Electronic Cigarettes in North America
History, Use, and Implications for Smoking Cessation

Caroline Franck, MSc*; Talia Budlovsky, BA*; Sarah B. Windle, MPH; Kristian B. Fillion, PhD; Mark J. Eisenberg, MD, MPH

Background—Designed to mimic the look and feel of tobacco cigarettes, electronic cigarettes (e-cigarettes) may facilitate smoking cessation. However, the efficacy and safety of e-cigarette use for this purpose remain poorly understood. Our objectives were to review the available data on the efficacy and safety of e-cigarettes for smoking cessation and to consider issues relevant to the context in which they are used, including product awareness and regulatory and ethical concerns.

Methods and Results—We systematically searched PubMed for randomized controlled trials and uncontrolled, experimental studies involving e-cigarettes. Included studies were limited to English or French language reports. Quality assessment was performed according to the Cochrane Risk of Bias tool. We identified 169 publications, of which 7 studies were included. Studies have concluded that e-cigarettes can help reduce the number of cigarettes smoked and may be as effective for smoking cessation as the nicotine patch. Although there is a lack of data concerning the safety and efficacy of e-cigarettes as a smoking cessation therapy, available evidence showed no significant difference in adverse event rates between e-cigarettes and the nicotine patch. E-cigarettes are widely used among smokers attempting to quit. However, significant international variation remains in the regulatory mechanisms governing the sale and distribution of e-cigarettes. Ethical concerns surround the use of e-cigarettes among minors and their potential to undermine efforts to reduce cigarette smoking.

Conclusion—Given the limited available evidence on the risks and benefits of e-cigarette use, large, randomized, controlled trials are urgently needed to definitively establish their potential for smoking cessation. (Circulation. 2014;129:1945-1952.)

Key Words: review ■ smoking cessation ■ tobacco use cessation products

Smoking-related diseases contribute to the death of >480000 North Americans each year, creating a heavy economic burden on both the Canadian and US healthcare systems. An estimated 52.9 million people (or 18.0% of adults ≥18 years of age) in North America currently smoke cigarettes. Smoking cessation has been shown to decrease the risk of coronary artery disease by 50% after 1 year of abstinence and the risk of lung cancer by ≈50% after 10 years of abstinence. Importantly, many who smoke report being motivated to quit, and approximately half have attempted to quit in the past year. However, most smokers who attempt to quit smoking without any assistance relapse within the first 8 days, with only 3% to 5% achieving prolonged abstinence of 6 to 12 months. Although the use of a smoking cessation therapy can increase the proportion of successful quitters at 12 months to >15%, this still represents a low likelihood of long-term success, even among smokers motivated to quit. Because available therapies remain insufficient, there is an urgent need to identify new and alternative smoking cessation therapies.

The Emergence of Electronic Cigarettes in North America

Since their patent in 2004, electronic cigarettes (e-cigarettes) have dramatically increased in popularity. They are sold directly to consumers and are designed to mimic the look and feel of conventional cigarettes, creating a smoke-free vapor (with or without nicotine) that is inhaled by the user. Most brands are marketed as lower-cost, tobacco-free alternatives to conventional cigarettes that are not subject to regular smoking laws and thus can be used in typically nonsmoking areas. Although the US Food and Drug Administration (FDA) permits e-cigarettes to be sold under the auspices of tobacco products rather than as drugs or devices, it does not permit e-cigarettes to be marketed for therapeutic purposes such as smoking cessation.

Nevertheless, research evidence suggests that smokers are attempting to use e-cigarettes to quit smoking. A survey of...
>10,000 adults reported that, of US smokers motivated to quit within the next 6 months, almost half had tried e-cigarettes. Smokers attempting to quit may be using e-cigarettes in place of proven therapies for smoking cessation (eg, nicotine replacement therapies [NRTs] such as the patch or gum, non-nicotine-containing pharmacotherapies such as bupropion or varenicline, or behavioral interventions). Given their increasingly popular use as a smoking cessation aid, there is reason for concern in light of the dearth of research evidence supporting their use in this context.

