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R STREET POLICY STUDY NO. 63  
June 2016

## DOCTOR'S ORDERS: E-CIGARETTES IN U.S. CLINICAL PRACTICE

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### ABSTRACT

E-cigarettes and related nicotine vapor devices have become extremely popular among smokers in the United States, while attracting remarkably few nonsmokers to continuing nicotine use. According to a May 2016 Reuters/Ipsos poll of 10,000 U.S. adults, about 10 percent vape regularly, which would be equivalent to 24.5 million adults nationwide. Of these adult vapers, about 30 percent have ceased smoking; 62 percent continue to smoke; and about 8 percent of U.S. vapers never smoked cigarettes.<sup>1</sup>

Despite this popularity and despite substantial evidence that e-cigs are far safer than cigarettes; that they have helped many smokers quit smoking; and that they have not, to date, attracted nonsmoking teens to continuing use, American medical and public-health authorities are near-unanimous in their condemnation of these products as unsafe, ineffective and a threat to the health of future generations of teenagers. In addition, the U.S. Food and Drug Administration

1. Jillian Mincer, "U.S. e-cigarette use stalls as health concerns grow: Reuters/Ipsos poll," Reuters, May 24, 2016. <http://www.reuters.com/article/us-usa-ecigarettes-poll-idUSKCN0YF0DE>

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(FDA) recently promulgated regulations that, if implemented, would eliminate all or almost all e-cig products from the American market by making it far too expensive for any but the largest big-tobacco cigarette companies to comply.

Authorities in the United Kingdom, looking at the same body of evidence, actively endorse e-cigs for harm reduction and smoking cessation. The factors influencing these divergent policy choices (to condemn e-cigs or endorse them) hinge on how the e-cig issue is framed. All agree that it is best never to start recreational use of nicotine delivery products. Once started, it is best to quit. However, if one is unable or unwilling to quit, the question becomes whether public-health endorsements of "switching" behavior – a smoker transitioning to a much lower-risk nicotine-delivery product – would do more harm than good. The British say yes. The Americans say no.

British authorities' review of the issue takes into account what we know about how and why some tobacco products cause addiction, illness and death, while other tobacco and nicotine products (though still addictive) appear to present little to no risk of potentially fatal tobacco-related illness. Supported by a critical review of those surveys and research studies, the United Kingdom has put forth policy guidelines to best protect and enhance public health.

By contrast, U.S. policy asserts that e-cig products must be presumed to be as harmful as cigarettes unless or until they are proven otherwise. No endorsement will be considered, including FDA approval, unless manufacturers can prove to the satisfaction of American authorities that each individual combination of vaping device, flavor and nicotine strength both presents far less risk of potentially fatal tobacco-related illness than cigarettes and will not attract nonsmokers to cigarette use.

In its proposed rules, the FDA requires that existing e-cig manufacturers submit to a multimillion dollar application process. These would necessitate large prospective and case-control studies on each individual product. British authorities have instead relied on the evidence provided by studies and surveys completed to-date on e-cigs as a class of product. In short, the divergent choices of British and American policymakers stem from the gap between relying on the best available evidence and demanding absolute proof.

## FRAMING THE DEBATE

Support for using e-cigarettes in smoking cessation and tobacco harm reduction is based on a substantial scientific literature and the concept of providing less-toxic sources of nicotine to smokers is widely supported, with important papers published in the *International Journal of Environmental Research and Public Health*,<sup>2</sup> *Harm Reduction Journal*,<sup>3</sup> *Addictive Behaviors*<sup>4</sup> and *Addiction*.<sup>5</sup> Such approaches also have become increasingly popular in clinical practice in both the United States and the United Kingdom. However, the official public-health position on e-cigarettes differs substantially between these two countries.

In April 2016, the Royal College of Physicians published a review of the most recent evidence,<sup>6</sup> which came to the following conclusions:

**E-cigarettes and quitting smoking** - among smokers, e-cigarette use is likely to lead to quit attempts that would not otherwise have happened, and in a proportion of these to successful cessation. In this way, e-cigarettes can act as a gateway from smoking.

**E-cigarettes and long-term harm** - the possibility of some harm from long-term e-cigarette use cannot be dismissed due to inhalation of the ingredients other than nicotine, but is likely to be very small, and substantially smaller than that arising from tobacco smoking. With appropriate product standards to min-

imise exposure to the other ingredients, it should be possible to reduce risks of physical health still further.

Just a week after release of the RCP's report, the FDA issued regulations to extend its authority over all tobacco-related products, including the broad spectrum of electronic cigarettes and nicotine vapor devices.<sup>7</sup> Under the rules, which are scheduled to go into effect Aug. 8, 2016, the FDA will prohibit the sale of any tobacco-related product to persons under the age of 18, will require warning labels be affixed to these products and will bar distribution of free samples of these products. These specific rules have been long-awaited and enjoy near-unanimous support from the public-health community.

