

E-cigarettes and Smoking Cessation in Real World and Clinical Settings: A Systematic Review and Meta-Analysis

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Appendix (Web Only)

DETAILED DESCRIPTION OF STUDIES IN THE SYSTEMATIC REVIEW

Cohort Studies of Real World Use of E-cigarettes

Studies with Control Groups, E-cigarette Use Assessed at Baseline

Borderud et al.¹ surveyed 1,074 cancer patients enrolled in a tobacco treatment program at Memorial Sloan Kettering Cancer Center from January 2012 to December 2013 to evaluate e-cigarette use at enrollment and its association with self-reported seven-day smoking abstinence 6-12 months after initial enrollment in the treatment program. Patients reporting any tobacco use in the past 30 days were recruited from all oncology clinics. Among patients who were available for follow-up (of 781 eligible for follow-up, excluding 82 deceased patients and 285 patients lost to follow-up, cessation outcomes were available for 414 patients), controlling for nicotine dependence, past quit attempts, and cancer diagnosis, those who had used e-cigarettes (defined as having used an e-cigarette in the past 30 days at enrollment) had similar odds of smoking to those who had not used e-cigarettes (aOR 1.0, 95% CI 0.5-1.7). In an intention-to-treat analysis (more e-cigarette users were lost to follow-up than those who did not use e-cigarettes: 66.3% vs 32.4%), those who smoked e-cigarettes had significantly lower odds of having stopped smoking compared to those who had not used e-cigarettes (aOR 0.5, 95% CI 0.3-0.8). Strengths of this study include controlling for a number of confounders including nicotine dependence and past quit attempts, and that the authors conducted both a complete case analysis and an intention-to-treat analysis. Limitations include that this study only focuses on individuals who are interested in quitting smoking (given that participants were drawn from a tobacco treatment program), and only includes individuals with cancer, and therefore may not be generalizable to a broader population.

Choi and Forster² evaluated e-cigarette use and cigarette smoking in 1,379 U.S. young adults (aged 22-26) from the Minnesota Adolescent Community Cohort who were recruited to complete a baseline survey in 2010-2011 with follow-up one year later (2011-2012). Among cigarette smokers at baseline who reported past-30 day use of e-cigarettes (n=346), 11% quit cigarettes at follow-up (defined as self-reported abstinence from smoking for at least 30 days) compared to 17% of smokers who reported no past 30-day e-cigarette use, yielding aOR 0.93 (95% CI 0.19, 4.63) after adjusting for baseline cigarette consumption (7.9 cigarettes per day in the e-cigarette users versus 7.4 in the never e-cigarette users) and demographics. One limitation of the study is that the sample is all Midwestern young adults, most of whom were white race/ethnicity, may not be generalizable to a more broad audience including adults of all ages. Additionally, they did not control for level of nicotine dependence.

Grana et al.³ evaluated the association between e-cigarette use and quitting cigarettes in 949 current US smokers recruited from the Knowledge Networks (now GfK) probability-based web-enabled panel. Baseline data were collected from 1549 participants in 2011, of whom 1189 were smokers and 81% completed follow-up one year later; 949 participants were included in the final analysis. No inclusion or exclusion criteria were reported. They found that the 9.3% of cigarette smokers who reported past 30-day use of e-cigarettes at baseline had lower odds of quitting cigarettes at one year follow-up compared to those who had not used e-cigarettes at baseline (aOR 0.76, 95% CI 0.36-1.60) when controlling for quit intention, cigarette consumption, and nicotine dependence. Quitting was defined as response of “Yes, I do not smoke now” to the question “Have you ever tried to quit smoking?” and reporting no use of cigarettes within the past 30 days. Strengths included controlling for potential confounding factors such as cigarettes smoked per day and nicotine dependence and follow-up over one year. Limitations included that frequency and duration of e-cigarette use were not assessed, therefore it cannot be determined whether

those who reported past 30-day use at baseline had just experimented with e-cigarettes once, or whether they were regular users. Additionally, quit rates were from participant self-report, and it is not clear what duration of cigarette abstinence represented quit.

Prochaska and Grana⁴ studied 956 adult daily smokers (at least five cigarettes per day) with serious mental illness recruited during acute psychiatric hospitalization between 2009-2013 in the San Francisco Bay Area. Participants were part of a randomized clinical trial evaluating brief and extended smoking cessation treatment (involving nicotine replacement therapy and cognitive behavioral counseling) compared to usual care. Exclusion criteria included non-English speaking, medical contraindications to NRT (such as pregnancy or recent myocardial infarction), and lack of capacity to consent. No participants used e-cigarettes in 2009, 1% percent of participants used e-cigarettes in 2010, 9% in 2011, 19% in 2012, and 25% in 2013. At 18-month follow-up, quitting (defined as past seven day point prevalence of tobacco abstinence through self-report and biochemical verification) was slightly, but not significantly, higher among those reporting e-cigarette use during the study period compared to those not reporting e-cigarette use (21% vs. 19%, $p=0.73$). A multivariate model controlling for demographics, study factors, psychiatric variables and tobacco-related variables found that e-cigarette use was associated with a non-significant increase in abstinence from cigarettes compared to no e-cigarette use (aOR 1.16, 95% CI 0.65-2.05). This study may not be generalizable to a broader audience given its focus on those with serious mental illness.

