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THE ROLE OF FLAVORING IN TOBACCO HARM REDUCTION

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EXECUTIVE SUMMARY

One of the great public health controversies of our time surrounds the debate over what role Electronic Nicotine Delivery Systems (ENDS),¹ of which e-cigarettes are the most common type, might play in tobacco harm reduction. A key element of this discussion concerns the role of flavorings.²

Regular users of ENDS declare that flavor is important in their ability to cease smoking. In the absence of flavors to soften the sometimes-harsh taste of nicotine vapor, they are likely to resume smoking cigarettes.

Some public-health officials have expressed concern that certain flavors might attract young people to experiment

1. Amy L. Fairchild and Ronald Bayer "Smoke and fire over e-cigarettes," *Science*, 347(6220):375-376, Jan. 23, 2015. <http://www.sciencemag.org/content/347/6220/375.summary>

2. Jessica L. Barrington-Trimis, Jonathan M. Samet and Rob McConnell, "MD1 Flavorings in electronic cigarettes: an unrecognized respiratory health hazard?" *JAMA: The Journal of the American Medical Association*, 312(23):2493-2494, Dec. 17, 2014. <http://jama.jamanetwork.com/article.aspx?articleid=1935097>

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with nicotine at an early age. Evidence for this thesis has not yet been demonstrated. Concerns about the safety of ENDS and whether ENDS might attract young people to nicotine use threaten to dominate what should be a far broader discussion about how tobacco-harm-reduction strategies could be used to improve public health.

INTRODUCTION

There are 42 million smokers in the United States. On average, they will live 10 fewer years than their nonsmoking peers.³ Although roughly 70 percent of U.S. daily cigarette smokers say they want to quit, fewer than half will attempt to do so in a given year. The long-term success rate of these quit attempts is about 6 percent.⁴

M. Bradley Drummond of Johns Hopkins University School of Medicine has estimated that at least 36 million U.S. adults are unwilling or unable to abstain completely from combustible cigarettes.⁵ If a substantial number of smokers switched to ENDS, the impact on death, disease and the cost of health care would be profound.

3. Boris D. Lushniak, "The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General, 2014," U.S. Department of Health and Human Services, Rockville, Md., 2014:171. <http://www.surgeongeneral.gov/library/reports/50-years-of-progress/>

4. Centers for Disease Control and Prevention, "Quitting smoking among adults--United States, 2001-2010," *MMWR: Morbidity and Mortality Weekly Report*, 60(44):1513, Nov. 11, 2011. <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6044a2.htm>

5. M. Bradley Drummond, "Electronic Cigarettes: Perhaps the Devil Unknown Is Better Than the Devil Known," *Annals of Internal Medicine*, 163(1):61-62, July 7, 2015. <http://annals.org/article.aspx?articleID=2292047>

In the debate around ENDS within the public-health community, the first question goes to the very nature of harm-reduction interventions: should they be entirely free of harm? A recent article in *Science* reviewed the rancorous dialogue among clinicians who argue either side of this question.⁶ Scholars agree that the differences between combusted smoke and vapor are substantial, but to some, any nicotine, or any chemical, is inherently harmful. A recurrent theme of the arguments used by those who oppose ENDS as a harm-reduction strategy is a strong distrust of tobacco business interests, with some stating flatly that nothing the tobacco industry says is to be believed.

Sometimes, this anti-industry posturing is quite intentional. Amy L. Fairchild of the Columbia University Mailman School of Public Health⁷ has explored the role of fear-based education programs in several public-health campaigns. The Centers for Disease Control and Prevention (CDC), public-health authorities and interested media frequently have exaggerated reports of e-cigarettes' possible toxicity. Michael Siegel, a professor at the Boston University School of Public Health, has documented many such examples.⁸ Demonization of the tobacco industry and of all nicotine products as equally harmful becomes a recurrent "theme amplifier" of general health messages and reduces the opportunity to form consensus around shared public-health goals.⁹