However, despite never considering even the possibility that any non-pharmaceutical nicotine-delivery product might offer personal or public health benefits, the FDA also introduced regulations that will eviscerate the e-cigarette industry. Manufacturers of e-cigs and other nicotine-vapor products developed and marketed after the effective date spelled out in 2009's Tobacco Control Act – Feb. 15, 2007 – must submit information within the next two years demonstrating the safety of their products. Those that do not meet the standards detailed by the FDA will not be permitted to be advertised or sold. If a product wishes to claim any personal or public-health benefit, its manufacturers must seek licensure as a drug, not as a tobacco product.

The detailed scientific assessments described in the FDA final rule are beyond the capacity of most e-cigarette manufacturers. Vape establishments that mix or prepare liquids for use in e-cigarettes are treated in the same manner as manufacturers. These regulations, taken in aggregate, will severely diminish consumer access to e-cigarettes. In the swirl of dueling press releases, it may be worthwhile to explore the common scientific foundations of these policy decisions.

An April 2016 in the *New England Journal of Medicine*<sup>8</sup> argued that the framing of harm-reduction interventions is the key distinction. The United Kingdom has a long tradition of encouraging harm reduction in the context of addiction, such as providing heroin and needles to heroin addicts. In the United States, methadone maintenance, needle exchange and similar interventions have been received more skeptical-

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2. Joel L. Nitzkin, "The case in favor of E-cigarettes for tobacco harm reduction," *International Journal of Environmental Research and Public Health*, 11(6): 6459–6471, June 2014. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4078589/>

3. Riccardo Polosa, Brad Rodu, Pasquale Caponnetto, Marilena Maglia and Cirino Raciti, "A fresh look at tobacco harm reduction: the case for the electronic cigarette," *Harm Reduction Journal*, 10(1):19, Oct. 4, 2013. <https://harmreductionjournal.biomed-central.com/articles/10.1186/1477-7517-10-19>

4. Karl O. Fagerstrom and Kevin Bridgman, "Tobacco harm reduction: the need for new products that can compete with cigarettes," *Addictive Behaviors*, 39(3):507-511, March 2014. <http://www.ncbi.nlm.nih.gov/pubmed/24290207>

5. David T. Levy, K. Michael Cummings, Andrea C. Villanti, et al., "A framework for evaluating the public health impact of e-cigarettes and other vaporized nicotine products," *Addiction*, April 25, 2016. <http://onlinelibrary.wiley.com/doi/10.1111/add.13394/abstract>

6. Tobacco Advisory Group, "Nicotine without smoke: Tobacco harm reduction," Royal College of Physicians, April 2016. <http://shop.rcplondon.ac.uk/products/nicotine-without-smoke?variant=1745137306>



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7. U.S. Food and Drug Administration, "Deeming Tobacco Products To Be Subject to the Federal Food, Drug, and Cosmetic Act, as Amended by the Family Smoking Prevention and Tobacco Control Act; Restrictions on the Sale and Distribution of Tobacco Products and Required Warning Statements for Tobacco Products," *Federal Register*, May 10, 2016. <https://www.federalregister.gov/articles/2016/05/10/2016-10685/deeming-tobacco-products-to-be-subject-to-the-federal-food-drug-and-cosmetic-act-as-amended-by-the>

8. Sharon H. Green, Ronald Bayer and Amy L. Fairchild, "Evidence, Policy, and E-Cigarettes — Will England Reframe the Debate?," *New England Journal of Medicine*, 374(14):1301-1303, April 13, 2016. <http://www.nejm.org/doi/full/10.1056/NEJMp1601154#t=article>

ly. When framed within the context of reducing the burden of tobacco-related illness, the evidence appears to favor use of e-cigarettes; when framed within a context of unknown harms, uncertainties regarding content, unintended consequences and the potential for utilization by youths, use of e-cigarettes generates red flags. For public-health officials steeped in a precautionary principle, the baseline directive is that no action should be taken until e-cigarettes are shown to be safe.

**FIGURE 1: SUBJECT FRAMING MATTERS**

	Focus on Youth	Focus on Smokers
		
Goal	Reduce any early adoption of nicotine	Reduce harm from combusted cigarettes
Concerns	Unknown health effects of e-cigs	Magnitude of smoking harms is very high
Unintended consequences	Renormalization of smoking	Unknown harms from e-cigs appear low
Conclusion	Limits all access to e-cigs, even if it affects adults	Promote use of e-cigs for cessation and harm reduction

### RELATIVE SAFETY OF TOBACCO-RELATED PRODUCTS



With respect to the safety of e-cigarettes, many authors share concerns about the large number of product types, which have been developed in the absence of regulatory standards. The vaping industry has made major progress in developing and implementing voluntary industry standards. One would expect a major benefit of regulation will be to protect the ethical manufacturers and vendors, and the public, by eliminating shoddy products from the marketplace and by eliminating predatory and other inappropriate marketing practices.

Some of the components of liquids used to produce vapor may be of unknown source and there are more than 8,000 different flavor combinations available. A small number studies have identified toxic substances in some types of e-cigarettes at very low concentrations. However, the safety concerns are eclipsed by the far more harmful effects of combusted cigarettes.

