E-cigarettes and vapes:
The popularity of electronic cigarettes (E-cigs) and “vapes” has grown dramatically, spawning a new industry of electronic nicotine delivery systems (ENDS). With the increasing use of E-cigs not only for smoking cessation, but also as a primary nicotine source, it is important for mental health professionals to be prepared to discuss use of these devices with patients. In this article, we will describe:

- the composition of E-cigs and their current use
- evidence for their use for smoking cessation
- adverse health effects
- recommendations of major regulatory agencies.

Finally, we will provide recommendations for E-cig use in clinical populations.

What is an electronic nicotine delivery system?
ENDS produce an aerosol with or without nicotine that is inhaled and is thought to mimic the use of combustible cigarettes. ENDS evolved from basic E-cigs into a less “cigarette-like” and more customizable product (Figure 1, page 32). ENDS include a range of designs and go by various names, including “personal vaporizers,” “e-cigars,” and “e-hookahs” (in this article, we will use the term “ENDS” to refer to these devices).

The general design of ENDS is a plastic tubing system that contains a mouthpiece, battery, electronic heating element (“vaporizer”), and a cartridge with liquid solvent with or without nicotine or flavoring (Figure 2, page 33). One draw on the mouthpiece or press of a button activates the...
device, heats the solution, and delivers a vapor in a similar manner to taking a puff of a cigarette. Although studies have shown that ENDS result in significant increases in plasma nicotine concentrations in 5 minutes, the plasma nicotine levels obtained with the first-generation “cigarette-like” ENDS are much lower than those caused by inhaling tobacco smoke. Over time nicotine delivery capability has improved as ENDS have evolved such that the rate of nicotine delivery and peak concentration obtained with newer models more closely mirror tobacco cigarettes.

Whether the rapid delivery of larger amounts of nicotine helps or hinders one’s efforts to break nicotine addiction remains to be determined because of the reinforcing properties of the drug.

The liquid in the E-cig cartridge typically contains not only nicotine but a number of chemical compounds with potentially deleterious or unknown health risks. The 3 main ingredients include:

- a solvent of glycerin and/or propylene glycol
- nicotine in various concentrations
- flavorings.

The glycerin or propylene glycol forms the basis for the aerosol. Nicotine concentrations vary from 0 (denicotinized) to 35 mcg per puff. A study reported 7,700 unique flavors available for vaping liquid. The liquid also contains impurities, such as anabasine, which has effects on the α-7 nicotinic acetylcholine receptor and its principal use is as an insecticide and β-nicotyrine, which inhibits cytochrome P450 2A.

**Epidemiology and end-user perspectives**

In 2014, 12.4% of U.S. adults classified themselves as “ever users” of ENDS (used at least once) and 3.7% of adults classified themselves as current users, according to the National Health Interview Study. Importantly, among E-cig users who had not used combustible cigarettes, young adults (age 18 to 24) were more likely to have tried ENDS than older adults. ENDS are becoming more popular across the globe. A study in the European Union found that ever users of ENDS most commonly were current cigarette smokers (31%) followed by former (10.8%) and never smokers (2.3%).

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ENDS use is relevant for mental health professionals because of the high rate of comorbid tobacco use disorder in individuals with psychiatric conditions. For example, 2 U.S. population surveys revealed those with mental health conditions were 1.5 to 2 times more likely to have tried ENDS and 2 to 3 times more likely to be current users. Those with psychiatric illness reported similar reasons for ENDS use as other individuals, including “just because,” use as a smoking cessation aid, ease of use, and perceived safety vs combustible cigarettes.

A recent review that included 9 studies focusing on ENDS use in those with mental illness reported mixed findings on the utility of these devices to reduce or stop use of combustible cigarettes. Additionally, it is important to monitor the use of cigarettes and ENDS in patients with psychiatric illness because the byproducts of tobacco smoke can affect the metabolism of some psychotropic medications. Although reduced use of combustible cigarettes could lead to lower dosing of some psychotropics, an unreported decrease in combustible cigarette use could lead to supratherapeutic drug levels. There are no data on the effect of ENDS on the metabolism of psychotropics.