Al-Delaimy et al.⁵ surveyed 1,000 cigarette smokers aged 18-59 in California at baseline (2011-2012) and one year later. The data were drawn from the California Smokers Cohort, a longitudinal survey of current and former smokers. They found that among those who had ever used e-cigarettes (defined as those who reported that they “have used e-cigarettes” at baseline and follow-up), after controlling for level of addiction, intention to quit, smoking status, and demographics had significantly decreased odds of self-reported 30-day abstinence from cigarettes (aOR 0.41, 95% CI 0.18-0.93) compared to those who said that they “will never use e-cigarettes” at baseline and follow-up (note that individuals who said that they “might use e-cigarettes” at both baseline and follow-up and those who used e-cigarettes at one time point but not the other were excluded). Strengths of this study are that they asked about ever e-cigarette use at both baseline and follow-up. Limitations are that the extent of e-cigarette use was not assessed and that data was collected from smokers in just one state, so is not nationally representative. Additionally, the final multivariate analysis included only 368 participants, and it is not clear to what extent these participants were lost to follow-up, versus those who had incomplete or inconsistent data on e-cigarette use.

Harrington et al.⁶ recruited 979 hospitalized smokers at a tertiary care medical center, collecting data at baseline and follow-up six months later, between 2012 and 2013. Of the 825 individuals (84%) who had complete data at both times, 171 (21%) reported e-cigarette use at baseline, 247 (30%) at follow-up, and 98 (12%) at both times. At six months, 12.2% of the baseline current e-cigarette users reported quitting smoking, compared to 13.4% of those who did not report current e-cigarette use at baseline ($p=0.80$); this corresponds to an odds ratio of 0.90 (0.54-1.50). Limitations include that they do not report data on nicotine dependence and the patients are all from one hospital.

Hitchman et al.⁷ surveyed 1,643 current cigarette smokers in Great Britain in 2012 with one-year follow-up in 2013, and estimated the odds of quitting smoking among those who used e-cigarettes in general as well as by type of e-cigarette at follow-up (cigalikes [disposable e-cigarettes or e-cigarette refillable with pre-filled cartridges] or and tank devices [commercial kit refillable with liquids or a modular system]). Participants were recruited from an online panel managed by Ipsos MORI and the study sample was derived from a total of 4064 current smokers who completed the baseline survey, of whom 1759 (43%) completed follow-up and 1643 had complete data on key variables. Quitting smoking was defined as individuals who said they smoked cigarettes either daily or nondaily at baseline, but reported that they “do not smoke cigarettes” or “have stopped smoking completely” at follow-up. Controlling for strength of urges to smoke at baseline, motivation to stop smoking at baseline, and demographics, use of e-cigarettes at baseline was associated with a nonsignificant decrease in quitting smoking at follow-up (aOR 0.83, 95% CI 0.52-1.30). The outcome depended on the product used and use pattern: nondaily (19.8% of sample) and daily (6.5% of sample) cigalike users at follow-up had decreased odds of reporting having quit smoking compared to those who had not used e-cigarettes (0.36, 0.20-0.60 and 0.74, 0.39-1.42, respectively), as did nondaily tank users (4.3% of sample; 0.70, 0.29-1.68). In contrast, daily tank users (4.2% of the sample) had significantly increased odds of reporting having quit smoking at follow-up (2.69, 1.48-4.89). Strengths of this study include adjustment for confounders including dependence, and looking at the different types of e-cigarette use at

follow-up. Limitations include differential loss to follow-up, which could limit the generalizability of the results, and that the definition of quitting cigarettes did not specify for what span of time people were quit.

Using the same dataset as Hitchman et al.⁷, Brose et al.⁸ found that controlling for baseline nicotine dependence and demographics, daily or nondaily e-cigarette use at baseline was associated with a nonsignificant decrease in quitting smoking (aOR 0.73, 95% CI 0.48-1.09) compared to no e-cigarette use at baseline. Both nondaily (0.77, 0.49-1.21) and daily (0.62, 0.28-1.37) e-cigarette use showed this pattern of decreased quitting.

Manzoli et al.⁹ surveyed 236 e-cigarette only users (used at least 50 puffs weekly of e-cigarettes for six months), 491 cigarette smokers (at least one cigarette per day for the past six months), and 232 dual users of cigarettes and e-cigarettes (used e-cigarettes and cigarettes within the same week for the past six months) in Italy in 2013 and one year later. Subjects were recruited through general practitioners, e-cigarette shops, internet advertising, and social networks, and data was collected through structured questionnaires. Exclusion criteria were age less than 30 or over 75, pregnancy or breastfeeding, illicit drug use, major depression, severe allergies, angina, and past smoking-related major diseases. At one year, controlling for demographics, body mass index, alcohol use, self-rated health, medical comorbidities, and years of tobacco smoking, they found that odds of past 30-day smoking abstinence from cigarettes was lower, but not significantly, among dual users compared to cigarette smokers (aOR 0.83, 95% CI 0.53-1.29). Abstinence was verified in a random sample of 25% of those reporting cigarette abstinence using exhaled carbon monoxide. Limitations include that they did not control for nicotine dependence and that 30% of the baseline sample was lost to follow-up.

Pavlov et al.¹⁰ interviewed 3,073 cigarette smokers enrolled in a smoking cessation program at a primary care clinic in Toronto, Canada that provides behavioral counseling and NRT at enrollment and three months later (years of data collection not provided). Through the program, participants received up to 26 weeks of brief behavioral counseling and nicotine replacement therapy at no cost to them. They found that the 363 (12%) of participants who did not use e-cigarettes at enrollment but began using e-cigarettes during participation in the program had significantly decreased odds of reporting quitting smoking compared to those who did not start using e-cigarettes (OR 0.68, 95% CI 0.54-0.87). Strengths of this study include that they looked at only individuals who began their e-cigarette use during their quit attempt. Limitations are that it is not clear whether the authors controlled for other factors such as demographics and smoking levels in their analyses, and that it was collected from a smoking cessation program in one city, so may not be generalizable to all smokers.