Some studies have compared the effects of vapor from select-

ed brands to that of combusted cigarettes. In all instances, the concentration of toxins found was lower in e-cigarettes. There have been no long-term epidemiological studies of e-cigarette users, as the products are too new in the market to allow time for appropriate follow-ups. There are long-term data on other pharmaceutical and non-pharmaceutical nicotine-delivery products, which give us excellent reason to anticipate little or no risk of potentially fatal tobacco-related illness and death from e-cigarettes. Regular users of e-cigarettes have reported a range of minor symptoms, such as minor throat irritation and mouth dryness.

**FIGURE 2: TOBACCO HARM VERSUS E-CIGARETTE HARM**

	Smoking	Vaping
		
Dangers	520,000 excess deaths per year	No reported diseases or conditions; Certain types of batteries may be flammable
Composition	Well-characterized source of toxin and mechanism of disease causation	Great variation in delivery systems and liquids
Experience	Decades	10 years
Users	Billions	Tens of millions
Scientific consensus	More harmful	Less harmful

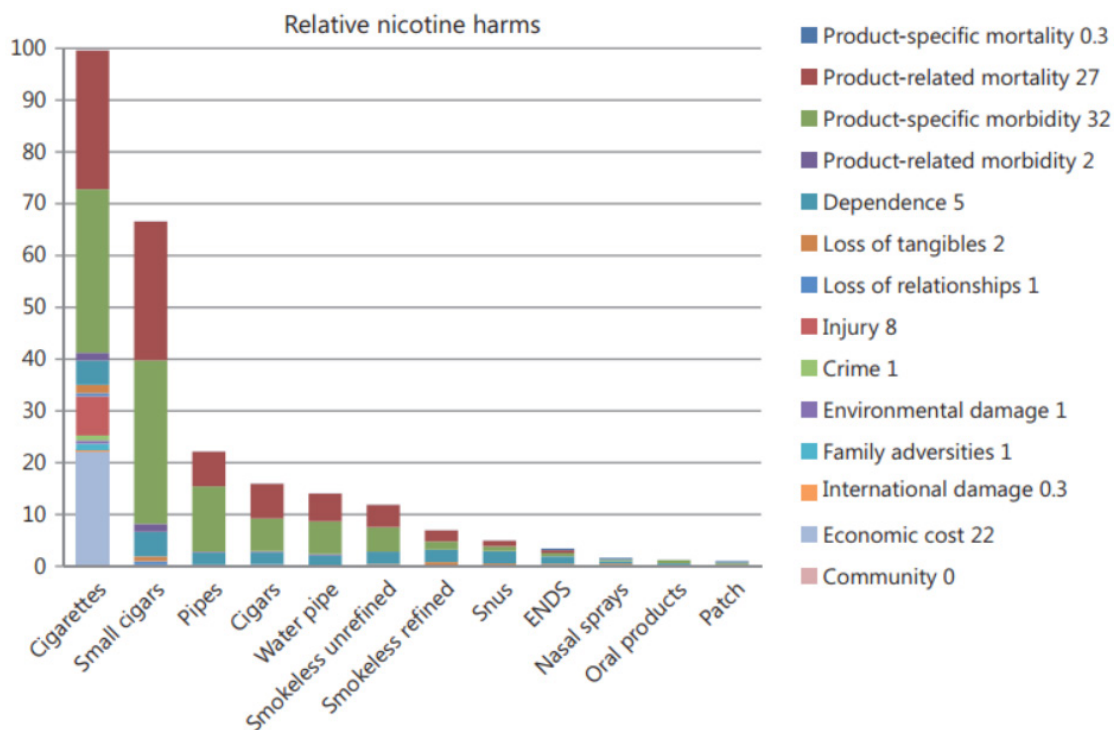
Experts can agree on some things:

- The number of known toxins and carcinogens in combusted cigarette smoke exceeds that of e-cigarettes by two orders of magnitude.
- The concentrations of the compounds in e-cigarette vapor known to be harmful are far lower than in combusted cigarette smoke.
- The magnitude of difference in safety is debated. The evidence summary on e-cigarettes from Public Health England estimates that e-cigarettes are 95 percent safer.<sup>9</sup> Another way to examine the safety of nicotine-containing products was laid out in 2014 by David J. Nutt, Lawrence D. Phillips, David Balfour and colleagues and can be seen in Figure 3.<sup>10</sup>

9. Ann McNeill, et al., "E-Cigarettes: An Evidence Update," Public Health England, Aug. 19, 2015. <https://www.gov.uk/government/publications/e-cigarettes-an-evidence-update>

10. David J. Nutt, Lawrence D. Phillips, David Balfour, et al., "Estimating the harms of nicotine-containing products using the MCDA approach," European Addiction Research, 20(5):218-225, April 3, 2014. <http://www.karger.com/Article/Pdf/360220>

**FIGURE 3: OVERALL WEIGHTED HARM SCORES OF NICOTINE PRODUCTS**



SOURCE: European Addiction Research

- No nicotine delivery product can be considered perfectly safe. However, we can say with confidence that e-cigarettes, having no tobacco and no combustion, are far safer than combustible cigarettes.

