E-cigarette Use for Smoking Reduction and Cessation in a Four-year Follow-up Study Among Young Swiss Men: Some may Benefit, but they are Few.

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Abstract

Background

Randomised controlled trials have shown some benefits to using e-cigarettes (ECs) to facilitate smoking reduction and cessation, but real-world observational studies have rarely confirmed this. The present study looked at EC use and smoking during a four-year longitudinal study of young men. It compares general population findings with a subgroup of individuals with a good prognosis for quitting smoking.

Methods

The smoking habits of 5353 young men at t1 (average 21.3 years old) were defined as either never-smoker, ex-smoker, initiates, relapsed smoker or persistent smoker. At follow-up (t2), smoking status was analysed using logistic regression, differences in the number of cigarettes smoked by persistent t1/t2 smokers were analysed using mixed linear models and the number of quit attempts was analysed using negative binomial models.

Results

At the general population level, EC use had no beneficial effects on reducing or ceasing smoking. Non-smokers (never- and ex-) and smokers at t1 were more likely to be smokers at t2 if they had begun to use ECs (e.g. among persistent smokers OR=4.56, 95% CI [2.75, 7.58]), but not significantly so if they had already used ECs at t1. Among smokers at t1, almost daily EC use at t1 was associated with a non-significant reduction in smoking at t2 (OR=0.74, 95% CI [0.33, 1.65]), but occasional EC use significantly increased smoking at t2 (OR=3.05, 95% CI [2.29, 4.06]). Both daily and occasional EC use increased smoking at t2 among t1 non-smokers. T2 smokers made more attempts to quit when using ECs at t2 (IRR=1.53, 95% CI [1.26, 1.85]). Beneficial effects were found among a subgroup of EC users with a good prognosis for quitting (using nicotine liquids and at least 2nd generation ECs, motivation to quit and daily EC use at t2, but not t1).

Conclusion

Some smokers may have benefitted from using ECs, but they were few. At the general population level, ECs are not predominantly used in a way, which might optimise reducing or ceasing smoking. Therefore, the public health effect on the general population of using ECs may be questionable, as may policy measures to facilitate EC use.

Introduction

Nicotine use creates dependence; however, it is unlikely to be directly responsible for much health harm. Most harm stems from nicotine delivery through smoking (1–3). Although smoking is decreasing in many—though not all—countries worldwide (4), its decline is seen as too slow (e.g., 1). This has led some scientists to ask whether harm reduction approaches may help to accelerate decreased smoking (3, 5). E-cigarettes, e-hookas or pod mods may be used as harm-reducing electronic nicotine delivery systems (ENDS): their use is not harmless but is considerably less harmful than smoking (3, 6–10). We will use the term e-cigarette (EC) as a generic term. Arguments against ECs include that dual use may lead to sustained smoking among smokers who would otherwise have quit, that EC use may re-normalise smoking-like behaviour (inhaling) in public, and finally that ECs may divert smokers who are motivated to quit away from evidence-based smoking cessation treatments (6). ECs may also seem attractive to young people and lead to nicotine use which would not have occurred otherwise and subsequently to smoking (gateway effect: 11). A recent review of the evidence (12) identified seven systematic meta-analytical reviews, of which two found a positive effect (13, 14), four were inconclusive (15–18) and one found a negative effect (19). The present paper argues that the mixed findings on the efficacy or effectiveness of using ECs for reducing or ceasing smoking may be related to the answers to our two research questions. Firstly, is there an overall general population, public health effect? Secondly, is there an effect among a subgroup of heavy smokers who are highly motivated to quit smoking? The present longitudinal study investigated vaping and its associations with smoking among young men aged around 21.3 years old at baseline, with a follow-up around four years later, and it distinguished between a general “real-world” population perspective and a group of smokers motivated to quit.

One reason for the different conclusions of the meta-analytical reviews may have been the types of studies included. Whereas reviews suggesting beneficial effects were predominantly based on randomised control trials (RCTs) (3), the sole review suggesting negative effects (19) included numerous observational studies, and even cross-sectional studies, which could not separate cause and effect. The review by Villanti et al. (20) set stricter criteria for studies on using ECs for reducing or quitting smoking. Only four studies fitted those criteria (21–24). All four were randomized controlled trials (RCT) and found, at best, small, but usually non-significant favourable effects for using nicotine ECs.

Commentaries on the paper by Villanti et al. (20) criticised its focus on RCTs and its assessment limited to EC users who were only motivated by smoking cessation (25, 26). To evaluate the potential impact of promoting ECs as a public health approach, there is a need to investigate how ECs are used in real-world clinical settings or, even more significantly, in the general population. Strict inclusion criteria limiting
investigations to smokers who desperately want to quit (and excluding others) do not reflect real-world EC use in the general population. Many vapers do so for other reasons, e.g. costs, the ability to use it where tobacco is banned or to maintain a similar habit as part of daily routines. Similarly, strict inclusion criteria as regards certain parameters of EC use, such as frequency of use, type, dose or duration, do not reflect real-world use either (26). Daily vaping and the use of more recent innovations in EC models (e.g. tank, mod and pod systems), which provide more effective nicotine delivery and therefore are sufficiently appealing to smokers, have shown promising effects in RCTs (for reviews see 3, 20, 27–29) but do not necessarily correspond to real-world use at the general population level (see 30).