Sutfin et al.¹¹ followed 3,146 college students in North Carolina and Virginia at baseline and with five follow-up surveys from 2010 to 2013, and studied 271 current cigarette smokers at baseline, who had not tried an e-cigarette at baseline, and had data on current cigarette smoking and covariates at wave 6. They found that by wave 5, 43.5% had ever tried e-cigarettes (defined as any use in the past six months at any study wave). Controlling for baseline smoking frequency, lifetime other tobacco use, demographics, membership in Greek organization (i.e. fraternity or sorority), sensation seeking at baseline, and number of friends and family who smoke, trying e-cigarettes was associated with cigarette smoking at wave 6 (aOR 2.48, 95% CI 1.32-4.66), or, alternatively, the odds of quitting were 0.40 (0.21-0.76). Strengths of this study include that they only looked at individuals who initiated e-cigarette use between baseline and follow-up. Limitations include that it only looked at college students in two US states, therefore may not be generalizable to other groups, and that they did not control for nicotine dependence.

Studies with Control Groups, E-cigarette Use Assessed at Follow-up

Adkison et al.¹² surveyed 5939 current and former smokers (who smoked at least 100 cigarettes in their lifetime) age 18 or older in Canada, the United States, the United Kingdom, and Australia as part of the International Tobacco Control Four-Country Survey at two different study waves one year apart (2008-2009 and 2010-2011). They found that 2.9% of the study population reported currently using e-cigarettes at the second study wave (2010-2011). People who were smokers at baseline (2008-2009) who were current e-cigarette users at follow-up (2010-2011) had a nonsignificant decrease in odds of having quit smoking at follow-up (OR 0.81, 95% CI 0.43-1.53) than people who were not using e-cigarettes at follow-up (OR obtained by contacting authors). Strengths of this study include data from a large number of participants from four different countries. Limitations include the lack of specific information on the extent of e-cigarette use, that e-cigarette use was assessed only at follow-up, and not controlling for confounders such as extent of cigarette consumption and nicotine dependence.

Vickerman et al.¹³ surveyed 2,758 adult callers to 6 U.S. state tobacco quitlines by telephone seven months after enrollment in quitline services from June 2011 to March 2012. They found that 11·3% of participants reported ever using e-cigarette for one month or more and 18·1% reported using or trying e-cigarettes for less than one month. Inclusion criteria for the study included being an adult tobacco user, consenting to evaluation follow-up at enrollment in quitline services, speaking English, providing a valid telephone number, and completing at least one intervention call with the quitline. Tobacco use data and demographics were collected at enrollment. The 30-day self-reported point prevalence of smoking abstinence at seven months was 21·7% in those who used e-cigarettes for one month or longer 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. The overall unadjusted odds of quitting cigarettes were 0·50 (95% CI 0·40-0·62) for those who had ever used e-cigarettes compared to those who never used e-cigarettes (calculated from the percentages provided in the paper), and the unadjusted odds of quitting for those who used e-cigarettes for one month or more compared to those who never used e-cigarettes was 0·61 (95% CI 0·45-0·83). These results are unadjusted for other variables associated with quitting cigarette smoking, and therefore the association may be different when adjusted. Additionally, participants were asked to recall their e-cigarette use at a seven-month assessment after enrollment in quitline services, therefore this is subject to recall bias.

Pearson et al.¹⁴ surveyed 2,123 current smokers in the U.S. participating in a web-based smoking cessation trial in 2012-2013 at recruitment and three month follow-up. The cessation trial randomized patients to a social network and/or to receive a free supply of NRT; the 2,123 participants in this study were those who completed three month follow-up from 3,408 participants that were originally randomized. At follow-up, 672 participants (32%) reported having used an e-cigarette to quit smoking cigarettes in the past three months. Adjusting for nicotine dependence, cigarettes per day, quitting-related variables, and demographics, those who had reported using e-cigarettes to quit at baseline had significantly decreased odds of 30-day smoking abstinence (aOR 0·68, 95% CI 0·53-0·87) compared to those who had not used e-cigarettes; when controlling for other cessation methods used during the three months of the study, the aOR was 0·77 (95% CI 0·59-1·00). Strengths included the adjustment for a number of quitting-related confounders such as dependence and use of NRT. Limitations include that this sample only looked at smokers that were participating in a cessation program, and therefore the results may not be generalizable to all smokers.

Biener and Hargraves¹⁵ assessed participant smoking status and e-cigarette use in two U.S. metropolitan areas (Fort Worth, Texas and Indianapolis, Indiana) in 2011-2012, with follow-up in 2014. They conducted a population-based survey of an address-based sample with data collection primarily through telephone. Of the original respondents to a survey, 1,675 were smokers and 1,374 (82%) agreed to be contacted for follow-up surveys; 695 participants were interviewed at follow-up (approximately 50%). Of participants completing follow-up, 111 (23 %) were intensive e-cigarette users (defined as daily e-cigarette use for at least one month at follow-up), 220 (29%) were intermittent e-cigarette users (defined as regular but not daily use for more than one month at follow-up), and 364 (48%) were either non-users of e-cigarettes or had tried e-cigarettes no more than twice. Controlling for baseline smoking level (heavy smokers were defined as smoking at least 20 cigarettes per day with the first cigarette within 30 minutes of waking) and demographics, intermittent e-cigarette users had a nonsignificant decrease in odds of quitting at follow-up (defined as self-reported abstinence from cigarettes for one month) compared to non-users/tryers (aOR 0·31, 95% CI 0·04-2·80) while intensive e-cigarette users significantly higher odds of quitting smoking up compared to non-users/tryers (6·07, 1·11-33·18). Strengths of this study include that e-cigarette users were separated by use patterns. Limitations include that e-cigarette use was only assessed at follow-up, only about half of their baseline sample was followed, and the sample is not nationally representative and therefore ability to generalize is unknown.