Unlike traditional NRTs, e-cigarettes combine properties of both pharmacological and behavioral smoking cessation interventions. Cigarette addiction is driven by a multitude of behavioral smoking cues that most pharmacological smoking cessation therapies fail to address. E-cigarettes mimic the action of smoking while mitigating withdrawal symptoms with nicotine replacement (in the case of nicotine-containing e-cigarettes). Studies among current smokers have also demonstrated the considerably higher product acceptability of e-cigarettes relative to NRTs. Although it remains understudied, the potential of e-cigarettes as a smoking cessation aid has garnered international interest. In 2008, the World Health Organization issued a press release stating that although it could not endorse the use of e-cigarettes as a smoking cessation aid because of the lack of rigorous evidence demonstrating their safety and efficacy, the “[World Health Organization] does not discount the possibility that the electronic cigarette could be useful as a smoking cessation aid. The only way to know is to test.”

E-Cigarette Device Components and Characteristics

E-cigarettes are typically composed of 3 parts: a plastic tube, an electronic heating component, and a cartridge containing a liquid solution of propylene glycol, with or without nicotine (Figure 1). When a sensor in the device detects airflow, the heating component in contact with the cartridge is activated, vaporizing the solution and producing a smoke-like aerosol that is subsequently inhaled. Because no combustion occurs, the inhalation of nicotine through an e-cigarette is believed to be a safer alternative to cigarette smoking by eliminating the inhalation of harmful compounds, including tar and carbon monoxide.

Two types of e-cigarettes may be purchased: disposable or rechargeable. Disposable e-cigarettes must be thrown away once the liquid contained in the cartridge is depleted. Rechargeable e-cigarettes may be used for an indefinite amount of time because the product battery is recharged with a computer USB port or wall outlet. In this case, the user replaces the atomizer cartridge as frequently as necessary. For both disposable and rechargeable products, cartridges are available in several flavors, including tobacco, menthol, chocolate, vanilla, and various fruit flavors. Cartridges can also be purchased in varying strengths of nicotine content, including nicotine free. The life span of a cartridge depends on several factors, including frequency of use and nicotine content per cartridge. Although the cost of an e-cigarette varies by brand, they are most often cheaper than tobacco cigarettes. The Internet is the primary medium of advertisement, with brands turning to platforms such as Facebook, YouTube, and Google to promote their products.

Despite their increasingly popular use for smoking cessation, little is known about their efficacy suited for this purpose and whether any adverse health effects are associated with their use. Consequently, we conducted a systematic review of experimental studies examining the safety and efficacy of e-cigarettes in the context of their use for smoking cessation.

Methods

We conducted a systematic search of PubMed to identify experimental trials examining the efficacy or safety of e-cigarettes for smoking cessation published before September 15, 2013. The search was conducted according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines for systematic reviews (Figure 2). Key search terms included “electronic cigarette” and “e-cigarette.” We searched PubMed, Google Scholar, and regulatory websites (eg, Health Canada, US FDA) manually for additional articles providing context for the awareness and use of e-cigarettes, their regulation, and potential ethical issues. Included publications from the systematic search contained experimental studies examining the efficacy or safety of an e-cigarette for smoking cessation. Exclusion criteria included articles without original data, articles limited to pharmacokinetic analyses, abstracts, conference proceedings, and articles not published in English or French. Data were extracted by 2 reviewers, with disagreements resolved by consensus or by a third reviewer. Extracted data included country of origin, study methods, study population, treatment type and duration, duration of follow-up, study results, and key takeaways. We used the Cochrane Collaboration tool for assessing risk of bias to determine the quality of included RCTs. This tool assesses the risk of selection bias, performance bias, detection bias, attrition bias, reporting bias, and other biases. Each trial is categorized on the basis of criteria determining the likelihood of potential threats to validity. Quality assessment was performed independently by 2 reviewers.

Results

Search Results

A total of 169 potentially relevant studies were identified in our initial literature search. After screening the titles and
abstracts of these studies, the full-length texts of 45 publications were retrieved and assessed for eligibility. Of these, 7 trials met our inclusion criteria and were included in our systematic review. No additional studies were identified through our manual search.

**Study Characteristics**

The earliest study we identified examining the use and efficacy of e-cigarettes for smoking cessation was published in 2010. Included studies had sample sizes ranging from 14 to 657 patients and treatment durations ranging from 1 day to 52 weeks (Table). Only 1 randomized controlled trial (RCT) examined the efficacy of an e-cigarette for smoking cessation among current smokers motivated to quit. Among the remaining 6 experimental studies, 2 randomized studies were conducted in current smokers (no information on motivation to quit), 1 randomized study among smokers not motivated to quit, and 3 nonrandomized studies among smokers not motivated to quit. Quality assessment was performed for 4 studies. The 3 nonrandomized studies were not evaluated with Cochrane criteria because they were uncontrolled and therefore of relatively poor quality. Not surprisingly, studies had a high risk of bias for allocation concealment and blinding (Table I in the online-only Data Supplement). Overall however, the risk of bias was low in other domains.

