



# HHS Public Access

Author manuscript

*Drug Alcohol Depend.* Author manuscript; available in PMC 2016 June 24.

Published in final edited form as:

*Drug Alcohol Depend.* 2015 February 1; 147: 68–75. doi:10.1016/j.drugalcdep.2014.12.007.

## Dependence levels in users of electronic cigarettes, nicotine gums and tobacco cigarettes

Jean-François ETTER, PhD<sup>1</sup> and Thomas EISSENBERG, PhD<sup>2</sup>

<sup>1</sup>Institute of Global Health, Faculty of Medicine, University of Geneva, Switzerland <sup>2</sup>Center for the Study of Tobacco Products, Dept. of Psychology, Virginia Commonwealth University, Richmond, VA, USA

### Abstract

**Objective**—To assess dependence levels in users of e-cigarettes, and compare them with dependence levels in users of nicotine gums and tobacco cigarettes.

**Design**—Self-reports from cross-sectional Internet and mail surveys. Comparisons of: a) 766 daily users of nicotine-containing e-cigarettes with 30 daily users of nicotine-free e-cigarettes; b) 911 former smokers who used the e-cigarette daily with 451 former smokers who used the nicotine gum daily (but no e-cigarette); c) 125 daily e-cigarette users who smoked daily (dual users) with two samples of daily smokers who did not use e-cigarettes (2206 enrolled on the Internet and 292 enrolled by mail from the general population of Geneva). We used the Fagerström Test for Nicotine Dependence, the Nicotine Dependence Syndrome Scale, the Cigarette Dependence Scale and versions of these scales adapted for e-cigarettes and nicotine gums.

**Results**—Dependence ratings were slightly higher in users of nicotine-containing e-cigarettes than in users of nicotine-free e-cigarettes. In former smokers, long-term (>3 months) users of e-cigarettes were less dependent on e-cigarettes than long-term users of the nicotine gum were dependent on the gum. There were few differences in dependence ratings between short-term (<=3 months) users of gums or e-cigarettes. Dependence on e-cigarettes was generally lower in dual users than dependence on tobacco cigarettes in the two other samples of daily smokers.

**Conclusions**—Some e-cigarette users were dependent on nicotine-containing e-cigarettes, but these products were less addictive than tobacco cigarettes. E-cigarettes may be as or less addictive than nicotine gums, which themselves are not very addictive.

---

**Correspondence:** Jean-François Etter. Institute of Global Health, University of Geneva, CMU, case postale, CH-1211 Geneva 4, Switzerland. +41.22.379.04.59. Fax +41.22.379.04.52. Jean-Francois.Etter@unige.ch.

#### Contributors

Both authors contributed to the design of the study, writing of the manuscript and interpretation of the data. JFE led the data collection and data analysis. Both authors have approved the final article.

#### Conflict of Interest

JFE was reimbursed by Dekang, a manufacturer of e-cigarettes and e-liquids for traveling to London and to China, to visit e-cigarette factories, but he received no honoraria for these meetings.

JFE's salary is paid by the University of Geneva.

TE: No competing interests.



## Keywords

Electronic Cigarette; Electronic Nicotine Delivery Devices (ENDS); Smoking; Nicotine; Dependence; Addiction; Internet Survey

---

## 1. INTRODUCTION

Electronic cigarettes (e-cigarettes) are increasingly popular (Hajek, Etter et al. 2014). E-cigarettes do not contain tobacco, but a liquid made of propylene glycol, glycerol, flavours, and most of the time nicotine. The liquid is heated electrically to produce a vapour for inhalation.

While there is considerable variability across products and individuals, some users are able to obtain substantial amounts of nicotine from e-cigarettes (Etter and Bullen 2011, Vansickel and Eissenberg 2013, Dawkins and Corcoran 2014, Etter 2014, Nides, Leischow et al. 2014). In many cases, plasma nicotine concentration after e-cigarette use is similar or higher than the concentration seen in users of nicotine replacement medications and, in some cases, it approaches that seen after tobacco cigarette smoking (Etter and Bullen 2011, Vansickel and Eissenberg 2013, Dawkins and Corcoran 2014, Etter 2014, Nides, Leischow et al. 2014, Spindle, Breland et al. 2014). The speed of nicotine delivery to the blood may be slower for e-cigarettes than for tobacco cigarettes, but is certainly similar to or faster than for nicotine medications (Choi, Dresler et al. 2003, Bullen, McRobbie et al. 2010, Dawkins and Corcoran 2014, Nides, Leischow et al. 2014, Spindle, Breland et al. 2014), including the nicotine gum (Henningfield 1995). Because the addictiveness of a drug-delivery device is in part determined by the speed of drug delivery to the brain (Le Houezec 2003), the differences across devices suggest the hypothesis that some e-cigarettes may be less addictive than tobacco cigarettes, but as or more addictive than nicotine medications, which themselves are not at all (patch), or not very addictive (gum, lozenge) (Hughes 1989, Shiffman, Hughes et al. 2003). This hypothesis is partially supported by data showing that the abuse liability of e-cigarettes is less than that of tobacco cigarettes, at least for smokers trying an e-cigarette for the first time (Vansickel, Weaver et al. 2012). Also, in experienced e-cigarette users (called “vapers” because they inhale a vapour), the number of minutes between waking up and first use (a good indicator of dependence) is longer for e-cigarettes than for tobacco cigarettes (Farsalinos, Romagna et al. 2013, Goniewicz, Lingas et al. 2013), and vapers report that e-cigarettes are less addictive than tobacco cigarettes (Farsalinos, Romagna et al. 2013, Goniewicz, Lingas et al. 2013, Foulds, Veldheer et al. 2014). Long-term e-cigarette users may be more addicted than short-term users, and new e-cigarette models may be more addictive than older models (Foulds, Veldheer et al. 2014). Otherwise, there is little published information on the addictiveness of e-cigarettes. Nevertheless, there is concern that some users may be addicted to nicotine when it is delivered via e-cigarettes.

