

CLINICAL COMMENTARY

Current Smoking Cessation Methods and the Potential Role of Electronic-Cigarettes

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Since 1965, there has been a remarkable decrease in the number of tobacco cigarette smokers in the United States. The number has fallen from over 40% of American adults in 1965 to below 20% in 2015.¹ Despite this, an estimated 480,000 smoking-related deaths occur in the United States each year.² On average, male smokers are dying 12 years earlier, while female smokers are dying 11 years earlier than non-smokers, which amounts to over 5 million years of life lost annually.³ It is estimated that \$170 billion is spent each year on smoking-related illnesses.⁴ Finding an effective means of curtailing addiction to tobacco is a vital health policy issue. The topic of smoking cessation becomes even more urgent when we consider that individuals who successfully quit smoking before the age of 35 can have a similar life expectancy as non-smokers.⁵ Similarly, those who quit by age 50 can cut their chances of dying in the next 15 years by half.⁶ In summary, smoking cessation at any age provides higher life expectancy, which provides a strong rationale for all physicians to ask every patient about tobacco cigarette smoking, including exposure to secondhand smoke.

The current methods to help a patient stop smoking can be categorized into two approaches: 1) behavioral and 2) pharmacological therapy. Each method has been shown to be effective alone, but they work best when combined. Behavioral interventions may include physician office visits and phone calls, one-on-one counseling with a trained professional, group counseling and printed or on-line self-help material (i.e. booklets and quit lines). Proven effective interventions include identification of a support system that can help individuals anticipate and avoid triggers for relapse. The UCLA-Health website (<https://www.uclahealth.org/Pages/patients/smoke-free/smoking-cessation-treatment.aspx#programs>) has an entire section dedicated to smoking cessation interventions for faculty, staff, and patients. Under the smoking cessation tab on uclahealth.org, there are several links to support groups, help lines, cessation programs, and a list of physicians who specialized in addiction.

The main pharmacological methods include the first line drugs bupropion and varenicline along with several forms of nicotine replacement therapies (NRT). All pharmacological therapies are contraindicated in pregnancies. All seem to be similarly effective, and the choice of which to start should be made in consultation with the patient to consider side effects and additional therapeutic effects. For example, bupropion is currently one of the best drugs available and is successful in approximately 1 in 5 people, as they remain abstinent through the first year of therapy.⁷ Bupropion is contraindicated in patients with seizure disorders but may be especially effective

in depressed tobacco cigarette smokers. It is also important to note bupropion should be avoided in patients taking MAO inhibitors. Patients often begin with 150mg/day of bupropion and depending on their tolerance can increase to 300mg/day after the third day of therapy. Bupropion, like most smoking cessation medications and NRT, is covered by many insurance plans including Medi-Cal.

Varenicline is another first-line drug that has been successful in promoting long-term smoking cessation. A review from 2013 reported that varenicline was more effective than any single form of NRT or bupropion.⁸ However, a combination of multiple NRT was as effective as varenicline in successfully leading to long-term smoking cessation. Although varenicline compared to bupropion was shown to have a higher quit rate initially, long-term quit rates were similar.⁷ The FDA recently required an addition to the boxed warning on varenicline indicating it can cause “changes in behavior, hostility, agitation, depressed mood, and suicidal thoughts or actions”.⁹

NRTs can be delivered through various methods including gum, patch, and nasal spray. No form of NRT is thought to work significantly better than any other, therefore the patient should choose the NRT that fits their lifestyle and budget best.¹⁰ Some prefer patches because they are thought to be the easiest to use; however, others prefer the gum or inhalers because they tend to be better at relieving acute nicotine cravings and may have the added benefit of providing some oral satisfaction. Regardless of what form is used, NRT is believed to increase likelihood of long-term cessation over placebo by 50-70%.¹⁰ It is also thought that a combination of NRT is superior to using only one form, although this was recently challenged in a study that showed there was no significant difference in efficacy among nicotine patch alone, varenicline, and combined NRT treatment.^{7,11} Combining the two forms of pharmacological therapies (NRT along with one of the drugs) has been thought to be a more successful approach. A Cochrane review showed combining NRT and bupropion had a higher quit rate when compared to bupropion alone.¹⁰

Although all of these pharmacological therapies are similarly effective, the long-term success rate of any of them is low. According to the CDC, nearly 70% of smokers are interested in quitting and just over half have attempted to quit in the past year. Unfortunately, only 6.2% were able to achieve this goal.⁵ Whether the problem is compliance, accessibility, cost, or simply ineffective cessation techniques, the bottom line is that even people who are determined to quit are frequently unsuccessful with the current cessation methods available. A

relatively new nicotine delivery device has become available, the electronic (e)-cigarette, which may provide one more tool in the pharmacological armamentarium to help smokers addicted to lethal tobacco cigarettes quit. Although not marketed or proven to help smokers quit, electronic cigarettes have been used by current tobacco cigarette smokers for this purpose.¹²