Although RCTs are commonly regarded as the strongest epidemiological designs, they do have inherent drawbacks. Simply participating in an experiment and having greater interaction with a therapist may increase motivation for the treatment, belief that the treatment is important and the behaviour typical of good subjects (31–33). Participants’ informed consent may be perceived as binding contracts which they do not want to break (34), and the inclusion and exclusion criteria of RCTs commonly lead to highly selective groups of participants. This does not reflect the groups of patients found in standard clinical settings (35) and even less so in the general population.

Longitudinal studies in the general population are particularly important when it comes to regulating ECs (e.g. maximum nicotine concentrations, taxes). Even critics of ECs generally admit that their use can result in decreased smoking and cessation for some smokers. However, whether the overall effect of EC use is harmful or beneficial depends on its predominant type of use in the general population. Those who regard EC use as more harmful than beneficial promote strong regulation (e.g. 11, 36, 37). Those who see its potentially beneficial effects, through decreased smoking and cessation, promote less regulation than for conventional cigarettes (CCs) (2, 12, 29).

Two of the recent systematic reviews (14, 15), deemed to be of high quality (38), included three general population studies. Brose et al. (39) found that after one year, daily EC users were more likely than non-users to have attempted to stop smoking (but not to have stopped) and to have reduced their number of cigarettes smoked by 50%. No effects were found for occasional EC users, and only about one fourth of all EC users were daily users. Al-Delaimy et al. (40) found that, after one year, ever-EC users had made a non-significant greater number of attempts to quit, but they were significantly less likely to quit and less likely to have decreased cigarette use. Manzoli et al. (41) compared formerly-smoking EC users with tobacco smokers and dual users, and they found that EC users were significantly more likely to have persisted in their tobacco abstinence; however, dual users were not more likely to become tobacco abstainers, and they also did not reduce tobacco use.

There are recent longitudinal studies on the general population. Many looked at the potential for ECs to introduce young people to smoking (42–44), confirming reviews that ECs expanded the nicotine market by attracting young people who may later use CCs (11, 45). A general population study of adults (18+) in the USA by Benharmina et al. (38) showed that ECs may increase the likelihood of tobacco abstinence among those attempting to quit. However, the vast majority relapsed to cigarette smoking, and those who did continued to use ECs in addition to CCs with no reduction of CC use. Findings from the same study (46) showed that at least high frequency of EC use at follow-up (but no use at baseline) may be associated with a reduction in CCs smoked. A general population study in France examined daily smokers and former daily smokers (47). After two years, regular (daily) vapers had reduced their daily CC use by about 1.7 cigarettes per day more than non-vapers. They also had a higher likelihood of quitting smoking. However, former smokers were more likely to relapse to CC smoking if they were vapers. Daily users, but not occasional users, were also shown to reach higher abstinence compared with non-vapers (48).

The present study examined EC use and its associations with smoking cessation, attempts to quit and CC use among a cohort of young men aged around 21.5 years old at baseline and continuing for 4 years of follow-up. It compared never-smokers, former smokers and persistent smokers in that population as a whole. This paper presents sensitivity analyses of the EC use modes assumed to have the most advantageous effects on smoking cessation (e.g. daily use, use of newer generations of ECs, use of nicotine liquids, and being motivated to reduce or cease CC smoking). The study was the continuation of an earlier one (49) which measured vaping at the baseline only.

**Methods**

**Sample**

Data come from the first three waves of the Cohort Study on Substance Use Risk Factors (C-SURF). Switzerland has a mandatory procedure for young men around 19 years old to determine their eligibility for military or civilian service. As men have to be at least 18 years old to be called for the procedure by the army, the youngest person in the sample was 18 years old. Conscripts were invited to participate in C-SURF during those procedures, but assessments were done independently of the army, at home, via the internet or on paper questionnaires. C-SURF is a larger study on substance use and behavioural addictions, not only exclusively on smoking and vaping. Questionnaires and other material is provided online at [www.c-surf.ch](http://www.c-surf.ch). English versions of the questionnaires are also provided as supplementary files 1 to 3. C-SURF was approved by the Human Research Ethics Committee of the Canton Vaud (C-SURF: Protocol No. 15/07).
Of the 7556 conscripts who provided written informed consent to participate in the study, 5987 (79.2%) completed the baseline assessment (t0) from September 2010–March 2012. Of these, 5479 responded (91.5% response rate) to the first follow-up assessment (t1) from March 2012–January 2014, and of these, 4981 responded (90.9% response rate) to the second follow-up assessment (t2) from April 2016–March 2018. We also invited consenting but baseline-non-respondent conscripts to participate in the t1 follow-up, and 391 completed both the t1 and t2 follow-ups and were thus included in the present study. These individuals had a known smoking status at t1 and t2, and logical imputation was used to impute their smoking status at baseline. Smokers and non-smokers at both t1 and t2 were also assumed, respectively, to have been smokers and non-smokers at t0. After eliminating 19 people with missing values on key variables, the final sample size consisted of 5353 participants.