Shi et al.¹⁶ surveyed 2,454 US cigarette smokers in the 2010 Tobacco Use Supplement to the Current Population Survey who were re-interviewed 12 months later. E-cigarette use was only assessed at follow-up. They found that, controlling for baseline cigarette dependence and demographics, those who reported using e-cigarettes for quitting cigarettes at follow-up had significantly lower odds of 30-day abstinence from cigarettes compared to those who did not use any smoking cessation aid (aOR 0·44, 95% CI 0·24-0·79). Those who used a pharmaceutical smoking cessation aid (i.e. NRT or prescription medication) also had significantly lower odds of 30-day abstinence from cigarettes compared to those using no smoking cessation aid (OR 0·67, 95% CI 0·50-0·88). Strengths of this study include use of a nationally representative sample and controlling for nicotine dependence. Limitations include that it is unclear whether participants were lost to follow-up between baseline and follow-up data collection, and data on the extent of e-cigarette use was not reported.

Studies without control groups

Berg et al.¹⁷ surveyed 36 adult cigarette smokers (smoking greater than or equal to five cigarettes on at least 25 of the past 30 days). The participants were current smokers at the time of recruitment, and were recruited from an e-cigarette vendor in one U.S. city (Atlanta, Georgia) in 2013; thus, they were recruited at the time they purchased their first e-cigarette. They found that among the 26 individuals surveyed at 8-week follow-up, six (23%) self-reported 30 day abstinence from cigarettes; assuming that those lost-to follow-up all continued smoking cigarettes, the authors report a 30-day point prevalence abstinence from combustible cigarettes of 16.7% at 8-week follow-up. Strengths included that the length of time that participants used e-cigarettes was clear given that none had used e-cigarettes at the time of enrollment and information about use was collected at follow-up. Limitations include a small sample size, the use of a convenience sample recruited from an e-cigarette vendor, and the lack of a comparison group that did not use e-cigarettes.

Etter and Bullen¹⁸ recruited 1,329 adults to complete an online questionnaire posted on a smoking cessation website (Stop-Tabac.ch) from 2011-2013, of whom 773 provided contact information to participate in a follow-up study (n=477 completed one-month follow-up and n=367 completed one-year). The questionnaire was in English and French, and participants were noted to be from U.S., France, UK, Switzerland, and other countries; a link to the questionnaire was also sent to forums and e-cigarette websites to publish on their websites. Among participants who reported using e-cigarettes daily and smoking daily or occasionally at baseline, 11/50 (22%) reporting quitting smoking at one month follow-up and 16/35 (46%) reported quitting smoking at one year follow-up. This study does not report smoking status of individuals who used e-cigarettes regularly but not daily, whose smoking behaviors may differ from that of daily e-cigarette users. There was no comparison with smokers who were not using e-cigarettes. In addition, they had a small sample size for whom they evaluated quitting (50 at one month and 35 at one year); overall only 28% of the original 1329 participants completed the one year follow-up survey, posing a high risk of bias in the results.

Polosa et al.¹⁹ followed 71 adult smokers (18 years old and older) who were making their first purchase of e-cigarettes at one of seven different vape shops in Italy in 2013 for six and 12 months to monitor their cigarette consumption. At one year, 29/71 (41%) participants reported past 30-day cigarette abstinence, with 22/71 (31%) participants lost to follow-up. The authors reported that demographics, extent of cigarette smoking, and cigarette dependence were not associated with smoking status at 12 months. One strength of this study is that participants were followed for one year. Limitations include no comparator group who had not used e-cigarettes and the small sample size of the study. Because all e-cigarette users were recruited from vape shops, the results may not be generalizable to all e-cigarette users.

Cross-Sectional Studies of Real World Use of E-cigarettes

Studies with control groups

Brown et al.²⁰ surveyed 5863 adult smokers in England in 2009-2014 as part of the Smoking Toolkit Study (in which individuals are selected to complete face-to-face computer-assisted surveys with a trained interviewer using random location sampling). They 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 (defined as those who answered “I am still not smoking” when asked “how long did your most recent serious quit attempt last before you went back to smoking”) were significantly higher than smokers who had made a quit attempt in the past year using unassisted over the counter NRT or no smoking cessation aids (unadjusted OR 2.23, 95% CI 1.70-2.93 versus NRT; 1.38, 1.08-1.76 versus no aid). After adjustment for nicotine dependence, demographics, time since start of quit attempt, past-year quit attempts, abrupt vs gradual quitting, year, and interaction terms for between time since last quit attempt and time spent with urges and between time since last quit attempt and strength of urges to smoke, odds of self-reported abstinence remained significantly higher among smokers who had made a quit attempt using e-cigarettes than those who had used NRT (1.63; 1.17-2.27) or no smoking cessation aids (1.61; 1.19-2.18). Strengths of this study include controlling for a large number of confounders and use of a large nationally representative population. Limitations include that this study did not compare e-cigarettes to assisted NRT or report the relationship between quitting and e-cigarette use among all smokers who used e-cigarettes. Additionally, classification of self-reported abstinence as those who said they were “still not smoking” does not give a sense of the duration of having quit.

Christensen et al.²¹ surveyed 9,656 adults in the telephone-based Kansas Adult Tobacco Survey in 2012-2013. They found that 11.8% of participants had ever used an e-cigarette and 3.4% had used an e-cigarette at least once in the past month (defined as current e-cigarette use). Among ever and former cigarette smokers who had their last cigarette in the past five years, the odds of past-month cigarette abstinence was significantly lower for both ever (0.43, 95% CI 0.24-0.79) and current (0.16, 95% CI 0.07-0.36) e-cigarette users, controlling for demographics. Limitations include that it is not clear whether individuals who do not currently smoke cigarettes started e-cigarette use before or after quitting cigarettes, that the analyses did not control for nicotine dependence, and the sample is drawn from a single U.S. state.

