# Review of: "Effectiveness of e-cigarettes as aids for smoking cessation: evidence from the PATH Study cohort, 2017–2019"

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We read with interest the article by Chen et al. on e-cigarettes as an aid for smoking cessation in the PATH Study cohort. [1]

Main aims were (i) to study effectiveness of e-cigarettes in smoking cessation among smokers with a recent quit attempt, and (ii) to study whether switching to e-cigarettes improves maintenance of cigarette abstinent among recent former smokers.

First, it is very interesting the choice of control group for the first objective. Authors compared recent quitters using e-cigarettes during their last quit attempts, and, as control group, recent quitters using any pharmaceutical aid. This choice allows to use a control group very homogeneous to the e-cigarette group. Instead, using all non-users of e-cigarettes as control group, i.e., both recent quitters and non-quitters, could bias results in favour of e-cigarettes.

Main findings were: (i) smokers who reported using e-cigarettes in their most recent quit attempt were less likely than other quit attempters to successfully quit; (ii) subjects who switched to e-cigarettes recorded a higher relapse rate than those who did not switch to e-cigarettes, although the difference was not significant.

As consumer products, i.e., e-cigarettes are bought in shops by the average consumer, in observational studies such as the one by Chen et al. [1], e-cigarettes were not associated with increased smoking cessation. The study by Chen is in line with a recent meta-analysis that considered 20 previous observational studies that, as Chen did, restricted participants to those who wanted to quit (OR=0.85; 95%CI=0.68-1.06). [2] Considering instead 35 observational studies that did not restrict sampling by motivation to quit, the effect of e-cigarettes was higher, even though close to the null (OR = 0.95; 95%CI = 0.77- 1.16).

Moreover, a recent systematic meta-analysis of longitudinal studies on the risk of smoking relapse with the use of e-cigarettes by former smokers, showed an increased 40-percent risk of relapse to conventional tobacco smoking associated with the use of e-cigarettes in former smokers. [3]

Finally, e-cigarette use among youth is associated with increased risk for cigarette initiation and use, particularly among youths at low risk to initiate tobacco smoking.[4]

Thus, on a population level, there may be significant harms associated with e-cigarettes, particularly among youth non-smokers. [5]

Moreover, country-specific characteristics, such as e-cigarette regulatory environment, and cost of e-cigarettes in

comparison to those of tobacco cigarettes and approved quitting methods, shape e-cigarette use. The hypothesis that e-cigarette users are a selected sample of quitters in relationship to the e-cigarette regulatory environment of their Countries, was an interesting suggestion by Yong et al. [6]: less restrictive environments shape e-cigarette users among quitters with higher likelihood of success (e.g., higher educated, less dependent); more restrictive environments allow a selection of e-cigarette users instead among quitters with lower probability of success (e.g., heavy smokers, lower social grades, smokers with many economic difficulties). In Italy, for instance, the low cost of e-cigarettes may have determined a selection of e-cigarette users among smokers with economic difficulties, since e-cigarettes are cheaper than tobacco cigarettes and approved smoking cessation medications. In Addition, these medications are not reimbursed through NHS. [7]

Finally, most tobacco smokers worldwide are not so attracted by e-cigarettes. In Italy, around 90% of smokers did not use e-cigarettes or Heated Tobacco Products [HTPs] at all. Moreover, around 60% of e-cigarettes users are dual users, i.e., keep on smoking conventional cigarettes. [8,9] Even though e-cigarettes are recommended as a safe and effective aids to smoking cessation by Public Health England since 2015, the situation in England is not very different from the Italian one: in 2021 almost 1/3 of e-cigarette users were dual users, and the proportion of adult smokers who currently used e-cigarettes stalled at around 17% from 2014, as if no more than 1 out of 6 smokers were satisfied with vaping. As a consequence, the vast majority of nicotine addicted subjects (83%) still are exclusive tobacco smokers.[10]

In contrast to the results from observational studies of e-cigarettes as consumer products, e-cigarettes as a smoking cessation method delivered in clinical studies was significantly associated with increased smoking cessation. [2,11] Thus, some e-cigarettes might be approved as a smoking cessation therapy administered under medical supervision as part of a cessation programme. Current findings from clinical studies also seem to suggest that e-cigarettes accompanied by intensive behavioural support delivered in a clinical setting improve cessation [12]. Therefore, on an individual level, e-cigarettes may be effective at quitting among adult smokers wto quit in a clinical setting. [5]

It is noteworthy to report here that two Countries that recorded quite different e-cigarette regulatory environments in the last 10 years (more restrictive: Australia; less restrictive: UK) seem to converge in 2021 to a similar strategy, the implementation of medical prescription of e-cigarettes for smoking cessation, using, however, different approaches. United Kingdom Government on October 29, 2021 announced that e-cigarettes could be prescribed on the NHS in England to help people stop smoking. Updated guidance to go through the regulatory approvals process for medicinally licensed e-cigarette products to be prescribed for smoking cessation, will be soon available for manufacturers. [13] This is not a new story: even though in 2016 one e-cigarette device was licensed for medical use by the UK medicines regulator, this approved device was never marketed, since developments in e-cigarette technology had left this product out of date. A license for medical use is very difficult to achieve for e-cigarettes, and manufacturers are more interested in extending consumer choice and delivering ever better next-generation e-cigarettes. [14]

Instead, in Australia from 1 October 2021, e-cigarettes containing nicotine cannot be sold unless the user has a prescription from a medical doctor. Even though in Australia nicotine vaping products are not recognised as a safe and effective aid to smoking cessation, some doctors may recommend use of e-cigarettes for long-term smokers who have tried to quit using approved medications but failed, and who still want to quit, and have discussed e-cigarette use with

their physicians. [15]

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