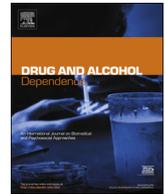




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Full length article

Does e-cigarette experimentation increase the transition to daily smoking among young ever-smokers in France?

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ABSTRACT

Introduction: According to multiple studies, e-cigarette use among adolescents is associated with subsequent smoking initiation. However, little is known about its effect on the transition from smoking initiation to daily smoking.

Methods: Using retrospective data from a French national representative survey collected in 2017 ($n = 39,115$), we analyzed the role of ever using e-cigarettes on daily cigarette smoking status at 17 among ever smokers ($n = 21,401$). Risk-ratios (RR) were computed through modified Poisson regressions with an inverse probability of treatment weighting (IPTW) approach.

Results: Among French adolescents aged 17, 16.8 % declared current e-cigarette use (1.9 % reported daily use) and 34.1 % cigarette smoking (25.1 % reported daily smoking). Among ever-smokers, adolescents who declared having ever used e-cigarettes were less likely than those who did not to transition to daily smoking at 17: RR = 0.62 95 %CI [0.60 – 0.64]. We found similar results for those who experimented with e-cigarettes before initiating smoking, RR = 0.76 95 %CI [0.66 – 0.89].

Conclusions: Our results found no evidence of an increased risk of transitioning to daily smoking at 17 among ever-smokers who also experimented with e-cigarettes. Further studies should investigate the longer-term role of vaping on future smoking habits with the use of causal inference methods.

1. Introduction

Tobacco smoking remains a major public health threat worldwide (U.S. Department of Health and Human Services, 2010). Among strategies used to decrease smoking prevalence, programs targeting adolescents are crucial since smoking initiation usually takes place during adolescence and early initiation is associated with later daily use and nicotine dependence (Sharapova et al., 2018).

The arrival of electronic cigarettes, or e-cigarettes, has disrupted the field of tobacco control. Vaping is considered to be drastically safer than conventional cigarette smoking (Newton et al., 2018), although it could generate diverse health effects, including among adolescents (U.S. Department of Health and Human Services, 2016). More research is needed to quantify the level of risk associated with their use (Glantz and Bareham, 2018; World Health Organization, 2019).

E-cigarettes are becoming more and more popular among adolescents. In the USA, vaping has even become more common than cigarette smoking and the use of any other tobacco products. In 2018, current use of e-cigarettes was 20.8 % among US high-school students (Gentzke et al., 2019). In France, this number was 10.0 % among high-school students in 2015 but increased to 16.0 % in 2018 (Spilka et al., 2019).

Researchers and decision-makers fear e-cigarette use could represent a gateway to tobacco smoking and thus jeopardize public efforts to reduce it. Several hypotheses have been proposed to explain the potential causal relation between e-cigarette experimentation and cigarettes smoking, including nicotine addiction, the fact that cigarettes could be more accessible to e-cigarettes users and the similarities of use between the two products (Schneider and Diehl, 2016). Another hypothesis, the common liability to drug use, considers that some people with unobserved characteristics could be predisposed to experiment

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with different products (Vanyukov and Ridenour, 2012).

A growing body of literature in the recent years has investigated the relationship between e-cigarette use and smoking experimentation. Thanks to adolescent cohort studies in the USA, Canada and the UK, smoking initiation has been shown to be highly correlated with ever previously using e-cigarettes (East et al., 2018; Hammond et al., 2017; Soneji et al., 2017). Conversely, experimentation with e-cigarettes (or, initiation of e-cigarette use) is found to be correlated with previous ever smoking (East et al., 2018). Although they considered temporality, the methods used in those studies do not allow concluding a causal relation between the two behaviors, because the results could simply illustrate the common liability to drug use (Lynn T. Kozlowski and Warner, 2017).

Few cohort studies have looked at the link between e-cigarette use and subsequent transition to regular smoking in adolescents. They have applied disparate definitions of transition to regular smoking, have not looked at daily smoking and have reached inconclusive results. For example, Conner et al. did not detect any association between e-cigarette use and subsequent smoking habits (defined as rarely, occasional or frequent cigarette smoking) among ever smokers from England aged 13–14 years at baseline (OR: 1.89, 95 % CI 0.82–4.33, N = 318) (Conner et al., 2018). Chaffee et al. (Chaffee et al., 2018) found that among US ever-smokers (age 12–17 years, N = 1295), e-cigarette experimentation was positively associated with a progression to an established cigarette smoking habit, defined as having smoked ≥ 100 cigarettes and having past-30 days smoking (OR: 1.80; 95 % CI: 1.04–3.12). Those studies have a number of limitations, including rather small samples, a follow-up at only 1 year after baseline, and use methods that are not appropriate to conclude on a causal relation between e-cigarette use and smoking habits later in life.