A second question in the debate concerns the threshold of proof needed to justify implementing a harm-reduction strategy. How much evidence is required to support use of a specific intervention? The contrast between the approach taken in the United Kingdom and the United States is revealing. This past spring, Public Health England issued a review of the health and safety implications of electronic cigarettes that concluded their use is about 95 percent safer than smoking.¹⁰

The authors conclude that smokers who have tried other methods of quitting without success could be encouraged to switch to e-cigarettes. In addition to encouraging their use as a cessation tool, encouraging

switching could help reduce smoking-related disease, death and health inequalities.¹¹

In the United States, that same evidence has been subject to radically divergent interpretation. The U.S. Preventive Services Task Force's recently updated clinical-practice guidelines concluded there is insufficient evidence to support the use of ENDS in smoking cessation.¹² For its part, the CDC has conducted a very aggressive public-relations campaign against ENDS, even though a close reading of available public-health information would counsel a nuanced understanding of the devices' health potential. A recent fact sheet distributed by the CDC stated:

In order for adult smokers to benefit from ENDS, they must completely quit combusted tobacco use. Smoking even a few cigarettes per day is dangerous to your health.

While this statement could be read as supportive of ENDS as a harm-reduction strategy, it fails to take into account that any reduction in combusted smoke would be a positive. The overwhelming thrust of the CDC's public-relations campaign has been vehement opposition to nicotine use in any form. For example, earlier this year, the agency trumpeted findings that "e-cigarette use among middle and high school students tripled from 2013 to 2014," without highlighting the very low levels involved or explicating what proportion of use was one-time experimentation and what proportion actually were teens who turned to e-cigarettes to help quit smoking.¹³ Clarity in this complex debate requires a nuanced understanding of the components of vapor, nicotine, flavoring and other compounds within the context of how they actually are used and how they can be tested.

NICOTINE SENSITIVITY AND THE YOUNGER BRAIN

It is well-established that the brains of younger persons are more vulnerable to alcohol, drugs and nicotine.¹⁴ The brain continues to mature into one's mid-20s. The younger the age of onset of any drug use, the greater difficulty the subject will

6. Fairchild and Bayer, 2015.

7. Amy L. Fairchild, Ronald Bayer and James Colgrove, "Risky Business: New York City's Experience with Fear-Based Public Health Campaigns," *Health Affairs*, 34(5):844-851, May 2015. <http://content.healthaffairs.org/content/34/5/844.abstract>

8. Michael Siegel, "Thanks to Invalid NEJM Formaldehyde Study, Public Is Being Told that Cancer Risk from Vaping is 15 Times Higher than from Smoking," *The Rest of the Story: Tobacco News Analysis and Commentary*, Nov. 24, 2015. <http://tobaccoanalysis.blogspot.com/2015/11/thanks-to-invalid-nejm-formaldehyde.html>

9. Theodore L. Wagener, Ellen M. Meier, Alayna P. Tackett, James D. Matheny and Terry F. Pechacek, "A Proposed Collaboration against Big Tobacco: Common Ground between the Vaping and Public Health Community in the United States," *Nicotine & Tobacco Research*, ntv241, June 11, 2015. <http://ntr.oxfordjournals.org/content/early/2015/10/26/ntr.ntv241.abstract>

10. Public Health England, "E-cigarettes: an evidence update," GOV.UK, London, England, Aug. 28, 2015. <https://www.gov.uk/government/publications/e-cigarettes-an-evidence-update>

11. *Ibid.*

12. Carrie D Patnode, Jillian T Henderson, Jamie H Thompson, Caitlyn A Senger, Stephen P Fortmann and Evelyn P Whitlock, "Behavioral Counseling and Pharmacotherapy Interventions for Tobacco Cessation in Adults, Including Pregnant Women: A Review of Reviews for the U.S. Preventive Services Task Force," *Evidence Syntheses*, No. 134, September 2015. <http://www.ncbi.nlm.nih.gov/books/NBK321744/>