Consequently, the aims of this study were to describe levels of dependence in users of e-cigarettes (current and former smokers), and to compare them with dependence levels in former smokers who used the nicotine gum and in cigarette smokers.

## 2. MATERIALS AND METHODS

We used comparisons to interpret dependence ratings. First, daily vapers who were former smokers compared their current level of dependence on e-cigarettes with their former level of dependence on tobacco cigarettes. Second, we compared dependence ratings in users of e-cigarettes with vs. without nicotine, hypothesizing that dependence would be present in the former only. Third, in former smokers, we compared dependence to the e-cigarette in daily vapers with dependence to the nicotine gum in daily users of the nicotine gum. Fourth, in daily e-cigarette users, we compared dependence on the e-cigarette in former smokers and in current smokers. Fifth, in daily smokers, we compared dependence on the e-cigarette in daily vapers (dual users) with dependence on tobacco cigarettes in two samples of daily smokers.

### 2.1. Participants

**E-cigarette users**—We collected data in e-cigarette users specifically for this study. We posted a questionnaire on the smoking cessation website Stop-tabac.ch, in English and French, between October 2012 and October 2013. Links to the survey were posted on health-related websites, smoking cessation websites, and websites informing about e-cigarettes or selling them. Eligible participants consisted of adults (>18 years), daily vapers only. E-cigarette use was assessed with the following question: “Are you currently using the electronic cigarette?” followed by 4 response options: “No, I have never used it”; “No, but I have used it in the past”; “Yes, occasionally (not daily)”; “Yes, I use it every day”. The study was approved by the ethics committee of the Geneva University Hospitals.

**Nicotine gum users**—Data for nicotine gum users were collected on the Internet between 2004 and 2007, in English, on the smoking cessation website Stop-tabac.ch (Etter 2009). We included only the 451 former smokers who used the nicotine gum daily and had not smoked in the past 7 days. Nicotine gum use was assessed with the following question: “Do you currently use nicotine gums?” followed by 4 response options: “Yes, I use them every day”; “Yes, occasionally (not every day)”; “No, but I have used them in the past”; “No, I never used them”.

**Daily smokers**—We included two samples of daily smokers as comparison groups. We posted a questionnaire on the Internet from 2004 to 2007, in English, on the website Stop-tabac.ch. This survey was answered by 2,206 daily smokers (Courvoisier and Etter 2008). We also drew a representative (i.e. random) sample of 2,000 people aged 18+ years from the accessible part of the registry of residents of Geneva, Switzerland, in 2006 (Etter 2009). We collected 1,487 questionnaires by mail (76.5% of 1,945 valid addresses). There were 391 smokers in this sample (26% of 1,487), but only the 292 daily smokers (75% of 391) were included in the present study.

### 2.2. Comparison of users of e-cigarettes with vs. without nicotine

We compared the 766 daily users of nicotine-containing e-cigarettes with the 30 daily users of nicotine-free e-cigarettes.

### 2.3. Comparison of e-cigarette users with nicotine gum users

In former smokers, we compared the 911 daily e-cigarette users with the 451 daily nicotine gum users. We also conducted this comparison in the subset of long-term users (>3 months) of these products, hypothesizing that dependence would be most apparent in long-term users (Foulds, Veldheer et al. 2014). Statistical tests for these comparisons were adjusted for age, sex, and duration of smoking abstinence.

### 2.4. Comparisons of ex-smokers who used the e-cigarette daily with daily dual users

We compared the 911 former smokers who used exclusively the e-cigarette with the 125 daily e-cigarette users who also smoked daily (daily dual users). Statistical tests for these comparisons were adjusted for age and sex.

### 2.5. Comparisons of daily dual users with other daily smokers

We compared the 125 daily e-cigarette users who also smoked daily (daily dual users) with the 2206 daily smokers in the Internet sample and the 292 daily smokers in the general population sample. We included a general population sample because all the Internet samples were not representative of the average users of pyro-cigarettes, e-cigarettes or nicotine gums. The comparison with the general population provides the reader with a useful benchmark that facilitates the interpretation of dependence ratings in the other samples. Statistical tests for these comparisons were adjusted for age and sex.

### 2.6. Assessment of dependence

There was no validated measure of dependence on the e-cigarette or the nicotine gum at the time of data collection (an e-cigarette dependence scale was published later) (Foulds, Veldheer et al. 2014). For tobacco cigarettes, commonly used instruments include the 6-item Fagerström Test for Nicotine Dependence (FTND) (Heatherton, Kozlowski et al. 1991), and the 19-item Nicotine Dependence Syndrome Scale (NDSS), which has an Overall score and 5 subscales: Drive (craving and withdrawal, and subjective compulsion to smoke), Priority (preference for smoking over other reinforcers), Tolerance (reduced sensitivity to the effects of smoking), Continuity (regularity of smoking rate), and Stereotypy (invariance of smoking) (Shiffman, Waters et al. 2004). A third instrument, the Cigarette Dependence Scale (CDS), is a brief (12 items), self-administered, single-dimension measure that covers DSM-IV and ICD-10 criteria of nicotine or tobacco dependence (Etter 2008, Courvoisier and Etter 2010). We modified FTND, NDSS and CDS to assess dependence on e-cigarettes. We labeled the modified scores e-FTND, e-NDSS and e-CDS for e-cigarettes, and g-FTND, g-NDSS and g-CDS for nicotine gum. For e-FTND and e-CDS, we used 10 puffs on e-cigarettes as equivalent to one tobacco cigarette, because smokers take about ten puffs from each cigarette (Etter and Perneger 2001). NDSS was not assessed in the population-based sample. We also used other indicators of dependence: unsuccessful attempts to stop using the product, perceived likeliness to succeed if they decided to stop using each product (included because inability to stop is the core feature of dependence), perceived addiction to the e-cigarette or nicotine gum compared with previous addiction to cigarettes. FTND, CDS and NDSS were defined a priori as the primary measures of dependence, all the other indicators of dependence were considered secondary. We also report reasons for using the

product (to deal with craving for tobacco, to quit smoking or avoid relapse, to deal with non-smoking situations).

