Association between age at first reported e-cigarette use and subsequent regular e-cigarette, ever cigarette and regular cigarette use

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ABSTRACT

Background and Aims: Association of electronic cigarette use and subsequent smoking has received considerable attention, although age of first use has not. This study tested differences in regular (e-cigarettes, cigarettes) and ever (cigarettes) use between e-cigarette user groups: early versus never users, late versus never users, early versus late users and effects of controlling for covariates.

Design: Prospective study with 12- and 24-month follow-up of e-cigarette/cigarette ever/regular use with data from an intervention.

Setting: Forty-five schools in England (Staffordshire and Yorkshire).

Participants: Never smokers (3289 13-14 year olds) who were part of a cluster randomised controlled trial.

Measurements: Sample divided into groups of e-cigarette users: *early users* (at 13-14 years), *late users* (at 14-15 years), *never users* (at 13-14 and 14-15 years). Dependent variables were self-reported regular e-cigarette and cigarette use, ever cigarette use at 15-16 years. Covariates were assessed.

Findings: Early users and late users compared with never users were significantly more likely to be regular e-cigarette users (early: OR=9.42, 95%CI=5.38, 16.49, $p<.001$; late: *OR*=6.89, 95%CI=4.11, 11.54, $p<.001$), ever cigarette users (early: *OR*=7.96, 95%CI=6.02, 10.53, $p<.001$; late: *OR*=5.13, 95%CI=3.85, 6.84, $p<.001$), and regular cigarette users (early: *OR*=7.80, 95%CI=3.99, 15.27, $p<.001$; late: *OR*=4.34, 95%CI=1.93, 9.77, $p<.001$) at age 15-16 years. Late users compared with early users had significantly lower rates of ever use of cigarettes at 15-16 years (*OR*=0.48, 95%CI=0.35, 0.66, $p<.001$), although this difference was non-significant at 12 months after first use of e-cigarettes (*OR*=0.89, 95%CI 0.64, 1.25, $p = .498$). Controlling for covariates did not change findings.

Conclusions: Adolescents in England who report using e-cigarettes at 13-14 years of age have higher rates of subsequently initiating cigarette use than adolescents who report using e-cigarettes at 14-15 years, a difference that may be attributable to a longer period of time to initiate cigarette use in former group.

Key words: electronic nicotine delivery systems; e-cigarettes; smoking; harm reduction; intervention.

INTRODUCTION

An increasing number of studies have assessed the impact of using e-cigarettes on subsequent initiation of smoking in adolescents. Various US [1-4] and UK [5-7] studies show e-cigarette use by adolescents to be positively associated with initiation of cigarette use 12-24 months later in 14-16 year olds. The evidence in relation to e-cigarette use and becoming a regular user of cigarettes is more mixed [7-8]. Few of the studies examining the relationship between e-cigarette use and subsequent smoking have examined the role of age of uptake (first reported use) of e-cigarettes. McCabe et al. [9] is one exception. They reported data comparing US adolescents who began using e-cigarettes in the ninth grade (14-15 years or earlier) versus the 12th grade (17-18 years). Those adolescents who initiated e-cigarette use earlier compared to later were significantly more likely to become ever users of cigarettes (AOR = 2.83, 95%CI 1.06, 7.51) when high school seniors. More recently, Evans-Polce and colleagues [10] show that age of first reported use of e-cigarettes is changing in US adolescents, while it appears to be remaining stable for first reported use of cigarettes, cigars and smokeless tobacco. In particular, between 2014 and 2018 the proportion of ever users of e-cigarettes at 14 years or younger increased from 8.8% to 28.6%. It is notable that the cross-sectional data reported by Evans-Polce et al. [10] do not indicate that earlier uptake of e-cigarettes is being translated into earlier uptake of cigarettes or other tobacco-containing products. The present research provides a further test of the impact of age of first reported use of e-cigarettes (i.e., early use versus late use) on subsequent ever cigarette use in a sample of UK adolescents. In addition, the present research provides a novel test of the impact of early versus late use of e-cigarettes on subsequent regular cigarette use and regular e-cigarette use.

The present data on e-cigarette and cigarette use in UK adolescents were collected as part of a trial to test an intervention to prevent smoking initiation [11]. Previous reports have focused on never smokers aged 13-14 years who reported having used e-cigarettes or not to predict initiation of cigarette smoking 12 months later when aged 14-15 years [5] and initiation and regular smoking 24 months later when aged 15-16 years [7]. We also collected data on use of e-cigarettes at age 14-15 years that we have not published previously, and this has allowed us to compare groups of never smoking adolescents who first reported e-cigarette use at different ages (*early users* [13-14 years] versus *late users* [14-15 years]) in relation to their

self-reported regular e-cigarette use, ever cigarette use, and regular cigarette use at 15-16 years of age. Such comparisons of early and late users confound age of first use of e-cigarettes with time delay between first reporting e-cigarette use and when outcomes are assessed (i.e., 24 months in early users versus 12 months in late users). To explore further the effect of time delay we also compared early users and late users of e-cigarettes at 12 months after first use (i.e., at age 14-15 years in early users versus 15-16 years in late users). Our analyses examined the effects of age of first reported use of e-cigarettes when not controlling and controlling for various covariates of adolescent smoking.