**Evidence for Use in Smoking Cessation**

An RCT from New Zealand conducted by Bullen et al recently published in *The Lancet* allocated 657 current smokers to 1 of 3 treatment arms: an e-cigarette (16 mg nicotine cartridge), a placebo e-cigarette, or a nicotine patch (21 mg nicotine per day). Participants were offered voluntary low-intensity behavioral counseling during the 12-week study period. At 6 months, biochemically validated continuous abstinence was reported in 7.3% of nicotine e-cigarette users, 5.8% of patch users, and 4.1% of placebo e-cigarette users (risk difference for nicotine e-cigarette versus patches, 1.51 [95% confidence interval (CI), –2.49–5.51]; for nicotine e-cigarettes versus placebo e-cigarettes, 3.16 [95% CI, –2.29–8.61]). Differences in adverse events were nonsignificant across treatment groups (incidence rate ratio for nicotine e-cigarettes versus patches, 1.05; 95% CI, 0.82–1.34; *P*=0.7), with 137 events among nicotine e-cigarette users, 119 events among patch users, and 36 events among placebo e-cigarette users. The study was underpowered to assess the superiority of e-cigarettes relative to the nicotine patch. Overall, however, the authors concluded that e-cigarettes, with or without nicotine, were modestly effective at helping smokers to quit.

Caponnetto et al conducted a prospective 12-month RCT in Italy examining smoking reduction and abstinence among 300 smokers not motivated to quit. This 3-arm trial compared e-cigarettes with 7.2 mg nicotine cartridges for 12 weeks (group A), 7.2 mg nicotine cartridges for 6 weeks followed by 5.4 mg nicotine cartridges for 6 weeks (group B), and nonnicotine e-cigarette cartridges for 12 weeks (group C). Results showed a reduction in daily cigarette smoking and exhaled carbon monoxide levels at each study visit across all 3 groups (*P*<0.001 versus baseline), with no differences between groups. With a few exceptions, there was no significant difference in quit rates between the study groups. At week 12, continuous abstinence was reported among 11% of group A, 17% of group B, and 4% of group C, whereas smoking reduction was observed in 22.3% of all participants. Similarly, at week 52, continuous abstinence was reported among 13% of group A, 9% of group B, and 4% of group C, and smoking reduction was reported among 10.3% of all participants. The most frequently reported adverse events included cough (26%), dry mouth (22%), shortness of breath (20%), throat irritation (17%), and headache (17%). No difference was found in the frequency of adverse events between 12 and 52 weeks. The authors conclude that e-cigarette use can cause the persistent modification of smoking behavior among smokers not intending to quit, resulting in important smoking reduction and abstinence.

Two randomized studies conducted by Dawkins et al and Bullen et al aimed to assess the impact of e-cigarettes on the short-term desire to smoke, rather than examining long-term cessation. Dawkins et al used mixed experimental methods, monitoring 86 smokers over the course of 1 day, during...
which participants were randomly allocated to 1 of 3 arms: using an e-cigarette (18 mg nicotine cartridge), using a placebo e-cigarette, or simply holding the e-cigarette. The authors concluded that e-cigarette use alleviated the desire to smoke and withdrawal symptoms 20 minutes after use. Similarly, Bullen et al^22^ conducted an RCT with a crossover design to measure the short-term desire to smoke, withdrawal symptoms, acceptability, pharmacokinetics properties, and adverse events...
among 40 participants randomized to use an e-cigarette (16 mg nicotine or placebo), a nicotine inhaler (six 10 mg nicotine cartridges), or a usual cigarette.22 Desire to smoke and withdrawal symptoms were assessed up to 60 minutes from the first puff of each product. Nicotine e-cigarette users reported less desire for a cigarette compared with nonnicotine e-cigarette users \((P=0.006)\). No significant difference was observed between the nicotine e-cigarette and nicotine inhaler, although participants reported a preference for the e-cigarette.