There is limited but promising data regarding e-cigarettes and smoking cessation. In a study of tobacco cigarette smokers who did not intend to quit smoking, e-cigarettes led to an 8.7% quit rate at 1 year.¹³ In another randomized study of e-cigarettes with nicotine, e-cigarettes without nicotine, and the NRT patch, all three groups had similar long-term quit rates.¹⁴ A systematic review from 2015 concluded that 18% of people using e-cigarettes had successfully quit smoking.¹² A Cochrane report from 2014 concluded that e-cigarettes were effective for long-term smoking cessation when compared to placebo e-cigarettes and that there was no evidence of health risks associated with short term e-cigarette use.¹⁵

Although e-cigarettes might be viewed as just another NRT, they are actually providing an element that goes beyond nicotine replacement alone. E-cigarettes satisfy more than just the chemical addiction to tobacco cigarettes through the mimicry of the bio-behavioral component. Anecdotal evidence shows people often relapse in their effort to quit smoking because they also miss the non-nicotine components of smoking (i.e., oral sensation, blowing smoke out of their mouths, and the socializing that is associated with smoking). Much of our current cessation techniques focus entirely on the addictive properties of nicotine but fall short in addressing the bio-behavioral aspect that is associated with most addictions. E-cigarettes successfully incorporate these bio-behavioral components of addiction while also satisfying the pharmacological needs.

Nonetheless, significant controversy surrounds the use of e-cigarettes as a smoking cessation strategy since they are not proven to be effective nor are they approved by the FDA as a smoking cessation tool. Furthermore, the long-term effects of e-cigarettes remain unknown. Finally, NRTs are only recommended for relatively short periods of time, although many are used for years by former tobacco cigarette smokers and without apparent harm.¹⁶ The concern that e-cigarette use will simply substitute one addiction for another is valid but contradicted by one study that showed 73.1% of participants who had successfully used e-cigarettes to quit smoking had also stopped using e-cigarettes after one year.¹³ On the other hand, it has been argued that smokers using e-cigarettes are less likely to quit smoking than smokers who do not use e-cigarettes.¹⁷ This claim has recently been challenged by a time series analysis of the prevalence of e-cigarette use among smokers, which demonstrated a direct association between e-cigarette use and successful smoking cessation.¹⁸

In summary, tobacco cigarettes lead to approximately half a million premature deaths in the United States each year, and with the current available smoking-cessation methods (behavioral therapy, bupropion, varenicline, and NRT) only 6.2% of smokers are successful in their quit attempts.⁵ The lack of reliable data regarding e-cigarettes as a smoking cessation

tool has made it nearly impossible for physicians to have a consensus.¹⁹ Nonetheless, it must be acknowledged that even if success rates are not better than other NRT, the broad appeal and popularity of e-cigarettes may significantly reduce the number of people addicted to lethal tobacco cigarettes. E-cigarettes should be considered as a potential resource for patients unable to quit tobacco cigarette smoking despite using traditional smoking-cessation strategies.

REFERENCES

1. *Centers for Disease Control & Prevention (CDC)*. N.p., Mar. 2016. Web. 19 July 2016. <http://www.cdc.gov/tobacco/data_statistics/tables/trends/cig_smoking/>.http://w
2. **US Department of Health and Human Services**. *The Health Consequences of Smoking-50 Years of Progress. A Report from the Surgeon General*. Atlanta, GA; USA: Department of Health and Human Services. Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, 2014.
3. **Jha P, Ramasundarathetige C, Landsman V, Rostron B, Thun M, Anderson RN, McAfee T, Peto R**. 21st-century hazards of smoking and benefits of cessation in the United States. *N Engl J Med*. 2013 Jan 24;368(4):341-50. doi:10.1056/NEJMSa1211128. PubMed PMID: 23343063.
4. **Xu X, Bishop EE, Kennedy SM, Simpson SA, Pechacek TF**. Annual healthcare spending attributable to cigarette smoking: an update. *Am J Prev Med*. 2015 Mar;48(3):326-33. doi: 10.1016/j.amepre.2014.10.012. PubMed PMID: 25498551; PubMed Central PMCID: PMC4603661.
5. **Centers for Disease Control and Prevention (CDC)**. Quitting smoking among adults--United States, 2001-2010. *MMWR Morb Mortal Wkly Rep*. 2011 Nov 11;60(44):1513-9. PubMed PMID: 22071589.
6. U.S. Department of Health and Human Services: The Health Benefits of Smoking Cessation. A Report of the Surgeon General. Rockville, Md: 1990. DHHS Publ No. (CDC) 90-8416.
7. **Wilkes S**. The use of bupropion SR in cigarette smoking cessation. *Int J Chron Obstruct Pulmon Dis*. 2008;3(1):45-53. Review. PubMed PMID: 18488428; PubMed Central PMCID: PMC2528204.
8. **Cahill K, Stevens S, Perera R, Lancaster T**. Pharmacological interventions for smoking cessation: an overview and network meta-analysis. *Cochrane Database Syst Rev*. 2013 May 31;(5):CD009329. doi: 10.1002/14651858.CD009329.pub2. Review. PubMed PMID: 23728690.
9. "FDA Drug Safety Communication: Safety review update of Chantix (varenicline) and risk of neuropsychiatric adverse events." *U.S. Food and Drug Administration (FDA)*. N.p., 2 Mar. 2016. Web. 19 July 2016. <<http://www.fda.gov/Drugs/DrugSafety/ucm276737.htm>>.
10. **Stead LF, Perera R, Bullen C, Mant D, Hartmann-Boyce J, Cahill K, Lancaster T**. Nicotine replacement therapy for smoking cessation. *Cochrane Database Syst Rev*. 2012 Nov 14;11:CD000146. doi:

