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**Do the associations between the use of Electronic Cigarettes and smoking reduction or cessation attempt persist after several years of use? Longitudinal analyses in smokers of the CONSTANCES cohort.**

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Conflicts of interest

GA has received speakers and/or consulting fees from Pfizer, Lundbeck and Pierre Fabre. ALLF has received speaker and consulting fees from Pfizer. CL has received speakers and/or consulting fees from Lundbeck, Boehringer Ingelheim, Janssen and Otsuka Pharmaceutical. FL has received speaker and/or consulting fees from AstraZeneca, Lundbeck, Janssen, Roche, Servier and Otsuka Pharmaceuticals. Other authors report no conflicts of interest.

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## **Abstract**

**Introduction.** We examined whether duration of electronic cigarette (e-cigarette) use could be associated with smoking reduction or cessation attempt.

**Methods.** 5,409 current smokers at baseline enrolled in the French CONSTANCES cohort in 2015 or 2016 were included. Duration of e-cigarette use was categorized as follows: never; former user for more than one year; former user for less than one year; new user for less than one year; return to use for less than one year; regular use for one to two years; regular use for more than two years. Two outcomes were considered at one-year of follow-up: change in the number of cigarettes per day and cessation attempt.

**Results.** Compared to never users, former users had an increase in the number of cigarettes per day at follow-up ( $B=0.95[95\%CI:0.57-1.33]$  and  $B=1.03[95\%CI:0.47-1.59]$  for former users of more than one year and less than one year, respectively). Compared to never users, all categories of current users had a decrease in the number of cigarettes per day ( $B=-3.31[95\%CI:-4.07;-2.54]$  and  $B=-4.18[95\%CI:-5.06;-3.29]$  for new users of less than one year and users of more than two years, respectively). Compared to never users, former users had a decreased likelihood of cessation attempt ( $OR=0.80[95\%CI:0.67-0.95]$  and  $OR=0.77[95\%CI:0.60-0.99]$  for former users of more than one year and less than one year, respectively). Compared to never users, all categories of current users had an increased likelihood of cessation attempt ( $OR=3.12[95\%CI:2.32;4.19]$  and  $OR=3.36[95\%CI:2.39;4.72]$  for new users of less than one year and users of more than two years, respectively).

**Conclusions.** E-cigarette use was associated with smoking reduction and cessation attempt for individuals who have used it for less than one year and additional benefits are expected to occur with a longer duration of use. Former users of e-cigarettes had poorer outcomes than those who have never used them.

## Introduction

Tobacco smoking remains the leading cause of premature death worldwide (Drummond & Upson, 2014). Alongside pharmacological treatments (Anthenelli, et al., 2016), electronic cigarettes have been developed in order to help smokers reduce or quit tobacco smoking (Etter, 2010; Shi, et al., 2016). These battery-powered devices vaporize a glycerol and propylene glycol-based liquid with or without nicotine at various concentrations and different flavors and are believed to be less toxic than conventional cigarettes. Electronic cigarettes are now used more frequently than pharmacological treatments to quit smoking in some countries (Adkison, et al., 2013; Adriaens, Van Gucht, Declerck, & Baeyens, 2014; Berlin, Nalpas, Targhetta, & Perney, 2019; Etter, 2010; Hartmann-Boyce, Begh, & Aveyard, 2018). In adult smokers, the use of electronic cigarettes is associated with a decreased number of cigarettes consumed per day and an increased likelihood of cessation attempt at follow-up in both randomized controlled studies (Adriaens, et al., 2014; Bullen, et al., 2013; S. H. Lee, Ahn, & Cheong, 2019; O'Brien, Knight-West, Walker, Parag, & Bullen, 2015) and observational studies (Brose, Hitchman, Brown, West, & McNeill, 2015; Etter & Bullen, 2014; Gomajee, et al., 2019), with a duration of follow-up ranging from 6 to 24 months. However, the length of time needed for the benefits of electronic cigarettes use on tobacco consumption to appear remains to be determined.