Several uncontrolled experimental studies have recently studied the use of an e-cigarette for smoking reduction and cessation. Polosa et al24 observed modifications in the smoking habits of 40 regular smokers not motivated to quit. Study participants were provided with e-cigarettes (7.25 mg nicotine per cartridge) over the course of 24 weeks and invited to attend 5 clinic visits. Thirteen participants reduced their cigarette consumption by 50%, 5 participants reduced it by 80%, and sustained abstinence was observed in 9 participants. In a follow-up study, Polosa et al25 reported that 12.5% of participants had sustained abstinence at 24 months. An 80% smoking reduction was observed \((P<0.001)\), with 27.5% showing a sustained 50% reduction in the number of cigarettes smoked per day. A second study by Caponnetto et al26 reported modifications in smoking behavior among 14 schizophrenic individuals using e-cigarettes (7.25 mg nicotine cartridges) over 12 months. Results showed 7 participants had reduced their cigarette consumption by at least 50%. Adverse events, including throat irritation, nausea, headaches, and dry cough, resolved spontaneously with time. Although these studies report promising reduction outcomes after e-cigarette use, all authors acknowledge the significant limitations of their study designs and call for more research before recommendations can be made.

Discussion

Our objective was to assess the efficacy and safety of e-cigarette use for smoking cessation. We found that, although the available literature on e-cigarettes is growing rapidly, much of it is centered on popular awareness and product acceptability. Only 1 study examined the efficacy of e-cigarettes for smoking cessation in a 3-arm, randomized study design, among smokers motivated to quit. Frequently reported adverse events were mild, often resolving with time. There is suggestive evidence that e-cigarettes may be at least as effective as existing NRTs. However, there remains a critical need for high-quality RCTs to examine this question in further detail.

Awareness and Use of E-Cigarettes

The exact number of current e-cigarette users is unknown, given that consumer data are withheld by private companies.9 However, the numbers of users and those aware of the product are steadily increasing. A US Centers for Disease Control survey reported that one third of American adults were aware of e-cigarettes in 2010, double the number who were aware of them in 2009.11 This estimate was even higher in current smokers, 50% of whom were aware of the existence of e-cigarettes. In addition, this survey revealed high intention to use e-cigarettes, especially among tobacco users compared with non-tobacco users \((odds ratio, 5.55; 95\% CI, 3.80–8.11)\).11 Results from a second survey examining e-cigarette use and product satisfaction among consumers showed that e-cigarettes are being used to assist in cigarette reduction and smoking cessation and to alleviate smoking-related health problems, despite a lack of regulatory approval as a smoking cessation therapy.14 Among smokers motivated to quit within the next 6 months, 48.5% had tried e-cigarettes (Figure 3).11 Widespread public interest in e-cigarettes has also stemmed an ever-growing Internet community of self-identified “vapers” who share their e-cigarette experiences in online discussion forums.27

The public demand for e-cigarettes has also gained the attention of Big Tobacco. In 2006, Reynolds American Inc, the second-largest tobacco company in the United States, purchased Conwood, the second-largest smokeless tobacco company in the United States, and has since launched 2 new e-cigarette brands, Vuse and Zonic.28,29 In 2011, Lorillard, the third-largest US tobacco company, purchased the brand Blu Ecigs for US $135 million.28 Most recently, Altria, one of the world’s largest tobacco corporations, is launching its first e-cigarette under the brand name MarkTen.30 Aside from the top 3 Big Tobacco companies, a number of independent e-cigarette manufacturers are currently operating in the United States. Among them, the top competitors include V2 Cigs, NJOY, and Green Smoke.28 In 2012, the e-cigarette market was estimated to generate between US $250 million and $500 million annually.28

Efficacy for Smoking Cessation

Study findings from Bullen et al13 provide suggestive evidence of the efficacy of e-cigarettes for smoking cessation. However, several methodological issues limit the conclusions they may generate. Power calculations overestimated the expected continuous abstinence, leading to an underpowered primary analysis. The study was also unable to examine the behavioral component of e-cigarettes because of the use of the nicotine patch as the comparator group and randomization in a 4:4:1 ratio to nicotine e-cigarettes \((n=289)\), nicotine patch \((n=295)\), or nonnicotine e-cigarette \((n=73)\). Other major problems included the lack of individual counseling and inadequate measurement of adherence. All participants were instructed to use the national quit line for telephone counseling; however, only a little more than one third of participants ever accessed the quit line. Self-reported adherence to allocated treatment was low; only 51% of participants in the nicotine e-cigarette group, 53% of those in the nonnicotine e-cigarette group, and 18% of those in the patch group remained adherent at the end of the treatment period. Additional concerns stem from the generalizability of these results to a North American context, given the sociodemographic characteristics of the study sample: one third of study participants were of New Zealand Māori origin, approximately half of whom had <12 years of education. The legal and social contexts of smoking in North America (banned indoor smoking, decline of a “smoking culture”) highlight the essential need for local, context-specific research.