13. Press release, "E-cigarette use triples among middle and high school students in just one year," Centers for Disease Control & Prevention, April 16, 2015. <http://www.cdc.gov/media/releases/2015/p0416-e-cigarette-use.html>

14. Richard J. Bonnie, Kathleen Stratton and Leslie Y. Kwan, "Public Health Implications of Raising the Minimum Age of Legal Access to Tobacco Products," Institute of Medicine, National Academies Press, March 12, 2015. <http://iom.nationalacademies.org/Reports/2015/TobaccoMinimumAgeReport.aspx>

face in trying to quit. This is especially true for smoking.¹⁵ The earlier nicotine use is initiated, the more difficult it is to cease later in life. As a result, there's near-universal agreement on the need to prevent ENDS sales to people under age 18.

Another interpretation of the same data might suggest that people with higher vulnerabilities start experimenting with nicotine and other drugs at earlier ages. Although a high proportion of young people experiment with nicotine, only a modest fraction adopt regular use. Self-medication with nicotine could explain much of the observed continued smoking in young people.¹⁶ The significance of this observation can't be underestimated, as more than 50 percent of all cigarettes consumed in the United States are smoked by people with one or more mental-health diagnoses.¹⁷

THE IMPORTANCE OF FLAVORING

Detailed study of smoking behavior shows that smokers' typical patterns of cigarette use help to maintain a relatively constant level of nicotine throughout the day.¹⁸ The same would be true of vapers.

The mechanisms by which ENDS and cigarettes each deliver nicotine to the lungs differ fundamentally in both process and outcome. The delivery of nicotine varies by device type, but measured nicotine levels in the blood of vapers show that ENDS consistently deliver lower levels than cigarettes. Additional puffs are required to sustain constant levels of nicotine.¹⁹ It is now well-established that, puff-for-puff, cigarettes deliver more nicotine than most ENDS.²⁰ Vapers compensate for the reduced availability of nicotine by taking in a larger number of puffs.

Vapers generally report their motivations are harm reduction and smoking cessation, and that they are well-aware

that ENDS use is not completely safe.^{21,22,23} More than half of users who responded to a large international Internet survey – with a sample size of 19,000 – reported symptoms that they attributed to ENDS; dry mouth and throat were the most common.²⁴ Given these issues, and the relatively greater number of puffs that ENDS users must make to obtain a comparable amount of nicotine, it's perhaps unsurprising that blogs and other websites geared toward the vaper community are filled with thousands of narratives about the significance of flavor. Some examples culled from the Internet include:

'I will celebrate my two year tobacco free. Due to quality flavors. Yes I use a Baked Cinnamon Roll, Strawberry Milk, Blue Raspberry, Blueberry fruits, Butter-scotch candy flavors...'²⁵

'BTW I'm 46 years old and I love the candy flavors, the bakery flavors and all the other things supposedly only kids are suppose to like and do not care for any of the tobacco flavors at all. I really wish people in general against these types of flavors and who create such ridiculous lies and false assumptions about them using 'The Children' as an aid to fight vaping would stop insulting the intelligence of the people of the world about this topic. The fact is whether you a baby or over 100 years old and can still taste age has nothing to do with what tastes good to an individual but it is a majot part of what keeps people from going back to smoking.'²⁶

'My very first juice I used was menthol tobacco flavor to help ease the transition. I have since only used fruity flavored juice as the tobacco juice smell also makes me sick. The different flavors have helped. It's like having a ham and cheese sandwich to eat everyday for months... you get sick of eating ham and cheese. The

15. Sadik Khuder, Hari H Dayal and Anand B Mutgi, "Age at smoking onset and its effect on smoking cessation," *Addictive Behaviors*, 24(5):673-677, September/October 1999. <http://www.ncbi.nlm.nih.gov/pubmed/10574304>

16. Athina Markou, Thomas R. Kosten and George F. Koob, "Neurobiological similarities in depression and drug dependence: a self-medication hypothesis," *Neuropsychopharmacology*, 18(3):135-174, March 1998. <http://www.ncbi.nlm.nih.gov/pubmed/9471114>