Indeed, a large number of patients don't quit smoking after they start using electronic cigarettes, so they use both (i.e. using conventional cigarettes and electronic cigarettes simultaneously). In fact, the prevalence of users of both electronic cigarettes and conventional cigarettes was near 60% in France in 2016 (Pasquereau A, 2017), and 41% in the US in 2018 (Owusu, et al., 2019). About half of the people who don't quit smoking after starting using electronic cigarettes keep on smoking at one year of follow-up (Owusu, et al., 2019). Although utilizing electronic cigarettes while smoking tobacco is thought to be a particularly harmful pattern of use (Bhatta & Glantz, 2020), it is unclear whether electronic cigarettes use remains associated with further smoking reduction and cessation attempt. In a prior study including 2,028 current smokers, using electronic cigarettes at both baseline and at two years of follow-up (*versus* only at baseline or only at follow-up) was associated with a higher chance of quitting smoking at follow-up (Giovenco & Delnevo, 2018; Zhuang, Cummins, Y Sun, & Zhu, 2016). Nevertheless, further longitudinal studies are needed to determine to length of time needed to observe a change in tobacco consumption after starting to use electronic cigarettes. Furthermore, studies need to examine whether these changes occur directly after starting to use electronic cigarettes (i.e. initiation for less than a year) or may be expected after a longer duration (i.e. initiation for more than two years). Moreover, it is also important to look at the changes in tobacco consumption in individuals with former electronic cigarettes use who start using it again. Finally, sociodemographic and clinical factors could moderate the association of electronic cigarettes on changes in tobacco consumption and need to be taken into consideration for information and prevention strategies (Chido-Amajuoyi, et al., 2020; Du, Shih, Shah, Weber, & Lightstone, 2019; J. E. Lee, Park, Chun, Park, & Kim, 2016; Lequy, et al., 2019; Wiernik, et al., 2019).

To address these issues, we took advantage of the French national population-based CONSTANCES cohort. Participants reported their smoking status and their electronic cigarettes use upon inclusion and at annual follow-ups. Duration of electronic cigarettes use was reported at baseline which permits the prospective assessment of changes in tobacco consumption as well as cessation attempts according to the duration of electronic cigarette use in a large sample of current smokers. If changes in tobacco consumption mostly occur in the first year of electronic cigarettes use, a greater reduction in tobacco consumption is expected in these participants than in those with a longer duration of electronic cigarettes use.

## **Material and methods**

### *Participants*

Since 2012, the CONSTANCES cohort has enrolled volunteers aged from 18 to 69 years at baseline according to a random sampling scheme stratified on age, gender, socioeconomic status and region of France (Goldberg, et al., 2017). Subjects completed annual self-administered questionnaires on their lifestyle, health, social, and personal characteristics. They were also invited to undergo an extensive health examination. CONSTANCES has obtained the authorization of the National Data Protection Authority (no. 910486) and was approved by the Institutional Review Board of the National Institute for Medical Research (no. 01-011). Informed consent was received from all of the subjects in the CONSTANCES cohort.

Established smokers were defined as those who had smoked at least 100 cigarettes over their lifetime at the time of inclusion in the cohort (World Health, 1998). These established smokers included both former smokers and current smokers. Questions regarding electronic cigarettes use were introduced in the baseline questionnaire in 2015 and, at the time of conducting this study, the most recent available follow-up data were in 2017. In the present study, we included the current daily smokers who were enrolled in the CONSTANCES cohort in 2015 and 2016 in order to allow for one-year of follow-up in the analyses (n=5,409) (**Supplemental Figure**).

### *Measurements of tobacco consumption and duration of electronic cigarette use*

Daily tobacco consumption was collected in number of cigarettes per day at both inclusion and at one year of follow-up. Change in tobacco consumption was defined as follows: the number of cigarettes per day at one-year of follow-up *minus* the number of cigarettes per day at baseline.

Reporting zero cigarettes per day at follow-up indicated a cessation attempt, whereas a consumption of one cigarette or more per day at follow-up was considered as a current use. Cessation attempt was consequently computed as a 'yes', 'no' variable.

Ever use of the electronic cigarette was assessed at baseline using the following question: "Have you ever smoked an electronic cigarette?". Distinction between current and former users was further obtained by the following two questions: "Are you currently using disposable electronic cigarettes?" or

"Are you currently using refillable electronic cigarettes?". Those who responded yes to at least one of these questions were classified as current electronic cigarette users. In former electronic cigarettes users at baseline, we had no information regarding the date on which they stopped using them or the duration of use. In current electronic cigarettes users at baseline, we were able to determine the duration of use before study enrollment by using the following question: "If you have ever used an electronic cigarette, for how many years did you do so?", with a binary answer as follows: "Less than one year" or "one year or more".

Based on the previous information, we were thus able to compute a categorical variable to define the electronic cigarette status at baseline as follows: never user, former user, regular user for less than one year, and regular user for more than one year. We had no data whether participants who declared using an electronic cigarette for more than one year had non-use periods since the initiation of their use.

Then, we used the questionnaire at one-year of follow-up to inform on the changes in the electronic cigarette status between baseline and follow-up, using the following question: "Do you currently use an electronic cigarette?".

Finally, based on both baseline and follow-up data, we computed a categorical variable reflecting the duration of electronic cigarette use as such: Never; Former for more than one year; Former for less than one year; New user for less than one year; Return to use for less than one year; Regular use for more than one year and less than two years; Regular use for more than two years.