ENDS are increasingly popular among adolescents. In 2015, there were an estimated 4.6 million current tobacco users among middle/high school youths in the United States and 3 million current ENDS users, according to the National Youth Tobacco Surveys. The shift from combustible cigarettes to ENDS is notable, with an increase in the percentage of current E-cig users and a decrease in the percentage of exclusive combustible cigarette users. In addition, there has been no change in the prevalence of lifetime tobacco users. This is a global issue, as reports of ever use of ENDS by adolescents range from 6.5% to 31% in the United States, 14.6% in Canada, and 4.7% to 38.5% in Europe. Based on these trends, the U.S. Surgeon General released a statement warning against the use of ENDS in youth because of the lack of safety data and strong association with use of tobacco products.

There are a number of possible reasons for the increasing popularity of ENDS, including the product’s novelty, lack of

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**Figure 2**

**Parts of an electronic cigarette**

- **Mouthpiece**
- **Heating element/atomizer**
- **Cartridge** (tank) holds the liquid “juice”
- **Microprocessor**
- **Battery**
- **Many devices have a switch to activate the heating element**
- **Some devices have a light-emitting diode on the end to simulate the glow of a burning cigarette**

*Source: United States Fire Administration*
regulations regarding their sale, availability of flavorings, and the perception that ENDS are safe alternatives to cigarettes. E-cig–using youths have described ENDS as “not at all harmful” and “not at all addictive” and believe that ENDS with flavoring are less harmful than those without.\textsuperscript{15} Although studies in adults show some users reporting that ENDS are less satisfying, they are seen as useful in decreasing craving and a safer alternative to cigarettes.\textsuperscript{16,17}

Are ENDS effective for smoking cessation? The evidence for ENDS as aids to smoking cessation remains murky (Table 1\textsuperscript{16-22}). There is a paucity of randomized controlled clinical trials (RCTs) investigating ENDS for smoking cessation or reduction, and it is difficult to quantify the amount of nicotine used in ENDS because of the variety of delivery systems and cartridges. In a recent Cochrane review, those using ENDS to quit smoking were more likely to be abstinent from combustible cigarettes at 6 months vs those using nicotine-free ENDS (relative risk = 2.29; 95% CI, 1.05 to 4.96), but there was no significant difference in quit rates compared with nicotine patches.\textsuperscript{23} However, the confidence in this finding was rated as low because of the limited number of RCTs. Of note, the authors found 15 ongoing RCTs at the time of publication that might be eligible for later evaluation.

Non-RCTs reveal mixed data. Positive results include 1 study with an odds ratio of 6.07 to quit for intensive ENDS users vs non-users,\textsuperscript{24} and another with dual users of combustible and electronic cigarettes having a 46% quit rate at 1 year.\textsuperscript{25} Additionally, in a pilot study providing ENDS to 14 patients with schizophrenia who had no previous desire to quit smoking, authors noted a reduction in the number of cigarettes smoked per day in users of E-cigs with nicotine\textsuperscript{26} Studies with neutral or negative results include those showing ENDS users to be current combustible tobacco smokers, and use of ENDS not predicting smoking cessation.\textsuperscript{4,27}

Continued on page 36.
Data also are mixed regarding the use of ENDS as a harm reduction strategy. One study found that ENDS decreased cigarette consumption, but did not increase the likelihood of quitting,28 while another reported that daily use of ENDS increased the odds of reducing smoking by as much as 2.5 times compared with non-use of such aids.29 In a 24-month prospective cohort study following tobacco users, there was no difference in the number of cigarettes smoked per day in those who started the trial as users of combustible cigarettes alone vs combustible cigarettes plus ENDS users.30 Interestingly, those who started the study as combustible cigarette users and switched to ENDS and those who had continued dual use throughout the 24 months smoked fewer combustible cigarettes per day than those who never tried ENDS or quit during the study period.