17. Ahmed Jamal, Israel T. Agaku, Erin O'Connor, Brian A. King, John B. Kenemer and Linda Neff, "Current cigarette smoking among adults - United States, 2005-2013," *MMWR: Morbidity & Mortality Weekly Report*, 63(47):1108-1112, Nov. 28, 2014. <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6347a4.htm>

18. Neal L. Benowitz and Jack E. Henningfield, "Establishing a nicotine threshold for addiction. The implications for tobacco regulation," *The New England Journal of Medicine*, 331, July 14, 1994. http://www.ihra.net/files/2011/07/13/Benowitz_-_Nicotine_Regulation.pdf

19. Konstantinos E. Farsalinos, Alketa Spyrou, Kalliroi Tsimopoulou, Christos Stefanopoulos, Giorgio Romagna and Vassilis Voudris, "Nicotine absorption from electronic cigarette use: comparison between first and new-generation devices," *Scientific Reports*, 4, Article number: 4133, Feb. 26, 2014. <http://www.nature.com/articles/srep04133/>

20. Farsalinos, et al., February 2014.

21. Amy McQueen, Stephanie Tower and Walton Sumner, "Interviews with 'vapers': implications for future research with electronic cigarettes," *Nicotine & Tobacco Research*, 13(9):860-867, May 12, 2011. <http://ntr.oxfordjournals.org/content/ear-ly/2011/05/12/ntr.ntr088.full.pdf+html>

22. 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://onlinelibrary.wiley.com/doi/10.1111/j.1742-1241.2011.02751.x/full>

23. 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, June 2013. <http://onlinelibrary.wiley.com/doi/10.1111/add.12150/abstract>

24. Konstantinos E. Farsalinos, Giorgio Romagna, Dimitris Tsiapras, Stamatis Kyzopoulos 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*, 112, April 22, 2014. <http://www.mdpi.com/1660-4601/11/4/4356>

25. Capt Donna, "Vaping Saved My Life," The American Vaping Association, accessed Dec. 15, 2015. <http://vaping.info/news/2015/vaping-saved-life>

26. Anonymous, "20+ yr Smoker Now Ex Smoker since 2008 quit because of Vaping," The American Vaping Association, accessed Dec. 15, 2015. <http://vaping.info/news/2015/20-yr-smoker-now-ex-smoker-since-2008-quit-vaping>

different flavors are to help keep people from getting sick of the same flavor and giving up on it.²⁷

Large-scale surveys of vapers show many users vary the use of flavors throughout the day. Konstantinos E. Farsalinos, a research fellow at Greece's Onassis Cardiac Surgery Center, conducted an Internet-based study of 4,618 ENDS users and found that 63 percent vary their flavors on a daily basis.²⁸ The significance of flavoring was further confirmed in a study of posts on ENDS flavors made to the news and social networking site Reddit.²⁹

SAFETY OF ENDS FLAVORING

ENDS products contain varying amounts of nicotine, but the greatest source of variation is flavoring. When ENDS users visit a vape shop, they generally have a selection of several hundred to several thousand flavors from which to choose. For the most part, these are well-established chemical products that have already entered the marketplace as additives to food. Most already fall under the classification of "generally regarded as safe"³⁰ as defined by Food and Drug Administration guidelines:

If a substance is not generally recognized as safe³¹ by qualified experts for its Intended use in food and does not qualify for any of the other exemptions from the food additive definition,³² it is a food additive. Many substances intentionally added to beverages and other conventional foods are food additives. Food additives require premarket approval based on data demonstrating safety. Usually, these data are submitted to us in a food additive petition, although we may also approve a food additive on our own initiative without first receiving a petition.