Although our focus was on the comparison of early versus late first users of e-cigarettes, groups of adolescents who had not used e-cigarettes were also created to enable comparison. The never users comparison group for early users of e-cigarettes were adolescents who were also never smokers at age 13-14 years and never users of e-cigarettes at both 13-14 and 14-15 years. The never users comparison group for late users of e-cigarettes were a subset of this group who additionally were never smokers at age 14-15 years. The user versus never user comparisons assessed the impact of e-cigarette use on subsequent cigarette use.

The present study extends knowledge in this area in four important ways. First, this is the only study to examine effects of early versus late use of e-cigarettes on regular e-cigarette, ever cigarette use, and regular cigarette use. Second, this study explored outcomes both at age 15-16 years and at 12 months post first reported use of e-cigarettes, in order to help differentiate between the effects of age of initiation and the duration from first use of e-cigarettes to assessment of outcome. Third, this study explored the effects of controlling for a number of covariates (gender, ethnicity, individual/school level socio-economic status, friends and family smoking, impulsivity, and intentions, attitudes, norms, perceived behavioural control and self-efficacy in relation to smoking). Fourth, self-reported measures of smoking at follow-up were validated against objective smoking measures.

The current study had three specific aims: 1. Test for differences between early users and never users of e-cigarettes in subsequent regular use of e-cigarettes, ever use of cigarettes, and regular use of cigarettes; 2. Test for differences between late users and never users of e-cigarettes in subsequent regular use of e-

cigarettes, ever use of cigarettes, and regular use of cigarettes; 3. Test for differences between early users and late users of e-cigarettes in subsequent regular use of e-cigarettes, ever use of cigarettes, and regular use of cigarettes.

METHOD

Design

Data were collected as part of a pre-registered, four-year cluster randomised controlled trial of a school-based intervention to prevent smoking initiation [11-12] using anti-smoking messages and implementation intentions [13-15]. The study was conducted in 45 schools in England with adolescents initially aged 11-12 years. The analyses reported here were performed controlling for condition.

Participants and Procedures

The data reported here are from wave 3 (September-December 2014; in 13-14 year olds), wave 4 (September-December 2015; in 14-15 year olds), and wave 5 (September-December 2016; in 15-16 year olds) of the trial when measures of e-cigarette use were added to data collection. Only respondents reporting having never smoked a cigarette at wave 3 were analysed here (i.e., this is a post-hoc analysis), although adolescents in both control and intervention conditions were included. Previous papers reported the impact of e-cigarette use (wave 3) on smoking 12 months later (wave 4; control condition only) [5] and 24 months later (wave 5; control plus intervention conditions) [7]. The University of Leeds, UK (Faculty of Medicine) ethical review committee approved the study (reference 12-0155).

Measures

Outcomes.

Cigarette use was assessed using standardised measures [16] at each wave (i.e., time point); adolescents ticked one of: 'I have never smoked; I have only tried smoking once; I used to smoke sometimes, but I never smoke cigarettes now; I sometimes smoke cigarettes now, but I don't smoke as many as one a week; I usually smoke between one and six cigarettes a week; and I usually smoke more than six cigarettes a week'. Only respondents marking the first response at wave 3 were retained for analysis. At

wave 4 and wave 5 this measure was converted into outcome measures of *ever smoked cigarettes* (first response coded 0; other responses coded 1) and *regularly smoked cigarettes* (last two responses coded 1; other responses coded 0). The self-reported smoking responses were validated against a measure of breath carbon monoxide (CO) levels (Micro+ Smokerlyzer® CO Monitor, Bedfont Scientific Limited, Kent, England), although we did not reclassify self-report measures based on CO level. Such measures are reliable and valid ways of assessing regular cigarette smoking [17-18] but not occasional smoking due to the short half-life (four-six hours) of breath CO.

E-cigarettes/vapourisers were described as 'a tube that sometimes looks like a normal cigarette and has a glowing tip. They all puff a vapour that looks like smoke but unlike normal cigarettes, they don't burn tobacco'. Use of e-cigarettes at each wave was tapped by one item ('Which ONE of the following is closest to describing your experience of e-cigarettes or vapourisers', I have never used them; I have tried them once or twice; I use them sometimes [more than once a month but less than once a week]; I use them often [more than once a week]'). This was converted into a measure of *ever used e-cigarettes* (first response=0; other responses=1) and *regularly used e-cigarettes* (last response coded 1; other responses coded 0). Ever used e-cigarettes at wave 3 and wave 4 was used to classify respondents into different user groups (see below). Regularly used e-cigarettes at wave 4 and wave 5 was used as an outcome measure.