McQueen et al. recruited 106 of 110 (96%) of eligible patients 19 years old or older with head and neck cancer to participate in an in-office electronic survey at an otolaryngology clinic in Alabama. Patients at all cancer stages were invited to participate, and only those with current or past daily tobacco use were enrolled. Total laryngectomy patients were excluded. Twenty-three (21.7%) of patients reported e-cigarette use as part of their quit program, and those who used e-cigarettes did not differ significantly from those who did not with respect to average age, sex, problem drinking (as defined by the Alcohol Use Disorders Identification Test), and socioeconomic variables. Nine of the e-cigarette users (39%) had successfully quit (defined as self-reported tobacco abstinence, including e-cigarettes), compared to 72.3% of the non-e-cigarette users (calculated OR 0.25 [95% CI 0.09-0.65]). Limitations include that these analyses are unadjusted, the definition of cessation is not clear, the sample is drawn from a single clinic with a very high percentage of Caucasian patients, and the definition of e-cigarette use may include individuals who have only used e-cigarettes once.

Studies without control groups

Siegel et al.²² surveyed 216 adults who had purchased Blu e-cigarettes online for the first time seven months earlier (during two weeks in 2009) via an online questionnaire. This sample was obtained by e-cigarette company Blu providing email addresses of customers that made purchases during its first continuous operation. Point prevalence of self-reported cigarette abstinence at six months after initial e-cigarette purchase was 31.0%; smoking abstinence was lower in those who were not using e-cigarettes at the time of the survey (26.8%), and highest in those with everyday use of e-cigarettes (54.2%). Limitations of this study include the very low response rate to the online survey (4.5% of the 4884 valid email accounts who were invited to participate), high likelihood of recall bias, and lack of comparison to individuals who were not using e-cigarettes to see how their cigarette abstinence rates compared.

Dawkins et al.²³ conducted an online survey of 1347 e-cigarette users from 33 different countries recruited from the websites of two e-cigarette brands (The Electronic Cigarette Company and Totally Wicked E-Liquid) in 2011-2012. When asked about tobacco consumption, 27/218 (12%) current smokers and 948/1123 (84%) former smokers reported that they had not smoked for several weeks or several months. Limitations of this study include the use of a convenience sample of consumers of two brands of e-cigarettes, risk of recall bias, and the lack of a comparison group that did not use e-cigarettes.

Gallus et al.²⁴ conducted an in-person survey of 3000 people 15 years of age and older in Italy in 2013. The data were collected through a survey on smoking conducted by DOXA (the Italian branch of the Worldwide Independent Network/Gallup International Association) across all Italian municipalities. They found that 5.6% had tried an e-cigarette in the past but were not regular users (determined by asking those who said they “have heard about e-cigarettes and have tried them” and “Do you regularly use e-cigarettes”) and 1.2% were regular e-cigarette users. Of the 36 participants who reported regular e-cigarette use, four (10.4%) said that they had quit smoking cigarettes. A strength of this study is that it uses a nationally representative sample of Italians. Limitations include the small number of regular e-cigarette users, the cross-sectional and self-reported nature of the data, and the lack of a comparison group for having quit smoking.

Tackett et al.²⁵ surveyed 215 adult e-cigarette store customers at four retail locations in the Midwestern U.S. in 2013 and found that 66% of the current e-cigarette users had quit smoking combustible cigarettes. (208/215 reported ever use of combustible cigarettes.) Self-reported cessation was verified biochemically with exhaled carbon monoxide. While it is not clear whether all of these individuals had initiated e-cigarette use prior to quitting combustible cigarettes, the fact that 86% of participants reported initiating e-cigarette use to quit smoking suggests that at least a large portion were still smoking combustible cigarettes when they started using e-cigarettes. Strengths of this study

include biochemical verification of smoking cessation. Limitations include that this was a convenience sample of e-cigarette store customers in one region of the U.S., the study was cross-sectional, and no assessment of non-users of e-cigarettes was done to compare quitting rates in a similar population.

Clinical Trials

Studies with control group not using e-cigarettes

Bullen et al.²⁶ conducted a randomized controlled trial of providing e-cigarettes for cessation compared to usual care (providing a coupon that could be redeemed at a pharmacy for NRT) in New Zealand. They recruited 657 adult cigarette smokers interested in quitting from 2011 to 2013 through newspaper advertisements; participants were randomized to receive nicotine e-cigarettes, nicotine patches, or no-nicotine e-cigarettes. Exclusion criteria included pregnant and breastfeeding women, people using cessation medications or in a smoking cessation program, those reporting a heart attack, stroke, or severe angina in the past two weeks, those with poorly controlled medical disorders, allergies, or other chemical dependence. Participants were also given access to telephone-based cessation support, however fewer than 10% of participants used it. Baseline characteristics were similar among treatment groups. The primary outcome was continuous smoking abstinence six months after their quit day, defined as self-reported abstinence during the entire six-month period, allowing five or fewer cigarettes total during this time, verified by exhaled carbon monoxide measurement. Among those randomized to receive 16 mg e-cigarettes for smoking cessation, 7.3% maintained abstinence from conventional cigarettes at six months, which was not significantly higher than those receiving a 21 mg nicotine patch (5.8%; RR 1.26, 95% CI 0.68-2.34) or e-cigarette containing no nicotine (4.1%; RR 1.77 (0.54-5.77)). A strength of this study is that it randomized participants to e-cigarettes and to standard of care therapy (NRT). Limitations included the fact that those randomized to NRT were mailed vouchers that could be redeemed for NRT patches at local pharmacies at no cost, whereas those in the e-cigarette group had the e-cigarette, battery, charger, and cartridges delivered to them. This difference may have biased the results against those in the NRT group, who had a higher loss to follow-up and withdrawal rate.