#### *Covariables assessed at baseline*

##### Sociodemographic factors

Age and gender were self-reported in the baseline questionnaire. Marital status was defined as single or living with a partner.

Education level was based on the 2011 International Standard Classification of Education (Schneider, 2013), and categorized as four options: levels 0 to 2 (from early childhood education to lower secondary education); levels 3 and 4 (upper secondary education and post-secondary non-tertiary education), levels 5 and 6 (short-cycle tertiary education and Bachelor's or equivalent level), and levels 7 and 8 (Master's or equivalent level and Doctoral or equivalent level).

Household income was categorized into four possibilities: less than 2100 euros, between 2100 and 2800 euros, between 2800 and 4200 euros, and more than 4200 euros per month.

Education and household income were treated as continuous variables since we assumed that these two variables were ordinal representation of underlying sets of continuous units (i.e. years of education and amount of money in Euros per month, respectively) (Winship & Mare, 1984).

##### Clinical factors

Three clinical factors relating to addictive behaviors were considered in the analyses: 1) The number of pack-year (i.e. (number of cigarettes per day/20) × number of years as a current smoker), 2) The total score at the Alcohol Use Disorder Inventory Test (AUDIT) (Gache, et al., 2005) and 3) Cannabis use in the previous 12 months, computed as a 'yes', 'no' variable.

Depressive symptoms were assessed using the total score at the Center of Epidemiologic Studies Depression scale (CESD) (Morin, et al., 2011).

Participants with at least one of the following reported diseases during the medical exam: chronic bronchitis, emphysema, asthma, hypertension, angina pectoris or myocardial infarction were considered as having a respiratory or a cardiovascular disease. Participants with none of the listed conditions were considered disease-free.

Self-rated health was measured using the following question: «How do you judge your general health compared to a person of your entourage of the same age?», using a 8-point Likert scale from 1 (very good) to 8 (very poor) (Lequy, et al., 2019).

Perceived respiratory health was measured using the following question: "Overall, over the past 10 years, would you say that the condition of your airways and breathing (excluding age-related effects)?", with three possible answers: "has not changed", "has improved", and " has deteriorated". The first two categories were merged and perceived respiratory health was computed as a binary variable.

#### *Statistical analyses*

Change in the number of cigarettes per day (i.e., number of cigarettes per day at one-year of follow-up *minus* the number of cigarettes per day at baseline) was considered as the dependent variable in general linear regressions models. Residuals were checked for normality and that they were not correlated to one another. Binomial logistic regressions were used when cessation attempt was the dependent variable, with no cessation attempt being the reference category.

In both sets of analyses, the first model, called the minimally-adjusted model, adjusted for age, gender and baseline number of cigarettes per day. The second model, called the fully-adjusted model, was further adjusted for all the covariables.

In the second model of the general linear regression, estimated means of changes in number of cigarettes per day according to electronic cigarette duration of use were computed.

#### *Exploratory analyses*

Interactions between the duration of electronic cigarette use and all the covariables were tested, as well as the interaction between the number of cigarettes per day at baseline and the covariables when the number of cigarettes per day at follow-up was the dependent variable. Further stratification was made in case of a significant interaction.

#### *Sensitivity analyses*

Sensitivity analyses were performed by re-conducting the general linear regressions among participants who were still smokers at follow-up (i.e. current smokers at follow-up irrespective of their use of electronic cigarettes,  $n = 3,977$ ), in order to examine whether the observed associations in the entire sample could be driven only by those with a cessation attempt.

Included subjects had complete data for the variables of interest, i.e., tobacco consumption at both baseline and follow-up and duration of electronic cigarette use at baseline. Except for age, gender and



prior quit attempt, we had missing data for the other covariables (mean percentage of missing data of 4.5%, ranging from 0.9% to 9.4%). Assuming a missing at random mechanism, we used stochastic regression imputations rather than complete-case analysis to limit the risk of selection bias (Newgard & Haukoos, 2007).

Statistical significance was determined using a two-sided alpha a priori set at 0.05 for both main analyses and exploratory analyses. These analyses were performed with IBM Statistics for Windows, Version 22.0, Released 2013 (Armonk, NY: IBM Corp).

## Results

### *Participants' characteristics*

The characteristics of the 5,409 included participants according to the duration of electronic cigarettes use are displayed in **Table 1**. Mean change in the number of cigarettes per day at follow-up was of -3.1 (SD=6.6). A total of 1,432 (26.5%) participants had a cessation attempt by one year of follow-up.

### *Change in tobacco consumption according to the duration of electronic cigarettes use*

Estimated parameters of the changes in tobacco consumption at one year of follow-up according to the duration of electronic cigarettes use are presented in **Table 2**.