But while many of the flavorings meet GRAS standard as food additives, there have been no petitions regarding their

27. Anonymous, "The hardest thing I've ever done," The American Vaping Association, accessed Dec. 15, 2015. <http://vaping.info/news/2015/hardest-thing-ive-ever-done>

28. Konstantinos E. Farsalinos, Giorgio Romagna, Dimitris Tsiapras, Stamatis Kyrzopoulos, Alketa Spyrou and Vassilis Voudris, "Impact of flavour variability on electronic cigarette use experience: an internet survey," *International Journal of Environmental Research and Public Health*, 10(12):7272-7282, Dec. 17, 2013. <http://www.mdpi.com/1660-4601/10/12/7272>

29. Lei Wang, Yongcheng Zhan, Qiudan Li, Daniel D. Zeng, Scott J. Leischow and Janet Okamoto, "An Examination of Electronic Cigarette Content on Social Media: Analysis of E-Cigarette Flavor Content on Reddit," *International Journal of Environmental Research and Public Health*, 12(11):14916-14935, Nov. 16, 2015. <http://www.mdpi.com/1660-4601/12/11/14916>

30. Jonathan E. Volk, Julia L. Marcus, Tony Phengrasamy, Derek Blechinger, Dong Phuong Nguyen, Stephen Follansbee and C. Bradley Hare, "No New HIV Infections with Increasing Use of HIV Preexposure Prophylaxis in a Clinical Practice Setting," *Clinical Infectious Diseases*, Sept. 1, 2015. <http://cid.oxfordjournals.org/content/early/2015/09/01/cid.civ778.abstract>

31. Volk, et al., 2015.

32. Barrington-Trimis, et al., 2014

use as inhalants. Furthermore, not enough is known about the changes that occur when these chemicals are heated in an ENDS. The FDA also does not have equivalent standards for GRAS for inhaled materials; oversight of inhaled substances has focused on the effective delivery of pharmacologic agents. On occasion, there has been discussion of the safety of propellants used to deliver aerosols, but the safety of inhaled flavorings has not been subject to extensive research. Concerns about the safety issues associated with flavorings have been debated in the medical literature, but little progress has been made to provide any measure of scientific certainty.³³

Some researchers, such as Jessica Barrington-Trimis of the University of Southern California Tobacco Center of Regulatory Science, have pointed to the number and variety of delivery devices and flavors as part of a call for more extensive regulation:

As of January 2014, there were 466 distinct brands of electronic nicotine products and at least 7,764 unique flavors, an increase of about 10.5 brands and 242 new flavor products per month from August 2013 to January 2014.³⁴

A recent article about a food flavoring used in some ENDS represents how information about possible harm associated with vapor becomes exaggerated in the media. In December 2015, the *Wall Street Journal* published an article headlined "Study Finds E-Cigarettes Contain Chemical Tied to 'Popcorn Lung,'" which bore the subhead:

Harvard researchers say 39 of the 51 flavors sold by leading brands contained diacetyl, which has been linked to severe respiratory diseases.³⁵

The original article, published in *Environmental Health Perspectives* and authored by a team led by Joseph G. Allen of Harvard University's T.H. Chan School of Public Health, argues that diacetyl is present in some ENDS flavors to create the taste of butter.³⁶ Allen goes on to argue that the chemical's presence represents a source of harm to all ENDS uses. High levels of acetyl was associated with the occurrence of

33. Konstantinos E. Farsalinos, Kurt A. Kistler, Gene Gillman and Vassilis Voudris, "Evaluation of electronic cigarette liquids and aerosol for the presence of selected inhalation toxins," *Nicotine & Tobacco Research*, 171, June 6, 2014. <http://ntr.oxfordjournals.org/content/early/2014/08/30/ntr.ntu176>

34. Barrington-Trimis, et al., 2014

35. Saabira Chaudhuri, "Study Finds E-Cigarettes Contain Chemical Tied to 'Popcorn Lung,'" *Wall Street Journal*, Dec. 9, 2015. <http://www.wsj.com/articles/study-finds-e-cigarettes-contain-chemical-tied-to-popcorn-lung-1449681247>