O'Brien et al.²⁷ conducted a secondary data analysis of data from 86 adults with mental illness (defined as self-report of taking a drug used to treat mental illness) who participated in Bullen et al.'s²⁶ trial in which they received either nicotine e-cigarettes (n=39), nicotine patches (n=36), or no-nicotine e-cigarettes (n=12). They found that 5% of those in the nicotine e-cigarette group quit smoking at six months, compared to 14% in the nicotine patch group and 0% in the no-nicotine e-cigarette group (p=0.25). Limitations include the small sample size, and the focus on adults with mental illness may limit generalizability to all smokers.

Hajek et al.²⁹ conducted a pilot study on 100 cigarette smokers by offering e-cigarettes to clients of Stop Smoking Services in London, UK in 2015. Clients also received weekly support and stop smoking medications including NRT and varenicline. 69% of clients accepted e-cigarettes, with 42% of them selecting tank systems and 58% selecting cig-a-like products. Participants were provided with e-cigarettes and refills for 4 weeks after their target quit date. At four week follow-up, 65% of those accepting e-cigarettes and 45% of those not using e-cigarettes had self-reported abstinence biochemically validated by exhaled CO. (The 2 participants with self-reported abstinence were not verified and were counted as not quit.) These results yield an RR of 1.44 (95% CI 0.94-2.21) for the association between e-cigarette use and quitting. Limitations of this study include that it was not randomized with the e-cigarette users self-selecting e-cigarettes, the sample size was small and limited to one geographic region, and the short follow-up period of 4 weeks.

Studies without control groups

Polosa et al.²⁸ conducted a prospective cohort study in 40 adult cigarette smokers recruited from staff of a hospital in Italy in 2010. Inclusion criteria included smoking at least 15 cigarettes per day for at least 10 years, and no interest in quitting cigarettes in the next 30 days. Exclusion criteria included history of alcohol or illicit drug use, major depression or other psychiatric conditions, recent myocardial infarction, and history of angina, hypertension, diabetes, severe allergies, or poorly controlled airways disease. Participants were given an e-cigarette kit and a four-week supply of 7.4 mg nicotine cartridges to use up to four cartridges/day. At six months, 27/40 participants were interviewed; nine (22.5%) had self-reported abstinence from cigarettes over the previous 30 days (verified by exhaled carbon monoxide). Polosa et al.²⁹ interviewed these patients again at 18 months and 24 months (23/40 participants available at the 18 and 24 month follow-ups). At 24 months, 5/40 (12.5%) of the participants had quit

smoking. Strengths of this study include the long follow-up period. Limitations include that they did not evaluate quitting rates among individuals not using e-cigarettes, and the authors reported frequent technical issues with malfunctioning of e-cigarettes. One of the authors (Polosa) was a consultant for the company that manufactured and supplied for free the e-cigarettes in this study.

Caponnetto et al.³⁰ conducted a randomized trial among 300 Italian adult smokers recruited from June 2010-February 2011 through newspaper advertisements. Inclusion criteria included smoking at least ten cigarettes per day for at least the past five years, age 18-70, in good general health, not currently attempting to quit smoking or wishing to do so in the next 30 days, and committing to follow the trial procedures. Exclusion criteria included symptomatic cardiovascular or respiratory disease, regular psychotropic medication use, current or past alcohol abuse, use of smokeless tobacco or NRT, and pregnancy or breastfeeding. One third of the participants were randomized to each intervention: (1) 12 weeks of treatment with a 7.2 mg nicotine e-cigarette, (2) 6 weeks of treatment with 7.2 mg nicotine e-cigarettes followed by 6 weeks of 5.4mg nicotine e-cigarettes and (3) 12 weeks of treatment with an e-cigarette not containing nicotine. There was no significant difference in having quit (defined as self-reported abstinence from tobacco smoking, verified by exhaled carbon monoxide measurements) at one year after enrollment among the three groups, with 13% for those using a constant dose of nicotine e-cigarettes, 9% for those using the tapering dose of nicotine e-cigarettes, and 4% of those using the non-nicotine e-cigarettes. (No P value was reported.) The one year follow-up was attended by 61% of the original sample, with 35-45% lost per each group. Strengths include randomization to e-cigarettes with or without nicotine. Limitations include the lack of a control group that did not use e-cigarettes and the authors report frequent e-cigarette device malfunctions.

Caponnetto et al.³¹ also studied 14 schizophrenic inpatients in Italy who smoked at least 20 cigarettes per day and were not intending to quit. Participants were given an e-cigarette kit and a 4-week supply of 7.4 mg nicotine cartridges to use up to four times a day. At one year follow-up, 2/14 (14%) participants had quit smoking (self-reported abstinence for the previous 30 days verified with exhaled carbon monoxide measurements). This study did not include a control group.

Ely³² recruited 44 individuals to participate in a smoking cessation program at a family practice clinic in rural northern Colorado that integrated e-cigarettes as an option in addition to standard smoking cessation interventions. Of 640 current smokers invited to participate in the study through a letter, 48 chose to participate and 44 completed the program. All participants were non-Hispanic/White, 57% had a high school education or less, and 66% were women. All participants were provided written information on BluCig and SmokeTip e-cigarettes with respect to cost, availability, and nicotine dosage options; and all participants used an e-cigarette at the start of the program, with 18 individuals also using bupropion or varenicline. After 6 months, 14/44 (32%) of participants were no longer using cigarettes or e-cigarettes (4/14 were also using either bupropion or varenicline), and 7/44 (16%) were using e-cigarettes but were no longer using cigarettes (four were also using bupropion). It is unclear what the definition of quitting was in this study or how it was determined. It is also unclear what the quit rates for the individuals not using e-cigarettes were in this smoking cessation program.