Similarly, the additional included studies provided hypothesis-generating evidence of the efficacy of e-cigarettes for smoking reduction and cessation. However, most had serious methodological or study design limitations. Several studies were conducted in highly nongeneralizable populations, including smokers not motivated to quit and diagnosed with schizophrenia. Others, including Bullen et al22 and Dawkins...
et al, 19 had a study follow-up period consisting of a single day. Three of the included studies 24–26 were nonrandomized, and only 2 studies 13, 22 compared the efficacy of e-cigarettes with approved NRTs. At present, because of the poor quality of the available literature, no conclusion can be drawn about the efficacy of e-cigarettes for smoking cessation.

Health and Safety Concerns

Although the FDA issued a warning in 2009 in response to detectable levels of carcinogens found in e-cigarette cartridges, 31 these levels are similar to those found in approved NRTs, including the nicotine patch. 32 In addition, none of the chemicals that occur in tobacco combustion have been found in e-cigarette cartridges or vapor in greater than trace quantities. 32 Adverse events reported in the included studies, typically consisting of throat and mouth irritation, cough, and nausea, were relatively minor and often were found to be self-resolving in studies with both short- and long-term (52-week) follow-up. There were no reported serious adverse events attributable to e-cigarette use. The current available evidence suggests that e-cigarettes are less harmful than tobacco cigarettes. However, e-cigarettes remain unregulated, and product contents may vary drastically between devices and manufacturer brands. Product variability will therefore continue to limit claims of safety and reliability until e-cigarette regulations are introduced to standardize device contents and characteristics.

E-Cigarette Regulation

E-cigarettes have been the target of much debate concerning the regulatory mechanisms that govern their distribution. The FDA allows the over-the-counter sale of nicotine and nonnicotine e-cigarettes, both of which have been available since 2007. In 2010, the e-cigarette brand NJOY sued the FDA to prevent e-cigarettes from being regulated as a drug or therapeutic device. The US Court of Appeals for the DC Circuit determined that e-cigarettes could be regulated as tobacco products and therefore would not fall under the regulation of drugs or devices, with the condition that they are not marketed for therapeutic purposes. 10 The FDA continues to monitor compliance with this stipulation and has issued warning letters to several distributors for claiming their products can successfully help their users to quit smoking. 33 Presently, the manufacturers and distributors of e-cigarettes appear unwilling to conduct the research necessary to clarify the potential role of e-cigarettes in smoking cessation.

In contrast to current US legislation, health officials around the world have responded to e-cigarettes with more restrictive product regulations governing their distribution. Canada, for instance, considers nicotine e-cigarettes to fall under the Food and Drug Act’s Medical Device Regulations, requiring scientific evidence supporting their safety, quality, and efficacy for their intended use. 34 Because no conclusive studies have been conducted to this effect, nicotine e-cigarettes are not currently authorized for sale in Canada. However, nonnicotine e-cigarettes, which do not come under the regulation of the Food and Drug Act, may be sold to adults at the same points of sale as conventional cigarettes, provided that these brands do not make health or smoking cessation claims. 35 Britain has recently determined that e-cigarettes will be licensed as medication beginning in 2016, when new tobacco laws will be introduced. 36 This licensing will ensure that e-cigarette use is regulated and will restrict access to minors. In New Zealand, Denmark, and Austria, e-cigarettes are already classified as medication and are subject to regulation. 36, 37 In Brazil, Norway, and Singapore, e-cigarettes are banned from sale entirely. 38 Many other countries have implemented restrictions on their sale, import, marketing, and use. Government officials in France, for example, announced their intention to ban e-cigarette use in public spaces. 39 Without rigorous research to support their claims, it remains difficult for governments and health policy makers to enact evidence-based product restrictions and regulations.
Ethical Considerations

The growing ubiquity of e-cigarettes lends itself to ethical scrutiny. Many have expressed concern about the potential for e-cigarettes to act as a “gateway” to cigarette smoking.19,20 Unlike other NRTs, e-cigarettes provide a recreational function and could feasibly entice unintended product users (eg, nonsmokers and youth) to engage in smoking-like behavior when they otherwise would not. However, it is unclear how many youth or nonsmokers are purchasing these products.32