**Measures**

**CC smoking**

At all three time points, participants were asked whether they had smoked in the past 12 months and, if so, how often on a 6-point scale from “once a month or less” to “daily”. All those smoking less than daily were considered “occasional smokers”. Past-12-months smokers were asked about the number of cigarettes smoked on days when they did smoke, and their number of cigarettes per week was calculated using quantity and frequency. Additionally, at t0, participants were asked whether they had smoked at least 50 cigarettes in their life. Five groups were constructed according to their “CC status t0–t1”: “never-smokers”, i.e. never-smokers at t0 and t1; “ex-smokers”, i.e. smokers at baseline but non-smokers at t1; “initiates”, i.e. never-smokers at t0 but smokers at t1; “relapsed-smokers”, i.e. ex-smokers at t0 but smokers at t1; and “persistent smokers”, i.e. smokers at t0 and t1. Participants were followed-up as parts of these five groups, and depending on sample size, some analyses required regrouping into smokers and non-smokers.

**Outcomes**

The primary outcomes considered were a) smoking cessation and b) a change in the number of cigarettes smoked by persistent smokers. The number of attempts to quit in the past 12 months was used as a secondary outcome. Possible responses were zero, one, two, three, and four or more attempts. Attempts to quit were defined as seriously trying to stop smoking and not smoking for several consecutive days.

**Vaping**

Questions about vaping were only asked at t1 and t2. Frequency of EC use was measured on the same 6-point scale as CC smoking, but only for those participants who had reported vaping in the past 12 months. As the number of vapers was relatively small at t1, “almost daily vaping” was defined as “5–6 days a week” or *daily*. For convenience, we named participants not vaping at t1 and t2 as “never-vapers”. It should be noted that they may have used ECs before t1, although this was rather unlikely, or they may have used after t1 assessment but having stopped again at t2.

**Dependence**

Higher nicotine dependence has been positively associated with the use of smoking cessation aids and negatively associated with successfully stopping, but many longitudinal studies on ECs have been criticised for not accounting for levels of nicotine dependence (12, 13, 38, 50). Nicotine dependence at t1 was assessed using the Fagerström Test for Nicotine Dependence (51) on a continuous scale scored from 0–10.

**Covariates**

Covariates were age, language (French, German), and the highest completed level of education at t1, which consisted of three categories: primary schooling (9 years); secondary vocational training (> 9–12 years); and post-secondary schooling (13 + years).

**Statistical analysis**

For descriptive purposes, we used percentages for ordinal and nominal variables and means with standard errors (SE) for continuous and count variables. Logistic regression models, stratified by t1 cigarette-smoking status (never-smokers, ex-smokers, initiates, relapsed-smokers, persistent smokers), were calculated to test associations between vaping and cigarette-smoking status at t2. Vaping was, if possible, analysed according to its occurrence at t1, t2 or both times. If sample sizes were too small, we grouped vaping at t1 with vapers using EC at both time points to distinguish users who used EC cigarettes already at t1 from those who used ECs only at t2. To estimate changes in the number of cigarettes smoked by persistent smokers at t1 and t2, we calculated linear mixed-models which considered correlations within subjects, vaping as the between-subject factor, time of assessment (t2 vs t1) as the within-subject factor, and the interaction between vaping and time of assessment. The interactions tested the differences in cigarette-smoking changes between never-vapers and groups of vapers (defined by their vaping status at t1 and t2). Associations between vaping and the number of attempts to quit by t2 among smokers were tested using negative binomial regression models for counts of attempts to quit.
**Subgroup analysis of smokers with good prognostic values for quitting**

As a subgroup analysis, we looked at daily smokers at t1 who might be assumed to have a higher likelihood/intention/motivation to stop smoking by using ECs than occasional smokers, who were less addicted and might use ECs for other reasons (e.g. curiosity). We also examined almost-daily vaping (at least 5 days/week) as vaping intensity has been shown to have a more beneficial impact on reducing or ceasing smoking. Following the suggestion by Villanti et al. (20), we tried to define a group of vapers who might have a good prognosis for reducing or ceasing smoking. Vapers in this group had to be using at least a second-generation EC (with rechargeable tanks or pod mods) with liquid nicotine and to claim at least one of the following motives: a) use it in the course of a quit attempt, or b) use to stop smoking or not to relapse to smoking. This information was asked at t2 only.

