PREVALENCE AND RISK FACTORS OF E-CIGARETTES AND NRT USE AMONG HIV-INFECTED AND UNINFECTED MEN WHO HAVE SEX WITH MEN

by

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Abstract

Background: The prevalence of e-cigarettes and NRT use is increasing among general population in recent years. With the shifting in HIV-infection paradigm, describing the prevalence and pattern among men with high risk of HIV infection is important in chronic disease prevention and improving their life expectancy and quality.

Objective: The aims of this study were 1) to provide a profile of current smoking, e-cigarettes use and NRT use; 2) to identify risk factors associated with initiation of e-cigarettes and NRT use among men with high risk of HIV infection.

Design: A longitudinal study based on The Multicenter AIDS Cohort Study (MACS). A total of 2285 men were included with follow-ups starting from June 2015.

Results: The prevalence of current smokers was constant from 2015 to 2017. Men without HIV had a similar prevalence as the general US adult men (16.7%-17.5%), at between 13.5% and 16.1%. Men with HIV had a higher prevalence at between 23.0% and 26.1%. The prevalence of e-cigarettes (ranged between 5.2% to 9.3% for HIV infected men and between 3.1% and 5.7% for uninfected men) and NRT use (ranged between 5.0% and 8.2% for infected men and between 3.5% and 4.6% for uninfected men.) did not differ by HIV status. The prevalence of e-cigarettes use was about 20% in current smokers, 4% in former smokers, and 0.3% for non-smokers. The prevalence of NRT use was about 12% in current smokers and about 3% in former smokers. Ever e-cigarettes and NRT users had a higher cumulative pack-year compared to never users. After adjusting for age, race, Hispanic ethnicity, education level, serostatus, detectable viral load, CD_4 count and cumulative pack-years, the cumulative incidence risk (RR) ratio of e-cigarettes use was 0.98 (95% CI, 0.97-0.99) for one year increase in age; 1.46 (95% CI,

1.01-2.10) for high school level education compared to 4 years' college and above, 1.55 (95% CI, 1.03-2.35) for less than high school education compared to 4 years' college and above, 1.09 (95% CI, 0.98-1.23) for HIV infection, and 1.02 (95% CI, 0.99-1.04) for 50% increase in cumulative pack-years. The cumulative incidence risk ratio of NRT use is 0.95(95% CI, 0.95-0.97) for one-year increase in age, 1.32 (95%CI, 1.00-1.73) for being back, 1.48 (95% CI, 1.02-2.15) for high school level education compared to 4 years' college and above, 1.31(95% CI, 0.99-1.72) and 1.10 (95% CI, 1.07-1.14) for 50% increase in cumulative pack-years.

Conclusion: The prevalence of current smoking was higher for men with HIV than men without. E-cigarettes and NRT use was mostly common among current smokers, the prevalence did not differ by HIV status. E-cigarettes and NRT users had a longer cumulative pack-years compared to never users. Risk factors associated with e-cigarettes and NRT use included younger age, lower education level, HIV infection and longer cumulative pack-years. Black race is associated with NRT use.

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Background

The overall prevalence of cigarette smoking in the United States was about 15.1% in 2015 and 15.5% in 2016 among adults (Jamal, 2018; Phillips, 2017). Adult men had a higher prevalence than women, the prevalence was 16.7% (95% CI, 15.9–17.6%) and 17.5% (95% CI, 16.6–18.5%) among males in 2015 and 2016; while for females was 13.6% (95% CI, 12.9–14.3%) and 13.5% (95% CI, 12.8–14.3%) (Jamal, 2018; Phillips, 2017).

Many studies have demonstrated that smoking causes many health conditions, including lung cancer, heart attacks, stroke, and chronic obstructive pulmonary disease (COPD). Tobacco use is therefore considered to be the biggest single cause of preventable death worldwide (Organization & Control, 2008). With the introduction of effective treatment including ART and HAART, the life expectancy of HIV-infected individuals is approaching the uninfected individuals. This shift in HIV infection paradigm makes it necessary to pay more attention to smoking cession among the infected individuals to prevent chronic diseases and to increase their life expectancy and quality (Althoff, 2016).

E-cigarettes is a novel electronic nicotine delivery device that mimics traditional cigarette smoking through heating liquid that usually contains nicotine. They are often used as a substitute for cigarettes among those trying to quit smoking or as a novel nicotine delivery system among those without a history of cigarettes smoking. In the U.S. general population, the prevalence of e-cigarettes smoking was 4.3%(95% CI, 3.9-4.8%) (Phillips, 2017) in the US adult men in 2015, and 4.0%(95% CI, 3.6–4.3%) in 2013-2014 (Hu, 2016). Among the adults, the prevalence of e-cigarettes use was highest among current smokers, and much

lower among former and never smokers (Carroll Chapman & Wu, 2014). However, studies have shown that the usage pattern was different among adolescents. There was a notable portion of adolescent users started smoking with e-cigarettes instead of tradition cigarettes (Arrazola et al., 2015). Among adults, e-cigarettes were mostly used as a substitute for cigarettes smoking and the users may not always intend to quit smoking (Carroll Chapman & Wu, 2014). Risk factors for e-cigarettes use often varies across different populations, commonly identified indicators including race(Camenga et al., 2014), sociodemographic characteristics (Rutten et al., 2015), currently smoking(Wang, Wang, Cao, Wang, & Hu, 2016), intention to quit smoking, and reliance on nicotine(Ramo, Young-Wolff, & Prochaska, 2015).

E-cigarettes were introduce into the US market in 2007, and the use has been increasing since then(Chen, 2013). They are often perceived to be less harmful since the quantity of harmful compounds and heavy metals produced by e-cigarettes is lower than those from traditional cigarettes. Although e-cigarettes are considered to be less addictive, the risk of nicotine addiction and renormalization of smoking behaviors remains (McMillen, Gottlieb, Shaefer, Winickoff, & Klein, 2015). Moreover, Bullen's study have revealed that e-cigarettes are very effective in helping quit smoking (Bullen et al., 2013). There was a review study on the prevalence in different age groups showing that the prevalence and use patterns varied among difference sub-populations. Current studies are mostly conducted among general population. In order to have a better understanding of the profile of e-cigarettes use, it necessary to describe the e-cigarette use in a representative population of older men who have sex with men (MSM).