Compared to participants who have never used electronic cigarettes, being a former user was associated with an increase in the number of cigarettes per day irrespective of the time elapsed since they stopped using electronic cigarettes (i.e. for less or for more than one year). In fully-adjusted model, estimated parameters were  $B = 0.95$  [95%CI: 0.57; 1.33] and  $B = 1.03$  [95%CI: 0.47; 1.59] regarding former users for more than one year and less than one year, respectively.

All electronic cigarettes users, whatever the length of time they have been using them, and including those who start using them again after a period of discontinuation, had a decrease in the number of cigarettes per day. In fully-adjusted model, estimated parameters were  $B = -3.31$  [95%CI: -4.07; -2.54] and  $B = -4.18$  [95%CI: -5.06; -3.29] for new users for less than one year and for more than two years, respectively.

Estimated means of change in the number of cigarettes per day are presented in **Figure 1**. Participants who have used electronic cigarettes for more than two years had a significant decrease in the number of cigarettes per day compared to those who used their electronic cigarette for one to two years (mean difference of -1.60 [95%CI: -2.82; -0.37],  $p=0.011$ ).

In exploratory analyses, we found interactions between the duration of electronic cigarettes use and the following four covariables: gender ( $p=0.011$ ), marital status ( $p=0.042$ ), packages-year ( $p<0.001$ ) and baseline number of cigarettes per day ( $p<0.001$ ). For baseline number of cigarettes per day, the interaction was also significant with the number of cigarettes per day at follow-up as the dependent variable ( $p<0.001$ ). Overall, a greater reduction in the number of cigarettes per day was found in men, in those living with a partner, having a higher number of pack-years and a higher number of cigarettes per day (**Supplemental Table 1**).

### *Likelihood of cessation attempt according to the duration of electronic cigarettes use*

Odds ratios of cessation attempt at one year of follow-up according to duration of electronic cigarettes use are presented in **Table 3**.

Compared to participants who have never used electronic cigarettes, being a former user was associated with a decreased likelihood of cessation attempt, irrespective of the time elapsed since they stopped using electronic cigarettes. In the fully-adjusted model, OR = 0.80 [95%CI: 0.67; 0.95] and OR = 0.77 [95%CI: 0.60; 0.99] for former users of less and more than one year, respectively.

All electronic cigarettes users, whatever the length of time they have been using them, and including those who start using them again after a period of discontinuation, had an increased likelihood of cessation attempt. In fully-adjusted model, OR = 3.12 [95%CI: 2.32; 4.19] and OR = 3.36 [95%CI: 2.39; 4.72] for new user of less than one year and more than two years, respectively. No statistical differences were found between the different categories of users when switching the category of reference from never to new user of less than one year (all  $p > 0.05$ ).

In exploratory analyses, we found interactions between the duration of electronic cigarettes use and the following four covariables: education ( $p=0.029$ ), marital status ( $p=0.021$ ), pack-year ( $p=0.001$ ) and baseline number of cigarettes per day ( $p=0.004$ ). Overall, ORs were higher in those with lower education, living with a partner and having a higher number of pack-years (**Supplemental Table 2**).

### *Sensitivity analyses*

The analyses of participants who were still smokers at follow-up (i.e. a positive number of cigarettes per day) are presented in **Supplemental Table 3**. In both sets of adjustments (i.e. minimally-adjusted and fully-adjusted), and for all categories of electronic cigarettes current use, the associations remained significant and in the same directions than in the main analyses.

## **Discussion**

This study aimed to examine whether the duration of electronic cigarettes use could be associated with a decreased tobacco consumption and an increased likelihood of cessation attempt at one year of follow-up in current smokers. Positive associations were observed in a duration of use of less than one year to more than two years, even after adjusting for potential confounders. In addition, returning to electronic cigarette use after a period of discontinuation was associated with similar benefits. However, individuals who had past electronic cigarettes use and have not started using them again, i.e. former users who remained as such, had the poorest outcomes with regards to tobacco consumption, irrespective of the time elapsed since they stopped using electronic cigarettes. In exploratory analyses, better outcomes were found in men, in those with lower level of education, living with a partner and having a higher number of pack-years.