**Results**

Smoking rates between t1 and t2 decreased from 47.4–41.2%, particularly occasional smoking. At the same time, the proportion of vapers almost doubled, from 5.2–9.8% (Table 1). Although the proportion of almost-daily vapers increased from 11.8–20.9%, the majority of EC users vaped occasionally: 712 of our 5353 participants were using ECs at at least one of the two time points, including 89 users at both.
Table 1
Sample descriptive statistics at t1, plus smoking status, EC use, attempts to quit and age at t2

| time measures                                  | n    | % or mean (SE) |
|------------------------------------------------|------|---------------|
| **t1** smoking status, number of cigarettes smoked and FTND |      |               |
| non-smoker                                      | 2816 | 52.6          |
| occasional smoker                               | 1363 | 25.5          |
| daily smoker                                     | 1174 | 21.9          |
| weekly cigarettes smoked (occas.)               | 1363 | 9.6 (0.508)   |
| weekly cigarettes smoked (daily)                | 1174 | 95.5 (1.316)  |
| FTND score (occas.)                             | 1363 | 0.48 (0.026)  |
| FTND score (daily)                              | 1174 | 3.19 (0.056)  |
| **t1** EC use                                   |      |               |
| non-user                                        | 5074 | 94.8          |
| occasional user                                 | 246  | 4.6           |
| almost daily user                               | 33   | 0.6           |
| **t1** linguistic region                        |      |               |
| French                                          | 3120 | 58.3          |
| German                                          | 2233 | 41.7          |
| **t1** education                                |      |               |
| primary schooling (9 years)                     | 404  | 7.5           |
| secondary vocational training (> 9–12 years)    | 2480 | 46.3          |
| post-secondary schooling (13 + years)           | 2469 | 46.1          |
| **t1** age                                      |      |               |
| age mean (SE)                                   | 5353 | 21.3 (0.017)  |
| **t2** smoking status, number of cigarettes smoked and number of attempts to quit |      |               |
| non-smoker                                      | 3149 | 58.8          |
| occasional smoker                               | 1087 | 20.3          |
| daily smoker                                     | 1117 | 20.9          |
| weekly cigarettes smoked (occas.)               | 1087 | 9.6 (0.516)   |
| weekly cigarettes smoked (daily)                | 1117 | 95.7 (1.416)  |
| attempts to quit (occas.)                       | 1087 | 0.39 (0.025)  |
| attempts to quit (daily)                        | 1117 | 0.49 (0.025)  |
| **t2** EC use                                   |      |               |
| non-user                                        | 4831 | 90.2          |
| occasional user                                 | 413  | 7.7           |
| almost daily user                                | 109  | 2.0           |
| **t2** age                                      |      |               |
| age mean (SE)                                   | 5353 | 25.4 (0.017)  |

Remarks: FTND = Fagerström Test for Nicotine Dependence  
SE = standard error  
occas. (occasional smokers), daily (daily smokers)

Initiation, relapse and cessation of smoking
Across almost all CC-smoking status, those who had not used ECs at t1 and t2 had the lowest adjusted odds ratios (AORs, Table 2). One exception was the never-smokers at t1 who had already vaped at t1, but they were only few (n = 11), which was one reason why t1-only vapers were grouped with persistent vapers (at t1 and t2). The two groups (t1-only vapers and persistent vapers) could only be separated among persistent smokers. Significantly higher AORs for smoking were found for participants starting EC use at t2. If a subgroup of persistent smokers was selected, namely daily-smokers at t1, then a small, but non-significant beneficial effect was found (AOR = 0.72, 95% CI [0.40, 1.30]). This group exhibited dual-use at t1 and had stopped EC use at t2.

**Table 2**

| smoking at time point 1 (incl. baseline, time point 0) | EC use | n  | unadjusted % of smokers at t2 | AOR | Lower | Upper | p-value |
|------------------------------------------------------|--------|----|-------------------------------|-----|-------|-------|---------|
| never-smokers                                        | never (reference) | 1891 | 5.3%                         | 1   |        |       |         |
| t1 only + t1 and t2                                  | 11     | 0.0% | 0.92                         | 0.26| 3.30  |       | 0.897   |
| t2 only                                              | 35     | 42.9%| 6.48                         | 3.36| 12.49 | < 0.001|         |
| ex-smokers                                           | never (reference) | 822  | 21.3%                        | 1   |        |       |         |
| t1 only + t1 and t2                                  | 15     | 20.0%| 1.10                         | 0.33| 3.64  |       | 0.874   |
| t2 only                                              | 42     | 64.3%| 5.22                         | 1.60| 17.05 | 0.006  |         |
| initiates*                                            | never (reference) | 232  | 36.2%                        | 1   |        |       |         |
| t1 only + t1 and t2                                  | 16     | 38.5%| 1.02                         | 0.13| 7.69  |       | 0.987   |
| t2 only                                              | 13     | 75.0%| 6.82                         | 1.87| 24.80 | 0.004  |         |
| relapsed smokers*                                    | never (reference) | 145  | 46.2%                        | 1   |        |       |         |
| t1 only + t1 and t2                                  | 5      | 60.0%| 1.34                         | 0.92| 1.96  |       | 0.127   |
| t2 only                                              | 20     | 85.0%| 4.56                         | 2.74| 7.57  | < 0.001|         |
| persistent smokers*                                  | never (reference) | 1551 | 77.0%                        | 1   |        |       |         |
| t1 and t2                                            | 83     | 89.2%| 1.85                         | 0.91| 3.78  |       | 0.091   |
| t1 only                                              | 152    | 81.6%| 1.18                         | 0.76| 1.82  |       | 0.461   |
| t2 only                                              | 320    | 94.7%| 4.56                         | 2.75| 7.58  | < 0.001|         |
| persistent t1 daily-smokers*                          | never (reference) | 727  | 87.3%                        | 1   |        |       |         |
| t1 and t2                                            | 66     | 89.4%| 1.14                         | 0.50| 2.60  |       | 0.751   |
| t1 only                                              | 98     | 84.7%| 0.72                         | 0.40| 1.30  |       | 0.279   |
| t2 only                                              | 220    | 91.4%| 2.66                         | 1.39| 5.08  | 0.003  |         |

**Remarks:** AOR = adjusted odds ratio, adjusted for age, education and language; * additional adjustment for the Fagerström Test for Nicotine Dependence score; persistent t1 daily smokers: smokers at t0 and t1, with daily smoking at t1.