Predictors.

Other measures were assessed as covariates that might account for the relationship between e-cigarette and cigarette use. Demographic variables analysed were gender (male=0; female=1), ethnicity (non-white=0, white=1), family affluence (based on the four-item Family Affluence scale [19]: scored 0-3, higher scores indicating greater affluence). Two school-level measures were also assessed: percentage of children per school eligible for free school meals (<median 20%=0; $\geq$20%=1) [20]; condition (control=0, intervention=1).

Friends' smoking was assessed using the question, 'How many of your friends smoke?', none of them; only a few; half and half; most but not all; all of them (none of them=0; a few or more=1). Family smoking was assessed using the question: 'Who smokes in your family now? Tick all the people who smoke

at the moment', followed by a list of 8 family members plus open-ended response to specify additional family member (no family members=0; one or more family members=1). Friends and family smoking were assessed at wave 3. Impulsiveness was measured at wave 5 based on a five item impulsivity scale (dichotomised into low impulsivity=0, high impulsivity=1) [20].

Health cognitions about smoking [14] were assessed at wave 3 as the mean of multiple questions on five-point scales: intention (3 questions; e.g., 'I plan not to smoke'; Cronbach's α=0·90); attitude (7 questions; e.g., 'For me, smoking would be… good-bad'; α=0·87); perceived norms (5 questions; e.g., 'Most of my friends think… I should smoke-I should not smoke'; α=0·79); perceived behavioural control (3 questions; e.g., 'I am confident I could resist smoking', strongly disagree-strongly agree; α=0·69); self-efficacy (6 questions; e.g., 'I can say no to smoking, even at school' strongly disagree-strongly agree; α=0·91). Questions were highly skewed towards negative views of smoking and so were dichotomised (negative views=0; less negative views=1).

Data Analysis

The analyses reported here were not pre-registered and as such the results reported should be considered exploratory. Missing data ranged from 0·0% (gender) to 1·1% (ethnicity) and 98% of the 3,289 never smokers in the sample would have been available for analysis under the traditional listwise deletion method across variables. Data were missing due to item non-response. As the level of missing values was low, missing at random was assumed to justify multiple imputation. Multiple imputation in SPSS generated five imputed datasets. Imputed values compared reasonably to observed values and results using listwise deletion were similar to multiple imputation, so imputed results are presented for all analyses. Adolescents were clustered by school and tests of differences between user groups (see below) controlled for clustering by school.

Based on responses to questions about ever use of e-cigarettes and cigarettes at wave 3 and wave 4, different *e-cigarette user groups* were created. *Early users* were defined as those who at wave 3 reported ever use of e-cigarettes plus never use of cigarettes, i.e., they had started using e-cigarettes but not cigarettes by age 13-14 years (N = 649). *Late users* were defined as those who at wave 3 reported never use of e-

cigarettes or cigarettes and at wave 4 reported ever use of e-cigarettes plus never use of cigarettes, i.e., they had started using e-cigarettes but not cigarettes by age 14-15 years (N = 419). *Never users* were defined as those who at both wave 3 and wave 4 reported never use of e-cigarettes plus at wave 3 reported never use of cigarettes (N = 2221). A sub-group of never users (labelled *never users who never smoked*) was defined as those who reported at both wave 3 and wave 4 that they never used e-cigarettes or cigarettes (N = 2172).

In the first set of analyses on e-cigarette user group, *early users* and *never users* were compared on regular use of e-cigarettes, ever use of cigarettes, and regular use of cigarettes at wave 4 and wave 5. The tests at wave 4 represent a 12-month follow-up; the tests at wave 5 represent a 24-month follow-up. These analyses overlap with those previously reported from this data [5,7]. In the second set of analyses on e-cigarette user group, *late users* and *never users who never smoked* were compared on regular use of e-cigarettes, ever use of cigarettes, and regular use of cigarettes at wave 5 (i.e., a 12-month follow-up). These comparisons have not previously been reported. In the third set of analyses on e-cigarette user group, *early users* and *late users* were compared regular use of e-cigarettes, ever use of cigarettes, and regular use of cigarettes at waves 4 and 5. Two comparisons between *early users* and *late users* were possible here although we focus on the former: comparisons at a specific age point, i.e., wave 5 (i.e., when adolescents were 15-16 years); comparisons on effects 12 months after e-cigarette use first reported (i.e., wave 4 outcomes for *early users*; wave 5 outcomes for *late users*). It is worth noting that time period since reporting e-cigarette use and age are confounded in these analyses. In the former analyses, time delay to outcome is different (*early users*: 24 months; *late users*: 12 months), although age when outcome is assessed is matched (15-16 years). In the latter analyses, time delay to outcome is matched (12 months) but age when outcome is assessed is different (*early* users: 14-15 years; *late users:* 15-16 years). Comparison of these analyses should give some indication of whether differences between early and late users are attributable to age of first reported use of e-cigarettes or time delay from first use to outcome reporting.