Nicotine replacement therapy (NRT) is most commonly used as a smoking cessation assistance to overcome highly nicotine dependent smokers' withdraw feelings and cigarette cravings. Also it could be used as a way to reduce the amount of cigarette smoking. NRT provides a small amount of nicotine to reduce the urge to smoke. The types of NRT varies from patches, gum, lozenges, inhalers and nasal sprays. Among US male smokers trying to quit in 2015, 27.0% (95% CI, 24.0–30.0%) of them used medication as a cessation assistance (Babb, 2017). A British study published in 2014 showed the highest prevalence of 34.8% of NRT use among smokers quitted in recent 3 months; 11.8% among current smokers, and 7.8% among smokers who quitted more than 3 months ago (Shahab, Beard, Brown, & West, 2014). A Canadian population based survey published in 2014 reveals the prevalence of NRT use among current smokers was about 27% (Zhang, Cohen, Bondy, & Selby, 2015). A study based on US adult current smokers with a quit attempt showed risk factors associated with the NRT use, including older age, male, higher education, higher smoking intensity, and nicotine dependence. (Shiffman, 2005).

NRT is proved to be effective in increasing the chance of success cessation by 50%-70% under standard use (Stead et al., 2012). The utilization of NRT increased recently in the general population. With a limited number of studies, the pattern of NRT use among MSM population remains unclear. An accurate description would be helpful in regulating and promoting the NRT use in order to support smoke cessation and prevent chronic diseases in this sub-population.

Compared with the general population, men at high risk of HIV infection are more likely to have substance abuse and addiction issues (Tetrault, Fiellin, & Sullivan, 2010). This might affect their smoking behaviors as well. There were evidence showing that men who have sex men had a higher prevalence of e-cigarettes usage (Gerend, Newcomb, & Mustanski, 2017). Study also suggested that poly-tobacco use was slightly higher among people with HIV than the general population (Pacek, Sweitzer, & McClernon, 2016). There are limited studies examining factors that might be associated with e-cigarettes or NRT use among men at high risk of HIV infection.

The Multicenter AIDS Cohort Study (MACS) is a comprehensive longitudinal study of nearly 30 years of follow-up on almost 7000 men who are at high risk HIV infection. This study used part of the MACS data, which contained 2285 participants with a follow-up time of 2.5 years started from June 2015. The large sample size and repeated measures of e-cigarettes and NRT use makes it an ideal dataset for addressing the prevalence and risk factors of e-cigarettes and/or NRT using among HIV-infected individuals. The purpose of this study is to 1) provide a description of current usage of cigarettes, e-cigarettes and nicotine replacement therapy, and 2) identify factors that are related to initiation of e-cigarettes smoking and NRT use among HIV-infected men and men at high risk of HIV infection in the US.

Methods

The Multicenter AIDS Cohort Study (MACS) is an ongoing multi-center prospective longitudinal study established in 1984 to describe the natural and treated histories of HIV infection in men high risk of HIV infection. A total of 6972 men were enrolled from four

centers (Baltimore/Washington DC, Chicago, Los Angeles, and Pittsburgh) in three recruitment waves (1984-85, n=4954; 1987-1991, n=668; 2001-03, n=1350). Demographic, clinical, laboratory testing, and behavioral data were collected at semi-annual visits. The study has been described in detail previously (Kaslow et al., 1987).

Behavioral questions related to tobacco use, e-cigarette and NRT use were collected since 2015 by primarily a separate self-administered web-based questionnaire, a computerized assisted direct interview (CADI) was used as a secondary option for administration. Overall, this study included all data after this time including 9877 person-visits contributed from 2285 people. The study populations used in the prevalence description and risk factor analyses are shown in the flow chart (Figure 1).

Outcomes

questions about e-cigarettes in each visit: "*1) Since your last visit, have you smoked E-cigarettes? 2) Are you smoking them now?"* E-cigarette use for a visit was defines as answer "yes" or "occasionally" to either of the two questions. Ever e-cigarette users were those who reported using e-cigarettes for at least one visit. Never e-cigarette users were those who never reported using e-cigarettes in any of the visits.

NRT using was defined as ever and never NRT using. There was one question about NRT usage: "*Since your last visit, have you used any stop-smoking medications, such as patch, gum, nasal spray, inhalers, or lozenges?"* NRT use for a visit was defines as answer "yes" or "occasionally" to the question. Ever NRT users were those who reported using NRT for

at least one visit. Never NRT users were those who never reported using NRT in any of the visits.

Exposures

This study also included several independent variables in the risk factor analysis, including age, race, education level, HIV treatment, detectable viral load and CD_4 count. These variables were included because previous studies had indicated that demographic, socioeconomic (Rutten et al., 2015), and health conditions (Pacek et al., 2016) might be related with e-cigarettes or NRT initiation.

Age at each visit was calculated by date of birth and was treated as a continuous variable. Race was characterized using race and Hispanic ethnicity. We grouped American Indian, Alaskan Native, Asian, Pacific Islander and others together as "Other" because of the small numbers (n=159,7.0%). Self-reported highest education level was collected at each visit and was categorized as high school or less, high school, some college and 4-year college and above.

HIV seroconversion status was assessed by enzyme-linked immunosorbent assay with confirmatory Western blot tests on all HIV-seronegative participants at each visit and dichotomized as HIV-seropositive (men with HIV) and HIV-seronegative (men without HIV). CD_4+ T-lymphocyte subset levels was measured by standardized flow cytometry at each visit and was grouped as below and above 350 cells/mm^3. Self-reported use of highly

active antiretroviral therapy (HAART) was defined as yes or no at each visit. Detectable viral load was defined as <20 copied/ml (measured by TaqMan® HIV-1 Test) at each visit.

Data analysis

We first calculated the visit-specific prevalence of smoking as the number of current smokers over the total number of participants under follow up in each visit. To describe the use of e-cigarettes, we then calculated the prevalence of ever e-cigarettes use among current and former smokers by seroconversion status, as the number of e-cigarette users divided by the total number of current or former smokers for each visit. Confidence intervals for the prevalence above were also calculated and depicted. Then for the NRT use, similar prevalence was calculated using the total number of current and former smokers as the denominator. Confidence intervals for the prevalence were calculated and depicted as well.

Univariate and multivariate Poisson regression models with robust variance were performed to identify risk factors for e-cigarettes use and cumulative incidence risk ratios (RR) were reported. Age, race, Hispanic ethnicity, education, HIV seroconversion status, HIV treatment, CD_4 count, and cumulative pack-years were included in the univariate and the multivariate models. All the covariates were included for adjustment in the multivariate Poisson regression model. For the Poisson regression models, each person has one row of data. Risk factors were obtained from the visit when a man first reported using e-cigarettes or NRT, or from last visit for men who never reported using e-cigarettes or NRT. A

complete case analysis approach that excludes those with missing data for any of the risk factors was used. Analyses were conducted using STATA 14.0.