A sensitivity analysis examined almost-daily EC use at: a) either t1 or t2; and b) t1 independent of the use frequency at t2 (Table 3). Among non-smokers at t1 (ex-smokers and never-smokers), almost-daily vaping at any time (AOR = 17.53, 95% CI [4.35, 70.61]) and vaping (but never daily), significantly increased the risk for smoking at t2 (AOR = 6.20, 95% CI [4.03, 9.54]). Looking at vapers who were already almost-daily vapers at t1, AORs were lower than 1, particularly for daily smokers with almost-daily vaping at t1 (AOR = 0.47, 95% CI [0.19, 1.15]). However, both findings were non-significant due to the small number of almost-daily vapers at t1.
### Table 3
Logistic regressions of smoking at t2 on the frequency of EC use stratified by smoking status at t1

| smoking status t1 | EC use | n     | crude % smokers time 2 | AOR   | Lower | Upper | p-value |
|-------------------|--------|-------|------------------------|-------|-------|-------|---------|
| non-smoker t1     | never an EC user | 2713  | 10.2%                  | 1     |        |       |         |
|                   | almost-daily EC user at any t | 9     | 66.7%                  | 17.53 | 4.35  | 70.61 | < 0.001 |
|                   | never a daily EC user | 94    | 41.5%                  | 6.20  | 4.03  | 9.54  | < 0.001 |
| smoker t1*        | never an EC user       | 1928  | 69.8%                  | 1     |        |       |         |
|                   | almost-daily EC user at any t | 126   | 80.2%                  | 1.26  | 0.79  | 2.01  | 0.327   |
|                   | never a daily EC user  | 483   | 90.5%                  | 3.57  | 2.58  | 4.93  | < 0.001 |
| smoker t1*        | never an EC user | 1928  | 69.8%                  | 1     |        |       |         |
|                   | almost-daily EC user at t1 | 32    | 71.9%                  | 0.74  | 0.33  | 1.65  | 0.463   |
|                   | EC user at any t, but not daily EC user at t1 | 577   | 89.3%                  | 3.05  | 2.29  | 4.06  | < 0.001 |
| daily smoker t1*  | never an EC user | 776   | 85.1%                  | 1     |        |       |         |
|                   | almost-daily EC user at t1 | 27    | 74.1%                  | 0.47  | 0.19  | 1.15  | 0.096   |
|                   | EC user at any t, but not daily EC user at t1 | 371   | 91.6%                  | 1.87  | 1.23  | 2.85  | 0.003   |

**Remarks:** AOR = adjusted odds ratio, adjusted for age, education and language; * additional adjustment for the Fagerström Test for Nicotine Dependence score.

### Smoking reduction among persistent smokers at t1 and t2.

Table 4 shows the results from the mixed models. The time effect indicates the change for the reference group, e.g. persistent (t1 and t2) smokers who had never vaped smoked a non-significant 1.62 more cigarettes weekly at t2 compared with t1. The EC-use estimates represent the relative difference in the adjusted number of cigarettes smoked at t1 compared with the reference group of never-vapers. For example, among all smokers, those vaping at t1 and t2 had smoked an average of 8.05 more cigarettes at t1, adjusted for covariates. The interesting estimates are the interaction effects which indicate the change between t1 and t2 relative to the change among the never-vapers. For example, daily smokers at t1 who vaped at both time points reduced their use by -7.65 (time) – 6.22 (interaction) = -13.87 cigarettes, whereas their corresponding never-vapers reduced weekly cigarettes smoked by only - 7.65 (time). Hence, the relative change of vapers at both time points was 6.22 fewer cigarettes smoked. Among all persistent smokers, never-vapers smoked 1.62 more cigarettes weekly (time effect). Vapers at t1 (but not t2) smoked 5.26 (-6.88 + 1.62) fewer cigarettes per week and vapers at both time points smoked 2.77 (4.39 + 1.62) fewer. None of these differences was significant except for the relative increase among occasional smokers at t1 who vaped at t1 and t2: they smoked an average of 25.85 more cigarettes weekly than occasional cigarette smokers at t1 who had never vaped.
Table 4
Mixed models of changes in the number of conventional cigarettes (CCs) smoked by persistent smokers at t1 and t2, by timing of EC use.