36. Joseph G. Allen, Skye S. Flanigan, Mallory LeBlanc, Jose Vallarino, Piers MacNaughton, James H. Stewart and David C. Christiani, "Flavoring Chemicals in E-Cigarettes: Diacetyl, 2, 3-Pentanedione, and Acetoin in a Sample of 51 Products, Including Fruit-, Candy-, and Cocktail-Flavored E-Cigarettes," *Environmental Health Perspectives*, 10.1289/ehp.1510185, Dec. 8, 2015. <http://ehp.niehs.nih.gov/15-10185/#tab2>

a serious lung disease among workers who produced butter-flavored popcorn. A small number of workers, exposed without environmental control or personal protective equipment, went on to require lung transplants. The association of acetyl and so-called “popcorn lung” is still under debate in the literature.³⁷ Writing about the paper on his blog, Michael Siegel has noted the quantities of acetyl measured in cigarette smoke is 750 times greater than that in e-cigarette vapor.³⁸

The complexities of evaluating all of these delivery systems and flavors is daunting, especially when one considers that the flavorings are heated and further interact with other compounds.³⁹ Research on the many compounds contained in ENDS products continues in many settings. However, assembling a sufficiently comprehensive data set may prove overwhelming.⁴⁰

ENDS AND ‘CHILDREN’S FLAVORS’

The availability of, e.g., “bubble gum” and “watermelon” flavors has been taken by some as a sign that ENDS producers seek to attract young people to experiment with nicotine, an extension of the thesis that tobacco companies seek to addict new generations of users. Concern about flavorings dates back to early tobacco-control efforts and specifically those efforts to stamp out targeted marketing to children. The Family Smoking Prevention and Tobacco Control Act banned, with the exception of menthol, cigarettes with characterizing flavors such as cherry, vanilla and grape. This ban did not apply to non-cigarette products, such as pipe tobacco or e-cigarettes.⁴¹

Research into the development of food preference suggests there are no flavorings that children inherently will prefer. The choices they make as consumers will reflect their previous experience, which is rooted in their individual

experience and the cultural norms of the society in which they develop.⁴²

However, there also is substantial research that shows U.S. children prefer certain flavors. The candy, confection, convenience store and related industries frequently survey which flavors are of greatest interest in their respective markets. A typical industry list of popular flavors includes: “fruit,” strawberry, cherry, watermelon, orange, blue raspberry, “sour,” grape, green apple and “multiple flavor.”

Flavoring frequently is taken into account to facilitate adherence to medical treatment, with a substantial literature on flavorings for over-the-counter medications for both children and adults. For example, Children’s Tylenol is available in “cherry blast” and grape flavors. It also should be noted that nicotine gum and lozenges generally are available in mint, cherry, cinnamon and other flavors.⁴³

Saul Shiffman of the University of Pittsburgh⁴⁴ examined interest in e-cigarettes among nonsmoking teens and adult smokers, and the effect of offering e-cigarettes under various flavor descriptors. The results did not support the conclusion that adding flavors to ENDS would attract nonsmoking teens. A review of the literature on flavor in a broad range of tobacco products by Shari P. Feirman of the Schroeder Institute for Tobacco Research and Policy Studies⁴⁵ concluded that flavored tobacco use is, in fact, associated with younger smokers. However, there is no data showing that young people are specifically drawn to what often are characterized as “children’s flavors.”

Discussion of the effect of flavoring on children also can be easily misrepresented. A team led by Bridget K. Ambrose of the Johns Hopkins Bloomberg School of Public Health studied 13,000 teenage users of tobacco products, who were asked about their first experiences.⁴⁶ The press interpreted

37. David Galbraith and David Weill, “Popcorn lung and bronchiolitis obliterans: a critical appraisal,” *International Archives of Occupational and Environmental Health*, 82(3):407-416, February 2009. <http://www.ncbi.nlm.nih.gov/pubmed/18548268>

38. Michael Siegel, “New Study Finds that Average Diacetyl Exposure from Vaping is 750 Times Lower than from Smoking,” *The Rest of the Story: Tobacco News Analysis and Commentary*, Dec. 10, 2015. <http://tobaccoanalysis.blogspot.com/2015/12/new-study-finds-that-average-diacetyl.html>