Results

Baseline demographic data for HIV-infected men and uninfected men are shown in Table 1. There were 2285 participants included in our study. The number of HIV-infected and uninfected men were roughly similar (46.9% were men with HIV). The infected men were younger than uninfected men (median age=60.3 vs. 54.5). HIV-infected men were more likely to black (44.6% compared with 18.5%) and to have Hispanic ethnicity (15.4% compared to 8.0%). The education level was also higher for uninfected men, over 85% of them had more than high school education while only above 75% of uninfected men went beyond high schools. Nearly all of the infected men were receiving HAART treatment (above 96%) and most of them had a CD_4 count more than 350 cells/mm^3 (93.4%). The prevalence of current smokers was higher among infected men (25.7%) compared with uninfected men (15.6%), but the prevalence of former smokers was slightly higher among HIV-infected men (52.3% compared with 44.6%). The prevalence of e-cigarettes use and NRT use both were higher among infected men (9.0% vs. 6.0% and 5.0% vs. 2.7%).

The current smoking prevalence in the MACS (by HIV infection status) and the general US population of adult men in 2015 and 2016 is shown in Figure 2. The prevalence of current smokers in HIV-infected men is depicted by the blue dots and corresponding 95% confidence intervals, and uninfected men depicted by the red dots. Gray dots represent the prevalence of current smokers in US adult men for the corresponding year. The prevalence of current cigarette smoking among US adult men was 16.7% in 2015 and 17.5% in 2016

(Jamal, 2018; Phillips, 2017). The prevalence among men without HIV was 15.7% and 16.1% for the two visits in 2015, respectively, and this was constant with the prevalence of US national adult men at 16.7%. The prevalence remained stable for year 2016 and 2017 (15.8%, 13.5%, 16.1%), also constant with the US national prevalence. However, the prevalence of smoking was higher among infected men, at 26.1% and 24.1% for 2015. The prevalence ranged from 23.0% to 25.1% in 2016 and 2017.

The prevalence of e-cigarettes smoking among all the participants is illustrated in Figure 3. Blue dots are for prevalence of e-cigarettes smoking among HIV-infected men, red dots for uninfected men and gray dots for US adult men in 2015. Overall, the prevalence was higher during April to September in 2015 (9.3% and 5.7%, for infected and uninfected men, respectively), which is the first time this question was added into the behavioral questionnaire, then it decreased and remained stable (between 5.2% and 6.7% for infected men; and between 3.1 and 4.7% for uninfected men). Men with HIV had a slightly higher prevalence, but the difference was not significant. The prevalence in this study was slightly higher than the prevalence in US male adults (4.3%) (Phillips, 2017). Among the e-cigarettes users, 73% were current smokers, 25% were former smokers, and 2% were never smokers.

Among the current smokers, the prevalence of ever e-cigarettes use was higher than the prevalence in all participants and in former smokers. The prevalence was about 20% in current smokers, 4% in former smokers, and very few for non-smokers, at about 0.3%. The prevalence is shown in Figure 4a and Figure 4b below. Prevalence of e-cigarettes smoking

among HIV-infected men is in blue and uninfected men in red. A similar pattern of change was seen in current smokers, with a higher prevalence for the first visit during April to September in 2015 (28.1% for infected men and 27.7% for uninfected men), then stably ranged from 15.6% to 19.7% for infected men and from 11.6% to 20.1% for uninfected men. Among former smokers, the prevalence of e-cigarettes use was stable, ranging from 2.7% to 3.8% for infected men, and from 2.0% to 2.6% for uninfected men. Again, the difference between infected and uninfected men were not significant.

Figure 5 compares the current and former smokers' cumulative pack-years (in the log scale) between ever e-cigarettes users vs. never e-cigarettes users. The median cumulative pack-years were greater for e-cigarettes users than the non-users. The difference in median cumulative pack-years between e-cigarette users and non-users ranged from 1.3 to 8 pack-years.

The prevalence of NRT use among current and former smokers is shown in Figure 6. Blue dots are for prevalence of NRT use among HIV-infected men, and red dots for uninfected men. Overall, the prevalence of NRT use ranged between 5.0% and 8.2% for infected men and between 3.5% and 4.6% for uninfected men. Infected men had a slightly higher but not significant higher prevalence then uninfected men. The prevalence of NRT use was consistent across time. Among the NRT users, 70.7% were current smokers and 26.8% were former smokers and 2.6% were never smokers.

Among current smokers, the prevalence of NRT use was higher than in former smokers. The prevalence was about 12% in current smokers and about 3% in former smokers. Figure 7a and 7b depict the prevalence and patterns. Prevalence of NRT use among HIV-infected men is in blue and uninfected men in red. For both current and former smokers, the prevalence did not change much during the study follow-up (Among current smokers: ranged from 10.6% to 17.3% for infected men; ranged from 9.2% to 12.9% for uninfected men. Among former smokers: ranged from 0.9% to 3.8% for infected men; ranged from 1.1% to 2.2% for uninfected men). Men living with HIV had a slightly higher prevalence of NRT use compared to uninfected men, but this difference was not significant.

Figure 8 shows the comparison of current and former smokers' cumulative pack-years between ever NRT users and never NRT users. The median cumulative pack-years were greater for NRT users than the non-users. The difference in median cumulative pack-years between NRT users and non-users ranged from 13.7 to 20.6 pack-years.

Table 2 summarizes the characteristics of ever e-cigarette users and never users and the potential risk factors. Among the 472 current smokers, 286 (60.1%) never reported using e-cigarettes and 186 (39.9%) ever reported using e-cigarettes during the follow-ups. Never e-cigarette users were older than ever users (median age= 55.1 vs. 49.4) and had higher education level. E-cigarette users had a higher proportion of less than high school education at 16.1%, compared to 11.0% for never e-cigarette users. They were similar in race, Hispanic ethnicity, seropositive proportion, detectable viral load, CD_4 count and cumulative pack-year. After adjusting for age, race, Hispanic ethnicity, education level,

serostatus, detectable viral load, CD_4 count and cumulative pack-years, the multivariate Poisson regression with robust variance showed that age, education level, HIV infection and cumulative pack years were significantly associated with initiation of e-cigarettes smoking. In the data, we observed a decrease in the cumulative incidence risk of initiating e-cigarettes smoking by 2% with one year increase in age (95% CI, 1%-3%). The cumulative incidence risk of initiating e-cigarette smoking increased by 46% for high school level men compared to men with 4 years' college and above (95% CI, 1%-210%), and increased by 1.55 times for men less than high school level education compared to men with 4 years' college and above (95% CI, 1.03- 2.35). Men with HIV have a 9% higher cumulative incidence risk than uninfected men (95% CI, 0.98-1.23). With 50% increase in cumulative pack-years, the cumulative incidence risk of e-cigarette use became 1.02 times greater (95% CI, 0.99-1.04).

