

# Cessation Treatment and E-Cigarettes

*A Report on Current Literature  
and Quitline Practices*



November 2014

## OVERVIEW

State quitlines receive about 1.3 million calls and 175,000 referrals for help in quitting tobacco use each year. Over the past two years, a growing number of smokers who contact state quitlines have had questions about electronic cigarettes and other electronic nicotine delivery systems (which will be referred to as “e-cigarettes” in this report). Quitlines have developed approaches for responding to questions about e-cigarettes and for treating smokers who are currently using e-cigarettes or who express an interest in using e-cigarettes as part of a quit attempt. The nascent research literature on e-cigarettes has provided some guidance to quitlines but few definitive answers. In the absence of definitive research findings and lacking clinical guidelines, the North American Quitline Consortium (NAQC) has synthesized the relevant literature and current quitline practices regarding e-cigarettes to share with the cessation and larger tobacco control communities. It is our hope that this report will help inform the field and lead to dialogue on two main questions:

- *Given the current level of knowledge about e-cigarettes, how should quitlines respond to smokers’ questions about them?*
- *What are the most important actions that quitlines can take to advance their practices related to e-cigarette use among callers seeking cessation treatment?*

While this report focuses on the impact of e-cigarettes on cessation treatment offered by state quitlines, NAQC recognizes that equally important questions exist regarding the impact of e-cigarettes on youth initiation and on maintaining a non-smoking norm across the country. The quitline community is committed to working with our colleagues in public health and health policy to ensure that the dynamic research and policy agendas related to e-cigarettes take into consideration issues of importance to cessation as well as tobacco prevention and eliminating exposure to secondhand smoke.

## QUESTIONS OF INTEREST AND SOURCES OF INFORMATION

The purpose of this report is to share the current experiences of quitlines in addressing questions about e-cigarettes in the context of a quit attempt as well as to share the current state of scientific knowledge on e-cigarettes. In gathering information, we sought responses to the questions below:

- *What questions are quitlines hearing from smokers about e-cigarettes?*
- *Do quitlines have policies and/or counseling protocols for e-cigarettes?*
- *What are quitlines telling smokers who ask about whether they should use e-cigarettes?*
- *Are quitlines asking screening questions about e-cigarettes?*
- *What are quitlines telling smokers about the relative harm of e-cigarettes as compared to combustible cigarettes?*
- *What messages do quitlines share with callers about dual use of e-cigarettes and combustible cigarettes?*
- *What messages are quitlines providing to callers about the importance of quitting e-cigarettes?*
- *What approaches are quitlines using with callers who ask for help quitting e-cigarettes?*
- *How do quitlines categorize callers who report quitting combustible cigarette use but who continue to use e-cigarettes?*
- *Among callers using e-cigarettes, what type of e-cigarettes are most common?*
- *Should FDA regulate e-cigarettes?*

The sources of information for this report are a literature review conducted in September 2014 and key informant interviews conducted by NAQC staff from August 25 through September 4, 2014, with the 12

quitline call centers currently providing services to state quitlines as well as one additional call center (Ceridian Health and Productivity Solutions based in Minnesota) which provided quitline service to the state of Tennessee through the end of June 2014. (See Appendix A for a list of individuals who were interviewed.) All quitline call centers participated in the interviews, so this report includes the full range of treatment practices with regard to e-cigarettes being provided by state quitlines in 50 states, the District of Columbia, Puerto Rico and Guam.

## **WHAT ARE E-CIGARETTES?**

E-cigarettes are battery-powered devices that deliver nicotine, flavorings and other chemicals via an inhaled aerosol. The battery heats the nicotine-containing liquid to produce an aerosol that is inhaled by the user. E-cigarettes have been sold in the United States since 2007,<sup>1</sup> and as of January 2014, there were at least 466 brands and 7,764 flavors available on the Internet.<sup>2</sup>

### **Patterns of Usage Among Adults**

Data from the National Adult Tobacco Survey in 2012-2013 showed that 14.1% of U.S. adults had tried e-cigarettes at least once in their lifetime, with 4.2% of ever e-cigarette users reporting using them “every day”, “some day”, or “rarely”.<sup>3</sup> E-cigarette users are more likely to be young, white race, and current or former smokers.<sup>4-6</sup> A 2012 study of 27 countries in the European Union found that 20.3% of adult current smokers, 4.7% of former smokers, and 1.2% of never smokers reported ever using e-cigarettes,<sup>7</sup> and a 2011-2012 study of 2,758 callers to 6 state tobacco quitlines in the U.S. found that 30.9% had ever used e-cigarettes.<sup>8</sup> The prevalence of exclusive e-cigarette use is low; findings from a 2012 national telephone survey found a prevalence of 0.4% for e-cigarette only use, compared to 1.9% for dual use of e-cigarettes and combustible cigarettes.<sup>9</sup>

### **Growth of E-cigarette Industry, Involvement of Tobacco Industry**

E-cigarette sales were estimated at over \$1.5 billion in 2013, and some analysts predict sales will reach \$10 billion by 2017.<sup>10</sup> The e-cigarette market includes both independent e-cigarette companies such as NJOY and major tobacco companies that developed their own e-cigarettes or that have acquired e-cigarette subsidiaries, such as Reynolds American Inc (Vuse) and Altria/Philip Morris (MarkTen and Green Smoke). In addition, e-cigarettes are distributed on the internet and via thousands of independent “vape shops” providing custom mixtures of e-liquid.<sup>11</sup> Over \$18 million was spent on e-cigarette advertising in 2012, and in a 2013 study of U.S. adults,<sup>12</sup> approximately half reported that they had been exposed to e-cigarette advertising through television, radio, print media, or online.<sup>13</sup> Additionally, there were increases in exposure to e-cigarette advertising on television among youth and young adults from 2011 to 2013 by 256% and 321%, respectively.<sup>14</sup>