**Health effects**

To better understand the adverse health effects of ENDS, one must consider potential short- and long-term consequences (Table 2). In the short-term, ENDS have been found to increase markers of inflammation and oxidative stress acutely as evidenced by in vivo laboratory studies.31,32 ENDS also have been linked to upper respiratory irritation, in part, because of the transformation of glycerin in the nicotine cartridge to acrolein upon combustion.33 Even 5 minutes of ad lib E-cig use has been found to significantly increase airflow resistance during pulmonary function tests—changes that have been shown to precede more persistent alterations in peak expiratory flow, such as those seen in chronic obstructive pulmonary disease. The more common patient-reported side effects include:

- daytime cough (27%)
- phlegm production (25%)
- headache (21%)
- dry mouth/throat (20%)
- vertigo, headache, or nausea (9%).35,36

A RCT investigating efficacy of E-cigs vs nicotine patches vs denicotinized E-cigs found no difference among the groups in the number of reported adverse events.18 Interestingly, another RCT found a decrease in adverse events, such as dry cough, mouth irritation, throat irritation, shortness of breath, and headache, compared with baseline in combustible cigarette smokers who used regular or denicotinized E-cigs.19

Although no studies have directly investigated long-term health consequences of ENDS because of their relative novelty, one can extrapolate potential harmful long-term effects based on knowledge of the products’ chemical constituents. For example, propylene glycol can degrade into propylene oxide, a class 2B carcinogen.37 Other potential carcinogens in the aerosol include formaldehyde and acetaldehyde. On a broader scale, many of the particulates have been shown to cause systemic inflammation, which is thought to increase cardiovascular and respiratory disease and death.38 Flavorings in ENDS include a variety of components including, but not limited to, aldehydes, which are irritants, and other additives that have been associated with respiratory disease.39

**Second-hand exposure.** There are no long-term studies of second-hand vapor exposure, but similar to long-term health on primary users, one can glean some observations from the literature. It is promising that compared with cigarettes, ENDS lack sidestream smoke and the vapor has not been found to contain carbon monoxide.40 Some research has demonstrated that the size and spray of fine particles in the aerosol is as large or larger than combustible cigarettes.41 Formaldehyde, acetaldehyde, isoprene, and acetic acid have been found in ENDS vapor.42 Interestingly, a simulated café study found elevated nicotine, glycerin, hydrocarbon, and other materials classified as carcinogens in the air.42

Although it is popularly thought that ENDS are less toxic than tobacco cigarettes, there is not enough evidence to estimate precisely as to how much less toxic or the consequences of use. ENDS are increasingly popular and are being used by never smokers who should be educated on the potential harm that ENDS pose.
Recommendations from agencies and medical organizations

The World Health Organization (WHO) recommended prohibiting the use of ENDS in indoor spaces to minimize potential health risks to users and non-users. The WHO also aims to prevent dissemination of unproven health claims, including claims that ENDS are effective—or not—or that the devices are innocuous. In the United States, the FDA has stated that ENDS are not recommended for safe quitting (2009). In August 2016, the FDA introduced regulations banning the sale of ENDS to individuals age <18 and required manufacturers to submit documents detailing all ingredients for review and possible approval.

The American Lung Association has stated its concerns about the use of ENDS but has not made any direct recommendations. The American Heart Association reports a potential negative public health impact and provides clinical guideline recommendations. Prominent psychiatric organizations such as the American Psychiatric Association, American Academy of Addiction Psychiatry (AAAP), the Substance Abuse and Mental Health Services Administration (SAMHSA), and the National Institute of Drug Abuse do not have official statements supporting or rejecting the use of ENDS. However, they do note the potential harm and lack of substantial evidence for efficacy of ENDS as a smoking cessation tool, and the AAAP and SAMHSA state that they will work with regulatory agencies to reduce the use of toxic products with addictive potential including ENDS.