Several causal inference methods can be applied to observational studies to estimate causal relationships. For instance, Inverse Probability of Treatment Weighting (IPTW) uses a propensity score to check and reach covariate balance between exposed and unexposed respondents (Austin, 2011; Austin and Stuart, 2015; Hernan, 2006; Imbens and Rubin, 2015). Timberlake et al. used a propensity score matching approach on data from the National Longitudinal Study of Adolescent Health to evaluate whether smokeless tobacco was a gateway to smoking (Timberlake et al., 2009). They found that the observed association between smokeless tobacco and smoking was not due to an effect of smokeless tobacco but only to baseline differences between users and nonusers of smokeless tobacco.

In France, daily smoking is still highly prevalent. In 2017, 25.1 % of 17-year-old adolescents declared having smoked at least one cigarette per day in the past month (Spilka et al., 2018). Looking at the transition from smoking initiation to daily smoking would provide useful information on the role of e-cigarette use on tobacco smoking trajectories at this critical period. The gateway effect hypothesis suggests that e-cigarette experimentation could cause smoking initiation and, potentially, subsequent transition to daily smoking. E-cigarette experimentation after smoking initiation could also reinforce smoking consumption and lead to daily smoking.

Objective: With an IPTW approach and retrospective cohort data, we analyze if e-cigarette ever use had an impact on the transition to daily smoking among French ever-smokers aged 17 using a large national representative survey. In additional analyses, we study if this impact differs with the sequence of the product experimented first.

2. Methods

2.1. Data source

The French Monitoring Centre for Drugs and Drug Addiction and the Department of National Civil Service and Youth conduct every three years the Escapad Survey (survey on health and substance use) to provide national representative estimates of prevalence of drug use

among French adolescents (Beck et al., 2006). All French nationals are required to attend a one-day compulsory session of civic and military information called the National Defense and Citizenship Day (JDC) shortly after having turned 17. Because the attendance certificate to the JDC is compulsory for all public exams, including a driving license, only a small proportion of youths ($\approx 4.1\%$) postpone their attendance. The Escapad data collection takes place during two weeks in March in all JDC centers across the French territory. All attending adolescents are requested to fill in a self-administered questionnaire, structured in line with recommendations by The European Monitoring Centre for Drug and Drug Addiction on patterns of substance use (Bless et al., 1997). Participation in the survey is confidential and anonymous and participants can refuse to participate, as explicitly stated to them. The survey has gained the Public Statistics general interest seal of approval from the National Council for Statistical Information (CNIS).

The data come from the 2017 Escapad in continental France. 43,892 adolescents attended the JDC, 42,751 completed the questionnaire, and 41,908 completed a valid questionnaire (aged 16–24). Among valid questionnaires, 6.7 % were completed by out of age respondents and thus removed. The final sample included 39,115 French adolescents with an average age of 17.4 years (min: 17; max: 18.5). Data are calibrated to guarantee representativeness based on gender and age for each of the 95 “départements” (level of administrative divisions of territory in France).

2.2. Study population

The sample included 23,095 respondents who declared having ever tried smoking. Smoking initiation was defined through the question: “During your life, have you ever smoked cigarettes, cigars or cigarillos” (never/yes). Individuals were classified as missing if they did not inform their cigarette consumption during the last 30 days, ever use of e-cigarette, age at e-cigarette initiation or age at transition to daily smoking. These variables were necessary for the definitions of exposure and outcome. As a result, the analytical study sample comprised 21,401 ever-smokers.

2.3. Outcome variable

The outcome variable was declaring daily cigarette smoking in the past 30 days. People who declared smoking one or more cigarettes per day were considered daily smokers at 17.