Studies of the safety of passively inhaled vapor or aerosol from e-cigarettes in nonusers have supported the supposition that the majority of toxic substances known to be present in combusted cigarettes are not reported in those e-cigarettes that have been studied. It is relatively straightforward to conclude that passive inhalation of vapor is far less harmful than passive inhalation of combusted smoke. As Dr. Joel Nitzkin explained in a 2014 paper:

E-cigarettes have no products of combustion. Nothing curls off the end of an e-cigarette when no one is puffing on it. The mainstream vapor exhaled by the user includes only the tiniest traces of chemical contaminants. E-cigarette vapor, as exhaled by the e-cigarette user, poses no significant risk to bystanders. A number of studies have been published dealing with the concentration of organic chemicals in exhaled e-cigarette vapor. Basically, these studies show that when the e-cigarette user exhales into a glass tube or similar container, trace quantities of a variety of organic chemicals can be detected, but, when in an eight-cubic meter test chamber or similar room, for a

half-hour or more, e-cigarette use does not measurably increase the trace quantities of these chemical substances above background levels, while cigarettes cause dramatic rapid increases.<sup>11</sup>

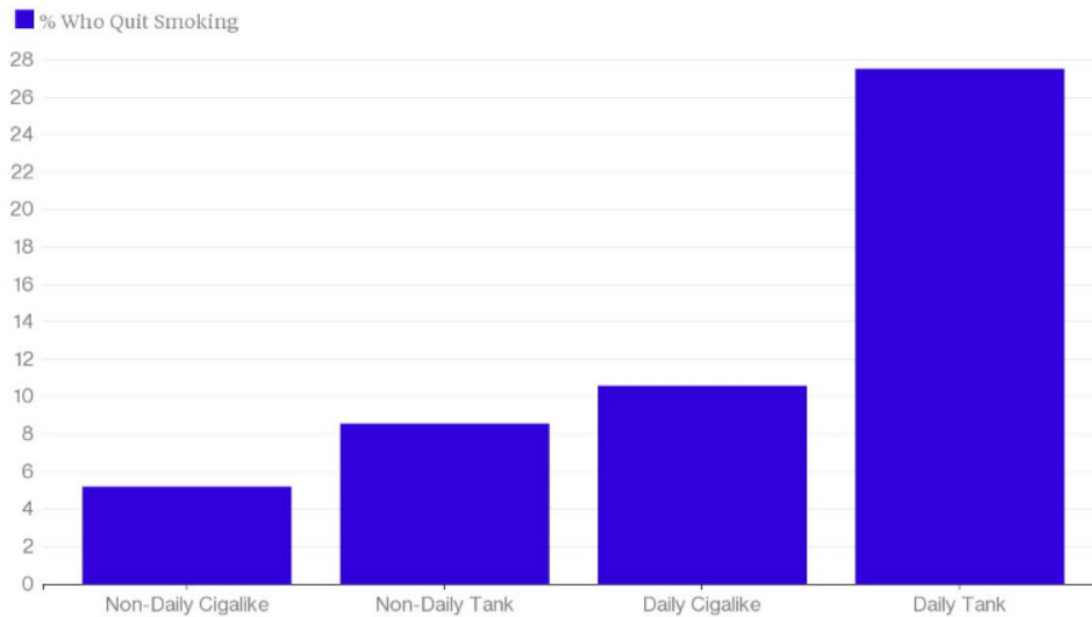
Despite the consensus recommendation on safety from Public Health England finding that e-cigarettes are about 95 percent less harmful than smoking, the FDA’s position remains that e-cigarettes are not safe until proven to be substantially less harmful than currently accepted tobacco products (as deemed by the Tobacco Control Act of 2009).

### EVIDENCE FOR CESSATION AND HARM REDUCTION

Whether e-cigarettes should be used for smoking cessation and tobacco harm reduction is a question that has been tested by differing sorts of investigations whose results nearly all point in the same direction. The most compelling and straightforward argument in favor of their clinical use concerns the mechanism for nicotine delivery. E-cigarettes provide vapers with sufficient nicotine to mitigate the need to smoke. For many users, the experience of vaping provides an acceptable alternative to combusted cigarettes. While most vapers’ initial experimentation likely is with the sort of “cig-a-like” products sold in convenience stores, the trend

11. Nitzkin, 2014.

FIGURE 4: COMPARISON OF E-CIGARETTE TYPES



SOURCES: King's College London, Bloomberg

for long-term users is to progress to tanks, mods and related vape-shop products.

Given the complexities of studying and confirming changes in the behavior of smokers, the data on cessation or reduction have not been as strong as some would expect. However, the studies point in the same general direction. The weight of the evidence has been sufficient to promote a change in government policy in the United Kingdom that now allows e-cigarettes to be dispensed for smoking cessation and harm reduction.<sup>12</sup> A significant number of physicians in the United States now routinely advise smokers to reduce the risk of tobacco-related disease by using e-cigarettes. Both physicians and their patients remain concerned about the many unknowns surrounding e-cigarettes, but this has not deterred widespread adoption.