Clinical recommendations

We do not recommend ENDS as a first-line treatment for smoking cessation because there is no evidence they are superior to the FDA-approved nicotine replacement therapies (NRTs), the paucity of research into the potential short- and long-term health risks of ENDS, and the fact that these products are not regulated for use as smoking cessation aids. It is, however, advisable to discuss ENDS use with patients by:

- asking if they are using the products
- assessing whether the user also is a smoker
- advising the patient to quit.

It also is important to assess the patient’s knowledge and attitudes regarding ENDS use and provide education about the products. Some patients firmly believe that ENDS are the lesser of 2 evils, and they are decreasing the harms of smoking by using these devices. While the debate over a potential harm reduction strategy unfolds, we think that because of the state of the evidence it is prudent to adopt a more precautionary stance and recommend that patients work toward abstinence from nicotine in any form.

For dual tobacco/ENDS users and for patients using ENDS who want to quit smoking, we recommend treatment with

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### Table 2

<table>
<thead>
<tr>
<th>Potential risks and benefits of ENDS use</th>
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<tbody>
<tr>
<td><strong>Benefits</strong></td>
</tr>
<tr>
<td>Reduction in combustible cigarette use could lead to reduction in dosing of some psychotropics</td>
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<tr>
<td>Less exposure to harmful/potentially harmful tobacco smoke constituents</td>
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<tr>
<td>Some evidence for higher combustible cigarette quit rate</td>
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<tr>
<td>Some evidence for reduction in the number of combustible cigarettes per day</td>
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<tr>
<td>Reduction in adverse events (cough, shortness of breath, headache)</td>
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<tr>
<td>Less expensive than combustible cigarettes</td>
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<tr>
<td><strong>Risks</strong></td>
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<tr>
<td>Unreported decrease in combustible cigarette use could lead to supratherapeutic levels of some psychotropics</td>
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<tr>
<td>Evidence for reduced pulmonary function with short-term use</td>
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<tr>
<td>Unknown effects of second-hand vapor</td>
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<tr>
<td>Exposure to potential carcinogens</td>
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<td>Use by never smokers</td>
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<tr>
<td>Unclear “addictiveness” potential</td>
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<tr>
<td>Unregulated dual use of ENDS and combustible cigarettes</td>
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<td>False perceptions of complete safety by some users</td>
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ENDS: electronic nicotine delivery systems
E-cigarettes

Current Psychiatry
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Box

Efficacy of smoking cessation aids: Where do electronic nicotine delivery systems fit in?

Meta-analyses have shown evidence for superiority of varenicline and combination nicotine replacement therapy (NRT) vs bupropion and monotherapy NRT. Recent studies suggest similar efficacy between E-cigs and nicotine patches, but the quality of this evidence is low. One can speculate that a combination of E-cigs and a nicotine patch might provide an advantage over either alone, as seen in trials of 2 NRTs. The patch is a long-acting nicotine source with the E-cig providing nicotine for breakthrough cravings as well as satisfaction of the behavioral component of smoking.

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\begin{align*}
\text{Varenicline} & > \text{Bupropion} \\
2 \text{NRTs} & > 1 \text{NRT} > \text{placebo} \\
\text{E-cig} + \text{NRT?} & > \text{E-cig alone?}
\end{align*}
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an approved pharmacotherapy (ie, NRTs, bupropion, and varenicline) combined with counseling. A 2013 Cochrane Review found that all pharmacotherapy options are more effective than placebo, and combination NRT and varenicline are superior to single NRT or bupropion (Box). References


### Related Resources

- The Tobacco Atlas. E-cigarettes should be regulated in such a way as to reduce smoking of combusted tobacco products to the greatest extent possible. www.tobaccoatlas.org/topic/e-cigarettes.

### Drug Brand Names

- Bupropion - Wellbutrin, Zyban
- Varenicline - Chantix

### Bottom Line

Many individuals use electronic nicotine delivery systems (ENDS) as a smoking cessation aid or because they think the devices are safer than tobacco cigarettes. However, because of the paucity of evidence regarding their efficacy as smoking cessation aids and concerns raised about their short- and long-term health consequences, we do not recommend using ENDS in psychiatric patients who smoke. The role these products may play in harm reduction remains to be seen.