IBM SPSS (version 26) or HLM (version 7) were used for the analyses. We assessed sample characteristics and validated cigarette smoking measures at waves 4 and 5 against breath CO levels (using logistic regressions). The main analysis assessed the frequencies of regular e-cigarette use, ever use of cigarettes, and regular cigarette use in each of the e-cigarette user groups at wave 5 (and for some groups at

wave 4). Analyses predicted regular e-cigarette use, ever cigarette use, and regular cigarette use (at wave 5) based on user group (Model 1) plus covariates (Model 2) using multilevel logistic regression (Bernoulli model) that controlled for clustering by school. The covariates were included as potential explanations of the relationship between e-cigarette use and later cigarette use (all were level 1 variables except free school meals and condition which were level 2 variables). For comparison purposes, we also compared the *early user* and *late user* groups at 12 months post first reported use (i.e., wave 4 outcomes for *early users* against wave 5 outcomes for *late users*). For group comparisons we report the odds ratio, 95% confidence interval and *p* value and examine the effects of controlling for covariates (based on the population average model with robust standard errors). The comparison between *early users* and *late users* report these statistics for group with and without covariates and the -2 log-likelihood to indicate model fit.

Full data are available from the first author.

RESULTS

Sample Description

Table 1 provides descriptive data on all measures for the full imputed sample. The sample of 3,289 never smokers at age 13-14 years (Table 1) comprised 47·0% boys and 83·5% white individuals, who mainly had no friends who smoked (66·8%) but did have one or more family member who smoked (61·3%). Health cognitions about smoking were all biased against smoking.

Objectively assessed breath CO levels were predictive of being classified as a regular cigarette smoker at wave 4 (Odds ratio = 2·52, 95%CI 1·54, 4·10, $p < ·001$) and wave 5 (Odds ratio = 2·10, 95%CI 1·71, 2·58, $p < ·001$). Objectively assessed breath CO levels were predictive of being an ever cigarette smoker at wave 5 (Odds ratio = 1·12, 95%CI 1·01, 1·24, $p = ·03$) but not wave 4 (Odds ratio = 1·11, 95%CI 0·94, 1·31, $p = ·23$). However, it is worth noting that the median and range of breath CO levels were very similar for different categories of smoker at both waves.

E-Cigarette User Groups

Table 2 shows the numbers of adolescents reporting different levels of regular e-cigarette use, ever cigarette use, or regular cigarette use in the different e-cigarette user groups at wave 4 (when aged 14-15

years) and wave 5 (when aged 15-16 years). At wave 4, rates of ever smoking were higher in *early users* compared to *never users* (Table 2, left-hand panel). Logistic regression analyses that controlled for clustering confirmed these differences to be significant when not controlling for covariates (Odds ratio = 16.69, 95%CI 12.45, 22.37, $p < .001$) and when controlling for covariates (Odds ratio = 1.39, 95%CI 1.29, 1.50, $p < .001$). Rates of regular e-cigarette and cigarette use were also higher in *early users* compared to *never users* at wave 4, although we did not test these differences in logistic regression given the low numbers involved (Table 2). At wave 5, *early users* again had higher rates of regular e-cigarette use, ever cigarette use and regular cigarette use compared to *never users* (Table 2, right-hand panel). After controlling for clustering, each of these differences was significant when not controlling (regular e-cigarette use: Odds ratio = 9.42, 95%CI 5.38, 16.49, $p < .001$; ever cigarette use: Odds ratio = 7.96, 95%CI 6.02, 10.53, $p < .001$; regular cigarette use: Odds ratio = 7.80, 95%CI 3.99, 15.27, $p < .001$) and controlling (regular e-cigarette use: Odds ratio = 1.21, 95%CI 1.11, 1.31, $p < .001$; ever cigarette use: Odds ratio = 3.55, 95%CI 2.82, 4.49, $p < .001$; regular cigarette use: Odds ratio = 1.25, 95%CI 1.16, 1.34, $p < .001$) for covariates. These findings parallel our previously reported findings [5,7].