The characteristics of ever NRT users and never users among current and former smokers and the potential risk factors are in Table 3. Among the 1501 former and current smokers, 1304 (86.9%) never reported using NRT and 197(13.1%) reported using NRT in at least one of the follow up visits. Never NRT users were older in age than ever users (median age=59.0 vs. 54.1). Ever users were more likely to be black (44.7% vs. 24.3%) but less Hispanic ethnicity (6.6% vs. 14.3%). Never users had a higher education level, with 78% more than high school level compared to 63% for ever users. The cumulative pack-years was significantly greater for those ever users (28.0 vs. 7.5). They were similar in seropositive proportion, detectable viral load, and CD_4 count. After adjusting for age, race, Hispanic ethnicity, education level, serostatus, detectable viral load, CD_4 count and

cumulative pack-years, the multivariate Poisson regression model with robust variance showed that age, black race, high school level education, HIV infection and cumulative pack-years were significantly associated with initiation of NRT use. The cumulative incidence risk of using NRT decreased by 5% with one year increase in age (95% CI, 3%-5%). Black men have a 32% higher cumulative incidence risk compared to white men (95% CI, 0%-73%). The cumulative incidence risk of NRT use increased by 48% for high school level men compared to men with 4 years' college and above (95% CI, 2%-215%). HIV infected men have 1.31 times the cumulative incidence risk than uninfected men (95% CI, 0.99-1.72). With 50% increase in cumulative pack-years, the cumulative incidence risk of NRT use was 1.13 times greater (95% CI, 1.09-1.16).

Discussion

This study reveals smoking behaviors and e-cigarettes and NRT use for men with high risk of HIV infection. Cigarettes smoking is more prevalent among HIV-infected men. E-cigarettes and NRT use are more common among current smokers. Very few never-smoked e-cigarettes and NRT users were captured in this study. A younger age, lower education level, HIV infection and longer cumulative pack-years are observed to be associated with e-cigarettes and NRT initiation. Future programs or policies regarding e-cigarettes or NRT behaviors among men with high risk of HIV infection should target to sub-populations with younger age, lower education level, HIV infection and greater smoking intensity.

The prevalence of current cigarette smoking among the uninfected men was similar to the prevalence in the US adult men, indicating that the uninfected men was a representative sample of smoking behaviors of the US adult men. Although the uninfected men in the

MACS study population was constructed mostly by men at high risk of HIV infection. The prevalence was higher among the infected men. The higher prevalence smoking might be explained by the higher prevalence of other risky behaviors including alcohol abuse and drug injection among HIV-seropositive men.

The prevalence of e-cigarette smoking among uninfected men was similar to the prevalence in the US adult men. HIV-infected men had a higher prevalence of e-cigarette smoking than the uninfected men and the US adult men. The prevalence of e-cigarette smoking was highest among current smokers. There was nearly no e-cigarette user among non-smokers in this study. A previous study reported that there was a notable portion of adolescent e-cigarettes users appeared to be never cigarette smokers, which means they started smoking with e-cigarettes instead of tradition cigarettes (Arrazola et al., 2015). However, we observed very few e-cigarette users among non-smokers here. This could be explained by the relative older population with an average age of more than 55 years at baseline in this study. Arrazola's study also revealed that the pattern of e-cigarettes use prevalence among adolescents and adults differed (Arrazola et al., 2015). E-cigarettes were introduced into US only after 2007. So the results from this study may not reflect the patterns in younger population. E-cigarettes users had a greater cumulative pack-years compared to non-users. These data from the MACS demonstrated that heavy smokers, as determined by cumulative pack years, were more likely to use e-cigarettes. They may have done so as a substitute for cigarette smoking or as a method to quit smoking, although these data were not collected.

NRT use was most common among current and former smokers. This is constant with the fact that NRT is mostly used as a method to stop smoking. We also notice that there were nine person-visits contributing from 8 persons that reported non-smokers and NRT use. We examined their other visits' data, the smoking status were constantly never smokers; seven of them reported NRT use only for one visits, and one person reported twice. It is highly possible to be a misclassification of NRT use. The analyses in this study were therefore performed only among current and former smokers. The prevalence of NRT use among infected and uninfected men were not significantly different in this study. The prevalence was higher among current smokers than former smokers. This concomitant use of NRT and cigarettes is worrisome since NRT products are not recommend to be used together with smoking or any other form of tobacco products. The results suggested that NRT users were more likely to be heavy smokers, as determined by cumulative pack years, than non-users. Also, NRT users had a longer cumulative pack years than the e-cigarette users. This makes sense since NRT are usually recommended to heavy smokers.

The risk factors associated with ever e-cigarette use and ever NRT use were similar.

Having a younger age, a lower level of education, infected with HIV, and a longer cumulative pack-years were associated with both the use of e-cigarettes and NRT. Black race is associated with NRT use only. The association between longer cumulative pack years and NRT use is understandable and is constant with a previous study (Shiffman, 2005). But Shiffman's study also revealed risk factors to be older age and better education, which are different from this study. This difference could be explained by the difference in study populations. NRT users was defined only as NRT users who were current smokers

and had made a quit attempt in Shiffman's study. While we included all e-cigarettes and NRT users regardless of quit attempt. Also, only men were included in this study while Shiffman's study included both sexes. So the difference in risk factors might have something to do with their pattern of NRT use, that is, whether they were use NRT together with cigarettes or only NRT to quit smoking. The association between young age and increase use of NRT and e-cigarettes might be explained by the relatively older population we have. The e-cigarettes and NRT are nicotine products that are relatively new. Younger people are more likely to accept new things and are more willing to do something to improve their health. The association between HIV infection and e-cigarettes/NRT use could be explained by the fact that HIV infected men are usually on regular medication and insurance plan. They are expose to more health improving information and are more motivated to quit or reduce the amount of smoking to improve their health condition. Men with lower education level are more likely to use e-cigarettes or NRT. This is because people with a lower education level usually have very limited access to other stop smoking assistance, such as individual counselling. E-cigarettes and NRT seem to be more accessible and affordable to them. Another interesting finding is that men with high school and less than high school education were more likely to use e-cigarettes, compared to men with higher than college level education. But only high school level education was associated with NRT use. This could be explained by the price difference. NRT are much more expensive than e-cigarettes. Less than high school education may limit the income level and therefore made NRT not affordable.

One of the strengths of this study is that MACS is a well-designed and well-conducted cohort with comprehensive information collected. This study utilized data from MACS consisting 2285 individuals and 2.5 years of follow-up time. With MACS study population being a representative sample of the MSM population, it is reasonable to say this study provided a good profile of the e-cigarettes and NRT use behaviors for the MSM population.

The limitations of this study are as follows: 1) There was no question about quit smoking attempts in the MACS questionnaires. We were therefore unable to address the association between e-cigarettes/NRT use and quit attempts. Although e-cigarettes users showed a higher smoking intensity than non-users, we were not able to identify whether they were using it as a substitute to cigarette smoking or as an assistance to quit smoking. 2) Questions regarding e-cigarettes and NRT use were added since 2015. There were only 5 visits afterwards, which leaves our follow-up time at 2.5 years. With such a short term follow-up, it is unlikely to capture any trend change in the prevalence of e-cigarettes and NRT use. 3) The risk factors included in this study is not a complete list of all possible factors due to the limitation of information collected. E-cigarettes and NRT are more expensive than traditional cigarettes so we think smokers' socioeconomic status and insurance plan might affect their behavior as well. Including more variables regarding socioeconomic status and insurance plan might be better than education level alone.

