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Impact of electronic cigarette and heated tobacco product on conventional smoking: an Italian prospective cohort study conducted during the COVID-19 pandemic

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ABSTRACT

Objective Debate continues about whether electronic cigarettes (e-cigarettes) and heated tobacco products (HTP) reduce or increase the probability of smoking, with many studies compromised by stated or unstated conflicts of interest. We undertook a longitudinal study in Italy.

Methods 3185 Italian participants aged 18–74 years provided baseline (April–May) and follow-up (November–December) responses in 2020, reporting smoking status and use of e-cigarettes and HTP. We tracked transitions over that period and reported risk ratios (RR) and corresponding 95% CIs for changes in smoking in relation to baseline use of e-cigarettes and HTPs.

Results Never cigarette smokers who used e-cigarettes at baseline were much more likely to start smoking (compared with never users, RR 8.78; 95% CI: 5.65 to 13.65) and current HTP users (RR 5.80; 95% CI: 3.65 to 9.20). Among ex-smokers, relapse (17.2%) at follow-up was more likely among e-cigarette (RR 4.25; 95% CI: 2.40 to 7.52) and HTP users (RR 3.32; 95% CI: 2.05 to 5.37). Among current smokers at baseline, those who had continued smoking at follow-up were 85.4% overall. These were more frequently current novel product users (compared with non-users, RR 1.10; 95% CI: 1.02 to 1.19 for e-cigarette users; RR 1.17; 95% CI: 1.10 to 1.23 for HTP users).

Conclusions Both e-cigarette and HTP use predict starting smoking and relapse, and appear to reduce smoking cessation. Due to the limited sample size within specific strata, the association with quitting smoking should be confirmed by larger prospective studies. These findings do not support the use of e-cigarettes and HTPs in tobacco control as a consumer product, at least in Italy.

INTRODUCTION

Over the last decade, electronic cigarettes (e-cigarettes) have entered markets in the majority of countries, globally.¹ Their entry into commerce has generated intense controversy within the health community, centred on safety (where the answer depends on whether they are being compared with smoking or not smoking),¹ and their role in smoking cessation, initiation or relapse.^{1,2}

WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ The entry into commerce of novel tobacco products has generated intense controversy within the health community on their role in smoking cessation.
- ⇒ Existing literature, mostly from cross-sectional studies, suggests that, outside clinical settings, e-cigarettes are not associated with any increase in smoking cessation and that their use might boost, rather than reduce, tobacco smoking in the adult population

WHAT THIS STUDY ADDS

- ⇒ The use of either e-cigarettes or HTPs predicts starting conventional cigarette smoking among never smokers and relapse among ex-smokers.
- ⇒ The use of e-cigarettes or HTPs does not increase -and might decrease- smoking cessation.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- ⇒ Our study reinforces the importance of regulating novel (tobacco) products the same way as conventional cigarettes, at least in Italy.

There is some evidence from clinical trials that e-cigarettes might be more effective than nicotine replacement therapy (NRT) when included with other forms of support as part of a time-limited clinical intervention.^{3,4} However, existing evidence suggests that e-cigarettes are not associated with any increase in smoking cessation outside of clinical settings.⁴

E-cigarette use predicts starting to smoke, particularly among young adults or adolescents,^{5,6} who are initially attracted by likable flavours and minimally regulated appealing advertisements, especially on social media.^{1,7,8} Once addicted to nicotine they may switch to conventional cigarettes, as shown in the few available longitudinal studies.^{9–11}

Most quitters using e-cigarettes as a smoking cessation tool use them for prolonged periods¹² and their continued dependence on nicotine might be expected to increase relapse to use of conventional tobacco. A recent meta-analysis of all available longitudinal studies showed that, among former



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smokers, e-cigarette users had twice the risk of relapse compared with e-cigarette never users.¹³

The situation is now becoming more complicated. Heated tobacco products (HTP) blur the line between e-cigarettes and combustible ones,¹ while the vast sums invested by the tobacco industry in research on harm reduction measures make it necessary to take care when interpreting data about any influence, stated or unstated, about the role of vested interests.^{14 15}

This study extends previous research in Italy that has used cross-sectional data, finding that use of e-cigarettes as consumer products in the general population is not associated with smoking cessation,¹⁶ that e-cigarette use might boost, rather than reduce, tobacco smoking in the adult population² and that a large proportion of people attracted by HTPs or HTP users were never smokers, or ex-smokers who had quit several years previously.^{17 18}

However, we need longitudinal data to track what happens over time. Here, we take advantage of a large prospective Italian cohort study, free of any industry support, to evaluate trajectories in conventional smoking, according to e-cigarette and HTP use in the general adult population.^{18 19} In this study, both the baseline and the follow-up interviews were conducted during the COVID-19 pandemic. In both time periods, although most social activities and shops were closed, e-cigarettes and HTPs have always been considered, like conventional tobacco, as basic necessities, and therefore they have always been accessible and purchasable in Italy.¹⁸

