (16.9, 20.1)   |
|                      | 2647           | 26.6 (24.9, 28.3)    | 24.6 (22.9, 26.2)| 12.7 (11.5, 14.0)   |
| NRT patch or gum     | 536            | 38.2 (34.1, 42.4)    | 36.9 (32.9, 41.0)| 17.3 (14.1, 20.6)   |
| Severe nicotine dependence |      |                      |                  |                      |
| Varenicline          | 2828           | 29.7 (28.1, 31.4)    | 28.4 (26.8, 30.1)| 14.7 (13.4, 16.0)   |
|                      | 2772           | 20.6 (19.1, 22.1)    | 19.3 (17.9, 20.8)| 10.5 (9.3, 11.6)    |
| NRT patch or gum     | 683            | 27.7 (24.3, 31.0)    | 26.2 (22.9, 29.5)| 14.1 (11.4, 16.7)   |
|                      | 815            | 30.1 (26.9, 33.2)    | 28.1 (25.0, 31.2)| 15.9 (13.4, 18.5)   |

Table 3. Multivariable models for point-prevalence abstinence comparing varenicline with NRT users

|                        | 7-day (%)     | 1-month (%)  | 6-month (%)  |
|------------------------|--------------|--------------|--------------|
| Overall population     | 1.21 (1.12, 1.32) | 1.24 (1.14, 1.34) | 1.11 (1.00, 1.24) |
| Varenicline            | 1 (reference) | 1 (reference) | 1 (reference) |
| p-value for medication × age | 0.05       | 0.05         | 0.05         |
| Age 25–54 years        | 1.34 (1.22, 1.47) | 1.37 (1.24, 1.50) | 1.23 (1.09, 1.39) |
| Varenicline            | 1 (reference) | 1 (reference) | 1 (reference) |
| Age 55 years or older  | 0.80 (0.67, 0.96) | 0.82 (0.69, 0.98) | 0.75 (0.60, 0.94) |
| Varenicline            | 1 (reference) | 1 (reference) | 1 (reference) |

NRT = nicotine replacement therapy; OR = odds ratios; CI = confidence interval.

NRT = nicotine replacement therapy; CI = confidence interval.

Adjusted for (per 1-year change, the overall population only), sex, categorical education level, marital status, smoke-years (per 1-year change), nicotine dependence (light/moderate or severe), medical institution (community clinics or hospital outpatient clinics), categorical number of clinic visits, and categorical duration of medication received. The bold estimates were statistically significant at alpha level of 0.05.
time they smoked. However, medications were prescribed before the phone survey, and there was no evidence suggesting that misclassification in abstinence rates would differ between two medication groups. In addition, the 7-day point-prevalence abstinence was 34% among varenicline users and 24% among NRT users in the current study, which agreed with the biochemically confirmed 7-day point-prevalence in the EAGLES study and a mobile smoking cessation program in Hong Kong.\(^2\)\(^3\) Second, participants may not have adhered to medications, and those who experienced medication-related adverse events may have discontinued medications, failed to quit smoking, or refused to respond. In sensitivity analyses, we considered nonrespondents to be smoking, and the results were consistent with those in the original analyses. Third, we were unable to control for unobserved potential confounding factors, such as comorbid conditions or health status. Fourth, the current study included a majority of male Asian participants of a government-sponsored tobacco cessation program in a single-payer health care system. Findings may not be applicable to populations in other health care systems or non-Asians. Women in Taiwan have low smoking rates (<2% for women aged 50 years or older), and the current study included relatively few women aged 50 years or older.\(^19\) Findings for female smokers need to be investigated in other populations.

**Conclusion**

The global population is aging, but the prevalence of tobacco smoking in older populations remains steady.\(^2\)\(^4\)\(^5\) The current prospective investigation suggests that varenicline does not offer a greater effectiveness than NRT patch or gum for older smokers, and accounting for sex or nicotine dependence does not modify these relationships. On the other hand, varenicline is superior to NRT patch or gum for smokers aged 54 years or younger. Health care providers should discuss with smokers the relative effectiveness between varenicline and NRT in choosing an appropriate treatment plan. Future investigation in female and non-Asian populations, including adverse events related to varenicline among older smokers, will provide further insights in tobacco control approaches.

**Supplementary Material**

Supplementary data are available at Nicotine and Tobacco Research online.

**Funding**

National Yang-Ming University received research funding from the revenues of tobacco health and welfare surcharges by the Health Promotion Administration, Ministry of Health and Welfare, Taiwan, for project, titled “International Collaborative Project for the Evaluation of Medical Services for Smoking Cessation.” Tsuo-Hung Lan, Po-Yin Chang, Pei-Yu Su and Hui-Chin Chang received grants (G1031227-105) from the Health Promotion Administration, Ministry of Health and Welfare, Taiwan (http://www.hpa.gov.tw/BHPNet/English/Index.aspx).

**Declaration of Interests**

All authors declare no competing interests.

**Acknowledgments**

We thank Professor Yi-Wen Ivy Tsai for her insightful comments and Mr. Imad Sawaya for editing the manuscript.

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