2.4. Exposure variable

The exposure variable was defined as “ever e-cigarette use in age similar or lower than that of the onset of daily smoking” (exposure = 1) vs never e-cigarette use (exposure = 0), resulting from the combination of three separate measures: “ever e-cigarette use”, “age of first e-cigarette use” and “age at transition to daily (tobacco) smoking” (if any). The ever e-cigarette use was defined through the question: “During your life, have you ever used an electronic cigarette” (never/yes). To make sure the exposure happened before the outcome, the age at first e-cigarette use (“What was your age the first time you used an electronic cigarette?”) and the age at transition to daily smoking (“If you are smoking daily, at what age did you start smoking every day?”) were used to classify respondents that had ever tried e-cigarette and were declaring a daily smoking habit at 17 (n = 7054). Respondents who tried e-cigarettes before, or at the same age as daily smoking, were considered as exposed (n = 4184), whereas those who tried e-cigarette after their transition to daily smoking were considered as unexposed (n = 2870) (Fig. 1). As a result, there were 13,055 exposed and 8346 unexposed in the study sample.

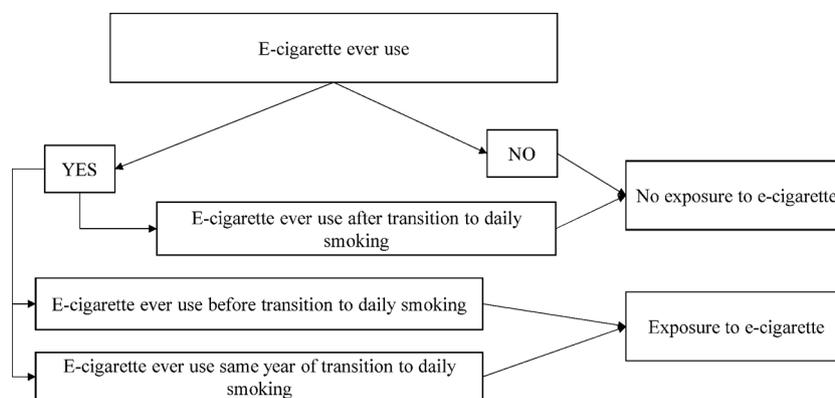


Fig. 1. Exposure classification.

2.5. Covariates

The following sociodemographic variables were considered: age (continuous), gender, parental occupational status (highest occupational category of either parent, recoded in 5 ordered categories: low; disadvantaged; middle; advantaged; high); family structure (members in the household, recoded in 3 categories: nuclear family; stepfamily; single-parent family/others) and the Family Affluence Scale (FAS) score (Currie et al., 2008). The FAS score was built into three categories (low; moderate; high) from four questions: number of cars owned by the family; whether the respondent's bedroom is shared with another household member; number of family holidays/travel in the past year; number of computers or digital tablets owned by the family.

Age at smoking initiation ("What was your age the first time you smoked a cigarette?") was included as it is a prominent factor predicting future daily smoking (Sharapova et al., 2018; Walker and Loprinzi, 2014).

School performance variables were declaring a grade repetition (no; yes), difficulties to read in French and difficulties to write in French (no; yes, sometimes; yes, often; recoded in "no" or "yes").

Substance use variables (licit or illicit) were used to approximate and control the effect of a common liability to addiction (Mayet et al., 2016). The experimentations with hookahs, alcohol, drunkenness and cannabis were included through the questions "During your life, have you ever: smoked tobacco with a hookah/drink alcohol/been drunk/smoked cannabis?" and "How old were you the first time?" For each, a categorical variable was created (never use; late initiation; early initiation). Early initiation was defined as an age at initiation under the 25th percentile (Mayet et al., 2016): 14 for hookah and alcohol and 15 for drunkenness and cannabis. The number of other illicit drug experimented with was included as a categorical variable coded from 0 to 7 products. Other illicit drugs included mushrooms, ecstasy/MDMA, amphetamine/speed, LSD, crack/freebase, cocaine, heroin.

2.6. Statistical analysis

The respondent sample and the analytical sample were described with percentages for categorical variables and means for continuous variables.

We used an IPTW approach by estimating stabilized inverse Propensity Scores (PS) as weights to estimate the impact of e-cigarette experimentation on the transition to daily smoking among smoking ever users. Such an approach allows for controlling for measured confounders and checking balance in such confounders between exposed and unexposed groups.

The propensity score represents for each individual the probability of being exposed based on baseline characteristics (Ali et al., 2016; Rosenbaum and Rubin, 1983). It was estimated by performing a multiple logistic regression on the exposure variable (e-cigarette ever use).