METHODS

Within the LOfckdown and lifeSTyles IN ITALY (Lost in Italy) project,¹⁹ we conducted a web-based longitudinal study on a large representative sample of Italian adults aged 18–74 years. The first interview was carried out during the nationwide COVID-19 lockdown (between 27 April and 3 May 2020) with a total of 6003 participants (2962 men and 3041 women) randomly selected from an online panel of DOXA, the Italian branch of the Worldwide Independent Network/Gallup International Association, comprising 140 000 Italian adults. We used a quota sampling method to obtain a sample representative of the Italian adult population in terms of age, sex and region.²⁰ All the participants accepted to be recontacted for a follow-up interview. Of them, 3185 (53.3%) completed the follow-up interview approximately 7 months later (between 27 November and 20 December 2020). A comparison of those who were retained versus lost to follow-up (online supplemental table 1) shows small but significant differences only in education (those retained were more likely to have a high level of education) and gender (they were more frequently men).

At baseline, participants completed an online self-administered questionnaire, including information on sociodemographic characteristics. One section focused on smoking and use of novel tobacco products. Smoking status was assessed at baseline and at follow-up using two questions: (i) Have you smoked at least 100 cigarettes during your life? and (ii) How many cigarettes/day do you smoke on average, including hand-rolled cigarettes? Ex-smokers were those reporting to have smoked at least 100 cigarettes during their lifetime but none (0 cigarettes/day) at the time of the interview. Current smokers reported having smoked at least 100 cigarettes during their life and were occasional smokers (ie, smokers of <1 cigarette/day) or people smoking 1 or more cigarettes/day at the time of the interview.

E-cigarette use was assessed by asking subjects if they had ever tried, used in the past or used e-cigarettes occasionally or

regularly (ie, daily). Past users were those who had used e-cigarettes either once or twice or in the past. Current e-cigarette users were using e-cigarettes occasionally or regularly. HTP use was determined asking subjects whether they were aware of HTPs, if they ever tried, used in the past or used occasionally or regularly HTPs, such as IQOS by Philip Morris or Glo by British American Tobacco. Past users were subjects reporting they had used HTP once or twice or in the past. Current HTP users were subjects using HTP occasionally or regularly.

Statistical analysis

We undertook separate log-binomial multiple regression models with current, ex and never smokers, adjusting for sex, age group and level of education, to derive risk ratios (RR) and corresponding 95% CIs of starting smoking at follow-up among never smokers at baseline, of relapsing among ex-smokers and of continuing smoking at follow-up among current smokers at baseline for both e-cigarette and HTP users versus never users. We also performed multiple logistic regression models, adjusting for sex, age group, level of education and geographic area, to derive ORs of starting smoking, relapsing and continuing smoking at follow-up. All statistical analyses were done with SAS V.9.4 (Cary, North Carolina, USA).

RESULTS

Table 1 shows the RRs for change in smoking status between baseline and follow-up according to use of e-cigarettes and HTPs at baseline. Among 2122 never smokers at baseline, the 99 (4.7%) who started smoking at follow-up were more frequently e-cigarette and HTP users at baseline: compared with never e-cigarette users, RRs were 4.81 for past and 8.78 for current e-cigarette users; compared with never HTP users, RRs were 3.67 for past and 5.80 for current HTP users. Among 344 ex-smokers at baseline, 59 (17.2%) relapsed at follow-up. Participants relapsing were more frequently e-cigarette users (RRs were 2.91 for past and 4.25 for current e-cigarette users) and HTP users (RRs were 2.51 for past and 3.32 for current HTP users). Among 719 current smokers at baseline, 614 (85.4%) continued smoking at follow-up (and 105, 14.6%, quit). Participants continuing smoking were more frequently current e-cigarette users and current HTP users, the crude RRs being 1.10 and 1.17, respectively. Online supplemental table 2 shows the corresponding analysis using ORs instead of RRs. The patterns did not substantially change. However, the multivariate ORs did not show significant differences in the probability of quitting among current smokers by use of novel products.

DISCUSSION

Our longitudinal study, which is free from any industry links, found that in Italy the use of either e-cigarettes or HTPs predicts starting conventional cigarette smoking among never smokers and relapse among ex-smokers. Use of novel products also appears to reduce smoking cessation. However, the association with quitting smoking should be confirmed by larger prospective studies. Nevertheless, our data are unlikely to be compatible with these products being effective as smoking cessation tools.