|                        | occasional smokers at t1 | daily smokers at t1 | all smokers at t1 |
|------------------------|--------------------------|---------------------|-------------------|
|                        | n                        | Estimate            | Std. Error        | Sig.   | n                        | Estimate            | Std. Error        | Sig.   | n                        | Estimate            | Std. Error        | Sig.   |
| Intercept              | 5.81                     | 10.94               | 0.596             | 0.596  | 49.96                    | 17.89               | 0.005             | 0.005  | 3.64                     | 12.21               | 0.766             |
| time effect t1 (ref.)  | 0                        | 0                   | 0                 | 0.000  | 0                        | 0                   | 0                 | 0.000  | 0                        | 0                   | 0.000             |
| time effect t2         | 10.55                    | 1.24                | 0.000             | 0.000  | -7.65                    | 1.84                | 0.000             | 0.000  | 1.62                     | 1.15                | 0.161             |
| never used EC (ref.)   | 685                      | 0                   | 660               | 0.000  | 1345                     | 0                   | 1345              | 0.000  | 3.64                     | 12.21               | 0.766             |
| EC use t1 and t2       | 17                       | -2.98               | 4.61              | 0.519  | 60                       | 4.90                | 4.54              | 0.281  | 77                       | 8.05                | 3.76              | 0.033  |
| EC use, t1 only        | 45                       | 6.93                | 2.89              | 0.017  | 84                       | -2.05               | 3.90              | 0.598  | 129                      | 3.28                | 2.95              | 0.267  |
| EC use, t2 only        | 116                      | 0.98                | 1.89              | 0.605  | 216                      | -0.68               | 2.64              | 0.796  | 332                      | 2.62                | 1.97              | 0.184  |
| Interaction time t2 *  | 0                        | 0                   | 0                 | 0.000  | 0                        | 0                   | 0                 | 0.000  | 0                        | 0                   | 0.000             |
| never used EC (ref.)   | 25.85                    | 7.94                | 0.001             | -6.22  | 6.39                     | 0.331               | -4.39             | 4.96   | 0.376                     |
| EC use t1 and t2       | -2.69                    | 4.98                | 0.589             | -4.64  | 5.49                     | 0.398               | -6.88             | 3.90   | 0.078                     |
| EC use, t1 only        | 1.72                     | 3.25                | 0.597             | 3.16   | 3.71                     | 0.395               | -0.25             | 2.59   | 0.922                     |

Remarks: Adjusted for age, education, language and the Fagerström Test for Nicotine Dependence score.

**t2 smokers’ attempts to quit**

Negative binomial models demonstrated that, among all smokers, those who were using ECs at t2, independently of whether they used them at t1, had a significantly higher incidence rate ratio of the number of attempts to quit smoking. However, when testing occasional and daily smokers at t2 separately, this effect was only significant for daily smokers (Table 5).

Table 5
Negative binomial regressions of smokers’ attempts to quit at t2 on the timing of EC use

|                        | occasional smokers at t2 | daily smokers at t2 | all smokers |
|------------------------|--------------------------|---------------------|-------------|
|                        | n                        | IRR                 | 95% CI      | 95% CI      | 95% CI      |
|                        |                          | Lower               | Upper       | Sig.        | Lower       | Upper       | Sig.        | Lower       | Upper       | Sig.        |
| Intercept              | 884                      | 0.06                | 0.01        | 0.36        | 0.002       | 0.08        | 0.01        | 0.51        | 0.007       | 0.07        | 0.02        | 0.25        | 0.000       |
| EC use t1 and t2       | 21                       | 1.37                | 0.67        | 2.79        | 0.390       | 0.56        | 0.59        | 1.02        | 2.47        | 0.040       | 0.040       | 0.040       | 0.000       |
| EC use t1 only         | 49                       | 1.35                | 0.83        | 2.20        | 0.228       | 0.83        | 0.91        | 0.59        | 1.42        | 0.686       | 0.686       | 0.686       | 0.000       |
| EC use t2 only         | 133                      | 1.08                | 0.77        | 1.52        | 0.652       | 0.241       | 0.76        | 1.39        | 2.23        | < 0.001     | < 0.001     | < 0.001     | 0.001       |

Remarks: Adjusted for age, linguistic region, education and the Fagerström Test for Nicotine Dependence score; IRR = incidence rate ratio.

**Subgroup of smokers with a good prognosis**

Finally, we looked at a group of vapers with a good prognosis for reducing and ceasing smoking. These were smokers at t1 using nicotine liquids in at least 2nd generation ECs and with the motivation to reduce or cease CC use. Vapers at t2 were stratified into four groups (no use
vs EC use at t1, and occasional use vs almost-daily EC use at t2) and compared to never-vapers. Models for smoking cessation did not converge for occasional EC users at t2 because they were all still smokers at t2. For almost-daily vapers at t2 who had been non-vapers at t1 (n = 35), the AOR for smoking at t2 was 1.42 (95% CI [0.56, 3.52]; p = 0.44), but it was 0.63 (95% CI: 0.20, 2.02) for those who had already been vapers at t1 (n = 13).

With regard to the number of cigarettes smoked weekly by persistent smokers, almost-daily EC users at t2 who had been non-vapers at t1 smoked significantly fewer weekly cigarettes (-22.92 + 1.62 = -21.30) than never-vapers, but this was not true for occasional vapers at t2. Similar reductions were found for those vaping at t1 and occasionally vaping at t2 (-25.23 + 1.62 = -23.62), but not for those with almost-daily use at t2 (Table 6). There were more attempts to quit among t2 smokers for all ever-vapers compared to never-vapers, which were non-significant for persistent vapers with almost daily vaping at t2.