Adriaens et al.³³ studied 48 smokers (at least three years of smoking, at least 10 cigarettes/day) in Belgium who had no interest in quitting and had not previously used an e-cigarette from 2012-2013. Exclusion criteria included self-reported diabetes, severe allergies, asthma or other respiratory disease, psychiatric disease, dependence on chemicals other than nicotine, pregnancy, breastfeeding, hypertension, cardiovascular disease, current use of smoking cessation therapy, and prior e-cigarette use. Participants were recruited using advertisements both on university campuses as well as in the local newspaper. As part of a randomized controlled trial, the participants were divided into three groups, two of which received e-cigarettes and one did not for an eight-week laboratory-based study in which the effect of e-cigarettes on craving and withdrawal were evaluated. After these eight weeks, all participants were provided with e-cigarettes (specifically of the second-generation type, i.e. tank system) and with information on how to further purchase refills, and followed up for six months. Assuming that those lost to follow-up continued to smoke, they found that 21% of participants had stopped smoking at six months (verified using exhaled CO measurements). Strengths include biochemical verification of smoking status. Limitations include that there was no control group that did not use e-cigarettes during the 6-month follow-up period and the small sample size.

Humair et al.³⁴ conducted a prospective cohort study of 17 patients at an outpatient clinic of an urban university hospital in Switzerland who were offered and chose to use nicotine e-cigarettes for smoking cessation since 2013. A psychiatric disorder was present in 82% of the sample. E-cigarettes were offered to those who wished to reduce

tobacco use or failed to stop smoking with nicotine replacement therapy or stop-smoking medication. At one year, 41% of participants had self-reported tobacco abstinence. Limitations of this study include the lack of a control group, the small sample, and lack of clarity on how long the participants used e-cigarettes and how they acquired the e-cigarettes.

McRobbie et al.³⁵ studied 40 smokers intending to quit at a clinic in England. They were recruited through newspaper advertisements, and exclusion criteria included pregnancy, breastfeeding, current serious medical illness, and e-cigarette use for more than one week in the past.^{35,36} One week prior to their target quit date, and at the target quit date, they were provided with nicotine e-cigarettes (GreenSmoke with 2.4% nicotine) and followed weekly for the next four weeks. Of the 33 participants that used e-cigarettes at the end of the treatment period (all were provided e-cigarettes), 16 (48%) had biochemically verified abstinence from smoking (with exhaled carbon monoxide) during the previous week. Limitations include lack of a control group that did not use e-cigarettes, the short period of cigarette abstinence (seven days), and small sample size. It is unclear if the seven participants who were not using e-cigarettes at the end of the treatment period had any changes in their smoking behavior, and for what period of time this group used e-cigarettes.

Polosa et al.³⁷ conducted another cohort study in which they recruited 50 healthy smokers aged 18-60 who had smoked at least 15 cigarettes per day for at least ten years and were not interested in quitting cigarettes in the next 30 days. No participants reported a history of alcohol and illicit drug use, major depression or other psychiatric conditions. Recruitment was done through anti-smoking leaflets and a kiosk promoting smoking cessation services at a university hospital in Italy. Participants were provided with second-generation e-cigarettes (i.e. personal vaporizers) and permitted to use them up to a maximum of a half vial per day. After 24 weeks, 18/50 (36%) of participants reported past-30 day cigarette abstinence (verified with exhaled carbon monoxide levels); 12/50 participants were lost to follow-up (24%). Strengths include the verification of smoking status biochemically, and the use of the same type of e-cigarette by all participants. Limitations of this study include the lack of a comparator group of smokers not using e-cigarettes and the small sample size.

RISK OF BIAS ASSESSMENT

All studies included in the meta-analysis were assessed for bias, using the ACROBAT-NRSI tool³⁸ for observational studies and the Cochrane Risk of Bias Tool³⁹ for clinical trials. These criteria were operationalized for assessment of the specific studies using the following rules:

Observational studies

- Selection of study population
 - Low risk: e-cigarette users and non-users selected from same population
 - High risk: e-cigarette users and non-users selected from different populations or at different time periods
- Exposure measurement
 - Low risk: duration of e-cigarette use assessed, those who could have used e-cigarettes just once excluded from analyses
 - Unclear risk: definition of e-cigarette use could include individuals who used e-cigarettes only once
 - High risk: assessment of e-cigarette use during the study period done at follow-up, definition of e-cigarette use not provided
- Outcome assessment
 - Low risk: smoking cessation verified by biochemical methods
 - Unclear risk: smoking cessation assessed by self-report
 - High risk: definition of smoking cessation does not specify duration of abstinence from cigarettes, definition of smoking cessation not provided
- Measurement of confounders
 - Low risk: adjustment for many confounders, including nicotine dependence

- Unclear risk: adjustment for some confounders, but not nicotine dependence
- High risk: unadjusted analyses
- Adequate follow-up
 - Low risk: low loss to follow-up, follow-up time 6 months or greater in longitudinal studies
 - Unclear risk: follow-up time 3 months or less in longitudinal studies, unclear loss to follow-up
 - High risk: loss to follow-up >25%, differential loss to follow-up

Clinical trials
















- Selection bias
 - Low risk: participants randomized to e-cigarette use
 - High risk: participants self-selecting to use e-cigarettes
- Performance bias
 - Low risk: blinding during phases of study where possible
 - High risk: participants and personnel unblinded to intervention
- Detection bias
 - Low risk: use of objective measures to assess smoking cessation (e.g. biochemical verification)
 - High risk: use of self-report only to assess smoking cessation
- Attrition bias
 - Low risk: low loss to follow-up
 - High risk: high loss to follow-up or differential loss to follow-up
- Reporting bias
 - Low risk: no evidence of under-reporting of results
 - High risk: evidence of selective reporting of results