Conclusion

The prevalence of current smoking was higher for HIV-infected men than uninfected men. E-cigarettes and NRT use was mostly common among current smokers, the prevalence does not differ by HIV status. E-cigarettes and NRT users had a longer

cumulative pack-years compared to never users. Risk factors associated with both e-cigarettes and NRT use included younger age, lower education level, HIV infection and longer cumulative pack-years. Black race is associated with NRT use.

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Tables and figures

Table 1. Baseline characteristics (HIV-infected vs. uninfected men) (N=2285)

	Uninfected	Infected	p-value
Total	1072	1213	
Age (median, IQR)	60.3 (53.2, 67.0)	54.5 (46.0, 61.1)	<0.001
Race			<0.001
White	822 (76.7%)	738 (60.9%)	
Black	198 (18.5%)	366 (44.6%)	
Other [a]	52 (4.9%)	107 (8.8%)	
Hispanic ethnicity	86 (8.0%)	187 (15.4%)	<0.001
Education level			<0.001
4 years' college and above	655 (61.1%)	545 (44.9%)	
Some college	263 (24.5%)	378 (31.2%)	
High school (12^{th} grade)	117 (10.9%)	204 (16.8%)	
Less than high school	37 (3.5%)	86 (7.1%)	
On HAART	NA	1176 (96.9%)	
CD_4 < 350 cells/mm^3	NA	92 (7.6%)	
Smoking status			<0.001
Never smoked	330 (32.0%)	354 (29.6%)	
Former smoker	539 (52.3%)	532 (44.6%)	
Current smoker	161 (15.6%)	306 (25.7%)	
Ever used e-cigarettes since last visit	60 (6.0%)	103 (9.0%)	0.009
Used NRT since last visit	27 (2.7%)	57 (5.0%)	0.007

[a] American Indian, Alaskan Native, Asian, Pacific Islander, and others

Figure 1. Flow chart showing study populations in each analysis step.