Variables were included in the PS logistic regression if they could influence the outcome (daily smoking at 17) or impact the probability of exposure without being influenced by the exposure: age and age at first cigarette use, sociodemographic, school performance, and drug use variables. All variables were added as main effects along with the following interaction terms: age at smoking initiation and gender, age at smoking initiation and FAS score, age at smoking initiation and difficulty to read, and hookah experimentation and gender. In addition, the survey weighting factors from the ESCAPAD 2017 survey were included in the PS model. Finally, stabilized inverse PS weights were computed (Austin and Stuart, 2015; Xu et al., 2010).

To assess balance between the two groups, absolute Standardized Mean Differences (SMD) of each selected covariate were computed between the exposed and unexposed groups before and after including the stabilized inverse PS as weights. We chose a conventional threshold, absolute SMD below 0.1, as an indicator of good balance in the weighted sample (Austin and Stuart, 2015; Linden and Samuels, 2013).

The impact of e-cigarette ever use on daily smoking was estimated through prevalence ratios (interpreted as risk ratios) obtained from a simple modified Poisson regression model with IPTW, which included daily smoking at 17 as the outcome and e-cigarette ever use as the exposure. Modified Poisson models directly allow the estimation of risk ratios (Zou and Donner, 2013). The robust variance option was chosen to correctly estimate confidence intervals (Zou, 2004). We conducted an additional Poisson model including the variables used to specify the propensity score as covariates to adjust for the potential residual imbalance of the covariates and provide doubly robust estimates (Imbens and Rubin, 2015).

2.7. Sensitivity analysis

The chronology between school performance variables and e-cigarette experimentation (as well as smoking experimentation) was unknown. School performance could have been impacted by the exposure to e-cigarette or other drug use (Legleye et al., 2010). Similarly, other drug experimentation could have happened after smoking and e-cigarette experimentation. Because of their potential roles as "post-treatment variables" (Imbens and Rubin, 2015), school performance and drug use variables were removed from the propensity score model in a sensibility analysis, everything else remaining unchanged.

2.8. Supplementary analyses

To evaluate a potential role of the order of experimentation between smoking and e-cigarette, we reproduced the primary analysis on two exposure subgroups. In both cases, the unexposed group, the specification of the propensity score and the final models remained unchanged, only the exposed group was modified (Fig. 2). In the first subgroup, the exposed group was composed of respondents who tried e-

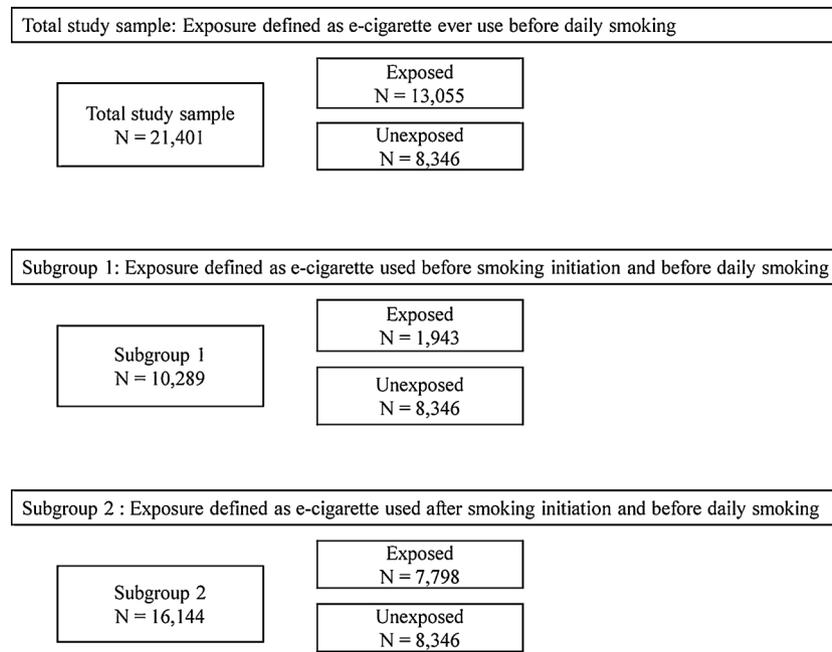


Fig. 2. Main and supplementary analyses.

cigarette strictly before smoking initiation, and in the second, respondents who tried e-cigarette strictly after smoking initiation. Those for which the order of experimentation was unknown (same age at first use for e-cigarette and smoking, $N = 2290$) were not included in those analyses.