The benefits of electronic cigarettes in the first year of their initiation that were found in our study are in line with prior literature, which already observed such benefits at 6-month (Bullen, et al., 2013; S. H. Lee, et al., 2019; Pasquereau, Guignard, Andler, & Nguyen-Thanh, 2017) and at one-year of follow-up (Brose, et al., 2015). However, a study by Zhuang et al. has not perceived such findings most probably

because the group of electronic cigarette users in their study included both new and former users (Zhuang, et al., 2016). Indeed, our results suggest that these groups display opposite patterns. Our findings also extend prior literature by showing that the benefits of electronic cigarettes use on smoking outcomes could be observed in both new users and those who start using them again after a period of discontinuation. In addition, further benefits are to be expected with a longer duration of electronic cigarettes use (i.e. a duration of more than one year and at least for up to two years). We believe that our results add complementary information compared to the potential harm of a dual use (i.e. using conventional cigarettes and electronic cigarettes simultaneously) when it does not result in tobacco cessation. Indeed, our findings might mitigate this position, since a continuous use of electronic cigarettes among smokers might ultimately increase the likelihood of tobacco cessation as suggested by further reduction in the number of cigarettes per day observed over time. Should these benefits continue for several years, it could eventually lead to tobacco cessation (Meneton, et al., 2018). As a matter of fact, our findings do suggest that the rate of tobacco cessation could increase over time among electronic cigarettes users. Furthermore, a duration of electronic cigarettes use for more than one year could reflect a greater motivation for smoking cessation while motivation for smoking cessation has been found to be associated with better outcomes among electronic cigarettes users (Vickerman, et al., 2017). A prolonged duration of use of electronic cigarettes may also be helpful to better alleviate the desire to smoke and withdrawal symptoms (Dawkins, Turner, Hasna, & Soar, 2012). In addition, some patients need time to learn how to use an electronic cigarette to successfully replace smoking (Hartmann-Boyce, et al., 2018). However, since comparable benefits were observed for both users for less and more than one year, longitudinal studies with more time points are needed to examine whether the likelihood of long-term use is associated with short-term benefits. Finally, exploratory analyses showed higher benefits on smoking outcomes in several subgroups. Regarding men and those living with a partner, these results are in line with prior findings showing that women could have more difficulty quitting smoking than men after a given cessation attempt (Rehm, et al., 2008), and that being married could be associated with an increased likelihood of smoking cessation (Frone, 2019; Hajek, et al., 2019; Martínez, et al., 2019). Our results also show that those with a higher number of pack-year and a lower education had higher benefits of using electronic cigarettes on their smoking outcomes. This knowledge would be of particular interest since belonging to one of these subgroups is usually associated with poorer outcomes (Holm, et al., 2017; Honjo, Iso, Inoue, Tsugane, & Group, 2010). Thus, further studies are needed to confirm whether using electronic cigarettes could present additional benefits in these subgroups and, if so, to understand the mechanisms underlying these associations.

Poorer outcomes were found in former electronic cigarettes users compared to individuals who have never used them. This result is in accordance with a prior cross-sectional study that found a decreased likelihood of smoking cessation among former electronic cigarette users (Giovenco & Delnevo, 2018). This finding might be explained by a transitory feeling of discouragement among former users, leading to lower successful rates. However, in the present study, poorer outcomes were also found in former electronic cigarette users of more than one year. Stopping electronic cigarette

after a smoking cessation failure could lead to increased tobacco consumption as a compensatory behavioral/biological mechanism in relation to nicotine dependence. This could explain, at least partially, the negative results of prior studies that examined smoking outcomes without distinguishing between former and current users of electronic cigarettes (Grana, Popova, & Ling, 2014; Manzoli, et al., 2015). Thus, our findings suggest the need to pay a particular attention to smokers who have stopped using electronic cigarettes, since they could experience an increase in tobacco consumption (Balmford, Borland, Hammond, & Cummings, 2010). At least when the liquid contains nicotine, stopping electronic cigarettes use may be associated with nicotine withdrawal symptoms that may be alleviated by increasing the number of cigarettes per day. Thus, after electronic cigarettes cessation, switching rapidly to validated treatments such as NRT and promoting self-efficacy may be particularly useful (Blevins, Farris, Brown, Strong, & Abrantes, 2016).

Our study presents some strength. The correlates of the duration of electronic cigarettes use on changes in tobacco consumption and cessation attempts were examined prospectively, in a large population-based cohort. Moreover, we took into consideration a broad range of clinical and sociodemographic variables to search for confounding effects and to identify potential moderators. However, this study has also some limitations. First, the CONSTANCES cohort is not representative of the general population due to selection effects associated with voluntary participation at inclusion and attrition at follow-up. Second, the observational nature of our study limits us from drawing causality. Even though the results were adjusted for several confounders, residual confounding cannot be ruled out. Third, the duration of electronic cigarettes use as well as former use for more than one year were self-reported retrospectively at baseline and we had no information about periods of discontinuation in tobacco smoking or electronic cigarettes use between the annual assessments. Thus, some smoking cessation attempts may have not been recorded. However, we have no reason to believe that it might influence our conclusions, but only by underestimating the strength of the associations. Fourth, searching for moderating effects of all the covariables leads to an inflation of the alpha risk. The aim of these analyses was exploratory, so the significance threshold was kept at a p-value below 0.05. Thus, these results need to be further confirmed in future studies. Fifth, the role of pharmacological treatments was not examined. Lastly, new models of electronic cigarettes have been marketed and may have better positive effects on smoking outcomes.