## 2.7. Statistical methods

We used *t* tests to compare means, Mann-Whitney *U* tests to compare medians and chi-square tests to compare proportions. For continuous variables, we used multivariate linear regression models to adjust for confounding factors. For dichotomous variables, we used multivariate logistic regression models to adjust for confounding factors. We used Holm-Bonferroni corrections for multiple comparisons. In the Tables, p-values that are statistically significant after this correction are shown in bold type.

## 3. RESULTS

### 3.1. Participation in the e-cigarette survey

We obtained 1,640 responses but retained only the 1,284 daily vapers, including 125 daily smokers (dual users: daily e-cigarettes and daily tobacco cigarettes), 1,033 former smokers (911 exclusive e-cigarette users who had not smoked any tobacco in the past 7 days, plus 122 recent quitters who had smoked in the past 7 days), 111 occasional smokers (dual users: daily e-cigarettes and occasionally tobacco cigarettes), and 15 of undeclared smoking status.

Participants lived in France (36%), the USA (25%), Greece (5%), Switzerland (3%), Belgium (3%), the UK (2%), Canada (2%) and other countries (24%). Most participants were men (Table 1). The 911 exclusive e-cigarette users reported using e-liquid with nicotine concentrations of 12 mg/ml on average, used refillable systems (99%) rather than disposable models (1%), took 200 puffs per day on their e-cigarette, took their first puff 32 minutes after waking, had been using the e-cigarette for 5 months and had also quit smoking for 5 months (medians). Twenty-three percent of exclusive e-cigarette users had e-FTND scores >4, 21% had e-CDS scores >43 (i.e. scores which reflect dependence (Etter 2008)), and 9% answered “very true” to the question: “I use e-cigarettes because I am addicted to them”. The 125 daily smokers (i.e. daily dual users) reported using e-liquid with nicotine concentrations of 13 mg/ml on average, took 100 puffs per day on their e-cigarette, took the first puff on their e-cigarette 30 minutes after waking up and had been using the e-cigarette for 3 months (Table 1).

### 3.2. Comparison of levels of dependence when vaping vs. smoking

In the 911 former smokers who used e-cigarettes daily, 74% rated their current dependence on e-cigarettes as “weaker” than their prior dependence on tobacco cigarettes, 21% as “same” and 3% as “stronger” (Table 2). These 911 exclusive e-cigarette users reported that when they were smoking tobacco cigarettes, they smoked their first cigarette 23 minutes after waking, whereas they currently took their first puff on their e-cigarette 32 minutes after waking (paired-samples *t* test:  $t=5.9$ ,  $p<.001$ ). Exclusive e-cigarette users rated their previous dependence on tobacco cigarettes at 90 on a scale of 0-100, whereas they rated their current dependence on e-cigarettes at 64 (paired-samples *t* test:  $t=24.2$ ,  $p<.001$ ).

Among the 125 daily smokers (daily dual users), 62% rated their current dependence on e-cigarettes as “weaker” than their current dependence on tobacco cigarettes, 28% as “same” and 3% as “stronger”. These dual users reported that they currently smoked 11.7 cigarettes per day, compared to 23.3 cigarettes per day before they started to use e-cigarettes (paired-samples *t* test:  $t=8.3$ ,  $p<.001$ ).

### 3.3. Comparison of e-cigarette users with vs. without nicotine

In the daily e-cigarette users who answered all the questions in this analysis ( $n=796$ , comprising daily, occasional and former tobacco smokers), users of nicotine-containing e-cigarettes ( $n=766$ ) reported taking 80 more puffs per day of their e-cigarettes than users of no-nicotine e-cigarettes ( $n=30$ ); they also had higher e-FTND scores (Table 3). Users of nicotine e-cigarettes were also more likely to say that the “throat hit” of their e-cigarette was “strong”, more likely to report that they enjoyed vaping, and were less likely to intend to stop vaping (Table 3).

### 3.4. In former smokers, comparison of users of e-cigarette vs. nicotine gum

In former smokers, e-FTND scores in exclusive e-cigarette users were slightly higher than g-FTND scores in exclusive nicotine gum users. The difference was mainly due to the shorter interval between waking and first use in vapers than in gum users (Table 1). In former smokers, e-CDS ratings in exclusive e-cigarette users were 7.6 points lower than g-CDS ratings in exclusive gum users (this difference amounts to half a standard deviation on this scale). In former smokers, e-NDSS ratings in exclusive e-cigarette users were 0.3 to 1 point lower than g-NDSS ratings in exclusive gum users (these differences amount to about half a standard deviation of these scales), except there was no difference for the NDSS *Priority* and *Tolerance* subscales.

In the subsample of long-term users (>3 months) of these products, e-CDS ratings in e-cigarette users were 13 points lower (that is, about one standard deviation) than g-CDS ratings in gum users, and e-NDSS ratings in e-cigarette users were 0.6 to 1.6 points lower (that is, about one standard deviation) than g-NDSS ratings in gum users. There was no difference in e-FTND/g-FTND scores in long-term users. Long-term users of the e-cigarette (11.4%) were also much less likely than long-term users of the gum (82.8%) to report they used these products because they were addicted to them, and that they had unsuccessfully tried to stop using these products in the previous 12 months (Table 4). In the subsample of short-term users ( $\leq 3$  months) of these products, there were few differences in dependence ratings between e-cigarette users and gum users.

### 3.5. In daily e-cigarette users, comparison of former smokers with daily smokers (dual users)

In daily users, former smokers took more puffs of vapor per day, they had higher e-CDS scores than daily smokers, but there was no significant difference for e-FTND and e-NDSS scores. Former smokers were also more likely than dual users to say that stopping vaping would be difficult, and that they used the e-cigarette because they were dependent on it (Tables 1 and 2).

