Therapeutics: Electronic cigarettes for smoking cessation

Jamie Hartmann-Boyce, Rachna Begh, Paul Aveyard

Nuffield Department of Primary Care Health Sciences, Radcliffe Observatory Quarter, University of Oxford, Oxford, UK OX2 6GG, Senior researcher, Jamie Hartmann-Boyce

Nuffield Department of Primary Care Health Sciences, Radcliffe Observatory Quarter, University of Oxford, Oxford, UK OX2 6GG, Post-doctoral research fellow, Rachna Begh

Nuffield Department of Primary Care Health Sciences, University of Oxford, Professor of Behavioural Medicine, Paul Aveyard

Corresponding author: Jamie Hartmann-Boyce, Jamie.hartmann-boyce@phc.ox.ac.uk, address as above

What you need to know [box]

- Electronic cigarettes (EC) were originally designed as a smoking cessation aid, and the limited evidence available suggests electronic cigarettes containing nicotine may help people stop smoking.
- Evidence suggests EC are considerably safer than traditional cigarettes.
- The technology used in EC has evolved considerably over time, and newer devices are typically better at delivering nicotine, which might enhance effectiveness.

Case

A 42 year old electrician has tried to stop smoking several times, including with the aid of pharmacotherapy and behavioural support. He asks you about using electronic cigarettes (EC). His work partner stopped smoking a year ago and is still using EC now. He has heard that EC are as damaging as the real things and worries that if he ends up addicted to EC he'll not have gained anything.

60% of current adult smokers in Great Britain have tried EC, and 18% are current EC users.(1) In England, over 40% of people who try to stop smoking do so with the aid of an EC.(2) 52% of current EC users are ex-smokers.(1) Some people who stop smoking with an EC are still using the EC a year later.(1) In this article we look at whether EC help people who smoke cut down and stop smoking, whether there are health risks from EC use, and how these compare with smoking.

Cigarette and nicotine addiction [box]

Most people who smoke cigarettes are addicted, and the main vehicle of that addiction is nicotine. When stopping smoking, people experience cravings for cigarettes, which drives return to smoking. These cravings for smoking are less intense when nicotine is substituted, thus replacing nicotine from sources other than cigarettes can facilitate achieving abstinence.

Transferring from cigarettes to other nicotine delivery devices, such as nicotine replacement therapy (NRT) or e-cigarettes, can transfer cigarette addiction to nicotine addiction. Around half of lifetime regular smokers will eventually die from smoking(3), whereas evidence on harms of addiction to NRT or e-cigarettes shows it is much less hazardous. Moreover, while cigarette smoking is tenacious, only a minority of people who transfer to NRT (and do not return to smoking) are persistent users.(4) While there is less evidence on persistent use of e-cigarettes after quitting smoking, one French cohort study found that over half of people who quit smoking with the aid of e-cigarettes were no longer using e-cigarettes (or tobacco cigarettes) six months later.(5) Persistent users of NRT and e-cigarettes report doing so primarily to avoid return to smoking.(6, 7)

All nicotine delivery devices, cigarettes, NRT, and e-cigarettes, provide nicotine dose information. It is not possible to use this to compare the nicotine dose delivered across the types of devices as the dose the user receives depends much more on how the device is used than the stated package dose.(8) Adding additional nicotine delivery devices, such as by using NRT or e-cigarettes while smoking, does not usually increase nicotine dose and tends to reduce tobacco dependence.(9-11)

What are electronic cigarettes?

Electronic cigarettes (EC) heat a liquid into an aerosol for inhalation, which usually comprises propylene glycol and glycerol, with or without flavours. Different models of EC are available, typically referred to as first, second, third, or fourth generation devices (see infographic [*not yet available, BMJ to draw*]). The 'e-liquid', or 'juice', is stored in disposable or refillable cartridges or a reservoir, depending on the type of device. E-liquid varies in its nicotine content, from liquid which contains no nicotine to liquid which contains doses over 20mg/nl. EC users are sometimes described as vapers, and EC use as vaping.