At wave 5, rates of regular e-cigarette use, ever cigarette use and regular cigarette use were higher in *late users* compared to *never users who never smoked* (Table 2, right-hand panel). Logistic regression analyses that controlled for clustering confirmed these differences to be significant when not controlling (regular e-cigarette use: Odds ratio = 6.89, 95%CI 4.11, 11.54, $p < .001$; ever cigarette use: Odds ratio = 5.13, 95%CI 3.85, 6.84, $p < .001$; regular cigarette use: Odds ratio = 4.34, 95%CI 1.93, 9.77, $p < .001$) and controlling (regular e-cigarette use: Odds ratio = 1.13, 95%CI 1.04, 1.23, $p = .004$; ever cigarette use: Odds ratio = 2.87, 95%CI 2.33, 3.53, $p < .001$; regular cigarette use: Odds ratio = 1.12, 95%CI 1.08, 1.16, $p < .001$) for covariates.

Table 3 reports the comparison of *early users* versus *late users* of e-cigarettes at wave 5 (i.e., 12 or 24 months after reporting first e-cigarette use for *late users* and *early users* respectively). Logistic regression controlling for clustering indicated that there were no significant differences between *early users* and *late users* for regular e-cigarette use when not controlling or controlling for covariates (Table 3, left-hand panel). Similarly there were no significant differences between *early users* and *late users* for regular

cigarette use when not controlling or controlling for covariates (Table 3, right-hand panel). In contrast, ever cigarette use was significantly lower in the *late users* compared to *early users* both when not controlling or controlling for covariates (Table 3, middle-panel).

The comparison of *early users* versus *late users* of e-cigarettes when focusing the 12-month period since first reporting e-cigarette use (i.e., wave 4 for early users, wave 5 for *late users*) revealed a slightly different pattern (Table 2). Logistic regression analysis controlling for clustering indicated that regular e-cigarette use was significantly lower in *late users* compared to *early users* (Odds ratio = 0.54, 95%CI 0.33, 0.87, $p = .013$), although this difference became marginally significant when controlling for covariates (Odds ratio = 0.87, 95%CI 0.76, 1.000, $p = .050$). Regular cigarette use was significantly higher in *late users* compared to *early users* (Odds ratio = 1.95, 95%CI 1.17, 3.25, $p = .012$), but this became non-significant when controlling for covariates (Odds ratio = 1.06, 95%CI 0.96, 1.18, $p = .235$). Ever use of cigarettes did not significantly differ between *late users* and *early users* (not controlling for covariates: Odds ratio = 0.89, 95%CI 0.64, 1.25, $p = .498$; controlling for covariates: Odds ratio = 1.07, 95%CI 0.81, 1.41, $p = .625$).

DISCUSSION

The present research shows that, compared to adolescents who had never used e-cigarettes, those who first reported using them either at age 13-14 (i.e., *early users*) or at age 14-15 years (i.e., *late users*) reported significantly higher rates of regular e-cigarette use plus ever and regular cigarette smoking at age 15-16 years (Table 2). In *early users* of e-cigarettes this pattern was present 12 and 24 months later (this pattern for ever and regular cigarette use in this sample has previously been reported) [5,7]. In *late users* of e-cigarettes this pattern was present 12 months later. These findings add to previous work showing that e-cigarette use is associated with subsequent ever [1-6] and regular use of cigarettes [7] and additionally shows it is associated with subsequent regular e-cigarette use at age 15-16 years. The current results are comparable to those reported in a recent meta-analysis of seventeen such studies (OR=4·59, 95%CI 3·60—5·85) for ever smoking based on comparing never versus ever users of e-cigarettes [21]. The reviewed studies were generally over a period of 12 months, focused on ever smoking, and controlled for the effects

of a number of covariates. Nevertheless these studies cannot conclusively rule out the idea that other pre-existing risk factors that were not assessed explain both c-cigarette and cigarette use (i.e., the common liabilities explanation).

The more novel aspect of the current findings was in assessing differences between *early users* and *late users* of e-cigarettes on subsequent regular e-cigarette use, ever cigarette use and regular cigarette use at age 15-16 years (Tables 2 and 3). At 15-16 years of age, *early users* were significantly more likely to be ever cigarette users than *late users*. This replicates previously reported findings [9]. There were no such significant differences for regular e-cigarette use or regular cigarette use. A problem with these comparisons is that *early users* had a 24-month period to start using cigarettes post using e-cigarettes compared to only 12 months in *late users*. Our comparison of *early users* and *late users* 12 months after first reporting using e-cigarettes (i.e., at age 14-15 years in early users versus 15-16 years in late users) revealed few differences. There were no significant differences in ever use of cigarettes (controlling or not for covariates). Regular e-cigarette use was significantly higher in *early users* compared to *late users*, while regular cigarette use was significantly higher in *late users* compared to *early users*. In both cases these differences became marginally or non-significant when controlling for covariates.