## **WHAT ARE QUITLINES?**

Quitlines are telephone-based programs to help smokers quit. All 50 states, the District of Columbia, Puerto Rico and Guam provide tobacco cessation services to their residents through state quitlines. Although specific services may vary from state-to-state, quitlines comply with the U.S. Public Health Services Clinical Guideline on Tobacco Dependence Treatment.<sup>15</sup> All state quitlines offer behavioral support (i.e., counseling) to tobacco users who want to quit. Forty-five state quitlines also offer some form of FDA-approved cessation medication at no cost.<sup>16</sup> In addition, quitlines may offer a variety of programs such as chat room and e-support for those attempting to quit as well as programs such as fax referral, electronic referral, and cessation training for health care providers. For information about the quitline services offered in a specific state, please refer to <http://map.naquitline.org/>.

According to the NAQC Annual Survey of Quitlines, quitlines received about 1.3 million calls in 2012.<sup>17</sup> Among callers who registered for services, the average age was 44.2 years, the average education was GED/high school, most (58%) were women and the vast majority of callers were non-Hispanic (90%) and white (73%). 40% of callers were uninsured, 24% were enrolled in Medicaid, 25% had private insurance and 11% had other government insurance.<sup>17</sup>

As of July 2014, 12 quitline call centers were providing quitline services to the 50 states, District of Columbia, Puerto Rico and Guam. The call centers providing services and the jurisdictions served are shown below.

**List of Quitline Call Centers and the States Served, July 2014**

12 Quitline Call Centers (U.S.)	53 States and Territories Served as of July 2014
Alere Wellbeing	Alaska, Arkansas, Connecticut, Delaware, Florida, Georgia, Guam, Hawaii, Idaho, Indiana, Iowa, Kansas, Louisiana, Maryland, Minnesota, Missouri, Nebraska, New Mexico, North Carolina, Oklahoma, Oregon, South Carolina, Texas, Utah, Virginia, Washington, Washington, D.C., Wisconsin
American Lung Association of Illinois	Illinois
Avera McKennan Hospital and University Health Center/ Black Hills Special Services	South Dakota
beBetter Health, Inc.	West Virginia
Information & Quality Healthcare	Mississippi, Tennessee
JSI Research & Training Institute, Inc.	Massachusetts, New Hampshire, Rhode Island
MaineHealth, Center for Tobacco Independence	Maine
National Jewish Health	Alabama, Colorado, Kentucky, Michigan, Montana, Nevada, North Dakota, Ohio, Pennsylvania, Vermont, Wyoming
Roswell Park Cancer Institute	New Jersey, New York
Telemedik	Puerto Rico
University of Arizona/Arizona Smokers' Helpline	Arizona
University of California, San Diego	California

## **I. QUITLINE PRACTICE**

Since 2013, state quitlines have noticed a substantial increase in the use of and interest in e-cigarettes among callers. Between August 25 and September 4, 2014, NAQC conducted key informant interviews with 100% of quitline call centers that operate (or recently operated) state quitlines, including the 12 quitline call centers shown on the table (above) and one additional call center (Ceridian Health and Productivity Solutions based in MN) which provided quitline service to the state of Tennessee through the end of June 2014. All quitline call centers participated in the interviews, so this report includes the full range of treatment practices being provided by state quitlines in all 50 states, the District of Columbia, Puerto Rico and Guam.

The quitline call centers served as a rich source of information about the use of e-cigarettes among callers and the challenges and questions that need to be addressed so that we can better serve callers. The information learned during the interviews is summarized below.

### *What questions are quitlines hearing from smokers about e-cigarettes?*

All quitline call centers reported that smokers' primary questions about e-cigarettes related to their safety and effectiveness as a quit aid. Many call centers noted that callers asked counselors what they think of e-cigarettes, whether they recommend them, how they compare to combustible cigarettes in terms of health risks, how they compare to FDA-approved medications as quit aids, and whether they are addictive. In addition, a few quitlines mentioned that smokers asked whether they would be tobacco-free if they used e-cigarettes, whether the quitline provides e-cigarettes, and how much nicotine replacement therapy (NRT) to use if they were also using e-cigarettes to quit.

During the interviews, quitline call centers emphasized that smokers who asked questions were interested in gaining credible information about e-cigarettes, especially as a tool for quitting or for replacing the use of combustible cigarettes. Often their questions lead to an in-depth dialogue with the counselor about nicotine, addiction, carcinogens and the role of pharmacotherapy in quitting.

### *Do quitlines have policies and/or counseling protocols for e-cigarettes?*

Three quitline call centers reported having official policies or protocols regarding e-cigarettes, six reported having policies that are in development or "unofficial" and four reported integrating their approaches to e-cigarettes into other longstanding policies such as a policy on whether e-cigarette users are eligible for services (e.g., the mission of the quitline is to provide cessation services to "tobacco users") or a policy related to increasing quit attempts (e.g., the call center has a commitment to support any callers who plan to make a quit attempt within the next 30 days). One call center noted that the available evidence is not sufficient to support a protocol given that we do not understand the different types of e-cigarettes, the dosage of nicotine they provide to users, or how to taper down the nicotine levels. All call centers noted that they support NAQC's efforts to share information about e-cigarettes and quitline practices regarding e-cigarettes among quitlines and many expressed a hope that they could work together through NAQC to discuss e-cigarettes and develop core principles for an evidence-based policy or protocol.