EC were originally designed as a smoking cessation aid. In those that contain nicotine, urges and withdrawal symptoms may be reduced by substituting the nicotine inhaled via tobacco smoke, as with more traditional forms of nicotine replacement therapy (e.g. patches, gum; Box 1).(12) However, EC may also facilitate smoking cessation by addressing the sensory and behavioural aspects of addictionsmoking to cigarettes .(13)

Licensing [box]

There are currently no countries where EC have been licensed as medical products, though applications are in the pipeline. Sales and marketing restrictions vary by country.

What the guidelines say [box]

In some countries, including Norway, Singapore and Brazil, EC are banned, whereas in the US and EU, it is legal to sell EC to adults. In the US, EC now fall under the remit of the Food and Drug Administration (FDA) through the "deeming rule" which subjects them to the same regulations as other tobacco products. In the EU, EC fall under the remit of the European Union Tobacco Products Directive, except where claims are made regarding therapeutic use or where nicotine content exceeds 20mg/ml, in which case medical licensing is required. At the time of writing, EC were not licensed anywhere in Europe. A 2016 report from the Royal College of Physicians (UK) recommends that, in the interest of public health, it is important to promote the use of EC, NRT and other non-tobacco nicotine products as widely as possible as a substitute for smoking.(14) However, medical guidelines have tended not to make definitive statements on the use of EC due to limited evidence, with some regulators citing concerns regarding uptake in children. A 2016 statement on EC from Public Health England and other UK public health organisations states that there is no circumstance in which it is better for a smoker to continue smoking, and that e-cigarette use among youth will continue to be closely monitored.(15) In 2017, Public Health England promoted the use of EC as a smoking cessation aid.(16)

Search strategy [box]

This article uses the search terms and inclusion criteria from the Cochrane review of electronic cigarettes for smoking cessation.(17) Searches were updated on 23 March 2017 and included: Cochrane Tobacco Addiction Group Specialized Register; Cochrane Central Register of Controlled Trials (CENTRAL); MEDLINE; Embase; and PsycINFO.

How well do they work for quitting smoking?

A 2016 Cochrane review of electronic cigarettes (2 radomized controlled trials, total number of participants 662) for smoking cessation found that EC with nicotine may help people stop smoking at six to twelve months compared to placebo EC without nicotine (4% vs 9%; relative risk 2.29, 95% confidence interval 1.05 to 4.96)).(17) However, certainty in this estimate was judged to be low due to imprecision (small number of trials and events) and indirectness (the two trials included in the review both used first generation devices which are no longer available due to poor nicotine delivery).(18, 19) Compared to other uncontrolled studies in which participants provided with EC showed quit rates ranging from 12.5% to over 50% at six months or longer, quit rates were relatively low in the randomized controlled trials, which could be due in part to the populations studied, relatively small sample sizes, devices tested, and the definitions of abstinence used.(17)

How well do they work for cutting down?

There is no definitive evidence that reducing cigarette consumption without quitting improves health.(20) For that reason, the 2016 Cochrane review of electronic cigarettes for smoking cessation did not address reduction.(17) However, people who want to reduce usually want to quit eventually, and there is evidence from a separate Cochrane review that, in people unmotivated to quit, providing NRT to help people initially reduce their cigarette consumption can lead to increased quit rates in the longer term.(21) It therefore follows that nicotine-containing EC may also be helpful in promoting reduction and abstinence, but the 2016 Cochrane review of tobacco harm reduction interventions included only one small study of e-cigarettes, meaning there was insufficient direct evidence to conclude this. (19, 21)

What are the harms?