These findings for *early user* and *late users* of e-cigarettes over different time periods can be interpreted in different ways. It is notable however how similar the two users groups are on ever use of cigarettes 12 months after first reported use of e-cigarettes and that differences only appear to emerge when the early user group had a longer time period to progress to ever use of cigarettes. Regular use of e-cigarettes and cigarettes use also increased over this period in early users of e-cigarettes. Future research with adolescents followed up for longer periods of time are required to better differentiate the effects of age of first use of e-cigarettes from time delay to outcome. In addition, future research might usefully explore effects in different age groups (e.g., first reported use of e-cigarettes before 13-14 years or after 14-15 years).

Like many studies, our research provides only limited insights into the mechanism relating ever use of e-cigarettes to subsequent smoking, meaning we need to remain cautious in making policy

recommendations based on these findings. Since we conducted our work, UK legislation has banned marketing and selling e-cigarettes to minors and UK agencies are required to enforce age of sale, child and tamper proof packaging, display age of sale signage and health warnings on e-cigarette packaging [22]. Nevertheless, our findings emphasise the value of regulating the marketing/sale of e-cigarettes to minors in countries where such measures are not in place.

Our study has a number of strengths including a large demographically diverse sample, low levels of missing data with replacement based on multiple imputation, assessment of effects over 12-24 months in groups who first reported e-cigarette use at different ages, exploration of effects on regular e-cigarette use, ever cigarette use, and regular cigarette use, validated self-reported smoking measures, and exploration of covariates. There are also weaknesses. First, our self-report measures of e-cigarette use were not validated against objective measures and all covariates were based on self-report. Second, we did not distinguish types of e-cigarette use (e.g., delivery method, presence or level of nicotine, presence of other substances) except at the final time point. Third, we were unable to differentiate effects due to age of first reported use of e-cigarettes from time delay to assessment of outcome at a range of ages and time points. Relatedly alternative groupings of e-cigarette by age may produce different findings. Fourth, we conducted a series of binary tests rather than an ordinal model that might allow examination of differences between ever and regular cigarette use (although such comparisons would be limited by the relatively small numbers in these groups).

In summary, this study shows that early use versus late use of e-cigarettes by adolescents is associated with significantly higher rates of ever cigarette use at 15-16 years of age. This may, or may not, be attributable to early users having a longer period of time to initiate cigarette use. Further research with a broader age-range of adolescents over longer periods of time is required.

Contributors

Dr Conner had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Declarations of Interest

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REFERENCES

1. Leventhal AM, Strong DR, Kirkpatrick MG, et al. Association of electronic cigarette use with initiation of combustible tobacco product smoking in early adolescence. *JAMA* 2015;**314**:700-707. doi:10.1001/jama.2015.8950.
2. Primack BA, Soneji S, Stoolmiller M, et al. Progression to traditional cigarette smoking after electronic cigarette use among US adolescents and young adults. *JAMA Pediatr* 2015;**169**:1018-1023. doi:10.1001/jamapediatrics.2015.1742.
3. Watkins SL, Glantz SA, Chaffee BW. Association of noncigarette tobacco use with future cigarette smoking among youth in the population assessment of tobacco and health (PATH) study, 2013-2015. *JAMA Pediatrics*;**172**:181-187. Doi:10.1001/jamapediatrics.2017.4173.
4. Barrington-Trimis JL, Kong G, Leventhal AM, et al. E-cigarette use and subsequent smoking frequency among adolescents. *Paediatrics* 2018;**142** doi:10-1542/peds.2018-0486.
5. Conner M, Grogan S, Simms-Ellis R, et al. Do electronic cigarettes increase cigarette smoking in UK adolescents? Evidence from a 12-month prospective study. *Tob Control 2017;* **27**, 365-372. doi:10.1136/tobaccocontrol-2016-053539
6. Best C, Haseen, F., Currie D, et al. Relationship between trying an electronic cigarette and subsequent cigarette experimentation in Scottish adolescents: a cohort study. *Tob Control 2017;**27**:*. doi:10.1136/tobaccocontrol-2017-053691
7. Conner, M., Grogan, S., Simms-Ellis, R., Scholtens, K., Sykes-Muskett, B., Cowap, L., Lawton, R., Armitage, C.J., Meads, D., Schmitt, L., Torgerson, C., West, R., & Siddiqi, K. (2019). Evidence that an intervention weakens the relationship between adolescent electronic cigarette use and tobacco smoking: A 24 month prospective study. *Tobacco Control*, 10.1136/tobaccocontrol-2018-054905
8. Shahab, L., Beard, E., & Brown, J. (2020). Association of initial e-cigarette and other tobacco product use with subsequent cigarette smoking in adolescents: A cross-sectional, matched control study. *Tobacco Control*, doi:10.1136/tobaccocontrol-2019-055283
9. McCabe, S.E., West, B.T., & McCabe, V.V. (2017). Associations between early onset of e-

cigarette use and cigarette smoking and other substance use among US adolescents: A national study. Nicotine and Tobacco Research, 2018, 20(8): 923-930.