One quitline call center has had a policy in place for about three years. Many quitlines provide resources for counselors that include research articles, fact sheets drawn from research articles, and in one case, a script with questions for callers and standard information about e-cigarettes. E-cigarettes are also addressed in staff meetings and training sessions. A number of call centers suggested that NAQC develop and maintain up-to-date fact sheets and/or web resources. (See Appendix B for examples of the policy, script and other quitline resources.)

### ***What are quitlines telling smokers who ask about whether they should use e-cigarettes?***

All 13 quitline call centers have either a policy or a counseling protocol to only recommend FDA-approved cessation medications to smokers as part of a quit attempt. They do not recommend the use of e-cigarettes, acupuncture, hypnosis, herbal remedies or other non FDA-approved cessation aids. However, all quitlines are supportive of their callers and will work with them in their quit attempts, even when the caller decides to use a cessation medication or aid that has not been proven effective.

Quitlines emphasized that counselors take a respectful and honest approach with callers. Although they do not recommend e-cigarettes, they also do not demonize them. They provide callers with factual information in a non-judgmental and neutral way, making it clear that there is much we do not yet know about e-cigarettes. Counselors provide science-based responses, noting that e-cigarettes are not FDA-approved or regulated and that we do not know if they are safe or effective as a cessation aid. We do not have adequate knowledge about the content of e-cigarettes, such as the amount of nicotine they contain and their other ingredients including possible toxins. Since the product is unregulated, the contents are likely to vary from brand to brand.

### ***Are quitlines asking screening questions about e-cigarettes?***

During key informant interviews in August/September 2014, 10 of the 13 call centers indicated that they ask callers about e-cigarette use at intake. One call center (serving one state) asks about use of e-cigarettes in the callers' quit attempts at "graduation" rather than at intake. One call center (serving a few states) is interested in asking questions at intake but has not yet developed questions. One multi-state call center mentioned that not all of their state funders have agreed to add the intake questions about e-cigarettes.

The questions asked by call centers were fairly similar, although some centers asked more questions than others. The most frequent questions were about current use (last 30 days) of e-cigarettes, the reason for using, the type of e-cigarette used (including whether it contains nicotine), frequency of use and whether the caller is thinking about quitting e-cigarettes (and if so, when). A few call centers provided preliminary data showing that prevalence of self-reported e-cigarette use among quitline callers was about 10% in 3 small eastern states and 16% in a large southwestern state. In one state that asked about use of e-cigarettes with and without nicotine, the great majority of callers reporting e-cigarette use (92%) reported that they use e-cigarettes with nicotine.

### ***What are quitlines telling smokers about the relative harm of e-cigarettes as compared to combustible cigarettes?***

Only one call center reported not providing any information about the harms of e-cigarettes compared to combustible cigarettes. Others mentioned using reliable websites (e.g., the website of the Centers for Disease Control and Prevention) and peer-reviewed journal articles as the basis for responding to the question.

Nearly all call centers mentioned that this information would only be shared with callers if the callers asked for it or gave permission for the counselor to share it with them. Counselors shared information with callers about the side effects of e-cigarette use such as coughing and throat irritation. They also informed callers about the small amount of research available on the potential harms of e-cigarettes, noting that the content of the e-cigarettes (i.e., nicotine levels, particulates and toxins) is not regulated or known and that the use of e-cigarettes may be associated with adverse health effects and disease. Many call centers expressed an opinion to NAQC that the use of e-cigarettes is safer for callers than combustible cigarettes in the short term, but all of them emphasized that we do not know about the adverse health effects associated with long-term use. Most call centers were knowledgeable about the risks of nicotine poisoning, especially for children who may find an e-cigarette cartridge, had heard about the rare cases of e-cigarettes exploding, and were aware that the exact

contents and health effects of e-cigarette aerosol were still being identified and that this aerosol may pose risks to bystanders in the vicinity of an e-cigarette user, and share this information with callers.

***What messages do quitlines share with callers about dual use of e-cigarettes and combustible cigarettes?***

Call centers report that when a caller mentions using e-cigarettes along with combustibles, the counselor asks if s/he intends to stop using both of them. Overall, callers using both combustible cigarettes and e-cigarettes usually expressed an intention to quit smoking combustible cigarettes first, and then may or may not have expressed an intention to quit e-cigarette use. As a principle, the majority of call centers would like callers to be completely tobacco-free and nicotine-free at some point, but they acknowledge that the intent of the caller will determine this (i.e., counselors use a client-directed motivational approach and do not tell callers what to do). Counselors may mention that it is harder to quit two nicotine products than a single product. They may also mention the importance of reducing nicotine levels.

The majority of dual users who call quitlines report using e-cigarettes to cut down on the number of combustible cigarettes they smoke or to help them quit using combustibles. When callers tell counselors they have made progress in cutting-down on combustible cigarettes, they are congratulated for this first step toward quitting.

Counselors will try to determine how much nicotine a caller is getting each day and will have a discussion with the caller about the importance of decreasing his/her nicotine levels. With e-cigarettes, it is difficult to determine nicotine levels. When callers ask about using other cessation aids such as NRT along with e-cigarettes, most counselors will discuss nicotine levels and may use this as an opportunity to talk about using an FDA-approved source of nicotine (e.g., the patch, gum, or lozenge) instead of e-cigarettes, noting among other things the benefits of knowing the nicotine levels of NRT. A growing number of call centers are recommending combination therapy (patch and gum) and may use a caller's dual use as an opportunity to explore past failures with NRT to assess whether combination therapy (e.g., patch and gum) may be beneficial to the caller and to ask the caller if s/he is interested in combination therapy as an alternative to e-cigarettes.