### 3.6. In daily smokers, comparison of e-cigarette users (dual users) vs. other smokers

In daily smokers, e-FTND scores in dual users were similar to FTND scores in the general population sample, but were 1.5 point lower than FTND scores in smokers in the Internet sample (this represents 0.7 standard deviation on the FTND scale) (Table 1). In daily smokers, e-CDS ratings in dual users were 9 to 20 points lower than CDS ratings in the two other samples of daily smokers (these differences amount to one to two standard deviations on this scale). In daily smokers, e-NDSS ratings in dual users were 0.3 to 1.6 points lower than NDSS ratings in daily smokers in the Internet sample (these differences amount to about half a standard deviation on these scales), except there was no difference for the NDSS *Tolerance*, *Continuity* and *Stereotypy* subscales.

In daily smokers, vapers (dual users) rated their dependence on e-cigarettes lower (44.9 on a scale of 0 to 100) than smokers rated their dependence on tobacco cigarettes (68.6 to 84.5 on a scale of 0 to 100, both  $p < .001$ ) (Table 1). In daily smokers, the reported interval between waking up and smoking was 58 minutes shorter in e-cigarette users than in smokers in the general population sample (Table 1). Among daily smokers, cigarette consumption was lowest (11.7 cig./day) among dual users of e-cigarettes and tobacco cigarettes, compared with the two other groups of daily smokers.

## 4. DISCUSSION

We used several methods to assess dependence on e-cigarettes: we used adapted versions of widely used dependence scales, we asked vapers to compare their dependence on e-cigarettes with their current or past dependence on tobacco cigarettes, and we compared dependence ratings in vapers, nicotine gum users and tobacco smokers. Overall, our results were convergent across measures and comparisons, and suggested that e-cigarettes are less addictive than tobacco cigarettes, a result congruent with the literature (Farsalinos, Romagna et al. 2013, Goniewicz, Lingas et al. 2013, Foulds, Veldheer et al. 2014). Our results also suggest that the e-cigarettes used by participants in this study were either as addictive or less addictive than the nicotine gum, which itself is not very addictive (Hughes 1989, Shiffman, Hughes et al. 2003). Nevertheless, some vapers may be dependent on nicotine when used in e-cigarettes. They probably were already dependent on nicotine when they started vaping, and most of them declared that they vaped to avoid relapsing to smoking.

Even though some vapers use e-cigarettes for long periods of time, it must be emphasized that there is no known adverse consequence of e-cigarette use (Hajek, Etter et al. 2014), except for the financial cost and the annoyance of permanent vaping. Thus, the potential benefits of long-term vaping (i.e., to prevent relapse to smoking) most probably outweigh the drawbacks as we know them today. As a comparison, even though some users of the nicotine gum use this product compulsively, some times for several months or years (Etter 2007, Etter 2009), long-term use of the gum is not perceived as a public health problem. Use of the nicotine gum over several years is not known to carry any health risks (Murray, Bailey et al. 1996, Murray, Connett et al. 2009), but the implications of long-term vaping to individual health are uncertain at this time. At the population level, the risks of e-cigarettes depend on various factors that need to be assessed in the long term, including the impact on smoking initiation and smoking cessation rates.

One third of smokers who have been abstinent for 12 months will eventually relapse to smoking during the following years (Etter and Stapleton 2006). Because long-term use of e-cigarettes may prevent late relapse, these products could help preserve the health of former smokers, so long as they do not themselves carry as yet undocumented long-term health risks. Prevention of relapse was a frequently cited reason for long-term vaping in our sample.

#### 4.1. Dual use

Dual use of e-cigarettes and cigarettes is considered by some as an additional risk for smokers (Lee, Hebert et al. 2014). Our data showed that after they started to vape, dual users cut by half their cigarette consumption. Dual users also rated their dependence on e-cigarettes as weaker than their dependence on cigarettes. Dual users were also less dependent on e-cigarettes than former smokers. However, our data provide no information on the impact of dual use on quit attempts and the duration of smoking.

#### 4.2. No-nicotine e-cigarettes

As in a previous report, users of no-nicotine e-cigarettes were less dependent than users of nicotine-containing e-cigarettes, (Foulds, Veldheer et al. 2014). Our data also suggest that nicotine is an important determinant of the “throat hit” (Farsalinos, Spyrou et al. 2014, Etter 2015). However, our analysis lacked statistical power to detect the effects of nicotine in e-cigarettes.

#### 4.3. Gum users

A comparison with users of the nicotine gum is useful because e-cigarettes are used somewhat like nicotine gums, as nicotine replacement tools (Etter and Bullen 2011), and because long-term, compulsive use of the nicotine gum has been reported in a minority of gum users (Etter 2007, Etter 2009). As explained in a previous study using the same data, long-term use of the nicotine gum in this sample was largely due to compulsive use or dependence, rather than to recreational use or relapse prevention (Etter 2009). In contrast, in our data, in exclusive e-cigarette users, the association between long-term use of the e-cigarette and indicators of dependence was less evident. Among former smokers, most long-term vapers used e-cigarettes for reasons other than dependence, in particular to avoid relapsing to smoking. Vapers also vape to decrease health risks and because vaping is cheaper than smoking (Etter and Bullen 2011). Thus, compulsive use and dependence were much more frequent in long-term users of nicotine gum than in long-term vapers. The dependence criterion of unsuccessful attempts to stop using the product was rare among vapers, compared with nicotine gum users. These results suggest either that current models of e-cigarettes are less addictive than the nicotine gum (even refillable tank systems, used by almost all of our participants), or that reasons for using each product differ across products. However, our samples of vapers and nicotine gum users should be compared with caution, because they differed on several aspects. For instance, it is possible that long-term gum users were more dependent on nicotine than long-term e-cigarette users, even before they started to use these products (Silla, Beard et al. 2014). Assessments of the dependence potential of nicotine medications and e-cigarettes in comparable samples of users are warranted.



#### 4.4. Study strengths and limitations

Strengths of the study include a large, international sample of long-term users of e-cigarettes, the use of multiple dependence measures, the multiple comparison groups, and the convergent results across analyses.