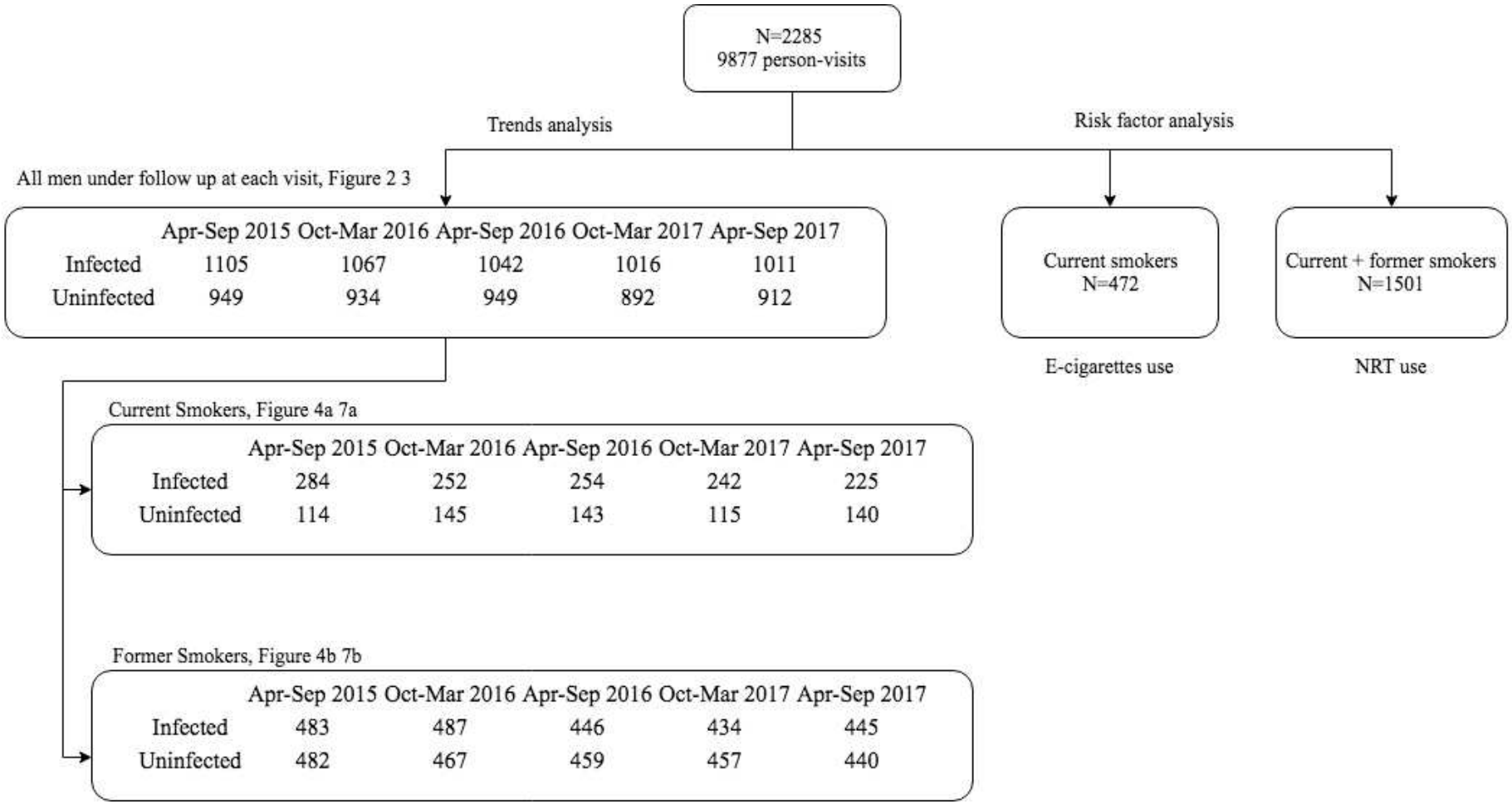

Figure 2. Prevalence of current smokers in MACS by visit, by serostatus

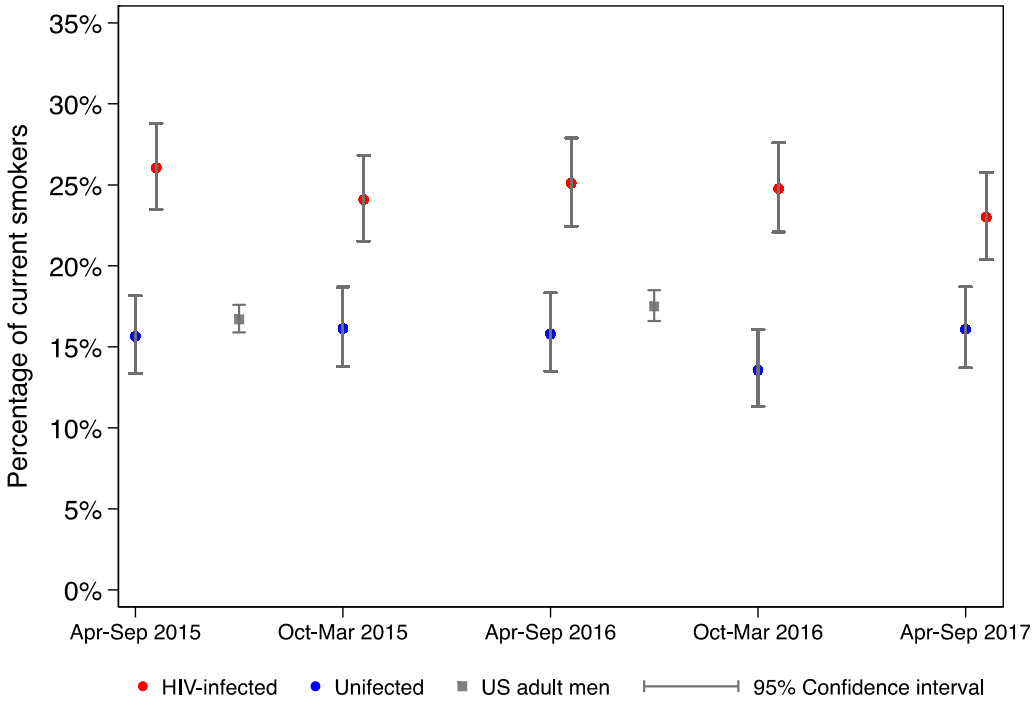

Figure 3. Prevalence of ever e-cigarettes users in MACS by visit, by serostatus

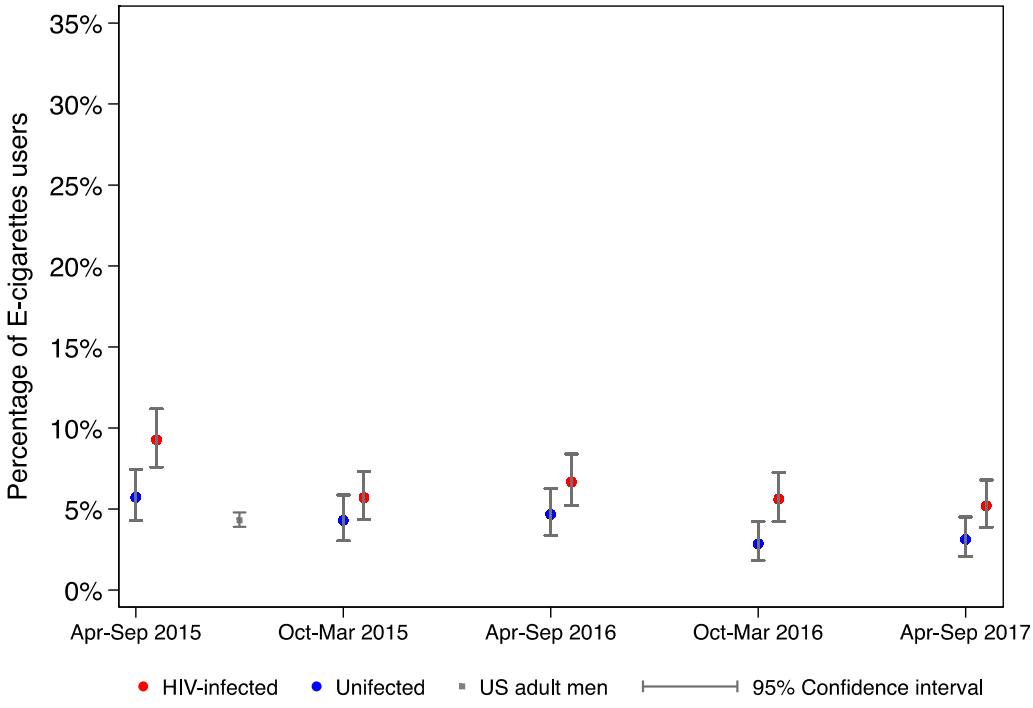

Figure 4a-b. Prevalence of ever E-cigarettes users among current smokers (left) and former smokers (right)in MACS by visit, by serostatus

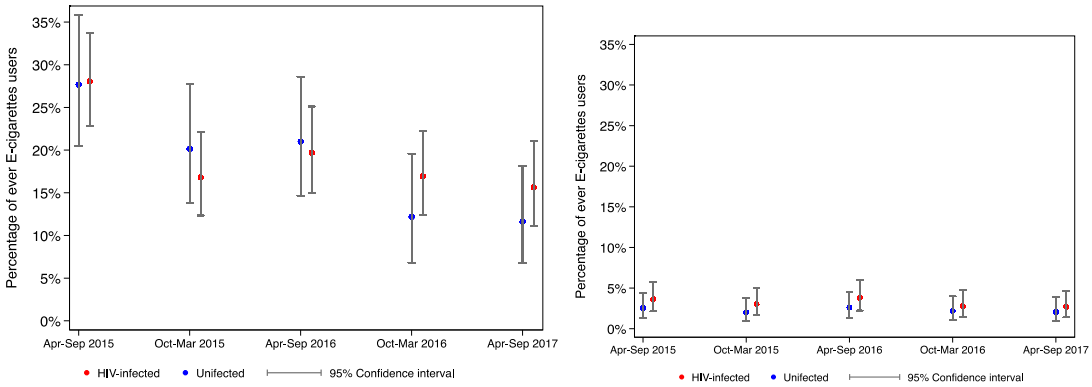

Figure 5. Cumulative pack-years among E-cigarettes users and non-users who are current and former smokers in MACS by visit