10. Evans-Polce, R., Veliz, P., Boyd, C.J., McCabe, V.V., & McCabe, S.E. (2019). Trends in e-cigarette, cigarette, cigar, and smokeless tobacco use among US adolescent cohorts, 2014-2018. and colleagues. *American Journal of Public Health*, e1-e3.
11. Conner, M., Grogan, S., West, R., Simms-Ellis, R., Scholtens, K., Sykes-Muskett, B., Cowap, L., Lawton, R., Armitage, C.J., Meads, D., Schmitt, L., Torgerson, C., & Siddiqi, K. (2019). Effectiveness and cost-effectiveness of repeated implementation intention formation plus anti-smoking messages on adolescent smoking initiation: A cluster randomized controlled trial. *Journal of Consulting and Clinical Psychology*, **87**, 422-432. doi: 10.1037/ccp0000387
12. Conner M, Grogan S, Lawton R, et al. Study protocol: A cluster randomised controlled trial of implementation intentions to reduce smoking initiation in adolescents. *BMC Public Health* 2013;**13**:54. doi:10.1186/1471-2458-13-54.
13. Gollwitzer PM, Sheeran P. Implementation intentions and goal achievement: A meta-analysis of effects and processes. *Adv Exp Soc Psychol* 2006;**38**:69-119. doi:10.1016/S0065-2601(06)38002-1.
14. Conner M, Higgins A. Long-term effects of implementation intentions on prevention of smoking uptake among adolescents: A cluster randomized controlled trial. *Health Psychol* 2010;**29**:529-538. doi:10.1037/a0020317.
15. Higgins A, Conner M. Understanding adolescent smoking: The role of the Theory of Planned Behaviour and implementation intentions. *Psychology, Health and Medicine*;**8:**177-190.
16. Jarvis L. Smoking among secondary school children in 1996: England. London: HMSO 1997.
17. Stookey GK, Katz BL, Olson CA, et al. Evaluation of biochemical validation measures in determination of smoking status. *J Dent Res* 1987;**66**:1597-1601.
18. Jarvis MJ, Tunstall-Pedoe H, Feyerabend C, et al. Comparison of tests used to distinguish smokers from non-smokers. *Am J Public Health* 1987;**77**:1435-1438.
19. Boyce W, Torsheim, T, Currie C, Zambon, A. The family affluence scale as a measure of

national wealth: validation of an adolescent self-report measure. *Soc Indic Res* 2006;**78**: 473-87.

20. Cloninger C, Przybeck T, Syrakic D, Wetzel R. *The Temperament and Character Inventory (TCI): A guide to its development and use*. St Louise, MO: Center for Psychobiology of Personality: 1994.
21. Khouja, JN, Suddell, SF, Peters, SE, Taylor, AE, Munafo, MR. Is e-cigarette use in non-smoking young adults associated with later smoking? A systematic review and meta-analysis. *Tob Cont* 2020; doi:10.11136/tobaccocontrol-2019-055433.
22. Medicine and Healthcare Products Regulatory Agency. E-cigarettes: Regulations for consumer products (UK Government). https://www.gov.uk/guidance/e-cigarettes-regulations-for-consumer-products. (accessed 7 Dec 2018).

Table 1: Descriptive data for the sample (N = 3289).

		N	(%)
Sex	Boy	1546	(47·0%)
	Girl	1743	(53·0%)
Ethnicity	Non-white	542	(16·5%)
	White	2747	(83·5%)
Family affluence[1]		2·72	(0·49)
Friend smokers	None	2196	(66·8%)
	A few or more	1093	(33·2%)
Family smokers	None	1272	(38·7%)
	One or more	2017	(61·3%)
Impulsivity	Low	1491	(45·3%)
	High	1798	(54·7%)
Intention	Low	3021	(91·9%)
	High	268	(8·1%)
Attitude	Low	2740	(83·3%)
	High	549	(16·7%)
Norms	Low	2859	(86·9%)
	High	430	(13·1%)
Perceived Behavioural Control	Low	2713	(82·5%)
	High	576	(17·5%)
Self-efficacy	Low	2688	(81·7%)
	High	601	(18·3%)
Free school meals[2]	Low	22	(48·9%)
	High	23	(51·1%)
Condition[2]	Control	20	(44·4%)
	Intervention	25	(55·6%)

1. Mean and standard deviation for this variable. 2. Number of schools.

Table 2: Frequency of e-cigarette and cigarette use at different waves (ages) split by e-cigarette user group.