In the decade since they were developed, e-cigarettes have become widely popular. It is estimated that 10 percent of U.S. adults use e-cigarettes.<sup>13</sup> Recent surveys show that 9.4 percent of smokers have used e-cigarettes in the past 30 days. As much as 80 percent of e-cigarette users continue to use combusted cigarettes, a practice clinicians dub “dual use.”<sup>14</sup> Surveys of current e-cigarette users show the main reason

vapers adopt e-cigarettes is for health reasons,<sup>15</sup> but they are well aware that use of e-cigarettes is not perfectly safe.<sup>16</sup>

Websites used by vapers provide tens of thousands of anecdotes and testimonials and offer support and encouragement to those who seek to reduce and eventually discontinue cigarette smoking.<sup>17</sup> Testimonials commonly focus on tactics and devices to help optimize the availability of nicotine. Some vapers use multiple flavors through the day to increase the amount of puffs taken to help meet their need for nicotine. Details of new devices and new types of e-liquids are also shared. Over the years, devices have continued to evolve in their capacity to deliver nicotine, require fewer refills and operate safely. There are now more than 600 types of devices available to deliver vaporized nicotine. With most vape-shop products, the flavor, nicotine strength and the device itself can be customized to the needs and preferences of the vaper, as well as changed at-will over time. Relative

12. See Tobacco Advisory Group, 2016; McNeil, 2015.

13. Mincer, 2016.

14. Ahmed Jamal, David M. Homa, Erin O'Connor, et al., “Current Cigarette Smoking Among Adults—United States, 2005–2014,” *Morbidity and Mortality Weekly Report*, 64(44):1233-1240, Nov. 13, 2015. <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6444a2.htm>

15. Jonathan Foulds, Susan Veldheer and Arthur Berg, “Electronic cigarettes (e-cigs): views of aficionados and clinical/public health perspectives,” *International Journal of Clinical Practice*, 65(10):1037-1042, Aug. 1, 2011. <http://www.pubfacts.com/detail/21801287/Electronic-cigarettes-e-cigs-views-of-aficionados-and-clinical-public-health-perspectives>; See also, Amy McQueen, Stephanie Tower and Walton Sumner, “Interviews with ‘vapers’: implications for future research with electronic cigarettes,” *Nicotine & Tobacco Research*, 13(9):860-867, April 5, 2011. <http://ntr.oxfordjournals.org/content/13/9/860.long>

16. Lynne Dawkins, John Turner, Amanda Roberts and Kirstie Soar, “‘Vaping’ profiles and preferences: an online survey of electronic cigarette users,” *Addiction*, 108(6):1115-1125, March 28, 2013. <http://onlinelibrary.wiley.com/doi/10.1111/add.12150/abstract>; See also, Jamal, 2015; Foulds, 2011.

17. Consumer Advocates for Smoke-free Alternatives Association, “CASAA Testimonials,” accessed June 20, 2016; See also, E-Cigarette Forum, “E-Cigarette Success Stories,” accessed June 20, 2016. <https://www.e-cigarette-forum.com/forum/forums/e-cigarette-success-stories.401/>

to pharmaceutical options and standardized convenience-store “cig-a-like” products, the ability to customize “mods” and “tanks” may enhance substantially their efficacy for both harm reduction (partial substitution of e-cigs for cigarettes) and smoking cessation.

A second batch of evidence comes from telephone and Internet surveys conducted in recent years. These surveys differ substantially in how they recruit smokers or e-cigarette users for questioning, survey methods used and how questions are worded. The evidence collected from these reports offer support for using e-cigarettes for smoking cessation and reduction.

- Jamie Brown and colleagues used a telephone survey to reach 5,863 people who made a quit attempt in the previous year. Among smokers who made a quit attempt without professional support, those who use e-cigarettes were more than twice as likely to report continued abstinence than those who used nicotine-replacement-products bought over the counter.<sup>18</sup>
- Konstantinos Farsalinos and colleagues surveyed an international sample of 19,414 e-cigarette users. Among respondents, 81 percent reported complete substitution of cigarettes.<sup>19</sup>
- Sara Hitchman and colleagues completed an online survey of 1,643 smokers, some of whom had used various e-cigarette devices. Users of e-cigarettes were more likely to have quit and users of tank systems were the most successful.<sup>20</sup>
- Leonie Brose and colleagues followed 1,759 smokers for one year. Daily use of e-cigarettes while smoking correlated with a greater number of quit attempts, but not greater rates of quitting. Nondaily use of e-cigarettes did not appear associated with quit attempts, cessation or reduced smoking. Daily users of e-cigarettes were 2.5 times as likely to reduce the amount smoked.<sup>21</sup>

18. Jamie Brown, Emma Beard, Daniel Kotz, Susan Michie and Robert West, “Real-world effectiveness of e-cigarettes when used to aid smoking cessation: a cross-sectional population study,” *Addiction*, 109(9):1531-1540, Aug. 8, 2014. <http://onlinelibrary.wiley.com/doi/10.1111/add.12623/abstract>