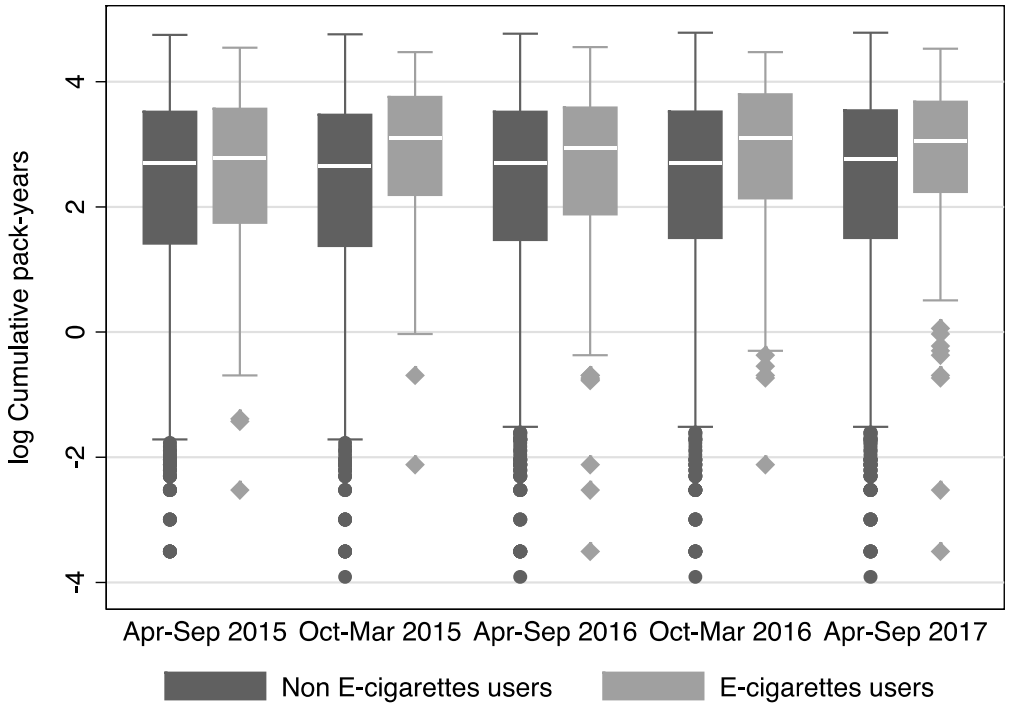

Figure 6. Prevalence of NRT use among current and former smokers in MACS by visit, by serostatus

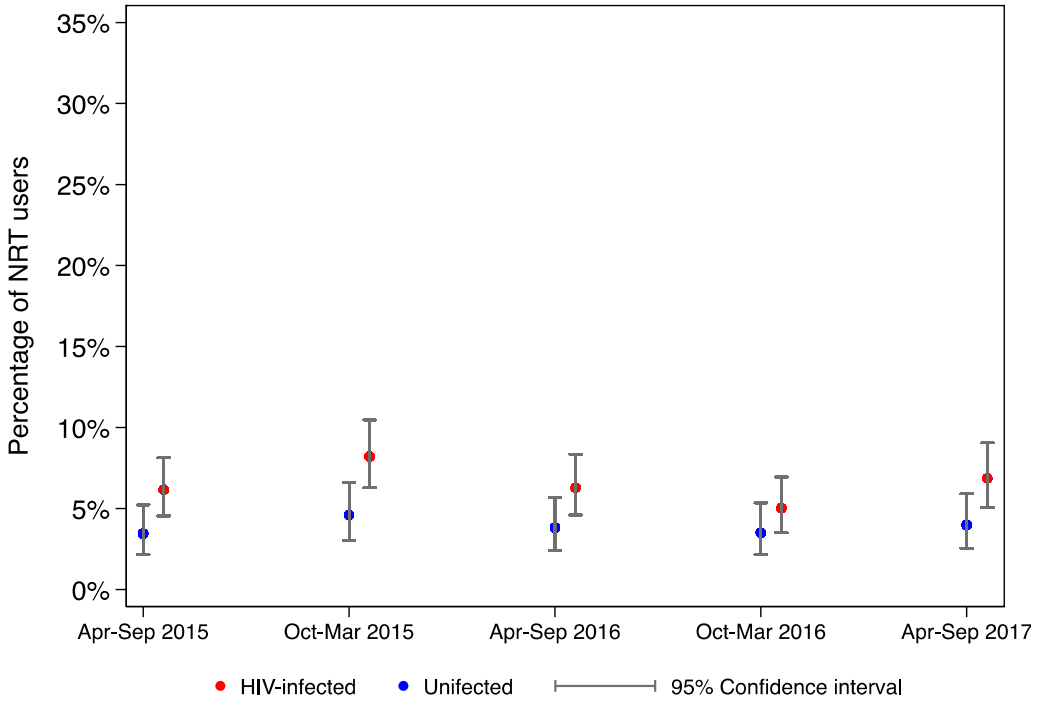

Figure 7a-b. Prevalence of NRT use among current smokers (left) and former smokers (right) in MACS by visit, by serostatus

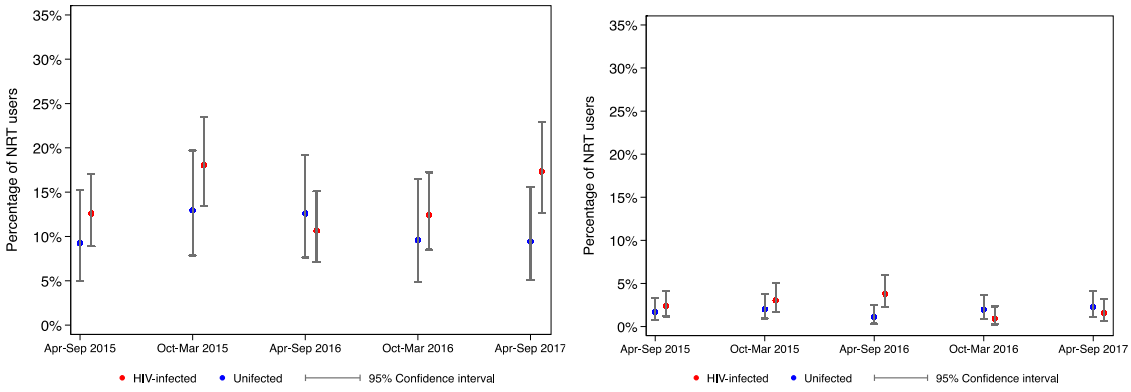

Figure 8. Cumulative pack-years among NRT users and non-users who are current or former smokers in MACS by visit