- 10.1002/14651858.CD000146.pub4. Review. PubMed PMID: 23152200.
11. **Baker TB, Piper ME, Stein JH, Smith SS, Bolt DM, Fraser DL, Fiore MC.** Effects of Nicotine Patch vs Varenicline vs Combination Nicotine Replacement Therapy on Smoking Cessation at 26 Weeks: A Randomized Clinical Trial. *JAMA*. 2016 Jan 26;315(4):371-9. doi: 10.1001/jama.2015.19284. PubMed PMID: 26813210; PubMed Central PMCID: PMC4824537.
 12. **Rahman MA, Hann N, Wilson A, Mnatzaganian G, Worrall-Carter L.** E-cigarettes and smoking cessation: evidence from a systematic review and meta-analysis. *PLoS One*. 2015 Mar 30;10(3):e0122544. doi: 10.1371/journal.pone.0122544. Review. PubMed PMID: 25822251; PubMed Central PMCID: PMC4378973.
 13. **Caponnetto P, Campagna D, Cibella F, Morjaria JB, Caruso M, Russo C, Polosa R.** Efficiency and Safety of an eElectronic cigAreTte (ECLAT) as tobacco cigarettes substitute: a prospective 12-month randomized control design study. *PLoS One*. 2013 Jun 24;8(6):e66317. doi: 10.1371/journal.pone.0066317. Erratum in: *PLoS One*. 2014;9(1). doi:10.1371/annotation/e12c22d3-a42b-455d-9100-6c7ee45d58d0. PubMed PMID: 23826093; PubMed Central PMCID: PMC3691171.
 14. **Bullen C, Howe C, Laugesen M, McRobbie H, Parag V, Williman J, Walker N.** Electronic cigarettes for smoking cessation: a randomised controlled trial. *Lancet*. 2013 Nov 16;382(9905):1629-37. doi: 10.1016/S0140-6736(13)61842-5. PubMed PMID: 24029165.
 15. **McRobbie H, Bullen C, Hartmann-Boyce J, Hajek P.** Electronic cigarettes for smoking cessation and reduction. *Cochrane Database Syst Rev*. 2014;(12):CD010216. doi: 10.1002/14651858.CD010216.pub2. Review. PubMed PMID: 25515689.
 16. **Schnoll RA, Goelz PM, Veluz-Wilkins A, Blazekovic S, Powers L, Leone FT, Gariti P, Wileyto EP, Hitsman B.** Long-term nicotine replacement therapy: a randomized clinical trial. *JAMA Intern Med*. 2015 Apr;175(4):504-11. doi:10.1001/jamainternmed.2014.8313. PubMed PMID: 25705872; PubMed Central PMCID: PMC4410859.
 17. **Kalkhoran S, Glantz SA.** E-cigarettes and smoking cessation in real-world and clinical settings: a systematic review and meta-analysis. *Lancet Respir Med*. 2016 Feb;4(2):116-28. doi: 10.1016/S2213-2600(15)00521-4. PubMed PMID: 26776875; PubMed Central PMCID: PMC4752870.
 18. **Beard E, West R, Michie S, Brown J.** Association between electronic cigarette use and changes in quit attempts, success of quit attempts, use of smoking cessation pharmacotherapy, and use of stop smoking services in England: time series analysis of population trends. *BMJ*. 2016 Sep 13;354:i4645. doi:10.1136/bmj.i4645. PubMed PMID: 27624188.
 19. **Yeh JS, Bullen C, Glantz SA.** CLINICAL DECISIONS. E-Cigarettes and Smoking Cessation. *N Engl J Med*. 2016 Jun 2;374(22):2172-4. doi: 10.1056/NEJMcld1602420. PubMed PMID: 27248625.