39. Sandra Costigan and Clive Meredith, “An approach to ingredient screening and toxicological risk assessment of flavours in e-liquids” *Regulatory Toxicology and Pharmacology*, May 27, 2015. <http://www.sciencedirect.com/science/article/pii/S0273230015001245>

40. Peyton A Tierney, Clarissa D Karpinski, Jessica E Brown, Wentai Luo and James F Pankow, “Flavour chemicals in electronic cigarette fluids,” *Tobacco Control*, 10.1136/tobaccocontrol-2014-052175, April 15, 2015. <http://tobaccocontrol.bmj.com/content/early/2015/03/27/tobaccocontrol-2014-052175>

41. Shari P. Feirman, Diana Lock, Joanna E. Cohen, David R. Holtgrave and Tianjing Li, “Flavored Tobacco Products in the United States: A Systematic Review Assessing Use and Attitudes,” *Nicotine & Tobacco Research*, 2015:ntv176, Aug. 7, 2015. <http://ntr.oxfordjournals.org/content/early/2015/08/26/ntr.ntv176.abstract>

42. Gary K Beauchamp and Julie A Mennella, “Early Flavor Learning and Its Impact on Later Feeding Behavior,” *Journal of Pediatric Gastroenterology and Nutrition*, 48:S25-S30, March 2009. <http://www.ncbi.nlm.nih.gov/pubmed/19214055>

43. Michael C. Fiore, et al., “Treating tobacco use and dependence: 2008 update,” U.S. Department of Health and Human Services, Public Health Service, May 2008. <http://bphc.hrsa.gov/buckets/treatingtobacco.pdf>

44. Saul Shiffman, Mark A. Sembower, Janine L. Pillitteri, Karen K. Gerlach and Joe G. Gitchell, “The impact of flavor descriptors on nonsmoking teens’ and adult smokers’ interest in electronic cigarettes,” *Nicotine & Tobacco Research*, 2015:ntu333, June 30, 2014. <http://ntr.oxfordjournals.org/content/early/2015/01/06/ntr.ntu333>

45. Feirman, et al., 2015.

46. Bridget K. Ambrose, Hannah R. Day, Brian Rostron, Kevin P. Conway, Nicolette Borek, Andrew Hyland and Andrea C. Villanti, “Flavored Tobacco Product Use Among US Youth Aged 12-17 Years, 2013-2014,” *JAMA : The Journal of the American Medical Association*, 314(17):1871-1873, Nov. 3, 2015.

the study as demonstrating that “first-time tobacco users” are “lured by flavors,”⁴⁷ with Ambrose herself reporting:

[T]he majority of youth ever-users reported that the first product they had used was flavored, including 88.7% of ever hookah users, 81.0% of ever e-cigarette users, 65.4% of ever users of any cigar type, and 50.1% of ever cigarette smokers.

However, those finding should not be taken to mean that flavor itself was responsible for youths’ decision to try tobacco products. It is as likely that most of the choices for nicotine use that are available to young people are flavored.

It may be important to consider the context in which young people may be tempted by flavor. A visit to a local newsstand shows an assortment of heavily marketed brands in familiar brightly colored packages. Compare this to the vape store experience, where a much larger assortment of products and containers are on display, few with recognizable names or packaging. Moreover, most ENDS merchants are reluctant to allow children in their shops at all and many communities have specific restrictions on sales to minors.⁴⁸

OTHER INGREDIENTS OF NICOTINE VAPOR

There are approximately 600 ingredients in cigarettes which, when burned, produce more than 7,000 chemicals. At least 69 of these chemicals are known to cause cancer and many are poisonous.

The chemical composition of nicotine vapor is less well-documented, given the large variation in sources and delivery systems. Common elements include water, nicotine, glycerin, propylene glycol and flavorings, all of which are heated to several hundred degrees. To the extent that some brands have been studied, the consensus is that the number of toxins and carcinogens is substantially smaller than in combusted cigarettes, as is the concern about their concentration.