Studies conducted in people using EC to quit smoking have not detected serious adverse effects and the devices appear well-tolerated by people who smoke. However, as EC have been used for only a few years, there is scant epidemiological data on the safety of EC when used as a long-term or permanent replacement for smoking. Most studies which report on safety of EC are small, uncontrolled, and follow-up participants for six months or less, and therefore the Cochrane review judged the quality of evidence on adverse events from electronic cigarettes as low.(17) As almost all regular use of EC occurs in former or current smokers, interpreting future epidemiological data will be difficult, though longer term studies are underway (see 'Ongoing studies' in Cochrane review (17)). Based on comparisons of the composition of carcinogens and toxicants in tobacco smoke and e-vapour, a 2016 Royal College of Physicians (UK) report estimated that the harm arising from long-term vapour inhalation from EC is unlikely to exceed 5% of the harm from smoking tobacco.(14) Although many have criticised this figure, there is consensus among public health experts that smoking is more dangerous than vaping.

Many studies – mostly small and uncontrolled – have investigated aspects related to the safety of EC. Findings on individual outcome groups and key biomarkers are summarized in Tables 1 and 2, drawing on the 2016 Cochrane review but updated to include relevant studies published since.(17)

Table 1. Summary of data on adverse events from longitudinal studies of EC in which EC were used for a week or longer

Event type	Summary of results	Sample size
Serious adverse events (SAEs)	None of the RCTs or intervention studies reported SAEs that were considered to be plausibly related to EC use, either in participants who had switched entirely to EC or were using EC as well as continuing to smoke. Longest follow-up was 2 years.(17)	14 studies (4 RCTs, 10 observational) Total n = 1,722
Adverse events (AEs)	No RCTs found statistically significant differences in adverse events by arm. These studies included people who switched entirely to EC and people who used EC alongside traditional cigarettes, with a longest follow up of 1 year. (17) Pooled results from three trials comparing EC with nicotine to EC without nicotine found a similar percentage of AEs between groups (RR 1.18, 95% CI 0.87 to 1.56, n=445).(18, 22, 23)	3 studies (RCTs) Total n = 421
	In the one RCT that compared EC to nicotine patch (six-month follow-up), 44.4% of participants in the nicotine EC arm reported any AEs, compared with 44.7% in the patch arm (RR 0.99, 95% CI 0.81 to 1.22).(17, 18)	1 study (RCT) Total n = 456
	The most frequently reported AEs across studies were mouth and throat irritation, cough, nausea, and headache, most commonly dissipating over time.(17)	14 studies (4 RCTs, 10 observational) Total n = 1,722

Table 2. Summary of longitudinal studies of EC in which change in toxicant exposure and biomarkers were studied in smokers who switched partially or fully to EC for at least a week[1]

Biomarker	Comparison[2]	Summary of results	Study duration	Sample size
Exhaled carbon monoxide (CO)	EC versus continuing smokers	Statistically significant declines observed in EC users; no significant changes in continuing smokers who did not use EC (17, 24)	4 weeks to 8 months	3 studies (2 RCT, 1 observational) N = 490
	Nicotine EC versus non-nicotine EC	No between group differences (22, 23)	1 to 3 weeks	2 studies (RCTs) N = 123

[1] includes only those biomarkers reported by three or more studies

[2] For studies comparing nicotine EC versus non-nicotine EC and before-after studies of EC provision, populations will include people who are using both EC and traditional cigarettes (dual users), as well as those who are using only EC (exclusive users). For comparisons between EC versus continuing smokers, 'EC' are exclusive EC users; continuing smokers may be dual users or may not use EC. For further detail on proportions of dual users, etc., see individual studies.