## **Conclusions**

Our findings showed that electronic cigarettes use may be associated with a decreased tobacco consumption and an increased likelihood of cessation attempts in those who have used them for less than one year, whether they are new users or have started using electronic cigarettes again. Additional benefits on these smoking outcomes can probably be expected in the case of longer electronic cigarette use, i.e., for more than one year and at least for up to two years. Benefits of electronic cigarettes use may be greater among subgroups that are difficult to treat such as individuals with a higher level of dependence and a lower education level (Holm, et al., 2017). However, stopping electronic cigarettes use may be associated with increased tobacco consumption. Future studies

comparing the effectiveness of electronic cigarettes use *versus* pharmacological treatments will be helpful to clarify whether these devices can be associated with better smoking outcomes in a personalized medicine approach (Berlin, Dautzenberg, et al., 2019; Hajek, et al., 2019). Furthermore, it would be also helpful to assess which of these different strategies might be most likely to lead to the cessation of all nicotine-containing substances (Martínez, et al., 2019).

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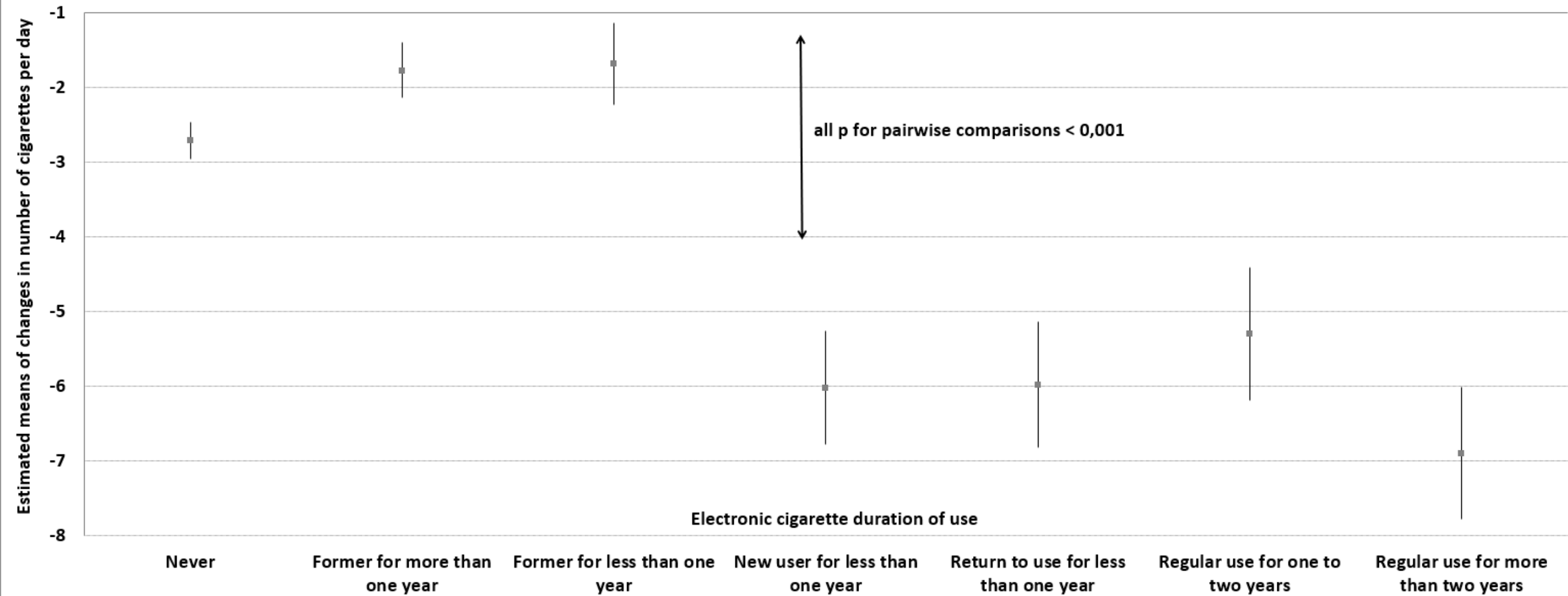
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# Estimated means of changes in tobacco consumption at one-year according to the duration of use of electronic cigarette and adjusting for sociodemographic and clinical factors among 5,409 smokers at baseline.