19. Konstantinos E. Farsalinos, Giorgio Romagna, Dimitris Tsiapras, Stamatis Kyrzopoulos and Vassilis Voudris, “Characteristics, perceived side effects and benefits of electronic cigarette use: a worldwide survey of more than 19,000 consumers,” *International Journal of Environmental Research and Public Health*, 11(4):4356-4373, April 22, 2014. <http://www.mdpi.com/1660-4601/11/4/4356>

20. Sara C. Hitchman, Leonie S. Brose, Jamie Brown, Debbie Robson and Ann McNeill, “Associations between e-cigarette type, frequency of use and quitting smoking: findings from a longitudinal online panel survey in Great Britain,” *Nicotine & Tobacco Research*, ntv078, April 20, 2015. <http://ntr.oxfordjournals.org/content/17/10/1187.long>

21. Leonie S. Brose, Sara C. Hitchman, Jamie Brown, Robert West and Ann McNeill, “Is the use of electronic cigarettes while smoking associated with smoking cessation attempts, cessation and reduced cigarette consumption? A survey with a 1-year follow-up,” *Addiction*, 110(7):1160-1168, April 23, 2015. <http://onlinelibrary.wiley.com/doi/10.1111/add.12917/abstract>

- At year-end 2015, CASAA, the Consumer Advocates for Smoke-free Alternatives Association surveyed its membership and identified 19,823 regular e-cigarette users. The group found that 87 percent indicated they quit smoking entirely after starting to use e-cigarettes.<sup>22</sup>

Longitudinal studies track the experience of current smokers over time on a periodic basis; study participants provide updates on their smoking status and quit attempts. The questions used in these studies vary considerable and do not make the distinction between “ever-use” of e-cigarettes and regular use. In aggregate these studies offer mixed results.

- Wael Al-Delaimy and colleagues surveyed a population of 1,000 smokers at two time-points, ending in 2011, and found that smokers who had ever used e-cigarettes were less likely to report cessation or reduction.<sup>23</sup>
- Sara Kalkhoran and Stanton Glantz published a meta-analysis of the previous year’s papers that showed a reduced impact of e-cigarettes on smoking cessation.<sup>24</sup> However, this paper has been criticized extensively on methodological grounds for excluding data showing vapers who have quit.<sup>25</sup>
- Lois Biener and J. Lee Hargraves followed a population of 695 cigarette smokers for two years. The sample was divided by e-cigarette use into three categories: intensive users (regular use for at least one month), intermittent users and never-users. Intensive users were six times more likely to quit smoking.<sup>26</sup>

Clinical trials provide a means to verify patient reports of behavior change by the use of chemical markers. This overcomes a major limitation of the many surveys which may have a biased participation or response rate.

22. Carl V Phillips, “CASAA ecig survey results,” Consumer Advocates for Smoke-free Alternatives Association, Jan. 4, 2016. <https://antithrillies.com/2016/01/04/casaa-ecig-survey-results/2016/>

23. Wael K. Al-Delaimy, Mark G. Myers, Eric C. Leas, David R. Strong and C. Richard Hofstetter, “E-cigarette use in the past and quitting behavior in the future: a population-based study,” *American Journal of Public Health*, 105(6):1213-1219, Nov. 25, 2014. [http://ajph.aphapublications.org/doi/abs/10.2105/AJPH.2014.302482?url\\_ver=Z39.88-2003&rft\\_id=ori%3Arid%3Aacrossref.org&rft\\_dat=cr\\_pub%3Dpubmed&](http://ajph.aphapublications.org/doi/abs/10.2105/AJPH.2014.302482?url_ver=Z39.88-2003&rft_id=ori%3Arid%3Aacrossref.org&rft_dat=cr_pub%3Dpubmed&)

24. Sara Kalkhoran and Stanton A. Glantz, “E-cigarettes and smoking cessation in real-world and clinical settings: a systematic review and meta-analysis,” *The Lancet Respiratory Medicine*, Jan. 14, 2016. [http://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(15\)00521-4/abstract](http://www.thelancet.com/journals/lanres/article/PIIS2213-2600(15)00521-4/abstract)

25. Peter Hajek, Hayden McRobbie and Chris Bullen, “E-cigarettes and smoking cessation,” *The Lancet Respiratory Medicine*, April 25, 2016. [http://www.thelancet.com/pdfs/journals/lanres/PIIS2213-2600\(16\)30024-8.pdf](http://www.thelancet.com/pdfs/journals/lanres/PIIS2213-2600(16)30024-8.pdf)

26. Lois Biener and J. Lee Hargraves, “A Longitudinal Study of Electronic Cigarette Use in a Population-based Sample of Adult Smokers: Association with Smoking Cessation and Motivation to Quit,” *Nicotine & Tobacco Research*, Oct. 9, 2014. <http://ntr.oxfordjournals.org/content/early/2014/10/07/ntr.ntu200.abstract>