Table 6
Smoking reduction and attempts to quit by t2 EC users with good prognosis* versus never-EC users

| t1 use frequency | t2 use frequency | n     | estimate | Lower  | Upper  | p-value |
|------------------|------------------|-------|----------|--------|--------|---------|
| no EC use        | no EC use (Reference) | 1345  | 1.62     | -0.61  | 3.85   | 0.156   |
| no EC use        | occasional       | 41    | 7.97     | -5.01  | 20.94  | 0.229   |
| no EC use        | almost daily     | 29    | -22.92   | -38.28 | -7.57  | 0.003   |
| EC use           | occasional       | 13    | -25.23   | -48.04 | -2.43  | 0.030   |
| EC use           | almost daily     | 8     | 9.67     | -19.34 | 38.69  | 0.514   |

95% CI IRR

| n     | IRR   | Lower | Upper | p-value |
|-------|-------|-------|-------|---------|
| no EC use (Reference) | 1621 | 1.00  |       |         |
| no EC use          | occasional | 45    | 2.57  | 1.68   | 3.91   | < 0.001 |
| no EC use          | almost daily | 32    | 2.52  | 1.53   | 4.14   | < 0.001 |
| EC use             | occasional | 13    | 2.48  | 1.15   | 5.34   | 0.020   |
| EC use             | almost daily | 8     | 1.61  | 0.52   | 4.96   | 0.407   |

Remarks: Adjusted for age, linguistic region, education and the Fagerström Test for Nicotine Dependence score.

Good prognosis: 2nd generation-type ECs, use of nicotine liquids, and motivation to reduce or quit CC use.

Estimate: weekly change in number of cigarettes smoked in mixed models and IRR for binomial count model.

Discussion

The present study of the effects of vaping on reducing and ceasing cigarette smoking used a 4-year longitudinal perspective to investigate a general population sample of young men (mean age 21.3 years old at t1, and 25.4 at t2). The results indicated that the more promising findings from RCTs (13, 14) and the inconclusive findings from observational studies (15–18) were not necessarily a contradiction. EC users in a general population may be more heterogeneous than the users motivated to quit in RCTs. In our general population as a whole, no significant beneficial effects of EC use were found with regards to reducing or ceasing smoking, but there was an increased number of attempts to quit, confirming other studies (52, 53). As in those other general population studies, some EC users, particularly regular EC users motivated to reduce or quit smoking, may indeed have benefitted, but they were relatively few compared to all vapers. Thus, although the effects of EC use were sometimes in a beneficial direction (fewer cigarettes smoked weekly or cessation), they were rarely significant. As the number of users in...
some subgroups was rather small, in line with Greenland et al. (54) or Rothman (55), we did not only interpret significant effects or claim that non-significant effects were not effects at all, but we also looked at the general picture of effects, e.g. whether they were consistently negative or mixed across different user groups.

Participants already vaping at t1 had similar or higher smoking rates at t2 than never-vapers. Vaping may have had a small beneficial effect for daily smokers at t1 who had been smokers at t0 (persistent smokers at t1), but this effect was non-significant, concerned 98 of the total 712 vapers and consisted of an unadjusted difference in cessation of 12.7% (no EC use at t1 and t2) versus 15.3% (smoking prevalence at t2: 87.3% vs 84.7%). Additionally, this effect was only found for those who also ceased EC use at t2. The beneficial effect was more pronounced if daily smokers at t1 had already vaped almost daily at t1 (OR = 0.47, 95% CI [0.19, 1.15]). However, this scenario concerned only 27 vapers, i.e. less than 4% of all vapers. Nevertheless, this was in line with other studies showing that daily vaping over a longer period may have beneficial effects (e.g., 3, 30). Approximating the suggestion made by Villanti et al. (20), the group with a good prognosis (i.e. daily vaping, long-term vaping, using nicotine liquids in at least a 2nd generation EC and being motivated to reduce smoking or quit) for meeting beneficial outcomes showed similarly beneficial effects towards smoking cessation, but the sample size was even smaller (n = 13).

Never-smokers and ex-smokers at t1 were not more likely than never-vapers to start smoking or relapse if they had already vaped at t1. Thus, once non-smoking has been achieved or maintained while already vaping, taking up smoking or relapsing is unlikely. Again, the number of such vapers was small compared with all vapers (11 never-smokers and 15 ex-smokers at t1). However, those who started vaping later were significantly more likely to be smokers at follow-up, i.e. to take up smoking or to relapse. This may confirm other studies on the greater likelihood of relapse (47) or taking up smoking among younger populations (12). However, as a caveat, for never-smoking, non-EC-users at t1 who smoked and vaped at t2, we do not know which habit began first. Thus, this finding about relatively young people may also be explained by their generally greater risk-taking and shared vulnerabilities (3, 56).