**Table 1. Characteristics of the 5,409 included participants.**

	Electronic cigarette duration of use							
	Total	Never	Former for more than one year	Former for less than one year	New user for less than one year	Return to use for less than one year	Regular use for one to two years	Regular use for more than two years
<b>N(%)</b>	5409(100)	3169(58.6)	1106(20.4)	437(8.1)	214(4.0)	171(3.2)	154(2.8)	158(2.9)
<b>CONTINUOUS VARIABLES (M(SD))</b>								
Age	42.9(13.1)	43.9(13.3)	40.5(13.0)	41.6(12.9)	44.5(11.3)	39.9(12.3)	43.0(10.8)	43.9(11.6)
Number of cigarettes per day	10.3(7.0)	8.9(6.8)	11.7(6.6)	12.4(7.2)	11.7(7.1)	13.2(6.7)	12.9(8.4)	13.2(6.7)
Number of pack-year <sup>1</sup>	11.8(11.8)	10.6(11.3)	12.9(11.9)	13.8(12.5)	13.4(11.6)	13.7(13.1)	14.1(13.0)	16.1(13.4)
Total AUDIT score	6.4(4.6)	6.3(4.4)	6.6(4.7)	6.8(5.4)	6.0(4.3)	7.0(5.3)	6.1(4.5)	6.9(4.7)
Total CESD score	15.5(6.4)	15.0(6.2)	15.9(6.3)	16.8(7.1)	15.3(6.6)	17.0(7.4)	16.1(7.1)	15.5(6.7)
Perceived global health status <sup>2</sup>	3.0(1.4)	2.9(1.4)	3.0(1.4)	3.2(1.6)	3.2(1.5)	3.4(1.5)	3.2(1.6)	3.1(1.6)
<b>CATEGORICAL VARIABLES (N, %)</b>								
Men	2588(47.8)	1496(47.2)	517(46.7)	218(49.9)	111(51.9)	81(47.4)	67(43.5)	98(62.0)
Education <sup>3</sup>								
0 to 2	418(7.7)	238(7.5)	77(7.0)	41(9.4)	27(12.6)	12(7.0)	10(6.5)	13(8.2)
3 and 4	1096(35.2)	1092(34.5)	412(37.3)	134(30.7)	93(43.5)	61(35.7)	50(32.5)	54(34.2)
5 and 6	1925(35.6)	1116(35.2)	400(36.2)	160(36.6)	59(27.6)	66(38.6)	65(42.2)	59(37.3)
7 and 8	1170(21.6)	723(22.8)	217(19.6)	102(23.3)	35(16.4)	32(18.7)	29(18.8)	32(20.3)
Household income in Euros								
Less than 2100	1619(29.9)	886(28.0)	357(32.3)	155(35.5)	73(34.1)	62(36.3)	44(28.6)	42(26.6)
Between 2100 and 2800	990(18.3)	562(17.7)	224(20.3)	68(15.6)	45(21.0)	34(19.9)	26(16.9)	31(19.6)
Between 2800 and 4200	1594(29.5)	942(29.7)	327(29.6)	127(29.1)	51(23.8)	47(27.5)	47(30.5)	53(33.5)
More than 4200	1206(22.3)	779(24.6)	198(17.9)	87(19.9)	45(21.0)	28(16.4)	37(24.0)	32(20.3)
Living with a partner	3202(59.2)	1931(60.9)	617(55.8)	241(55.1)	131(61.2)	94(55.0)	93(60.4)	95(60.1)
Existence of a prior quit attempt	3683(68.1)	2048(64.6)	794(71.8)	333(76.2)	136(63.6)	132(77.2)	116(75.3)	1242(78.5)
Cannabis use in the previous 12 months	1486(27.5)	837(26.4)	336(30.4)	136(31.1)	41(19.2)	53(31.0)	42(27.3)	41(25.9)
Respiratory and cardiovascular diseases	1091(20.2)	597(18.8)	230(20.8)	96(22.0)	58(27.1)	41(24.0)	25(16.2)	44(27.8)
Poorer perceived respiratory health <sup>4</sup>	2306(42.6)	1176(37.1)	581(52.5)	223(51.0)	88(41.1)	105(61.4)	76(49.4)	62(39.2)

N: Number of subjects; M: mean; SD: Standard Deviation; AUDIT: Alcohol Use Disorder Identification Test; CESD: Center for Epidemiologic Studies Depression Scale; <sup>1</sup> Defined as follows: (number of cigarettes per day/20) × (years as a current smoker); <sup>2</sup> Measured on a 8-points Likert scale from 1 (very good) to 8 (very poor); <sup>3</sup> Based on the 2011 International Standard Classification of Education; <sup>4</sup> Reporting of a deterioration compared to no change or an improvement.