A challenging topic for call centers is deciding whether to provide NRT for callers who are using e-cigarettes, either alone or in combination with combustible cigarettes, and determining what dosage of NRT to recommend. In the case of a smoker using both e-cigarettes and combustible cigarettes, most call centers would attempt to determine the caller's nicotine level and would provide NRT to the smoker with the caveat that they quit using both combustible cigarettes and e-cigarettes on their quit date, and use only NRT after the quit date. Many call centers expressed a lack of confidence in assessing the caller's current nicotine level (because the actual levels in e-cigarettes may vary from the level on the label) and as a result, a lack of confidence in being able to advise callers what dosage of NRT they should use. As a result, the counselor may not provide NRT in some cases but instead advise the caller to talk to a physician. In a few call centers, a policy/protocol prohibits the provision of NRT to dual users.

***What messages are quitlines providing to callers about the importance of quitting e-cigarettes?***

As mentioned above, if callers are using both combustible cigarettes and e-cigarettes, they usually express an intention to quit smoking combustible cigarettes first and then may or may not express an intention to quit using e-cigarettes. All call centers express concerns to callers about using an unregulated product (i.e., e-cigarette) for which little information is available on safety and efficacy and, if the client is open to discussing it, advise switching to an FDA-approved cessation medication to make a quit attempt. All call centers encourage callers to quit e-cigarettes. If clients express an intention to quit e-cigarettes, the counselors will strongly support this decision. Although many call centers expressed an opinion to NAQC that they do not view short-term use of e-

cigarettes in negative terms, all of them raised concerns about the safety of long-term use and the difficulty of quitting two nicotine-containing products. Many call centers also raised concerns about the ongoing hand-to-mouth behavior of e-cigarette use as a possible trigger for relapse to combustible cigarettes.

Some call centers reported that the cost of e-cigarettes may motivate callers to quit using them, especially if the call center provides free FDA-approved medications or if the caller has insurance coverage for cessation medications. This may help motivate e-cigarette users to switch to FDA-approved medications. Although every call center acknowledged the importance of caller-directed decision-making about quitting, many mentioned that the ultimate goal of their work is to help callers become completely tobacco- and nicotine-free.

#### ***What approaches are quitlines using with callers who ask for help quitting e-cigarettes?***

One call center noted that a caller exclusively using e-cigarettes would not be eligible for services from the quitline because its mission is to help callers quit using tobacco products and they consider e-cigarettes to be a nicotine product rather than a tobacco product. All other call centers would provide counseling and ten of them may recommend NRT depending on the caller's level of nicotine dependency (as determined by the caller's smoking history and time of first use of e-cigarettes). Two call centers reported they do not recommend NRT to anyone using tobacco products other than cigarettes. One call center reported that this is a theoretical question as the quitline has not received any calls from people who exclusively use e-cigarettes. After this interview, we asked the remaining call centers about calls from people exclusively using e-cigarettes and were told that calls from this group were either rare or had never been received.

#### ***How do quitlines categorize callers who report quitting combustible cigarette use but who continue to use e-cigarettes?***

Four quitline call centers consider those who quit combustibles but still use e-cigarettes as "quit", 6 consider them as "not quit" and 3 did not have an opinion. Most call centers noted that their 7-month follow up (evaluation) data can display separately a caller's use of cigarettes, other tobacco products and nicotine-containing products. Most call centers expressed an interest in having a dialogue or participating in workgroup meetings to discuss the development of standard intake and follow up (evaluation) questions for the NAQC Minimal Data Set as well as how to classify e-cigarette users.

#### ***Among callers using e-cigarettes, what type of e-cigarettes are most common?***

Five quitline call centers do not collect information about the type of e-cigarettes used by callers. Two call centers noted that disposable e-cigarettes were most popular, two mentioned tank systems and rechargeable e-cigarettes, two mentioned the brand Blu and rechargeable e-cigarettes, one mentioned rechargeable e-cigarettes and one mentioned tank systems. Over time, call centers have noticed changes in the type of e-cigarettes used by callers. One call center observed that disposable e-cigarettes may be used by dual users in places where they cannot smoke but that smokers who are serious about quitting are more likely to use the tank system so that they have more control over the nicotine dosage and can modify this dosage.

#### ***Should FDA regulate e-cigarettes?***

Quitline call centers are supportive of having FDA move forward with regulations of e-cigarettes. When asked about whether FDA should take action to regulate e-cigarettes, 7 call centers responded strongly in the affirmative, 2 supported regulation, and 4 were not prepared to respond to what they viewed as a political question or felt that they should defer to the state funder on this issue. In discussions, all call centers agreed that it would be beneficial to know the ingredients of e-cigarettes, the level of each ingredient (especially nicotine) and the likely adverse health effects that these ingredients may pose to e-cigarette users (especially long-term users) and to bystanders in the vicinity of e-cigarette aerosol.

## **II. LITERATURE REVIEW**

A literature review was conducted in September 2014 to advance our understanding of key questions about e-cigarettes and cessation. The findings are presented below.