	Before-after provision of/instruction to use EC	Statistically significant declines from baseline to follow-up. Declines observed both in exclusive EC users and in dual users.(17, 25-27)	1 week to 2 years	8 studies (3 RCTs, 5 observational) N = 344
Known tobacco-related carcinogens	EC versus continuing smokers	Declines in four carcinogens in both groups, but greater declines in EC group (24)	12 weeks	1 study (RCT)
	Before-after study of provision of/instruction to use EC	Statistically significant reductions in at least some of the measured toxicants; reductions were found in both exclusive EC users and in dual users. No studies found increases in any of the toxicants measured. (17, 26, 28)	10 days to 4 weeks	3 studies (1 RCT, 2 observational) N = 97
Blood pressure	EC versus continuing smokers	General population: no clinically or statistically significant within or between groups differences (24) People with hypertension: systolic and diastolic blood pressure statistically significantly lower at 12 months in EC (exclusive and dual) users than in continuing smokers (29)	12 weeks to 2 years	2 studies (1 RCT, 1 observational) N = 497
	Nicotine EC versus non-nicotine EC	No significant (clinical or statistical) changes observed among or between study groups (30)	1 year	1 study (RCT) N = 300
Heart rate	EC versus continuing smokers	No evidence of clinically significant changes in people who switched from smoking alone to partial or full use of an EC (24, 30)	12 weeks to 1 year	2 studies (RCTs) N = 708
	Nicotine EC versus non-nicotine EC	No significant changes (clinical or statistical) observed among or between study groups (30)	1 year	1 study (RCT) N = 300
Lung function (including FEV1, FVC)	EC versus continuing smokers	No clinically significant changes observed (one study in healthy volunteers, one in people with COPD) (24, 31)	12 weeks to 2 years	2 studies (1 RCT, 1 observational) N = 456
	Before-after provision of/instruction to use EC	Statistically significant improvements observed over a 2 year period (study in people with asthma)(32)	2 years	1 study (observational) N = 18

Safety in people with pre-existing conditions

Results from individual studies in people with COPD, asthma, and hypertension have generally shown improvements in symptoms and have not detected serious adverse effects. We found no studies providing evidence regarding the safety of electronic cigarette use during pregnancy. Findings in these populations from retrospective chart reviews are summarized in Table 3.

Table 3. Summary of findings from studies of EC in people with pre-existing conditions

Condition	Study details	Findings
Asthma	Uncontrolled study of people who smoked and switched to e-cigarettes using 2 years of data from medical records(32) N = 18	• No evidence of harm • Statistically significant improvements in asthma control questionnaire (ACQ) scores and lung function parameters observed over the study period
Hypertension	2-year study of blood pressure readings from medical records comparing people with hypertension who continued smoking with those who switched (29) N = 89	• EC use appeared to be well tolerated • No severe adverse reactions or acute decompensation in blood pressure reported in EC users • Statistically significantly lower systolic and diastolic blood pressure readings in EC users than in matched tobacco smokers at 12 months ($p<0.001$)
COPD	2-year study using data from medical records comparing people with COPD who continued smoking with those who switched(31) N = 48	• Statistically significant reduction in COPD exacerbations observed over 12 months in EC users, from 2.3 (SD 1.0) at baseline to 1.8 (SD 1.0, $p = 0.002$) at 1 y and 1.4 (SD 0.9, $p < 0.001$) at 2 y • No changes observed in matched controls

What happens in people who cut down but don't stop?

Most studies of electronic cigarettes (EC) compare people using them exclusively with people exclusively using combustible forms of tobacco. However, in the population dual use is common; for example, 18% of British smokers are dual users.(1) There are no long-term data on the safety of dual use, but data from one short term study detected reductions in toxicants in people who switched from using only combustible tobacco to using combustible tobacco and EC.(33) None of the included studies in the Cochrane review found an increase in adverse events or undesirable changes in biomarkers in people who began using EC in addition to combustible tobacco.(17) However, there is no definitive evidence that reducing cigarette consumption without quitting improves health.

How do they compare with other nicotine replacement therapies?