In its fact sheet on ENDS, the CDC states:

ENDS generally emit lower levels of dangerous toxins than combusted cigarettes. However, in addition to nicotine, ENDS aerosols can contain heavy metals, ultrafine particulate and cancer-causing agents like acrolein. ENDS aerosols also contain propylene glycol or glycerin and flavorings. Some ENDS manufacturers claim that the use of propylene glycol, glycerin, and food flavorings is safe because they meet the FDA

47. Melissa Healy, “First-time tobacco users lured by flavorings, report says,” *Los Angeles Times*, Oct. 26, 2015. <http://www.latimes.com/science/sciencenow/la-sci-sn-first-time-tobacco-flavorings-20151026-story.html>

48. Preventing Tobacco Addiction Foundation, “State-by-State: List Of All Tobacco 21 Cities,” accessed Dec. 16, 2015. <http://tobacco21.org/state-by-state/>

definition of ‘Generally Recognized as Safe.’⁴⁹ However, GRAS status applies to additives for use in foods, NOT for inhalation. The health effects of inhaling these substances are currently unknown.

A comparison of the toxic elements contained in ENDS vapor with those contained in cigarette smoke shows the majority of harmful compounds are absent. Where they are present, toxins in ENDS are at far lower concentrations.

Notwithstanding these uncertainties, public-health authorities concede that ENDS are probably safer than cigarettes, despite those same authorities’ reluctance to recommend them. The first major challenge to earning acceptance from the public-health community is acquiring better understanding of the extraordinary proliferation of ENDS products and flavorings in an entirely unregulated marketplace.

ENDS products have been available for more a decade. There have not, to date, been reports of clinical syndromes associated with ENDS use. News reports have focused on fire dangers associated with some types of devices and the Transportation Safety Administration has required that travelers stow ENDS devices on their person or in carry-on baggage – not in checked luggage that would be stored in cargo holds.⁵⁰ Also of concern have been poisoning risks associated with children or household pets who accidentally ingest nicotine e-liquids.⁵¹

The absence to date of evidence of adverse health outcomes does not prove the long-term effects of ENDS device use is minimal. But consumer behavior has been a positive sign. A recent Reuters poll concluded that 10 percent of the adult population uses ENDS alone or together with cigarettes.⁵² Two recent studies of practicing physicians find that half report their smoking patients ask about e-cigarettes and one out of three of these physicians recommend their use for harm reduction or cessation.^{53,54}

49. Volk, et al., 2015.

50. Harriet Baskas, “DOT bans e-cigarettes in checked luggage,” *USA Today*, Oct. 27, 2015. <http://www.usatoday.com/story/travel/flights/todayinthesky/2015/10/27/electronic-cigarette-checked-luggage-ban/74670944/>

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CONCLUSION

Notwithstanding broader concerns about ENDS, their use as a strategy for smoking cessation and harm reduction is now very common. In order to reap the benefits of harm reduction, public-health authorities in the United States might consider an approach more in line with that taken in the United Kingdom. This would require a greater focus on the harm-reduction possibilities of smokers switching to ENDS, rather than excessive scrutiny of the residual risks inherent in ENDS.

In this larger context, concerns about the use of flavoring as a tool to recruit children are overblown. There are no “kid’s flavors,” per se, nor is there any evidence that children are drawn to tobacco products specifically because of flavor. Restricting the sale of nicotine products to people over the age of 18 should address most concerns regarding the effect of nicotine on younger brains. ...

Although there remains insufficient information about the full range of flavoring additives, until demonstrated to the contrary, most flavorings used in ENDS should be considered safe relative to the risk of smoking combusted tobacco.

A great deal of additional research is required to resolve many of the possible safety questions regarding ENDS. But surveys of smokers who already are using the products to cease an unquestionably deadly habit demonstrate that the public has already made up its mind on the matter.

ABOUT THE AUTHORS

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