3. Results

3.1. Smoking and e-cigarette use among French adolescents aged 17 ($n = 39,115$)

59.0 % of French adolescents aged 17 reported having tried smoking, only a slightly higher number than e-cigarette experimentation (52.4 %). The use in the past month was two times more common for cigarettes than for e-cigarettes (34.1 vs 16.8 %). For cigarettes, the use in the past month was mainly daily smoking (25.1 %) whereas the daily use of e-cigarette was only 1.9 % (Table 1).

At 17, 44.8 % had already experimented with both products (dual ever users), 33.5 % had not experimented with any product, and 14.1 % had only tried smoking while 7.6 % had only tried of e-cigarette.

The mean age at smoking initiation was 14.4, the mean age at transition to daily smoking was 15.1 and the mean age at e-cigarette initiation was 15.4. Among dual ever users, 71.4 % had tried e-cigarette after having tried smoking while 13.2 % tried e-cigarette before, and 15.4 % the same year. Among daily smokers who tried e-cigarette ($N = 7,054$), 40.2 % ($N = 2,870$) tried it after the transition to daily smoking, 27.2 % ($N = 1,882$) before and 32.7 % ($N = 2,302$) the same year.

Table 1

Prevalence of e-cigarette use and cigarette smoking at 17, in France in 2017 (ESCAPAD 2017, OFDT).

	E-cigarette Weighted percentage (observations)	Cigarette smoking Weighted percentage (observations)
Ever use	52.4 (20,373)	59.0 (23,095)
Current use (at least once in the past month)	16.8 (6540)	34.1 (13,332)
Daily use (at least once per day in the past month)	1.9 (740)	25.1 (9820)

3.2. Role of e-cigarette ever use on transition to daily smoking at age 17 among ever smokers ($n = 21,401$)

In our population of interest, 32.1 % of those who experimented with e-cigarette (exposed group, $n = 13,055$) were daily smokers compared to 49.6 % among those who did not (unexposed group, $n = 8,346$). Their characteristics are presented in Table S1 of the supplementary materials.

Table 2 summarizes the estimated impact of e-cigarette use on the transition to daily smoking among ever smokers. The simple weighted regression gave an estimate of $RR = 0.62$ 95 %CI [0.60 – 0.64]. Adolescents who experimented with e-cigarette were less likely than those who did not to transition to daily smoking at 17. Adding covariates yielded very similar results (not shown). The propensity score specification allowed for good balancing of the exposed and unexposed respondents on the chosen covariates (highest absolute SMD = 0.01) (Table S2). The stabilized inverse PS showed a reasonable dispersion, a condition for estimation reliability (Table 3).

Removing the variables describing other substance use and school from the propensity score specification very slightly reduced the negative effect of e-cigarette on the transition to daily smoking (from $RR = 0.62$ 95 %CI [0.60 – 0.64] to $RR = 0.66$ 95 %CI [0.63 – 0.68]) (Table S3).

When considering the chronology of e-cigarette and tobacco smoking experimentation, the negative effect of e-cigarette on the transition to daily smoking was still present when individuals experimented with e-cigarette before they experimented with smoking ($RR = 0.76$ 95 %CI [0.66 – 0.89]). When they experimented with e-cigarette after smoking, the effect was $RR = 0.66$ 95 %CI [0.64 – 0.69] (Tables S4 and S5).

Table 2

Effect estimate of e-cigarette ever use on the transition to daily smoking among French ever smokers aged 17 in 2017 (ESCAPAD 2017, OFDT).

Model	Observations			RR	95 %CI
	Total population	Exposed	Unexposed		
Simple IPTW regression	17,862	10,981	6,881	0.62	[0.60 – 0.64]

RR: risk ratio; 95 %CI: 95 % confidence interval; IPTW: inverse probability of treatment weighting.

Table 3

Distribution of the stabilized inverse propensity scores in the analytic sample (ESCAPAD 2017, OFDT).

Observations	Mean	CV	P1	P99	Min-max
17,862	1.00	30.11	0.56	1.99	0.41-7.52

CV: coefficient of variation; P1: 1st percentile; P99: 99th percentile.

4. Discussion

Our results show that among French ever smokers aged 17, those who had experimented with e-cigarette were less likely to later transition to daily smoking than those who had not. This was the case even when e-cigarette was tried before initiating smoking, in contradiction with the gateway hypothesis.

Many studies have shown an association between ever e-cigarette use and subsequent smoking initiation among adolescents from the USA, the UK or Canada (Soneji et al., 2017). As mentioned earlier, experimenting with e-cigarette and smoking seem to be highly associated behaviors. Our results do not question those findings since our outcome (daily smoking) and objectives were different.