### ***What do we know about the nicotine concentration in the context of e-cigarettes?***

The exact design and composition of an e-cigarette is variable,<sup>18</sup> and this, combined with variability in individual usage patterns, contributes to differences in the amount of nicotine and other toxicants delivered to the user.<sup>19,20</sup> Furthermore, inconsistencies have been found in the amount of nicotine present in e-cigarettes compared to the amount noted on their labels.<sup>21,22</sup> In one study, an e-cigarette from the CIXI brand labeled as having 0mg of nicotine was found to have up to 21.8mg of nicotine per cartridge, while another labeled as having 24mg of nicotine was found to have 0.09mg of nicotine per cartridge;<sup>23</sup> in this study, cartridges from the NJOY brand also had discrepancies in actual and labeled nicotine content. This raises concerns about the actual contents of e-cigarettes and points to the need for more standardized quality control.

### ***What do we know about the potential adverse health effects of e-cigarettes compared to combustible cigarettes?***

Given that the long-term health effects of e-cigarette use remain unknown, analysis of their health risks has primarily focused on the chemical contents of the e-cigarette liquid and aerosol and adverse effects noted by users. User-reported adverse effects from e-cigarettes are typically symptoms such as nausea/vomiting, cough, and throat irritation, however more serious events such as burns have also occurred, though rarely, from use.<sup>24</sup>

### **Risks of Nicotine Toxicity**

Nicotine is not a benign substance. A recent report from the U.S. Surgeon General highlights the vulnerability of certain populations, especially youth, pregnant women and their fetuses, and concludes that:<sup>25</sup>

- \* At high-enough doses, nicotine has acute toxicity.
- \* Nicotine exposure during fetal development, a critical window for brain development, has lasting adverse consequences for brain development.
- \* Nicotine adversely affects maternal and fetal health during pregnancy, contributing to multiple adverse outcomes such as preterm delivery and stillbirth.
- \* Nicotine exposure during adolescence, a critical window for brain development, may have lasting adverse consequences for brain development.

An early study of e-cigarettes suggested levels of nicotine delivery were low,<sup>26</sup> but later studies demonstrated experienced users receiving higher levels of nicotine that may approach levels found in combustible cigarettes.<sup>27</sup> As e-cigarette products continue to evolve and some “tank system” variants produce more aerosol at higher temperatures, nicotine delivery may be greater. The high variability in nicotine levels (within a single product and across different products) may increase the potential for toxicity.<sup>21</sup> In addition, there is risk of harm from the liquid nicotine in e-cigarettes from oral or cutaneous contact, particularly in children.<sup>28</sup> From September 2010 to February 2014, monthly calls to poison centers in the U.S. for exposure to e-cigarettes increased from one to 215, and over half of these calls were for children less than 5 years of age.<sup>29</sup> It is thus important to ensure child-resistant packaging for e-cigarettes and refill cartridges, and prevent children’s access to these products.

### *Toxicants and Carcinogens in E-cigarettes*

Carbonyl compounds and volatile organic compounds have been isolated from e-cigarette aerosol, including known carcinogens such as formaldehyde and acetaldehyde. In one study of 12 brands of e-cigarettes, up to 56.1ug of formaldehyde and 13.6 ug of acetaldehyde were detected in e-cigarette vapor compared to levels of 2ug and 1.1 ug, respectively, from a nicotine inhaler,<sup>30</sup> a form of FDA-approved NRT that delivers nicotine through inhalation without heating. The authors reported that the levels of these toxins in e-cigarette aerosol were 9 to 450 times lower on average compared to combustible cigarettes.<sup>30</sup> For reference, the California Environmental Protection Agency reports a “No Significant Risk Level” (i.e., the daily intake of a chemical estimated to result in 1 excess case of cancer among 100,000 exposed individuals) of 40 ug/day for formaldehyde and 90 ug/day for acetaldehyde.<sup>31</sup> The level of carbonyl compounds in e-cigarette aerosol varies depending on factors such as battery voltage and nicotine solvent,<sup>32</sup> and therefore exposure to toxic compounds from e-cigarettes may vary considerably. In a study of 159 samples of e-liquid from 36 manufacturers, diacetyl, an organic compound associated with respiratory disease, was found in sweet-flavored e-cigarettes at levels higher than deemed safe for exposure by the National Institute for Occupational Safety and Health in over 40% of samples.<sup>33</sup>

Tobacco-specific nitrosamines such as N'-nitrosonornicotine (NNN) and 4-(methylnitrosoamino)-1-(3-pyridyl)-1-butanone (NNK), which are also carcinogenic, have been detected in some e-cigarettes at levels much lower than combustible cigarettes,<sup>30,34</sup> but these were not found in a nicotine inhaler. Carcinogenic metals such as cadmium, nickel, and lead have also been detected at low levels, however in one study were not significantly different from the level in nicotine inhalers.<sup>30</sup> It is not clear whether the concentrations of these compounds in e-cigarettes increases cancer risk, and it will likely be several years before the true effects become apparent.

While the production of carcinogens and toxins from e-cigarettes is lower than combustible cigarettes, presence of ultrafine particulate matter is another important consideration in risk assessment. E-cigarettes deliver levels of particles comparable to or greater than cigarettes, and these particles are of smaller size. Particle concentrations in multiple studies have been in the range of  $10^9/\text{cm}^3$ ,<sup>35,36</sup> with higher particle number seen with higher liquid nicotine concentrations and longer e-cigarette puffs.<sup>35</sup> Particle distribution modes of 100-200nm have been found in e-cigarettes,<sup>35,37</sup> which is similar to that of combustible cigarettes. Ultrafine particles from combustible cigarettes, even at low levels, increase risk of cardiovascular<sup>1</sup> and pulmonary diseases,<sup>2</sup> and the production of these particles by e-cigarettes may also pose these risks.