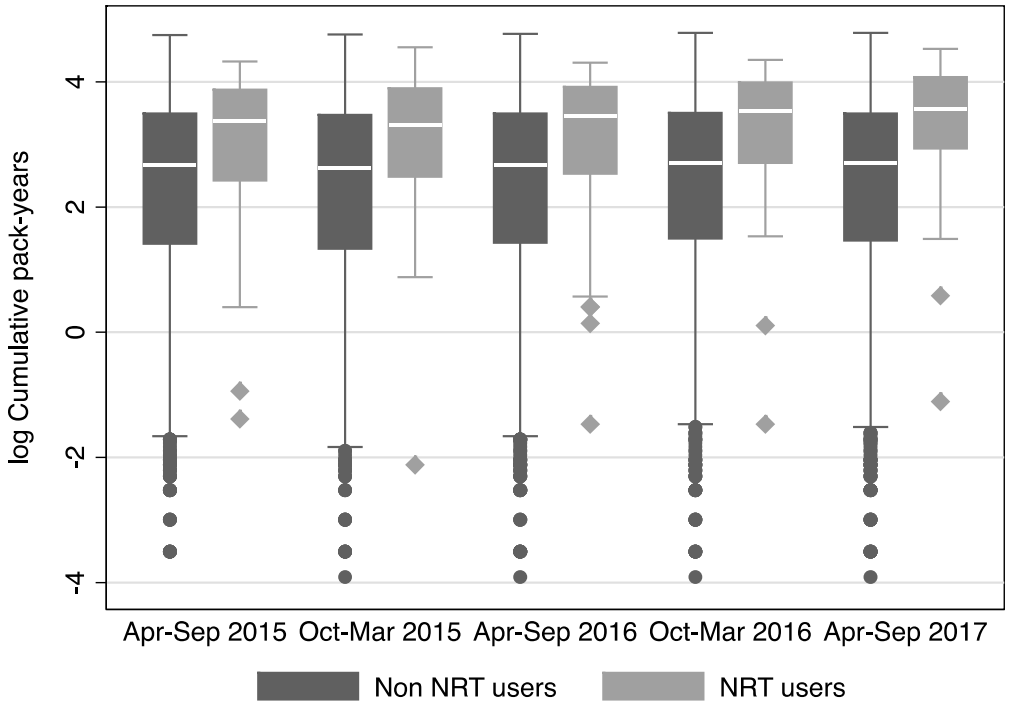

Table 2. Descriptive statistics of characteristics of E-cigarette users vs. non-users, among current smokers and their association with ever e-cigarette use based on univariate and multivariate Poisson regression models with robust variance. (N=472)

	Never E-cigarette users	Ever E-cigarette users	Univariate cumulative incidence risk ratio (RR) (95% CI)	Multivariate[b] cumulative incidence risk ratio (RR) (95% CI)
Total	282	186		
Age (median, IQR)	55.1 (45.9, 61.0)	49.4 (39.4, 56.0)	0.98**(0.97, 0.99)	**0.98** (0.97, 0.99)**
Race				
White	121 (43.1%)	82 (44.1%)	ref	ref
Black	141 (50.2%)	92 (49.5%)	0.98 (0.73, 1.32)	0.82 (0.64, 1.05)
Other [a]	19 (6.8%)	12 (6.5%)	0.96 (0.52, 1.76)	0.66(0.34, 1.27)
Hispanic ethnicity	26 (9.2%)	22 (11.8%)	1.17 (0.75, 1.83)	1.10 (0.71, 1.71)
Education level				
4 years' college and above	94 (33.3%)	37 (19.9%)	ref	ref
Some college	95 (33.7%)	67 (36.0%)	1.46 (0.98, 2.19)	1.26 (0.90, 1.76)
High school (12^{th} grade)	62 (22.0%)	52 (28.0%)	1.61* (1.06, 2.46)	**1.46* (1.01, 2.10)**
Less than high school	31 (11.0%)	30 (16.1%)	1.74* (1.08, 2.82)	**1.55* (1.03, 2.35)**
Seropositive	177 (62.8%)	126 (67.7%)	1.14 (0.84, 1.55)	**1.09 (0.98, 1.23)**
Detectable viral load [c]	177 (62.8%)	126 (67.7%)	0.80 (0.53, 1.21)	0.79 (0.50, 1.26)
Current CD_4 < 350 cells/mm^3 [c]	16 (5.7%)	10 (5.4%)	1.00 (0.53, 1.91)	1.07 (0.54, 2.14)
Cumulative pack-years, median (IQR)	19.9 (7.6, 41.5)	20.1 (6.8, 36.7)	0.99[d] (0.97, 1.01)	**1.02[d] (0.99, 1.04)**

[a] American Indian, Alaskan Native, Asian, Pacific Islander, and others

[b] Adjusted for age, race, Hispanic ethnicity, education level, serostatus, detectable viral load, CD_4 count and cumulative pack-years

[c] Restricted to men with HIV-infection, additionally adjust for detectable viral load and low CD_4 count

[d] Per 50% increase in cumulative pack-years

*p<0.05 **p<0.01

Table 3. Descriptive statistics of characteristics of NRT users vs. non-users, among current and former smokers and their association with ever e-cigarette use based on univariate and multivariate Poisson regression models with robust variances. (N=1051)

	Never NRT users	Ever NRT users	Univariate cumulative incidence risk ratio(RR) (95% CI)	Multivariate[b] cumulative incidence risk ratio(RR) (95% CI)
Total	1304	197		
Age (median, IQR)	59.0 (50.7, 66.0)	54.1 (47.2, 59.4)	0.98**(0.97, 0.99)	**0.95** (0.95, 0.97)**
Race				
White	884 (67.8%)	103 (52.3%)	ref	ref
Black	317 (24.3%)	88 (44.7%)	2.08** (1.57, 2.77)	**1.32* (1.00, 1.73)**
Other [a]	102 (7.8%)	6 (3.0%)	0.53 (0.23, 1.21)	0.59 (0.25, 1.36)
Hispanic ethnicity	186 (14.3%)	13 (6.6%)	0.46** (0.26, 0.81)	0.71 (0.38, 1.30)
Education level				
4 years' college and above	642 (49.2%)	54 (27.4%)	ref	ref
Some college	381 (29.2%)	70 (35.5%)	2.00** (1.40, 2.85)	1.36 (0.97, 1.91)
High school (12^{th} grade)	203 (15.6%)	51 (25.9%)	2.59** (1.77, 3.79)	**1.48* (1.02, 2.15)**
Less than high school	78 (6.0%)	22 (11.2%)	2.84** (1.73, 4.66)	1.36 (0.85, 2.16)
Seropositive	693 (53.1%)	132 (67.0%)	1.66** (1.24, 2.24)	**1.31 (0.99, 1.72)**
Detectable viral load [c]	99 (30.1%)	24 (24.0%)	0.80 (0.51, 1.27)	0.72 (0.44, 1.16)
Current CD_4 < 350 cells/mm^3 [c]	61 (4.7%)	11 (5.6%)	1.08 (0.58, 2.00)	1.19 (0.61, 2.34)
Cumulative pack-years, median (IQR)	7.5 (0.3, 26.3)	28.0 (11.8, 48.2)	1.07**[d] (1.04, 1.09)	**1.10**[d] (1.07, 1.14)**

[a] American Indian, Alaskan Native, Asian, Pacific Islander, and others

[b] Adjusted for age, race, Hispanic ethnicity, education level, serostatus, detectable viral load, CD_4 count and cumulative pack-years

[c] Restricted to men with HIV-infection, additionally adjust for detectable viral load and low CD_4 count

[d] Per 50% increase in cumulative pack-years

*p<0.05 **p<0.01

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