Some studies have looked at regular smoking as an outcome. Barrington-Trimis et al. found that adolescents who experimented with e-cigarette were more prone than the others to become tobacco ever users and regular tobacco smokers, although they did not find a significant difference between the two outcomes. In France, most adolescents start by experimenting with smoking and then experiment with e-cigarettes, which could explain some of the difference. Coherent with our results, among ever smokers at baseline, they found that those who had ever used e-cigarettes at baseline did not differ in their smoking progression sequence than those who did not (OR = 0.76; 95 % CI: 0.41-1.42 for reporting past-30-days frequent use of cigarettes, defined as 3–5 or more days) (Barrington-Trimis et al., 2018). It seems that although e-cigarettes and smoking are associated behaviors, e-cigarettes might not seem to increase smoking behaviors among ever smokers.

In France, smoking remains much more common than in countries where other studies have been conducted, which could explain diverging results found in the literature. In 2018, 27.3 % of French high-school students declared smoking in the past 30-days (Spilka et al., 2019). In comparison, current use of cigarette smoking was 8.1 % among American high school pupils the same year (13.9 % for any combustible tobacco product) (Gentzke et al., 2019) and it was 15 % at age 15 in the UK in 2016 (National Health Service Digital, 2017). Moreover, highly addictive devices delivering high doses of nicotine salts were not available in France at the time of the survey, contrary to the US situation where most e-cigarettes used by adolescents contain nicotine. Similarly, as for smoking, vaping in France is strongly regulated and advertising is forbidden, which is not the case, for example, in the USA (Marynak et al., 2018).

France has recently implemented strong tobacco control policies including plain packaging and regular price increases (Lermenier-Jeannet, 2018). At the same time, the prevalence of daily smoking among adults is currently decreasing sharply (Andler et al., 2019). Our results could illustrate this ongoing denormalization of smoking. E-cigarettes could represent an alternative to tobacco smoking for a

growing proportion of adolescents that, although they might experiment with both products, are losing interest in smoking. To test this hypothesis, motivations for smoking and for e-cigarette use among French adolescents will have to be further investigated through both qualitative and quantitative analyses.

E-cigarette use, especially among adolescents, remains a controversial topic among public health professionals (Chapman et al., 2019; Kozlowski and Warner, 2017; Newton et al., 2018). However, in France, smoking still represents the main health threat. In this context and in the light of our results, we recommend continuous tobacco control efforts and the production of more robust data to better understand e-cigarettes' risks and role in smoking behaviors. Data on the role of e-cigarettes from countries with various smoking prevalence are needed to add to the existing literature.

4.1. Limitations

Our conclusions are provisional and only concern ever smokers aged 17. People who at 17 are not daily smokers could pursue two potential trajectories: later becoming daily smokers, or remaining non-daily smokers. Our analyses should be repeated in cohorts that survey older age groups to investigate the impact of e-cigarette use on smoking behaviors later in life.

We use self-reported age at smoking and e-cigarette initiation as well as age at transition to daily smoking to construct retrospective trajectories of use. We acknowledge a recall bias could be possible but limited for those questions (Henriksen and Jackson, 1999; Johnson and Mott, 2001; Parra et al., 2003). Those events have mostly happened within a 5-year period and smoking initiation is commonly considered an important "rite of passage" for adolescents in France. We thus assume that the sequence of use between e-cigarette, cigarette and daily smoking should be well recalled.

We only considered e-cigarette initiation (and not regular or daily use) as exposure. This limitation is a minor one given the relatively low proportion of regular e-cigarette use at 17. Finally, since the type of e-cigarette device and the presence of nicotine within the liquid was unknown; we could not take them into account.

In conclusion, our results represent additional insights on the potential role of e-cigarette on smoking habits by focusing on the transition to daily smoking. They rely on the robustness of the ESCAPAD 2017 survey method and a rigorous analytical approach. They illustrate the French context where smoking is still highly common although less and less popular and where experimenting with e-cigarettes could reflect a lack of interest for smoking. However, adolescent vaping will have to be closely monitored to prevent any public health issue.

Contributors

SL, SC and TB designed the statistical analysis plan. FB and SS supervised the work. SC conducted the data analysis and wrote the manuscript. SL, TB, FB and SS provided critical feedback on the manuscript and analyses. All authors have read and approved the final manuscript.

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Declaration of Competing Interest

No conflict declared.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.drugalcdep.2020.107853>.

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