	Behaviour at wave 4 (age 14-15 years)			Behaviour at wave 5 (age 15-16 years)		
	E-cigarette Use	Cigarette Use		E-cigarette Use	Cigarette Use	
Group	Regular	Ever	Regular	Regular	Ever	Regular
Never users (N=2221)	0 (0·0%)	49 (2·2%)	1 (0·0%)	15 (0·7%)	185 (8·3%)	13 (0·6%)
Never users who never smoked (N=2172)	-	-	-	14 (0·6%)	149 (6·9%)	13 (0·6%)
Early users (N=649)	46 (7·1%)	182 (28·0%)	6 (0·9%)	38 (5·9%)	268 (41·3%)	26 (4·0%)
Late users (N=419)	-	-	-	17 (4·1%)	117 (27·9%)	10 (2·4%)

Table 3: Prediction of regular e-cigarette use (left-hand panel), ever cigarette use (middle panel) or regular cigarette use (right-hand panel) at wave 5 (15-16 years) by e-cigarette user group plus covariates (N = 1063) controlling for clustering by school.

	Regular e-cigarette use			Ever cigarette use			Regular cigarette use		
Predictors	OR	(95% CI)	*p*	OR	(95% CI)	*p*	OR	(95% CI)	*p*
Model 1 without covariates									
Early user	1·00			1·00			1·00		
Late user	0·76	(0·45—1·28)	·292	0·48	(0·35—0·66)	< ·001	0·69	(0·35—1·37)	·282
Model 2 with covariates									
Early user	1·00			1·00			1·00		
Late user	0·96	(0·84—1·11)	·602	0·61	(0·46—0·81)	< ·001	0·94	(0·83—1·07)	·347
Male	1·00			1·00			1·00		
Female	0·89	(0·78—1·01)	·068	1·72	(1·34—2·21)	< ·001	0·95	(0·84—1·07)	·363
Ethnicity = non-white	1·00			1·00			1·00		
Ethnicity = white	0·84	(0·70—1·01)	·063	1·08	(0·75—1·55)	·678	0·91	(0·77—1·07)	·250
Family affluence	1·00	(0·95—1·04)	·861	0·98	(0·91—1·05)	·532	0·98	(0·95—1·02)	·336
Free school meals = low	1·00			1·00			1·00		

Free school meals = high	0·91	(0·77—1·07)	·244	1·04	(0·82—1·34)	·727	1·07	(0·95—1·20)	·245
Friend smokers = none	1·00			1·00			1·00		
Friend smokers = more than none	1·02	(0·86—1·21)	·834	0·96	(0·69—1·33)	·791	0·96	(0·85—1·08)	·474
Family smokers = none	1·00			1·00			1·00		
Family smokers = one or more	1·02	(0·91—1·15)	·691	1·11	(0·85—1·46)	·432	0·91	(0·81—1·04)	·150
Impulsivity=low	1·00			1·00			1·00		
Impulsivity=high	1·24	(1·11—1·40)	<·001	2·22	(1·75—2·82)	< ·001	1·22	(1·11—1·35)	< ·001
Intentions = low	1·00			1·00			1·00		
Intentions = high	0·94	(0·78—1·14)	·538	1·22	(0·82—1·83)	·314	0·95	(0·75—1·21)	·691
Attitude = low	1·00			1·00			1·00		
Attitude = high	1·16	(1·01—1·33)	·034	1·12	(0·81—1·56)	·468	1·16	(1·03—1·31)	·020
Perceived norms = low	1·00			1·00			1·00		
Perceived norms = high	1·12	(0·96—1·30)	·139	0·96	(0·75—1·23)	·738	1·21	(1·06—1·39)	·006
Perceived behavioural control = low	1·00			1·00			1·00		
Perceived behavioural control = high	0·86	(0·75—0·99)	·032	1·05	(0·79—1·39)	·745	0·97	(0·85—1·12)	·696
Self-efficacy = low	1·00			1·00			1·00		

Self-efficacy = high	1·04	(0·90—1·20)	·572	1·10	(0·83—1·46)	·492	0·91	(0·82—1·02)	·116
Control condition	1·00			1·00			1·00		
Intervention condition	0·93	(0·78—1·11)	·403	0·73	(0·57—0·95)	·018	1·01	(0·90—1·13)	·859

Regular e-cigarette use: model 1 without covariates, -2 log-likelihood function = -1474·5; model 2 with covariates, -2 log-likelihood function = -1208·9; Ever cigarette use: model 1 without covariates, -2 log-likelihood function = -1507·8; model 2 with covariates, -2 log-likelihood function = -1440·7; Regular cigarette use: model 1 without covariates, -2 log-likelihood function = -1515·3; model 2 with covariates, -2 log-likelihood function = -1180·9.