**Table 2. Estimates and 95%CI for the change in tobacco consumption at 1-year according to electronic cigarette duration of use (N=5,409).**

	B <sup>1</sup>	95%CI		p
		min	max	
<b>MINIMALLY-ADJUSTED MODEL<sup>2</sup></b>				
Never	Ref	.	.	.
Former for more than one year	<b>0.97</b>	<b>0.57</b>	<b>1.36</b>	<b>&lt;0.001</b>
Former for less than one year	<b>0.92</b>	<b>0.35</b>	<b>1.50</b>	<b>0.002</b>
New user for less than one year	<b>-3.27</b>	<b>-4.01</b>	<b>-2.48</b>	<b>&lt;0.001</b>
Return to use for less than one year	<b>-3.33</b>	<b>-4.21</b>	<b>-2.45</b>	<b>&lt;0.001</b>
Regular use for one to two years	<b>-2.80</b>	<b>-3.72</b>	<b>-1.87</b>	<b>&lt;0.001</b>
Regular use for more than two years	<b>-4.41</b>	<b>-5.32</b>	<b>-3.50</b>	<b>&lt;0.001</b>
<b>FULLY-ADJUSTED MODEL<sup>3</sup></b>				
Never	Ref	.	.	.
Former for more than one year	<b>0.95</b>	<b>0.57</b>	<b>1.33</b>	<b>&lt;0.001</b>
Former for less than one year	<b>1.03</b>	<b>0.47</b>	<b>1.59</b>	<b>&lt;0.001</b>
New user for less than one year	<b>-3.31</b>	<b>-4.07</b>	<b>-2.54</b>	<b>&lt;0.001</b>
Return to use for less than one year	<b>-3.27</b>	<b>-4.12</b>	<b>-2.41</b>	<b>&lt;0.001</b>
Regular use for one to two years	<b>-2.58</b>	<b>-3.48</b>	<b>-1.69</b>	<b>&lt;0.001</b>
Regular use for more than two years	<b>-4.18</b>	<b>-5.06</b>	<b>-3.29</b>	<b>&lt;0.001</b>

<sup>1</sup> Estimated parameter of change in tobacco consumption computed as follows: number of cigarettes per day at follow-up minus number of cigarettes per day at baseline; <sup>2</sup> Adjusted for age, gender and number of cigarettes per day at baseline; <sup>3</sup> Adjusted also for education, household income, marital status, pack-year, total score at the alcohol use disorder identification test, total score at the center for epidemiologic studies depression scale, existence of respiratory or cardiovascular disease, perceived global health status and perceived respiratory health status. Significant results are presented in bold.

**Table 3. Odds ratios of cessation attempt at one-year according to electronic cigarette duration of use (N= 5,409).**

	OR <sup>1</sup>	95%CI		p
		min	max	
<b>MINIMALLY-ADJUSTED MODEL<sup>2</sup></b>				
Never	Ref	.	.	.
Former for more than one year	<b>0.81</b>	<b>0.69</b>	<b>0.97</b>	<b>0.019</b>
Former for less than one year	0.82	0.64	1.06	0.133
New user for less than one year	<b>2.91</b>	<b>2.19</b>	<b>3.87</b>	<b>&lt;0.001</b>
Return to use for less than one year	<b>2.20</b>	<b>1.59</b>	<b>3.04</b>	<b>&lt;0.001</b>
Regular use for one to two years	<b>2.22</b>	<b>1.58</b>	<b>3.12</b>	<b>&lt;0.001</b>
Regular use for more than two years	<b>3.61</b>	<b>2.59</b>	<b>5.02</b>	<b>&lt;0.001</b>
<b>FULLY-ADJUSTED MODEL<sup>3</sup></b>				
Never	Ref	.	.	.
Former for more than one year	<b>0.80</b>	<b>0.67</b>	<b>0.95</b>	<b>0.012</b>
Former for less than one year	<b>0.77</b>	<b>0.60</b>	<b>0.99</b>	<b>0.047</b>
New user for less than one year	<b>3.12</b>	<b>2.32</b>	<b>4.19</b>	<b>&lt;0.001</b>
Return to use for less than one year	<b>2.13</b>	<b>1.53</b>	<b>2.98</b>	<b>&lt;0.001</b>
Regular use for one to two years	<b>2.14</b>	<b>1.51</b>	<b>3.03</b>	<b>&lt;0.001</b>
Regular use for more than two years	<b>3.36</b>	<b>2.39</b>	<b>4.72</b>	<b>&lt;0.001</b>

<sup>1</sup> Odd Ratio of qui attempt; <sup>2</sup> Adjusted for age, gender and number of cigarettes per day at baseline; <sup>3</sup> Adjusted also for education, household income, marital status, pack-year, total score at the alcohol use disorder identification test, total score at the center for epidemiologic studies depression scale, existence of respiratory or cardiovascular disease, perceived global health status and perceived respiratory health status. Significant results are presented in bold.