### ***What is the current evidence of efficacy of e-cigarettes for smoking cessation?***

As of September 2014, studies on the use of e-cigarettes have not met scientific standards for demonstrating efficacy as a smoking cessation aid. One cross-sectional study in England found that in cigarette smokers who made at least one quit attempt in the preceding year and had used an e-cigarette as part of a quit attempt, the odds of self-reported abstinence from smoking were higher than that of smokers who had made a quit attempt in the past year using unassisted over the counter NRT or no smoking cessation aids (OR 2.23, 95% CI 1.70-2.93 versus NRT; 1.38, 1.08-1.76 versus no aids).<sup>38</sup> (They did not compare e-cigarettes with assisted NRT.) In contrast, pooled analysis from 4 longitudinal population-based studies<sup>4,8,39,40</sup> and one cross-sectional study<sup>41</sup> looking at all e-cigarette users (rather than just those who used e-cigarettes as part of a quit attempt) found decreased odds of quitting by over 30% in those using e-cigarettes.<sup>1</sup> One of these studies specifically focused on callers to U.S. quitlines in 6 states, and found that the 30-day point prevalence of smoking abstinence, assessed at 7 months after registration for cessation services, was lower in those who had ever used e-cigarettes compared to those who had never used e-cigarettes (point prevalence of smoking abstinence: 21.7% in those who used e-cigarettes for longer than one month and 16.6% in those who used e-cigarettes for less than one

month, compared to 31.3% in those who never used e-cigarettes).<sup>8</sup> These studies suggest that while a subset of smokers attempting to quit may find success with use of e-cigarettes in their quit attempt, the cessation rates of the overall population of smokers using e-cigarettes remains associated with lower rates of smoking cessation (based on currently available literature). In a study of 1,074 cancer patients who enrolled in a tobacco treatment program, odds of self-reported smoking 6 months after study enrollment was similar between e-cigarette users and non-users (OR 1.0, 95% CI 0.5-1.7); using intention-to-treat analysis, the odds of self-reported smoking was twice as high in e-cigarette users compared to non-users (2.0, 1.2-3.3).<sup>42</sup>

The one randomized controlled trial comparing e-cigarette use to NRT did not find a significant difference in cessation between the two groups.<sup>43</sup> This trial, which was conducted in New Zealand among cigarette smokers interested in quitting, found that 7.3% of those randomized to receiving 16mg e-cigarettes for smoking cessation maintained abstinence from combustible cigarettes at 6 months, which was not statistically significant compared to those receiving a 21mg nicotine patch (5.8%) or e-cigarette containing no nicotine (4.1%). In this trial, those randomized to NRT were mailed cards to redeem for patches at local pharmacies and vouchers to cover costs, whereas those in the e-cigarette group had the e-cigarette, battery, charger, and cartridges delivered to them; this may have introduced bias towards those in the NRT group, who had a higher loss to follow-up and withdrawal rate.

#### ***Based on the current literature, should smokers use e-cigarettes for smoking cessation?***

While cigarette smokers are more willing to use e-cigarettes than nicotine inhalers (the only form of FDA-approved inhaled NRT) in quit attempts,<sup>44</sup> evidence does not support the promotion of e-cigarettes as a primary cessation aid. Furthermore, the long-term effects of e-cigarette use, in the context of continued exposure to nicotine, toxicants, carcinogens, and ultrafine particles, often in unregulated and unspecified amounts, remains unknown. While evidence on strategies for helping users quit e-cigarettes are lacking, these users should be informed about the uncertainties in e-cigarette content and long-term health risks, and encouraged to set a quit date for e-cigarettes as well.<sup>1</sup>

#### ***How should we classify someone who reports quitting combustible cigarette use (but continuing to use e-cigarettes)?***

At this point in time, no standard classification scheme exists. The field may want to classify them as no longer smoking cigarettes but continuing to use e-cigarettes. A 2014 policy statement from the American Heart Association<sup>45</sup> recognizes three different groups based on tobacco/e-cigarette usage patterns: (1) users interested in quitting who should receive assistance, (2) users not interested in quitting who should receive intervention to increase motivation to quit, and (3) users who recently quit in whom prevention of relapse should be promoted. Individuals should be asked about use of any tobacco products and e-cigarettes, and it would be informative to specify use of e-cigarettes and combustible cigarettes separately so that it is clear whether they quit use of one product, continue to use another, or continue using both. This information may prove to be important in determining relapse.

#### ***What do we know about dual use of combustible cigarettes and e-cigarettes?***

E-cigarette users who also use combustible cigarettes, i.e. dual users, remain at risk of negative health effects from smoking cigarettes. Dual use also arises if e-cigarettes are being used by current smokers as a substitute for cigarettes where smoking combustible cigarettes is prohibited (a common marketing claim<sup>46</sup> and frequently reported reason for trying e-cigarettes among users<sup>47</sup>), to cut down the number of cigarettes they smoke without quitting, or if current smokers who use e-cigarettes for smoking cessation are unsuccessful in quitting.