The patterns of e-cigarette use in this study were comparable to patterns observed in previous studies of vapers : 120 puffs/day (Etter and Bullen 2011); 175 puffs/day (Etter 2010); 200 puffs/day (Etter and Bullen 2011, Foulds, Veldheer et al. 2011); 235 puffs/day (Dawkins, Turner et al. 2013); 4 mL e-liquid per day (Farsalinos, Romagna et al. 2013). This suggests that participants in this study were not particularly intensive users and that our results are generalizable to most daily vapers. However, the samples used as comparison groups (nicotine gum users, smokers) were collected in different surveys at different times using different enrollment methods, and the statistical adjustments may not have compensated for all the differences between these groups. Therefore, these comparisons, although informative, should be interpreted with caution.

Importantly, this study should not be interpreted as a prevalence study, and our results should not be extrapolated to other populations. However, our aim was not to produce prevalence estimates, but to assess whether dependence criteria were present in e-cigarette users.

One limitation is that we did not proceed to a psychometric validation of the versions of the dependence scales adapted for the e-cigarette and nicotine gum. In particular, we arbitrarily used 10 puffs on e-cigarettes as equivalent to one tobacco cigarette, because smokers also take about 10 puffs per cigarette (Etter and Perneger 2001). Furthermore, many items in NDSS, CDS and FTND are not well suited for e-cigarettes (e.g. use despite risks). Thus, the comparison of scores for these scales across different products must be interpreted with caution.

It is unclear why there were more men than women in our sample of e-cigarette users, since such differences are not consistently observed in surveys of vapers conducted in the general population (Hajek, Etter et al. 2014). Technology is rapidly progressing and future models may deliver nicotine more efficiently than those available to participants in this study. If future models are able to deliver nicotine with the dose and speed of tobacco cigarettes (Spindle, Breland et al. 2014), then nicotine dependence among e-cigarette users may mirror that of cigarette smokers. Thus, dependence assessment among e-cigarette users is a moving target that will require methods that are sensitive to the evolving nature of these devices.

#### 4.5. Conclusions

Some e-cigarette users were dependent on nicotine when used in e-cigarettes, but these products were less addictive than tobacco cigarettes. E-cigarettes may be as addictive or less addictive than the nicotine gum, which itself is not very addictive.

### Acknowledgments

#### Role of Funding Source

*Drug Alcohol Depend.* Author manuscript; available in PMC 2016 June 24.

This study was partly funded by the Swiss Tobacco Prevention Fund (Swiss Federal Office of Public Health), grant 12.000189 to JFE. The Swiss Tobacco Prevention Fund had no role in the design or conduct of the study, interpretation of the data or decision to submit the paper for publication.

TE is supported by the National Institute on Drug Abuse of the U.S. National Institutes of Health under Award Number P50DA036105 and the Center for Tobacco Products of the U.S. Food and Drug Administration. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the Food and Drug Administration.

## REFERENCES

- Bullen C, McRobbie H, Thornley S, Glover M, Lin R, Laugesen M. Effect of an electronic nicotine delivery device (e cigarette) on desire to smoke and withdrawal, user preferences and nicotine delivery: randomised cross-over trial. *Tob Control*. 2010; 19(2):98–103. [PubMed: 20378585]
- Choi JH, Dresler CM, Norton MR, Strahs KR. Pharmacokinetics of a nicotine polacrilex lozenge. *Nicotine Tob Res*. 2003; 5(5):635–644. [PubMed: 14577980]
- Courvoisier D, Etter JF. Using item response theory to study the convergent and discriminant validity of three questionnaires measuring cigarette dependence. *Psychol Addict Behav*. 2008; 22(3):391–401. [PubMed: 18778132]
- Courvoisier DS, Etter JF. Comparing the predictive validity of five cigarette dependence questionnaires. *Drug Alcohol Depend*. 2010; 107(2-3):128–133. [PubMed: 19926407]
- Dawkins L, Corcoran O. Acute electronic cigarette use: nicotine delivery and subjective effects in regular users. *Psychopharmacology (Berl)*. 2014; 231(2):401–407. [PubMed: 23978909]
- Dawkins L, Turner J, Roberts A, Soar K. ‘Vaping’ profiles and preferences: an online survey of electronic cigarette users. *Addiction*. 2013; 108(6):1115–1125. [PubMed: 23551515]
- Etter J, Bullen C. Cotinine levels in users of electronic cigarettes. *European Respiratory Journal*. 2011; 38(5):1219–1220. [PubMed: 22045788]
- Etter JF. Addiction to the nicotine gum in never smokers. *BMC Public Health*. 2007; 7:159. [PubMed: 17640334]
- Etter JF. Comparing the validity of the Cigarette Dependence Scale and the Fagerstrom Test for Nicotine Dependence. *Drug Alcohol Depend*. 2008; 95(1-2):152–159. [PubMed: 18328641]
- Etter JF. Dependence on the nicotine gum in former smokers. *Addict Behav*. 2009; 34(3):246–251. [PubMed: 19022585]
- Etter JF. Perceived priorities for prevention: change between 1996 and 2006 in a general population survey. *Journal of Public Health (Oxford)*. 2009; 31(1):113–118.
- Etter JF. Electronic cigarettes: a survey of users. *BMC Public Health*. 2010; 10:231. [PubMed: 20441579]
- Etter JF. Levels of saliva cotinine in electronic cigarette users. *Addiction*. 2014; 109:825–829. [PubMed: 24401004]
- Etter JF. Throat hit in users of the electronic cigarette: an exploratory study. 2015 Submitted manuscript.
- Etter JF, Bullen C. Electronic cigarette: users profile, utilization, satisfaction and perceived efficacy. *Addiction*. 2011; 106(11):2017–2028. [PubMed: 21592253]
- Etter JF, Bullen C. Saliva cotinine levels in users of electronic cigarettes. *Eur Respir J*. 2011; 38(5):1219–1220. [PubMed: 22045788]
- Etter JF, Perneger TV. Measurement of self reported active exposure to cigarette smoke. *J Epidemiol Community Health*. 2001; 55(9):674–680. [PubMed: 11511648]
- Etter JF, Stapleton JA. Nicotine replacement therapy for long-term smoking cessation: a meta-analysis. *Tob Control*. 2006; 15(4):280–285. [PubMed: 16885576]
- Farsalinos K, Romagna G, Tsiapras D, Kyrzopoulos S, Voudris V. Nicotine levels, associated side effects and dependence potential of electronic cigarettes in ‘vapers’ who have completely substituted smoking with electronic cigarette use: implications for public health policy. *Int. J. Environ. Res. Public Health*. 2013; 10 Online first.
- Farsalinos KE, Romagna G, Tsiapras D, Kyrzopoulos S, Voudris V. Evaluation of electronic cigarette use (vaping) topography and estimation of liquid consumption: implications for research protocol