Only one randomized controlled trial with long term follow up is available comparing electronic cigarettes (EC) with nicotine replacement therapy. In the ASPIRE trial, participants were randomized to EC with nicotine, EC without nicotine (placebo), or nicotine patch for 13 weeks. Neither adverse events nor quit rates were significantly different between those assigned to EC with nicotine and

those assigned to patch, though confidence intervals do not rule out an important difference for six-month cessation (RR 1.26, 95% CI 0.68 to 2.34; 584 participants).(18) Multiple trials are ongoing comparing EC with traditional forms of nicotine replacement therapy.(17) At present there are only two completed randomized controlled trials of EC for smoking cessation with follow-up at six months or longer, whereas there are over 100 definitively establishing the efficacy and safety of nicotine replacement therapy for smoking cessation.(17, 34) The Royal College of Physicians (UK) has stated that, as EC are not currently made to medicines standards, they are probably more hazardous than NRT.(14)

How cost effective are they?

Though other forms of NRT are often paid for by healthcare systems, EC are not as they are not medically licensed. There are no cost-effectiveness evaluations.

Tips for patients [box]

- Smoking is uniquely deadly and the evidence we have so far suggests electronic cigarettes with nicotine may help you quit.
- There is strong evidence that behavioural support and commonly used stop smoking medications, including nicotine replacement therapy, varenicline, and bupropion, help people stop smoking and are safe to use. There is less evidence available on the effectiveness and safety of electronic cigarettes as they are relatively new products.
- It is probably best to try a second generation e-cigarette (often referred to as vape pens). First generation devices (cig-a-likes that look like cigarettes) deliver less nicotine and may be less satisfying and not work as well. Third and fourth generation devices may be more complicated to use for people new to EC.
- It takes time to learn to use an e-cigarette to replace smoking, so persevere by changing the dose of nicotine, type of device, and the flavours. Ask a friend or ask for help in a vape shop. Once you are finding your electronic cigarettes satisfying, plan a day on which you will quit smoking regular cigarettes as soon as you can.
- Though we can't say electronic cigarettes are 100% safe, experts overwhelmingly agree that they are considerably less harmful than traditional cigarettes. Some experts estimate that electronic cigarettes are 95% safer than traditional cigarettes.
- The harm from smoking comes from burning the tobacco, not from the nicotine. As with other forms of nicotine replacement therapy, try not to worry about continued use of nicotine – the most important thing is to stop smoking.

How patients were involved in the creation of this article [box]

We thank three members of the UK Centre for Tobacco and Alcohol Studies smokers' panel with whom we held discussions before drafting the article; these discussions informed what was included in the sections on safety and tips for patients. Panel members also commented on the full article, resulting in revisions to the tips for patients.

Education into practice [box]

- How could you share the learning from this article with colleagues who work in different disciplines?
- Now you have read this article, how will you discuss the available evidence about the benefits and harms of e-cigarettes with patientswho have tried other ways to quit?

Figures

Figure 1. Different generations of electronic cigarettes (*BMJ to draw*)

Disclosure statements

Competing interests

We have read and understood the BMJ policy on declaration of interests and declare the following interests: There was no specific funding for this article. JHB and RB receive support from the National Institute of Health Research. PA is funded by the UK Centre for Tobacco and Alcohol Studies and is supported by the NIHR Biomedical Research Centre, Oxford and the NIHR CLAHRC, Oxford. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health. JHB, PA, and RB have no other competing interests to declare.

Contributors

JHB, RB and PA all contributed to the conception and design of the work; the acquisition, analysis, and interpretation of the data; the drafting and revision of the manuscript critically for important intellectual content; and final approval of the version to be published. JHB is guarantor.

Patient consent

Patient consent not required (patient case hypothetical).

Licence

The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, a worldwide licence to the Publishers and its licensees in perpetuity, in all forms, formats and media (whether known now or created in the future), to i) publish, reproduce, distribute, display and store the Contribution, ii) translate the Contribution into other languages, create adaptations, reprints, include within collections and create summaries, extracts and/or, abstracts of the Contribution, iii) create any other derivative work(s) based on the Contribution, iv) to exploit all subsidiary rights in the Contribution, v) the inclusion of electronic links from the Contribution to third party material where-ever it may be located; and, vi) licence any third party to do any or all of the above.