- Pasquale Caponnetto and colleagues completed a one-year pilot study with 23 schizophrenic patients who had no intention to quit and no smoking-cessation counseling offered. Sustained smoking abstinence was shown in 14 percent and 80 percent showed a sustained reduction in the number of cigarettes smoked.<sup>27</sup>
- Riccardo Polosa and colleagues studied 40 regular smokers who were not ready to quit. At six months, 32.5 percent of participants showed a 50 percent reduction in the number of cigarettes smoked.<sup>28</sup>
- Peter Hajek, in a pilot study in London, provided e-cigarettes to smokers seeking to quit. At four weeks, 68 percent had biochemically validated abstinence.<sup>29</sup>

The so-called “gold standard” for evidence of clinical efficacy for a drug used to cure a disease is the randomized clinical trial. In a 2013 study, Christopher Bullen and colleagues randomized 289 smokers to e-cigarette, patch and placebo e-cigarette groups and measured six-month abstinence.<sup>30</sup> The overall reduction in cigarettes smoked for the e-cigarette group was statistically significant, at 0.0001. E-cigarettes were as effective as the patch in smoking cessation, with a quit rate of 7.3 percent.

Davide Campagna and colleagues examined subjective and objective measures of respiratory function in smokers who either fully or partially replaced combusted cigarettes with e-cigarettes. Both groups showed significant improvement.<sup>31</sup>

Some important conclusions can be drawn from this body of research. For many smokers, smoking and use of other nicotine products is a behavior, not a disease. As a behavior, product use is heavily influenced by public and private communications, marketing and other factors that do not

influence the efficacy of a drug. This being the case, a randomized clinical trial, which presumes use is totally dependent on pharmaceutical efficacy, is not an appropriate study design to address initiation, continuation and/or cessation of cigarette use or use of other non-pharmaceutical nicotine products. There is no practical way to adjust for these communication issues in an open society and no practical way to blind the study.

Use of e-cigarettes has been observed to prompt successful quitting in persons who were not interested in quitting. The surveys and clinical trials reflect “real world” experience and measured cessation and cigarette reduction in the absence of behavioral interventions. Some data suggest that more recent studies generate better outcomes, because smokers only relatively recently have gained access to nicotine-delivery systems that produce higher levels of nicotine.<sup>32</sup>

## E-CIGARETTES IN CLINICAL PRACTICE

In February 2016, the United Kingdom’s National Centre for Smoking Cessation Training published training materials guiding the use of e-cigarettes for cessation and harm reduction in that country.<sup>33</sup> In the United States, a growing number of physicians are recommending e-cigarettes. Two studies have found that doctors report two-thirds of their smoking patients ask about e-cigarettes and about one-third of U.S. physicians advise smokers to use them.<sup>34</sup> A larger and more recent survey of practicing physicians presented at the recent Society for Research on Nicotine and Tobacco reported that 57.8 percent of physicians advise using e-cigarettes for smoking cessation or harm reduction.<sup>35</sup> One author has suggested that electronic nicotine delivery systems, such as e-cigarettes, have had a public health impact by reducing the number of regular smokers.<sup>36</sup>

Clinical investigations into the effects of e-cigarettes on patients have been limited by many pragmatic issues, not the

27. Pasquale Caponnetto, Roberta Auditore, Cristina Russo, Giorgio Carlo Cappello and Riccardo Polosa, “Impact of an electronic cigarette on smoking reduction and cessation in schizophrenic smokers: a prospective 12-month pilot study,” *International Journal of Environmental Research and Public Health*, 10(2):446-461, Jan. 28, 2013. <http://www.mdpi.com/1660-4601/10/2/446>

28. Riccardo Polosa, Pasquale Caponnetto, Jaymin B Morjaria, Gabriella Papale, Davide Campagna and Cristina Russo, “Effect of an electronic nicotine delivery device (e-Cigarette) on smoking reduction and cessation: a prospective 6-month pilot study,” *BMC Public Health*, 11(1):1, Oct. 11, 2011. <http://bmcpublihealth.biomedcentral.com/articles/10.1186/1471-2458-11-786>

29. Peter Hajek, et al., “Adding E-Cigarettes to Specialist Stop-Smoking Treatment: City of London Pilot Project,” *Journal of Addiction Research & Therapy*, Sept. 30, 2015. <http://www.omicsonline.org/open-access/adding-ecigarettes-to-specialist-stopsmoking-treatment-city-of-london-pilot-project-2155-6105-1000244.php?aid=60562>

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least of which is standardization, but observational studies are possible. Instructions for how to advise patients to quit smoking using e-cigarettes have started to appear in the literature<sup>37</sup> and they are being introduced to active treatment programs. As a behavioral intervention that does not involve health-insurance reimbursement, e-cigarette use puts the smoker, not the doctor, in control. It also arguably reduces the need for continuing medical follow-up.