- standards definition and for public health authorities' regulation. *International journal of environmental research and public health*. 2013; 10(6):2500–2514. [PubMed: 23778060]
- Farsalinos KE, Spyrou A, Tsimopoulou K, Stefanopoulos C, Romagna G, Voudris V. Nicotine absorption from electronic cigarette use: comparison between first and new-generation devices. *Sci Rep*. 2014; 4:4133. [PubMed: 24569565]
- Foulds J, Veldheer S, Berg A. Electronic cigarettes (e-cigs): views of aficionados and clinical/public health perspectives. *Int J Clin Pract*. 2011; 65:1037–1042. [PubMed: 21801287]
- Foulds J, Veldheer S, Yingst J, Hrabovsky S, Wilson SJ, Nichols TT, Eissenberg TT. Development of a questionnaire to assess dependence on electronic cigarettes in a large sample of ex-smoking e-cig users. *Nicotine Tob Res*. 2014
- Goniewicz ML, Lingas EO, Hajek P. Patterns of electronic cigarette use and user beliefs about their safety and benefits: An Internet survey. *Drug and Alcohol Review*. 2013; 32(2):133–140. [PubMed: 22994631]
- Hajek P, Etter JF, Benowitz N, Eissenberg T, McRobbie H. Electronic cigarettes: review of use, content, safety, effects on smokers and potential for harm and benefits. *Addiction*. 2014 Epub ahead of print.
- Heatherton TF, Kozlowski LT, Frecker RC, Fagerstrom KO. The Fagerstrom Test for Nicotine Dependence: a revision of the Fagerstrom Tolerance Questionnaire. *Br J Addict*. 1991; 86(9): 1119–1127. [PubMed: 1932883]
- Henningfield JE. Nicotine medications for smoking cessation. *N Engl J Med*. 1995; 333(18):1196–1203. [PubMed: 7565976]
- Hughes JR. Dependence potential and abuse liability of nicotine replacement therapies. *Biomed Pharmacother*. 1989; 43(1):11–17. [PubMed: 2659095]
- Le Houezec J. Role of nicotine pharmacokinetics in nicotine addiction and nicotine replacement therapy: a review. *Int J Tuberc Lung Dis*. 2003; 7(9):811–819. [PubMed: 12971663]
- Lee YO, Hebert CJ, Nonnemaker JM, Kim AE. Multiple tobacco product use among adults in the United States: Cigarettes, cigars, electronic cigarettes, hookah, smokeless tobacco, and snus. *Prev Med*. 2014; 62:14–19. [PubMed: 24440684]
- Murray RP, Bailey WC, Daniels K, Bjornson WM, Kurnow K, Connett JE, Nides MA, Kiley JP. Safety of nicotine polacrilex gum used by 3,094 participants in the Lung Health Study. *Lung Health Study Research Group*. *Chest*. 1996; 109(2):438–445. [PubMed: 8620719]
- Murray RP, Connett JE, Zapawa LM. Does nicotine replacement therapy cause cancer? Evidence from the Lung Health Study. *Nicotine Tob Res*. 2009; 11(9):1076–1082. [PubMed: 19571249]
- Nides MA, Leischow S, Bhattar M, Simmons M. Nicotine blood levels and short-term smoking reduction with an electronic nicotine delivery system. *American Journal of Health Behavior*. 2014; 38(2):265–274. [PubMed: 24629555]
- Shiffman S, Hughes JR, Di Marino ME, Sweeney CT. Patterns of over-the-counter nicotine gum use: persistent use and concurrent smoking. *Addiction*. 2003; 98(12):1747–1753. [PubMed: 14651507]
- Shiffman S, Waters A, Hickcox M. The nicotine dependence syndrome scale: a multidimensional measure of nicotine dependence. *Nicotine Tob Res*. 2004; 6(2):327–348. [PubMed: 15203807]
- Silla K, Beard E, Shahab L. Characterization of long-term users of nicotine replacement therapy: evidence from a national survey. *Nicotine Tob Res*. 2014; 16(8):1050–1055. [PubMed: 24610398]
- Spindle TR, Breland AB, Karaoglanian NV, Shihadeh AL, Eissenberg T. Preliminary Results of an Examination of Electronic Cigarette User Puff Topography: The Effect of a Mouthpiece-Based Topography Measurement Device on Plasma Nicotine and Subjective Effects. *Nicotine Tob Res*. 2014
- Vansickel AR, Eissenberg T. Electronic cigarettes: effective nicotine delivery after acute administration. *Nicotine Tob Res*. 2013; 15(1):267–270. [PubMed: 22311962]
- Vansickel AR, Weaver MF, Eissenberg T. Clinical laboratory assessment of the abuse liability of an electronic cigarette. *Addiction*. 2012; 107(8):1493–1500. [PubMed: 22229871]

**Table 1**

Dependence on e-cigarette or nicotine gum in former smokers, and dependence on tobacco cigarette in two samples of daily smokers enrolled on a stop smoking website and in the general population