References

1. Action on Smoking and Health (ASH). Use of e-cigarettes (vapourisers) among adults in Great Britain 2017 [Available from: http://ash.org.uk/information-and-resources/fact-sheets/use-of-electronic-cigarettes-vapourisers-among-adults-in-great-britain/.
2. West R, Beard B, Brown J. Trends in electronic cigarette use in England: Smoking Toolkit Study. wwwsmokinginenglandinfo/latest-statistics2016.

3. Doll R, Peto R, Wheatley K, Gray R, Sutherland I. Mortality in relation to smoking: 40 years' observations on male British doctors. BMJ. 1994;309(6959):901-11.
4. Hajek P, Jackson P, Belcher M. Long-term use of nicotine chewing gum: Occurrence, determinants, and effect on weight gain. JAMA. 1988;260(11):1593-6.
5. Pasquereau A, Guignard R, Andler R, Nguyen-Thanh V. Electronic cigarettes, quit attempts and smoking cessation: a 6-month follow-up. Addiction. 2017;112(9):1620-8.
6. Etter J-F, Bullen C. Electronic cigarette: users profile, utilization, satisfaction and perceived efficacy. Addiction. 2011;106(11):2017-28.
7. Borup G, Mikkelsen KL, Tonnesen P, Christrup LL. Exploratory survey study of long-term users of nicotine replacement therapy in Danish consumers. Harm Reduct J. 2015;12:2.
8. Jarvis MJ, Boreham R, Primatesta P, Feyerabend C, Bryant A. Nicotine Yield From Machine-Smoked Cigarettes and Nicotine Intakes in Smokers: Evidence From a Representative Population Survey. JNCI: Journal of the National Cancer Institute. 2001;93(2):134-8.
9. Fagerstrom KO, Hughes JR. Nicotine concentrations with concurrent use of cigarettes and nicotine replacement: a review. Nicotine Tob Res. 2002;4 Suppl 2:S73-S9.
10. McRobbie H, Phillips A, Goniewicz ML, Smith KM, Knight-West O, Przulj D, et al. Effects of Switching to Electronic Cigarettes with and without Concurrent Smoking on Exposure to Nicotine, Carbon Monoxide, and Acrolein. Cancer Prevention Research. 2015;8(9):873.
11. Rahman MA, Hann N, Wilson A, Worrall-Carter L. Electronic cigarettes: patterns of use, health effects, use in smoking cessation and regulatory issues. Tobacco Induced Diseases. 2014;12(1):21.
12. Stead LF, Perera R, Bullen C, Mant D, Hartmann-Boyce J, Cahill K, et al. Nicotine replacement therapy for smoking cessation. The Cochrane database of systematic reviews. 2012;11:CD000146.
13. Rose JE. Nicotine and nonnicotine factors in cigarette addiction. Psychopharmacology. 2006;184(3-4):274-85.
14. Tobacco Advisory Group of the Royal College of Physicians. Nicotine without smoke: tobacco harm reduction. London: Royal College of Physicians; 2016.
15. Public Health England. E-cigarettes: a developing public health consensus. London, UK; 2016.
16. Public Health England. Highest smoking quit success rates on record. 2017:https://www.gov.uk/government/news/highest-smoking-quit-success-rates-on-record (accessed 7 November 2017).
17. Hartmann-Boyce J, McRobbie H, Bullen C, Begh R, Stead LF, Hajek P. Electronic cigarettes for smoking cessation. The Cochrane Library. 2016.
18. Bullen C, Howe C, Laugesen M, McRobbie H, Parag V, Williman J, et al. Electronic cigarettes for smoking cessation: a randomised controlled trial. Lancet. 2013;382(9905):1629-37.
19. Caponnetto P, Campagna D, Cibella F, Morjaria JB, Caruso M, Russo C, et al. EffiCiency and Safety of an eLectronic cigAreTte (ECLAT) as tobacco cigarettes substitute: a prospective 12-month randomized control design study. PloS One. 2013;8(6):e66317-e.
20. Begh R, Lindson-Hawley N, Aveyard P. Does reduced smoking if you can't stop make any difference? BMC Med. 2015;13(1):257.
21. Lindson-Hawley N, Hartmann-Boyce J, Fanshawe TR, Begh R, Farley A, Lancaster T. Interventions to reduce harm from continued tobacco use. The Cochrane database of systematic reviews. 2016;10:CD005231.
22. Meier E, Wahlquist AE, Heckman BW, Cummings KM, Froeliger B, Carpenter MJ. A Pilot Randomized Crossover Trial of Electronic Cigarette Sampling Among Smokers. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2017;19(2):176-82.
23. Tseng TY, Ostroff JS, Campo A, Gerard M, Kirchner T, Rotrosen J, et al. A Randomized Trial Comparing the Effect of Nicotine Versus Placebo Electronic Cigarettes on Smoking Reduction Among Young Adult Smokers. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2016;18(10):1937-43.