But there is strong data to support the use of behavioral interventions in smoking cessation. Indeed, the medications used for smoking cessation are approved as adjuncts to behavioral interventions. According to the evidence review presented in the clinical practice guideline produced by the U.S. Preventive Services Task Force, the more sessions provided, the longer the duration and the longer the course of treatment, the better the outcome.<sup>38</sup> The focus on using medication or e-cigarettes for smoking cessation has been aligned to the “real world” experience of quitting, where counseling is not readily available. Clearly, the enhanced availability of smoking-cessation counseling would help people trying to quit by whichever means they chose.

There has been considerable criticism of the standard model of smoking cessation, which some see as rejecting smokers who are not ready to change. In the current model of treatment, smokers who state that they are not ready to quit are provided no treatment. In 2013, a detailed survey of quit attempts in the Behavioral Risk Factor Surveillance System revealed that approximately two-thirds of smokers had made a quit attempt in the preceding year.<sup>39</sup> Previous surveys show that 6.2 percent are successful in any given year.<sup>40</sup> Successful quitters make eight to 11 attempts before they are able to abstain. Smokers who make repeated efforts to quit over time get “better” at abstaining for longer periods, in a process that may last several years.

Given the chronic relapsing course of smoking cessation, Michael Steinberg and colleagues have proposed that

tobacco use be approached as a chronic disease.<sup>41</sup> Steinberg goes on to propose extended medication with nicotine as a means to treat this chronic condition.

Kimber Richter and Edward Ellerbeck have argued for an opt-in treatment approach, wherein every smoker seen by a clinician is provided with an intervention, regardless of their readiness for change.<sup>42</sup> There is substantial evidence that interventions for smokers not ready to change nonetheless promote quitting and reduce the amount smoked.

Positive outcomes for this type of proactive approach also have been reported by others authors.<sup>43</sup> Steven Fu and colleagues randomized 5,000 smokers under the care of the U.S. Department of Veterans Affairs to compare the standard model of usual care versus proactive care. At one year, the proactive group had a sustained six-month abstinence rate of 13.5 percent, compared with 10.9 percent in usual care.<sup>44</sup> Jennifer Vidrene and colleagues evaluated an alternative, more proactive approach to refer patients to smoking-cessation quit-lines. Most smokers referred passively never call for help. But after doctors shifted to an “Ask-Advise-Connect” protocol, Vidrene observed a tenfold increase in smokers’ enrollment.<sup>45</sup>

The application of any intervention – be it e-cigarettes, medication or simply counseling – is likely to have some impact. Smokers concerned about their health are switching to e-cigarettes and many of these are able to quit. Although many smokers consult their doctors about e-cigarettes, the majority do not. They represent empowered consumers who seek to improve their health.

## CONCLUSION

There can be little question that many adult smokers would benefit by switching from combusted cigarettes to e-cigarettes. Some would quit use of all nicotine products or entirely replace combusted cigarettes. A large fraction of

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the others would be able reduce the number of cigarettes smoked. Those vapers who use higher levels of nicotine, as can be obtained through tank systems, are more likely to succeed. Early surveys and studies understated the impact of e-cigarettes because tank systems were not yet available.

The effectiveness of vaping in smoking cessation is equal to use of the nicotine patch, when purchased over the counter. In fact, the majority of surveys and studies of e-cigarettes report unassisted quitting. The addition of counseling services to offer insights into effective e-cigarette use, could expand their impact significantly. Telephonic and online support systems, which already are shown to enhance performance of medications, could have a similar effect on quit rates for vapers.

At the Centers for Disease Control and Prevention's Public Health Grand Rounds on E-cigarettes in October 2015, CDC Director Tom Freiden was quoted saying: "For the individual smoker, there is no question that e-cigarettes are safer."<sup>46</sup> The use of e-cigarettes for smoking cessation and tobacco harm reduction among adults has become a cultural norm. Rather than resist it, we should do what our counterparts in the United Kingdom already have done: embrace it and find ways to make it even better.

#### ABOUT THE AUTHOR

Dr. Edward Anselm is medical director of Health Republic Insurance of New Jersey and a senior fellow of the R Street Institute.

Edward is a frequent speaker at population health conferences and has been a strong advocate for reimbursement of smoking-cessation services. Most recently, he implemented the first harm reduction strategy sponsored by a health plan. Building on reimbursement for smoking cessation and enhanced coverage of FDA-approved smoking-cessation medications, the program seeks to engage patients and their doctors in a dialogue about harm reduction.

He previously served as chief medical officer of Freelancers Health Service Corp./Health Republic Insurance of New York, HIP Health Plan and Fidelis Care of New York. As a health care executive, his focus has been implementation of disease management and case management programs.

Trained in internal medicine at the Rosalind Franklin University of Medicine and Science, Edward for several years ran a primary-care clinic. During his residency at Montefiore Medical Center, initiated a smoking cessation clinic. Since then, he has organized and led a number of clinics at hospitals and in workplace settings.

Edward is a fellow of the New York Academy of Medicine and serves on the board of the New York-metro chapter of Physicians for a National Health Plan. He also teaches courses on tobacco control and other public health topics as an assistant clinical professor of medicine at the Icahn School of Medicine at Mount Sinai.

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