	Former smokers		Daily smokers			Former smokers	Daily e-cig users	Daily smokers	
	Daily gum users	Daily e-cig users	Daily e-cig users	Internet	Gen. popul.	Gum users vs e-cig users	Former smokers vs daily smokers	E-cig users vs Internet	E-cig users vs general popul.
N participants	451	911	125	2206	292	P value	P value	P value	P value
Age (mean)	44.7	40.9	44.6	37.8	40.1	<b>0.001</b>	<b>0.001</b>	<b>&lt;.001</b>	<b>0.001</b>
Men (%)	38.6	68.9	57.1	36.8	58.4	<b>0.001</b>	<b>0.010</b>	<b>&lt;.001</b>	0.8
Days since quit smoking (median)	379	147	--	--	--	<b>&lt;.001</b>	--	--	--
Duration of use of [product] (days, median)	365	152	91	--	--	<b>&lt;.001</b>	0.019	--	--
Minutes to first cigarette of the day, mean	--	--	34.9	41.1	93.3	--	--	0.86	<b>&lt;.001</b>
Minutes to 1 <sup>st</sup> gum or 1 <sup>st</sup> e-cig of the day	59.7	32.1	41.0	--	--	<b>&lt;.001</b>	0.12	--	--
Cigarettes/day, mean	--	--	11.7	20.3	16.2	--	--	<b>&lt;.001</b>	<b>&lt;.001</b>
Puffs per day on e-cigs, mean	--	217	140	--	--	--	<b>0.001</b>	--	--
Self-rated addiction to [product] on a scale of 0–100 (mean)	70.6	63.7	44.9	84.5	68.6	0.33	<b>&lt;.001</b>	<b>&lt;.001</b>	<b>&lt;.001</b>
CDS (e-CDS, g-CDS), mean	41.1	33.5	27.5	48.1	36.9	<b>&lt;.001</b>	<b>&lt;.001</b>	<b>&lt;.001</b>	<b>&lt;.001</b>
FTND (e-FTND, g-FTND), mean	3.4	3.9	3.2	4.7	3.2	<b>&lt;.001</b>	0.013	<b>&lt;.001</b>	0.94
NDSS (e-NDSS, g-NDSS) Overall	-0.45	-1.21	-1.33	-0.26	--	<b>&lt;.001</b>	0.19	<b>&lt;.001</b>	--
NDSS Drive	-0.12	-1.13	-1.27	0.40	--	<b>&lt;.001</b>	0.28	<b>&lt;.001</b>	--
NDSS Priority	-0.71	-0.73	-0.69	-0.29	--	0.73	0.59	<b>&lt;.001</b>	--
NDSS Tolerance	-0.84	-1.15	-0.98	-0.48	--	0.022	0.16	0.007	--
NDSS Continuity	0.11	-0.87	-0.68	-0.69	--	<b>&lt;.001</b>	0.34	0.31	--
NDSS Stereotypy	0.60	-0.13	-0.18	0.13	--	<b>&lt;.001</b>	0.60	0.009	--

FTND: range 0 to 10; CDS: range 12 to 60; NDSS: range -4 to +4

Bold: statistically significant values after Holm-Bonferroni adjustment.

**Table 2**

Other indicators of dependence on e-cigarette or nicotine gum in former smokers, and dependence on tobacco cigarettes in two samples of daily smokers

	Former smokers			Daily smokers		Former smokers	Daily e-cig users	Daily smokers	
	Daily gum users	Daily e-cig users	Daily e-cig users	Internet	Gen. popul.	Gum users vs e-cig users	Former smokers vs daily smokers	E-cig users vs Internet	E-cig users vs general popul.
N participants	451	911	125	2206	292	P value	P value	P value	P value
I am a prisoner of [product] (% fully agree)	41.1	6.2	3.6	57.2	27.7	<b>&lt;.001</b>	0.003	<b>&lt;.001</b>	<b>&lt;.001</b>
Stopping [product] would be: (% very difficult / impossible)	44.9	29.2	21.1	65.1	28.8	0.20	<b>0.001</b>	<b>&lt;.001</b>	<b>&lt;.001</b>
Serious attempt to stop [product] in past 12m (yes, %)	27.7	1.3	5.3	52.5	31.8	<b>&lt;.001</b>	0.03	<b>&lt;.001</b>	<b>0.001</b>
Likely to succeed if decided to stop using [product] (%)	28.8	32.9	39.0	36.1	--	0.82	0.09	0.89	--
Perceived addiction to e-cigs / gums, compared with previous addiction to cigarettes (same or stronger, %)	35.5	23.6	31.0	--	--	<b>&lt;.001</b>	0.18	--	--
<i>Reasons for use:</i>									
Use e-cig / gum because is addicted to it (%)	68.8	46.1	20.7	--	--	<b>&lt;.001</b>	<b>&lt;.001</b>	--	--
Use e-cig / gum to deal with craving for tobacco (%)	60.6	87.4	90.6	--	--	<b>&lt;.001</b>	0.51	--	--
Use e-cig / gum to quit smoking or avoid relapse (%)	67.8	96.1	75.4	--	--	<b>&lt;.001</b>	<b>&lt;.001</b>	--	--
Use e-cig / gum to deal with situation where can't smoke (%)	26.6	43.6	66.6	--	--	<b>&lt;.001</b>	0.003	--	--
I fear that I will start smoking again if I stopped vaping / using nicotine gums (%)	57.7	75.4	--	--	--	<b>&lt;.001</b>	--	--	--

Bold: statistically significant values after Holm-Bonferroni adjustment.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

**Table 3**

Characteristics of current and former smokers who used the e-cigarette daily, with or without nicotine, Internet, 2012-2013