Another concern relates to the potential of e-cigarettes to interfere with large-scale smoking cessation efforts. E-cigarettes retain the most powerful identifier of cigarettes, the production of smoke, which brings to mind a recent public smoking culture.41 Their use could undermine years of antitobacco efforts, which tobacco control agencies have fought hard to institutionalize. In addition, the promotion of “safe alternatives” to cigarette smoking may also displace smokers’ addiction, the lack of research examining the safety and efficacy of e-cigarettes is concerning. At present, there is genuine medical uncertainty about the therapeutic merits of e-cigarettes. Consequently, their study lends itself well to further research. Rigorous scientific data are urgently needed to determine the relative potential of e-cigarettes to aid in smoking cessation compared with available therapies.

Conclusions

Given their increasing availability and use across the United States and Canada, particularly in the context of smoking cessation, the lack of research examining the safety and efficacy of e-cigarettes is concerning. At present, there is genuine medical uncertainty about the therapeutic merits of e-cigarettes. Consequently, their study lends itself well to further research. Rigorous scientific data are urgently needed to determine the relative potential of e-cigarettes to aid in smoking cessation compared with available therapies.

Source of Funding

This study was supported by a Knowledge Synthesis grant from the Canadian Institutes of Health Research (CIHR, grant number KRS-134302).

Disclosures

Dr Eisenberg has received funding from Pfizer Canada Inc to conduct the Evaluation of Varenicline (Champix) in Smoking Cessation for Patients Post-Acute Coronary Syndrome (EVITA) trial (NCT00794573) of varenicline versus placebo after acute coronary syndrome. The other authors report no conflicts.

References

20. Deleted in proof.
Clinical Perspective

Electronic cigarettes (e-cigarettes) are currently not licensed to be sold as smoking cessation aids in either the United States or Canada. However, e-cigarettes are rapidly growing in popularity among smokers attempting to quit. We reviewed the available data on the efficacy and safety of e-cigarettes for smoking cessation and considered issues relevant to the context in which they are used, including product awareness and attitudes. Most research findings revealed a reduction in cigarette consumption with e-cigarette use, regardless of nicotine content. However, studies had various limitations, including very small sample sizes and short follow-up periods (eg, 1 day), or included smokers not motivated to quit. The authors of one randomized controlled trial concluded that e-cigarettes may be as effective as the nicotine patch. However, methodological considerations, including an underpowered primary analysis, limit the robustness of these results. In addition, there remains a lack of data regarding the long-term safety of e-cigarette use. Until results from large, generalizable, randomized controlled trials become available, the efficacy and safety of e-cigarettes for smoking cessation remain uncertain, particularly in light of variable product restrictions and regulations. Clinicians who are asked to comment on the efficacy of e-cigarettes for smoking cessation should err on the side of caution and recommend proven smoking cessation therapies, including nicotine replacement therapies, bupropion, and varenicline.
Electronic Cigarettes in North America: History, Use, and Implications for Smoking Cessation
Caroline Franck, Talia Budlovsky, Sarah B. Windle, Kristian B. Filion and Mark J. Eisenberg

Circulation. 2014;129:1945-1952
doi: 10.1161/CIRCULATIONAHA.113.006416
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2014 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/129/19/1945

Data Supplement (unedited) at:
http://circ.ahajournals.org/content/suppl/2014/05/13/129.19.1945.DC1

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/
Supplemental Table 1. Cochrane risk of bias assessment of randomized experimental studies evaluating the efficacy and/or safety of e-cigarettes for smoking cessation.

<table>
<thead>
<tr>
<th>Domain</th>
<th>Adequate sequence generation</th>
<th>Allocation concealment</th>
<th>Blinding</th>
<th>Incomplete outcome data addressed</th>
<th>Free of selective outcome reporting</th>
<th>Free of other bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bullen et al. (2013)</td>
<td>Low</td>
<td>High</td>
<td>High</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Caponnetto et al. (2013)</td>
<td>Low</td>
<td>Low</td>
<td>Unclear</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Dawkins et al. (2012)</td>
<td>Unclear</td>
<td>High</td>
<td>High</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Bullen et al. (2010)</td>
<td>Low</td>
<td>High</td>
<td>High</td>
<td>Low</td>
<td>Low</td>
<td>High</td>
</tr>
</tbody>
</table>