Even those who smoke just a few cigarettes per day remain at increased risk of cardiovascular disease<sup>48</sup> and resultant mortality,<sup>49</sup> and such health risks are expected to persist if cigarette smoking continues, even at lower amounts. While there are no data on the health effects of e-cigarette and combustible cigarette dual use, studies of smokeless tobacco and combustible cigarette dual use suggest dual tobacco product use carries significant health risks. In the 52-country INTERHEART trial, dual users of smokeless tobacco and cigarettes had significantly increased odds of acute myocardial infarction (odds ratio 4.09, 95% CI [2.98-5.61]) compared to never smokers; this was higher than the odds of acute myocardial infarction associated with chewing tobacco alone (2.23, [1.41-3.52]) and the odds of non-fatal myocardial infarction in current smokers compared to never smokers (2.95, [2.77-3.14]).<sup>50</sup> Additionally, among patients hospitalized for myocardial infarction in Sweden from 2005 to 2009, the mortality risk of those who quit snus (a form of smokeless tobacco) was nearly half of that of those who continued to use snus, an effect similar in magnitude to smoking cessation,<sup>51</sup> suggesting that cardiovascular patients benefit from cessation of use of a noncombustible low nitrosamine tobacco product. Another study found a greater increase in lung cancer mortality with more years of cigarette smoking compared to more cigarettes smoked per day,<sup>52</sup> suggesting that the risk of lung cancer death will persist even with a reduction in daily cigarette consumption. Therefore, while some studies have found that many smokers using e-cigarettes reduce the number of cigarettes they smoke per day,<sup>43,53</sup> the effects on mortality from some cardiovascular diseases and malignancies are likely to persist unless complete abstinence from cigarette smoking follows.

### ***Are there special concerns or considerations related to e-cigarettes for special populations such as youth and those with substance abuse or mental health illnesses?***

The use of e-cigarettes in certain populations, such as those with mental health illness, has not been as well-studied as in the general population. One study found that 14.8% of individuals with self-reported depression, anxiety, or other mental health condition endorsed ever use of e-cigarettes and 3.1% reported current use, compared to 6.6% and 1.1% of individuals without reported mental health conditions endorsing ever use and current use, respectively.<sup>54</sup> Among current smokers, 40.3% of individuals with mental health conditions reported ever use of e-cigarettes, compared to 28.7% of individuals without mental health conditions. In a small study of 14 cigarette smokers with schizophrenia that tried e-cigarettes, none of whom had intentions to quit, a 50% reduction in cigarettes smoked per day was seen after one year of follow-up in 7 (50%) of the participants, and smoking abstinence was seen in 2 (14%) individuals after a year; no changes in the positive and negative symptoms of schizophrenia were noted.<sup>55</sup> Given that this is a small uncontrolled study, the ability to interpret these results and apply them in a larger context is limited. Further studies are needed on e-cigarette use in the population with mental health illness.

There are special concerns related to e-cigarettes for youth. E-cigarette use is rising among youth: from 2011 to 2012, the National Youth Tobacco Survey showed approximate doubling in ever-use of e-cigarettes among students in grades 6-12 from 3.3% to 6.8%;<sup>56</sup> among middle school students, over 20% had never used a combustible cigarette. In 2013, 263,000 youth who had never smoked cigarettes reported ever using e-cigarettes, and those who had ever used an e-cigarette had increased intentions to smoke combustible cigarettes.<sup>57</sup>

## **III. FINDINGS, DISCUSSION AND NEXT STEPS**

This report aims to inform the field on two questions: 1) Given the current level of knowledge about e-cigarettes, how should quitlines respond to smokers' questions about them? and 2) What are the most important actions that quitlines can take to advance their practice in this area?

### ***How Should Quitlines Respond to Smokers' Questions About E-cigarettes?***

The practices of quitlines regarding e-cigarettes are noteworthy first for their consistency across 13 independent organizations, and second for their careful balancing of the paucity of relevant scientific findings and the importance of providing evidence-based treatment to smokers who want to quit. The main findings about quitline practice are:

- It is rare for quitlines to receive a call from an individual who exclusively uses e-cigarettes.
- Quitline call centers tend to receive similar questions from callers about e-cigarettes. The majority of callers ask about the safety of e-cigarettes and their effectiveness as a cessation aid.
- Nearly all quitlines have developed or are developing policies to guide their approach to e-cigarettes.
- All quitline call centers only recommend FDA-approved cessation aids. However, they provide support to all smokers making a quit attempt, even when the smoker chooses to use a non FDA-approved cessation aid such as e-cigarettes.
- Most quitline call centers are either already asking or developing screening questions about e-cigarettes. Call centers expressed interest in developing standard screening questions. A few state agencies that fund quitlines have not approved the use of screening questions.
- Most quitline call centers collect follow-up (evaluation) data in separate categories (use of cigarettes, use of other tobacco products, and use of nicotine products). However, there was a lack of consistency in whether they considered callers who continue to use e-cigarettes to be “quit.”
- All quitline call centers except one have information about the possible harms of e-cigarettes available to share with callers. However, this information was inconsistent across call centers; many call centers expressed an interest in identifying common credible sources of information and/or developing standard fact sheets.
- Most quitlines have a consistent approach to working with callers who are using both combustible cigarettes and e-cigarettes (i.e., dual users). Many had questions about whether it is advisable to provide NRT to dual users and how to calculate NRT dosage in these individuals.
- All quitline call centers encourage callers to quit e-cigarettes if the issue is raised by the caller. Although many call centers did not view short-term use of e-cigarettes negatively, all of them raised concerns about the safety of long-term e-cigarette use and the difficulty of quitting two nicotine products.

The literature review provides important new research information for quitlines filling some knowledge gaps and helping to address some of the outstanding questions. In summary, current evidence is not sufficient to suggest that e-cigarettes are effective aids for smoking cessation. E-cigarettes lack quality control, and, as a result, their exact components are often unknown. While research suggests that e-cigarettes produce fewer and lower levels of carcinogens and toxicants than combustible cigarettes, it is not yet clear whether the concentration of these compounds found in e-cigarette aerosol poses long-term health risk and further studies are needed to evaluate this. E-cigarettes also produce ultrafine particles, which may pose short- and long-term health risks. In the case of dual use of e-cigarettes and combustible cigarettes, evidence suggests that even if consumption of combustible cigarettes is reduced, certain health risks will remain elevated in the absence of complete cessation.