	E-cig with nicotine	E-cig without nicotine	P value
Number of participants	766	30	
Age (mean)	41.7	47.1	0.008
Men (%)	64.5	60.7	0.68
Former smokers (%)	83.2	80.0	0.75
In current smokers, cig./day (median)	4	15	0.10
In former smokers, time since quit smoking (days, median)	142	123	0.86
Duration of current episode of use (days, median)	152	91	0.48
Puffs per day on e-cigs (median)	170	90	<b>&lt;.001</b>
Throat hit of current e-cig is "strong" (%)	42.0	13.7	<b>&lt;.001</b>
Minutes to 1 <sup>st</sup> e-cig of the day, median	20	30	0.039
FTND-ecig	3.9	2.5	<b>&lt;.001</b>
FTND e-cig score $\geq 5$	36.7	20.0	0.06
CDS-e-cig	33.2	27.8	0.017
NDSS-e-cig : Overall	-1.2	-1.5	0.12
NDSS-e-cig : Drive	-1.1	-1.7	0.019
NDSS-e-cig : Priority	-0.7	-0.7	0.98
NDSS-e-cig : Tolerance	-1.1	-0.8	0.09
NDSS-e-cig : Continuity	-0.9	-1.1	0.35
NDSS-e-cig : Stereotypy	-0.2	-0.4	0.29
Stopping using the e-cig would be "very difficult" + "impossible" (%)	28.2	14.8	0.010
Made a serious attempt to stop using e-cig in past 12 months (%)	1.5	7.4	0.018
Intention to stop using e-cig in next 6 months	8.2	30.9	<b>0.002</b>
If decided to stop e-cig, unlikely to succeed (%)	30.7	14.8	0.08
Feels the urge to smoke while vaping (%)	11.9	32.1	0.016
Easy to abstain from smoking when vaping (%)	89.6	79.3	0.019
<i>Reasons for use (% very + extremely true)</i>			
Because I am addicted to the e-cig	8.4	0	0.13
To deal with my cravings for cigarettes	64.7	59.3	0.88
To quit smoking or avoid relapsing	81.8	79.3	0.53
Because I enjoy it	55.4	35.7	<b>0.002</b>
<i>Reasons for NOT stopping e-cigarette (% agree)</i>			
I am a prisoner of the e-cig	26.9	18.5	0.07
I am unable to stop vaping	27.5	14.8	0.10

Bold: statistically significant values after Holm-Bonferroni adjustment.

**Table 4**

Characteristics of former smokers who used the e-cigarette or the nicotine gum daily, according to the duration of product use, Internet, 2004-2013

	Used e-cig for ≤3 months	Used e-cig for >3 months	P-value e-cig ≤3m vs >3m	Used gum for ≤3 months	Used gum for >3 months	P-value gum ≤3m vs >3m	P value e-cig vs gum ≤3 months	P value e-cig vs gum >3 months
Number of participants	244	331		152	295			
Men (%)	63.2	67.2	0.3	41.2	36.8	0.32	<b>&lt;.001</b>	<b>&lt;.001</b>
Age (median)	40	42	0.07	38.0	47.0	<b>&lt;.001</b>	0.49	0.016
Time since they quit smoking (days, median)	77	520	<b>&lt;.001</b>	15	960	<b>&lt;.001</b>	0.38	<b>&lt;.001</b>
Duration of current episode of e-cig or gum use (days, median)	49	365	<b>&lt;.001</b>	14	730	<b>&lt;.001</b>	0.006	<b>&lt;.001</b>
Minutes to 1 <sup>st</sup> puff on e-cig or to 1 <sup>st</sup> gum of day - median	20	15	0.16	60	20	<b>&lt;.001</b>	<b>&lt;.001</b>	0.016
- mean	38.2	27.8	0.015	110.0	34.6	<b>&lt;.001</b>	<b>&lt;.001</b>	0.016
Made a serious attempt to stop using e-cig or nicotine gum in past 12 months (%)	0.9	1.3	0.7	12.9	37.2	<b>&lt;.001</b>	0.011	<b>&lt;.001</b>
FTND-e-cig or FTND-gum	3.7	4.1	0.009	2.0	4.0	<b>&lt;.001</b>	<b>&lt;.001</b>	0.61
CDS-e-cig or CDS-gum	32.7	34.1	0.19	28.4	47.0	<b>&lt;.001</b>	0.37	<b>&lt;.001</b>
NDSS-e-cig or NDSS-gum : Overall	-1.2	-1.2	0.55	-1.5	0	<b>&lt;.001</b>	0.27	<b>&lt;.001</b>
NDSS-e-cig or NDSS-gum : Drive	-1.1	-1.2	0.19	-1.2	0.4	<b>&lt;.001</b>	0.91	<b>&lt;.001</b>
NDSS-e-cig or NDSS-gum : Priority	-0.8	-0.7	0.05	-0.7	-0.7	0.67	0.38	0.71
NDSS-e-cig or NDSS-gum : Tolerance	-1.2	-1.1	0.37	-1.4	-0.5	<b>&lt;.001</b>	0.034	<b>&lt;.001</b>
NDSS-e-cig or NDSS-gum : Continuity	-0.9	-0.9	0.91	-0.2	0.7	<b>&lt;.001</b>	<b>&lt;.001</b>	<b>&lt;.001</b>
NDSS-e-cig or NDSS-gum : Stereotypy	-0.2	-0.1	0.92	-0.1	0.9	<b>&lt;.001</b>	0.11	<b>&lt;.001</b>
Addiction to e-cig or to nicotine gum compared with former addiction to cigarettes (% "same" or "stronger")	26.4	21.8	0.25	9.0	49.5	<b>&lt;.001</b>	<b>&lt;.001</b>	0.12
If you decided to stop vaping / to stop all NRTs, likely to succeed? (% not likely)	30.8	32.9	0.45	16.1	42.7	<b>&lt;.001</b>	0.07	0.21
<i>Reasons for using the e-cig or gum (% very true)</i>								
To deal with nicotine withdrawal symptoms	68.7	59.9	0.20	72.8	59.6	<b>0.001</b>	0.046	<b>&lt;.001</b>
To quit smoking or avoid relapsing to smoking	87.7	85.2	0.09	92.3	42.0	<b>&lt;.001</b>	0.66	<b>&lt;.001</b>
Because I am addicted to the e-cig / to the gum	8.0	11.4	<b>&lt;.001</b>	6.8	82.8	<b>&lt;.001</b>	<b>&lt;.001</b>	<b>&lt;.001</b>

Bold: statistically significant values after Holm-Bonferroni adjustment.