Among never smokers at baseline, the proportion of current e-cigarette and HTP users who then started smoking was approximately 9 and 6 times higher, respectively, than never users, suggesting that in Italy the use of novel (tobacco) products was a frequent passage towards conventional cigarette smoking. Our results are in line with those from the few longitudinal studies available, from the USA, showing that e-cigarettes act as

Table 1 Distribution of 3185 Italians according to changes in their conventional tobacco smoking status at follow-up, overall and by use of electronic cigarettes (e-cigarettes) and heated tobacco products (HTP), Italy, 2020*

Characteristics	Never smokers at baseline			Ex-smokers at baseline			Current smokers at baseline		
	N	Starting smoking at follow-up		N	Relapsing at follow-up		N	Continuing smoking at follow-up	
		%	RR (95% CI)		%	RR (95% CI)		%	RR (95% CI)†
Total	2122	4.7		344	17.2		719	85.4	
E-cigarette use									
Never	1684	2.1	1.00‡	209	7.7	1.00‡	572	84.6	1.00‡
Past	259	10.8	4.81 (2.98 to 7.77)	71	25.4	2.91 (1.58 to 5.37)	87	85.1	1.01 (0.91 to 1.11)
Current	179	19.6	8.78 (5.65 to 13.65)	64	39.1	4.25 (2.40 to 7.52)	60	93.3	1.10 (1.02 to 1.19)
HTP use									
Never	1861	3.2	1.00‡	277	11.2	1.00‡	646	84.5	1.00‡
Past	152	12.5	3.67 (2.24 to 6.02)	43	32.6	2.51 (1.48 to 4.25)	42	88.1	1.04 (0.93 to 1.17)
Current	109	19.3	5.80 (3.65 to 9.20)	24	58.3	3.32 (2.05 to 5.37)	31	100.0	1.17 (1.10 to 1.23)§

*Estimated through generalised linear models (log-binomial models) after adjustment for sex, age and level of education; estimates in bold type are statistically significant at 0.05.
†The multivariable model did not converge. Consequently, univariate (crude) RRs are provided.
‡Reference category.
§Crude RR provided, with 0.5 added to all cells, as there were some zero-cells causing problems with computation of the RR or its SE.
RR, risk ratio.

a gateway to smoking conventional cigarettes particularly among young adults.^{6 9 11}

A recent study showed that in Europe approximately 50% of ex-smokers using HTPs had quit smoking before this product entered the local market.²¹ This suggests that a large proportion of people who had successfully quit smoking fall back to nicotine addiction when using these novel products. Our findings add to evidence from other longitudinal studies conducted in the USA, the UK and France, showing that use of e-cigarettes and HTPs is associated with a higher risk of cigarette smoking relapse among former cigarette smokers.^{13 22}

A cohort study from Italy, partially supported by the tobacco industry, found no increase in smoking cessation or reduction due to e-cigarettes.²³ This is in line with current evidence suggesting that in observational studies of adult cigarette smokers, e-cigarettes are not associated with higher smoking cessation.⁴ Our findings further confirm that an effectiveness of e-cigarettes—and HTPs—as smoking cessation tools is unlikely, at least outside of clinical setting.²⁴

The substantial changes in smoking observed in our cohort in such a short time frame (around 7 months) could be the consequence of the unique context since early 2020, when governments imposed unprecedented measures in response to the COVID-19 pandemic. Indeed, cross-sectional data from the first confinement period have already shown unusual large changes in smoking behaviour,²⁰ and in e-cigarette and HTP use.¹⁸ Thus, we cannot assume that our results reflect transitions in smoking behaviour in normal conditions. For this reason, it will be important to confirm our findings in subsequent research.

As with all longitudinal studies there is risk of bias from attrition of the sample. However, any differences in measured characteristics of those who were or were not retained were very small and mostly statistically insignificant, as with the key variables on smoking and use of novel products. Due to the limited sample size within specific strata, analyses of current smokers are likely to be underpowered. Moreover, the limited sample size did not allow us to separate occasional and regular product users. In addition, it is possible that HTP users misinterpreted the question on conventional smoking, erroneously considering the use of HTP as smoking. In this study, we followed a portion of a nationally representative sample but, as we could not use

statistical weights, we are not able to guarantee the representativeness of this subsample. However, the distributions by age, sex and geographic area of the subsample were not substantially different from the baseline sample.

In conclusion, this prospective cohort study helps fill the gaps in knowledge of the effects on smoking of novel (tobacco) products, particularly HTPs. In the general Italian population, both e-cigarette and HTP use predict starting conventional cigarette smoking among never smokers, relapsing among ex-smokers and appears to act as barriers for smoking cessation among current smokers. E-cigarettes might have a role in smoking cessation as part of clinical interventions, but as consumer products, e-cigarettes and HTPs appear deleterious for tobacco control, and, ultimately, population health, at least in Italy.

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Contributors SG had the original study idea; RP and AO obtained the funding. AL and CS did the statistical analysis; SG drafted the article in collaboration with CS and AL; all other authors made substantial contributions to conception, design and data interpretation; all the authors approved the final version of the manuscript. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Competing interests None declared.

Patient consent for publication Consent obtained directly from patient(s).

Ethics approval The ethics committee of the Fondazione IRCCS Istituto Neurologico Carlo Besta approved the study protocol (file number 71-73, April 2020). All participants gave their informed consent to participate in the study. The dissemination plan aims to target an extensive audience, including members of the public, current smokers, health professionals and policy makers. It will be achieved using various channels: media outreach via press release from Istituto di Ricerche Farmacologiche Mario Negri, scientific networks and social media.

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