Recommendations for quitline practice based on the available scientific evidence are shown below:

- Quitlines should continue to tell callers that the overall health risks of e-cigarette use are unknown. There are no long-term studies on the health effects of e-cigarettes, and it will likely be years until such data becomes available. Regulatory standards and quality control measures for e-cigarettes are often inconsistent or lacking, and therefore the exact composition of these products is unknown. Quitlines should inform callers, as appropriate, that aerosol from some e-cigarettes has been found to contain carcinogens and toxicants, including carbonyl compounds, volatile organic compounds, tobacco-specific

nitrosamines, and metals. Additionally, ultrafine particles produced by e-cigarettes are comparable in size and number to those produced by cigarettes, and may pose the same cardiovascular risk.

- Quitlines should continue to advise against using e-cigarettes for smoking cessation. Evidence is insufficient to suggest that e-cigarettes can help smokers quit combustible cigarettes. As of September 2014, the studies on use of e-cigarettes for smoking cessation have had varied results, with studies in some populations showing increased cessation in those using e-cigarettes, and others showing lower smoking cessation rates in those using e-cigarettes. Overall, studies on the use of e-cigarettes have not met scientific standards for demonstrating efficacy as a smoking cessation aid.
- Quitlines should continue to discourage dual use of combustible cigarettes and e-cigarettes. The long-term risk profile of dual users of combustible cigarettes and e-cigarettes is unknown. Research demonstrates that individuals who continue to smoke even a few cigarettes a day have elevated risk of cardiovascular disease. Therefore, even if dual use of e-cigarettes and combustible cigarettes leads to reduction in number of cigarettes smoked per day, while some of the cancer risk associated with cigarette smoking may decrease, cardiovascular risk will likely remain elevated without complete abstinence from cigarettes.

In the past six months, a number of associations, committees and experts have published articles and commentaries regarding the advice health care providers should provide to current smokers about use of e-cigarettes. (See Appendix C for a list of the publications.) The recommendations made in these publications and the concerns raised align closely with quitline practice and concerns.

### ***Important Actions Quitlines May Take to Advance Their Practices Related to E-cigarettes***

There are many important issues to consider as we move forward. Quitline call centers raised a number of important issues for consideration during the key informant interviews. Other members of NAQC and the team responsible for this report have contributed their ideas as well. Below, selected ideas have been compiled into next steps.

NAQC should:

- Convene a workgroup of members to develop standard intake and follow-up questions on e-cigarettes for NAQC's minimal data set (MDS).
- Facilitate sharing and/or development of resources on e-cigarettes, including protocols for treating e-cigarette users, messages, and fact sheets.
- Develop a NAQC policy statement on e-cigarettes and compile resources to support quitline call centers (e.g., policy statements from other national organizations and treatment specialist organizations, resources for quitline callers and the public, updated literature reviews on e-cigarettes). We should share materials and avoid duplication of effort.
- Encourage the development of formal scientific guidance on whether and under what circumstances NRT should be recommended to help e-cigarette and dual users quit, and how to calculate recommended dosage of NRT for e-cigarette users and dual users.
- Explore whether the increase in e-cigarette use has resulted in fewer smokers making formal evidence-based quit attempts. Two call centers raised concerns about decreasing call volumes and questioned whether the availability of e-cigarettes has decreased smokers' interest in becoming both tobacco- and nicotine-free.
- Engage health care providers and their societies (including the authors listed in Appendix C) in a dialogue about advice for smokers and dual users regarding the use of e-cigarettes and quitting.
- Monitor issues related to youth experimentation with and use of e-cigarettes, and a related concern about child poisonings.

- Keep the quitline community informed about new research findings as well as legislative and regulatory actions that are being considered and can be taken at the state and national levels.

A number of recommendations are beyond the scope of NAQC's activities, but are important to mention.

- Encourage randomized trials to determine the effectiveness of e-cigarettes as a cessation aid and the safety of long-term use.
- Engage tobacco control and cessation organizations in a discussion about e-cigarettes and their impact on population health and individual health.
- Monitor tobacco companies' acquisitions of e-cigarette companies.

#### **IV. CONCLUSION**

An increasing number of callers to state quitlines are raising questions about the use of e-cigarettes. Many of these questions concern the overall safety of e-cigarettes as well as their efficacy for smoking cessation. The research literature on e-cigarette use is nascent. As a result, the long-term health risks of using these products, as well as long-term patterns of e-cigarette use and dual use, and how e-cigarettes impact smoking cessation remain to be seen. Given these limitations, the practices of quitlines regarding e-cigarettes are noteworthy first for their consistency across 13 independent organizations, and second for their careful balancing of the paucity of relevant scientific findings and the importance of providing evidence-based treatment to smokers who want to quit. Smokers should be supported in their quit attempts, regardless of what products they are currently using as a cessation aid, and they should be encouraged to use FDA-approved, evidence-based therapies. Important actions that quitlines may take to advance their practice include working through NAQC to: a) establish standard intake and follow-up (evaluation) questions for callers; b) develop some standard materials (especially on the potential harms of e-cigarettes), and c) monitor new research findings on e-cigarettes that may influence quitline practice. Research should continue to evolve to address the growing number of questions and concerns about e-cigarettes, which will ultimately aid policymakers and the FDA in establishing standards, as well as tobacco cessation specialists in treating individuals who use these products.

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