Among daily smokers at t1 who were persistent smokers at t2, there was a small, non-significant reduction of 5–7 fewer CCs smoked weekly by EC users than by never-EC-users, but only if they were already vaping at t1 and either continued to vape at t2 or ceased vaping at t2. No relative reduction was found among daily smokers at t1 who initiated vaping by t2. This may mean that EC users have to vape for longer before a reduction in CC smoking appears. These results support findings from a general population study in France (47), but also from RCTs (21), that the reduction of CC smoking among dual users may be rather small. On the one hand, the few occasional smokers at t1 who persistently used ECs at t1 and t2 (n = 17) had significantly increased their smoking by 26 CC more per week than never-vapers. This could indicate that EC use may reinforce smoking-like behaviour (6, 57), which could result in heavier CC use among occasional smokers. On the other hand, following the recommendations of Villanti et al. (20), some but not all vapers with the best prognosis for our desired outcomes significantly reduced CC use by more than 20 cigarettes a week. Even for smokers with a good prognosis, findings were mixed. Those already using ECs at t1, but only irregularly at t2, reduced their CC use, which was in line with studies showing that long-term EC use may result in a reduction of CC use (58), but probably only if ECs were also reduced. No reduction in use was found for persistent EC users with almost-daily use at t2. Those who did not vape at t1 but did so daily at t2 showed a reduction of more than 20 cigarettes per week. This may suggest that smoking reductions among dual users may be achieved in the short term, but not in the long term (23). Overall, it seems that dual users may get little direct benefit from their EC use as regards their CC consumption (6, 41).

Consistent with other studies is the finding that that dual smokers and EC users at t2, regardless of whether they had used ECs at t1, demonstrated a higher number of attempts to quit. The number of attempts to quit was even higher in the subgroup with a better prognosis than the overall sample. The finding concerning more attempts to quit is well documented in the literature, and it is suggested that this may lead to smoking cessation in the future (3). However, increased numbers of attempts to quit without necessarily increased cessation rates have also often been found (39, 40), and our findings supported this.

The present study's findings come with some caveats. The sample consisted solely of relatively young men—we can say nothing about women. Young people often only experiment with ECs (29) or try it out of curiosity (13), which the present study supported, showing that few vaped daily or almost daily. Young people are commonly at the beginning of their lives as smokers, and there may be much greater benefits of EC use among older, long-time, heavy smokers with stronger urges, needs and perhaps motivations to quit smoking. With the past twelve months assessment at t1 and t2, and a long, average follow-up period of four years, we could not investigate relapses and uptakes of smoking and vaping in between. However, this has also been true for most studies with shorter follow-ups. When co-occurrences of smoking and vaping begin at the same time during the 12 months before assessment, we cannot investigate which came first. However, we do know that before t1, EC use was very rare in Switzerland, and we know whether people were smokers before t1. Thus, almost all smokers at t1 had started smoking before their EC use, and we were able to monitor for vapers at t1 to t2—and similarly for smokers and non-smokers with regards to simultaneous or subsequent EC use. We were also able to say something about dual users at t1 and how they compared when they did or did not continue with EC use at t2. The present study overcame some of the problems inherent in other longitudinal studies: we were able to adjust for nicotine dependence and we followed-up with people who had quit smoking, not only treatment failures (13).
Conclusion

Even critics of vaping do not deny that it may have benefits for some smokers, particularly if newer vaping devices are used, they are used for longer durations and with greater intensity (daily use), and they are used to aid the motivation to quit. The present study supports such findings. However, for an evaluation of vaping’s overall impact, studies at the general population level are needed (21, 38), particularly when it comes to policy decisions, such as giving a price advantage to ECs through the higher taxation of CCs (2, 11, 12, 37). Many vapers have no plans to quit but rather use ECs to circumvent smoke-free policies or to maintain a similar habit as part of their daily routine. Thus, they do not fit the strict inclusion criteria of RCTs as regards frequency of EC use, type of CC, dose or duration (15, 25, 57). Thus, the use of RCTs or the selection of subgroups with good prognostic outcomes does not reflect real-world use (26). The present study showed that for young men, although a few may have benefitted from ECs, at the general population level, vaping probably had no benefit and probably even a negative impact on their smoking behaviour.

Abbreviations

AOR: adjusted odds ratio; CC: conventional cigarettes; C-SURF: cohort study on substance use risk factors; EC: e-cigarettes; FTND: Fagerström Test for Nicotine Dependence; IRR: incidence rate ratio; OR: Odds ratio; RCT: randomized control trial; SE: standard error

Declarations

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Authors’ contributions

AG analysed and interpreted the data and drafted the manuscript. MW, SM & JS revised the manuscript critically for important intellectual content, helped with the analysis plan and statistical analysis, have given final approval of the version to be published, and have agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Availability of data and materials

The study questionnaires are available at www.c-surf.ch. The dataset analysed during the current study, will be made available at ZENODO. All data of the project, properly anonymized are available via C-SURF’s homepage www.c-surf.ch upon detailed research request.

Ethics approval and consent to participate

All participants of the study gave written consent to participate. C-SURF was approved by the Human Research Ethics Committee of the Canton Vaud (C-SURF: Protocol No. 15/07).

Consent for publication

Not applicable.

Competing interests

Authors have no conflict of interest.
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