24. Cravo AS, Bush J, Sharma G, Savioz R, Martin C, Craige S, et al. A randomised, parallel group study to evaluate the safety profile of an electronic vapour product over 12 weeks. Regulatory toxicology and pharmacology : RTP. 2016;81 Suppl 1:S1-S14.
25. Pratt SI, Sargent J, Daniels L, Santos MM, Brunette M. Appeal of electronic cigarettes in smokers with serious mental illness. Addict Behav. 2016;59:30-4.
26. Pulvers K, Emami AS, Nollen NL, Romero DR, Strong DR, Benowitz NL, et al. Tobacco Consumption and Toxicant Exposure of Cigarette Smokers Using Electronic Cigarettes. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2016.
27. Strasser AA, Souprountchouk V, Kaufmann A, Blazekovic S, Leone F, Benowitz NL, et al. Nicotine Replacement, Topography, and Smoking Phenotypes of E-cigarettes. Tobacco regulatory science. 2016;2(4):352-62.
28. Goniewicz ML, Gawron M, Smith DM, Peng M, Jacob P, 3rd, Benowitz NL. Exposure to Nicotine and Selected Toxicants in Cigarette Smokers Who Switched to Electronic Cigarettes: A Longitudinal Within-Subjects Observational Study. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2017;19(2):160-7.
29. Polosa R, Morjaria JB, Caponnetto P, Battaglia E, Russo C, Ciampi C, et al. Blood Pressure Control in Smokers with Arterial Hypertension Who Switched to Electronic Cigarettes. Int J Environ Res Public Health. 2016;13(11).
30. Farsalinos K, Cibella F, Caponnetto P, Campagna D, Morjaria JB, Battaglia E, et al. Effect of continuous smoking reduction and abstinence on blood pressure and heart rate in smokers switching to electronic cigarettes. Intern Emerg Med. 2016;11(1):85-94.
31. Polosa R, Morjaria JB, Caponnetto P, Prosperini U, Russo C, Pennisi A, et al. Evidence for harm reduction in COPD smokers who switch to electronic cigarettes. Respiratory research. 2016;17(1):166.
32. Polosa R, Morjaria JB, Caponnetto P, Caruso M, Campagna D, Amaradio MD, et al. Persisting long term benefits of smoking abstinence and reduction in asthmatic smokers who have switched to electronic cigarettes. Discovery medicine. 2016;21(114):99-108.
33. McRobbie H, Phillips A, Goniewicz ML, Smith KM, Knight-West O, Przulj D, et al. Effects of switching to electronic ccigarettes with and without concurrent smoking on exposure to nicotine, carbon monoxide, and acrolein. Cancer Prevention Research (Philadelphia, Pa). 2015;8(9):873-8.
34. Stead LF, Perera R, Bullen C, Mant D, Hartmann-Boyce J, Cahill K, et al. Nicotine replacement therapy for smoking cessation. Cochrane Database of Systematic Reviews. 2012(11).