Table A1. Search strategy with specific search terms

electronic cigarette
e-cigarette
electronic nicotine delivery
1 or 2 or 3
stop
quit
cessation
abstain
abstinence
5 or 6 or 7 or 8 or 9
4 and 10

Table A2. Risk of Bias in Observational Studies (derived from ACROBAT-NRSI tool)³²						
Study	Selection of study population	Exposure measurement	Outcome assessment	Confounders	Adequate follow-up	Comments
Cohort Studies of Real World Use of E-cigarettes, E-cigarette Use Assessed at Baseline						
Borderud 2014 ⁴⁹						Exposure assessment of self-reported any past-30 day e-cigarette use may include those who have only used once; cessation measured as self-reported past 7 day abstinence; >25% lost to follow-up
Choi 2014 ²¹						Exposure assessment of self-reported any past-30 day e-cigarette use may include those who have only used once; cessation measured as self-reported past-30 day abstinence; did not control for nicotine dependence
Grana 2014 ²²						Exposure assessment of self-reported any past-30 day e-cigarette use may include those who have only used once; cessation measured as patient self-report of “I do not smoke now” and duration of abstinence is unclear
Prochaska 2014 ⁵⁷						Exposed participants defined as those who answered “e-cigarettes” to question about use of other tobacco products
Al-Delaimy 2014 ⁵²						Exposure assessment was done at baseline and follow-up but could still include those who have just tried e-cigarettes once; outcome assessment done by self-report; final analysis included only 368 participants, and it is not clear to what extent these participants were lost to follow-up, had incomplete or inconsistent data on e-cigarette use
Harrington 2015 ⁵³						Exposure assessment of self-reported any past-30 day e-cigarette use may include those who have only used once, unclear definition of quitting smoking; analysis did not control for confounders
Hitchman 2015 ⁴⁸						Exposure assessment of self-reported any e-cigarette use may include those who have only used once; quitting defined as “do not smoke cigarettes at all” or “stopped smoking completely” with no indication of duration; differential loss to follow-up
Manzoli 2015 ⁵⁶						Did not control for nicotine dependence; loss to follow-up of 30%
Pavlov 2015 ⁵⁰						Definition of e-cigarette use unclear; definition of quitting smoking was unclear; unclear if results controlled for confounders; 3-month follow-up time
Sutfin 2015 ⁵⁵						Exposure assessment of self-reported any past-6 month e-cigarette use may include those who have only used once; quitting derived from inverse of those reporting cigarette smoking; did not control for nicotine dependence

Study	Selection of study population	Exposure measurement	Outcome assessment	Confounders	Adequate follow-up	Comments
Cohort Studies of Real World Use of E-cigarettes, E-cigarette Use Assessed at Follow-up						
Adkison 2013 ²³						Unclear if current use of e-cigarettes could include those only having used e-cigarettes once; unclear what duration of quit was used as the outcome; OR derived from numbers provided by authors and therefore unadjusted
Vickerman 2013 ²⁴						Participants asked to recall e-cigarette use at follow-up, increasing risk of recall bias; cessation measured as self-reported past 30 day abstinence; OR derived from numbers provided by authors and therefore unadjusted
Pearson 2014 ⁵⁴						Exposure assessment of e-cigarette use may include those who have only used once; cessation measured as self-reported past 30 day abstinence; follow-up time 3 months
Biener 2015 ⁷						Outcome assessed as self-reported abstinence; only about 50% of baseline sample was followed
Shi 2015 ⁵¹						Exposure assessment of e-cigarette use may include those who have only used once; cessation measured as self-reported past 30 day abstinence; loss to follow-up unclear
Cross-Sectional Studies of Real World Use of E-Cigarettes						
Brown 2014 ¹⁸					n/a	Definition of e-cigarette use as having used an e-cigarette as part of a quit attempt may include individuals who only used e-cigarettes once; definition of quitting as “still not smoking” does not indicate duration of quit
Christensen 2014 ⁵⁸					n/a	Exposure assessment of e-cigarette use may include those who have only used once; cessation measured as self-reported past 30 day abstinence; did not control for any confounders besides demographics
McQueen 2015 ²⁸					n/a	Exposure assessment of e-cigarette use may include those who have only used once; cessation measured by self-report; did not control for any confounders
Overall Risk of Bias						
Low	18	2	2	9	7	
Unclear	0	14	9	4	3	
High	0	2	7	5	5	
Not applicable					3	
= low risk of bias, =unclear risk of bias, =high risk of bias, n/a = not applicable since cross-sectional study						

Table A3. Risk of Bias in Clinical Trials (using Cochrane Risk of Bias Tool) ³³							
Study	Selection bias	Performance bias	Detection bias	Attrition bias	Reporting bias	Other bias	Comments
Randomized Clinical Trial with Control Groups							
Bullen 2013 ¹⁴						none detected	Those randomized to NRT were mailed vouchers to redeem for NRT patches at no cost, whereas the e-cigarette group had the e-cigarette, battery, charger, and cartridges delivered to them. The NRT group had a higher loss to follow-up and withdrawal rate.
Non-Randomized Clinical Trial with Control Groups							
Hajek 2015 ²⁹						none detected	Participants were not randomized and had chosen to use e-cigarettes.
Overall Risk of Bias							
Low 	1	0	2	1	2	0	
High 	1	2	0	1	0	0	
 =low risk of bias,  =unclear risk of bias,  =high risk of bias							

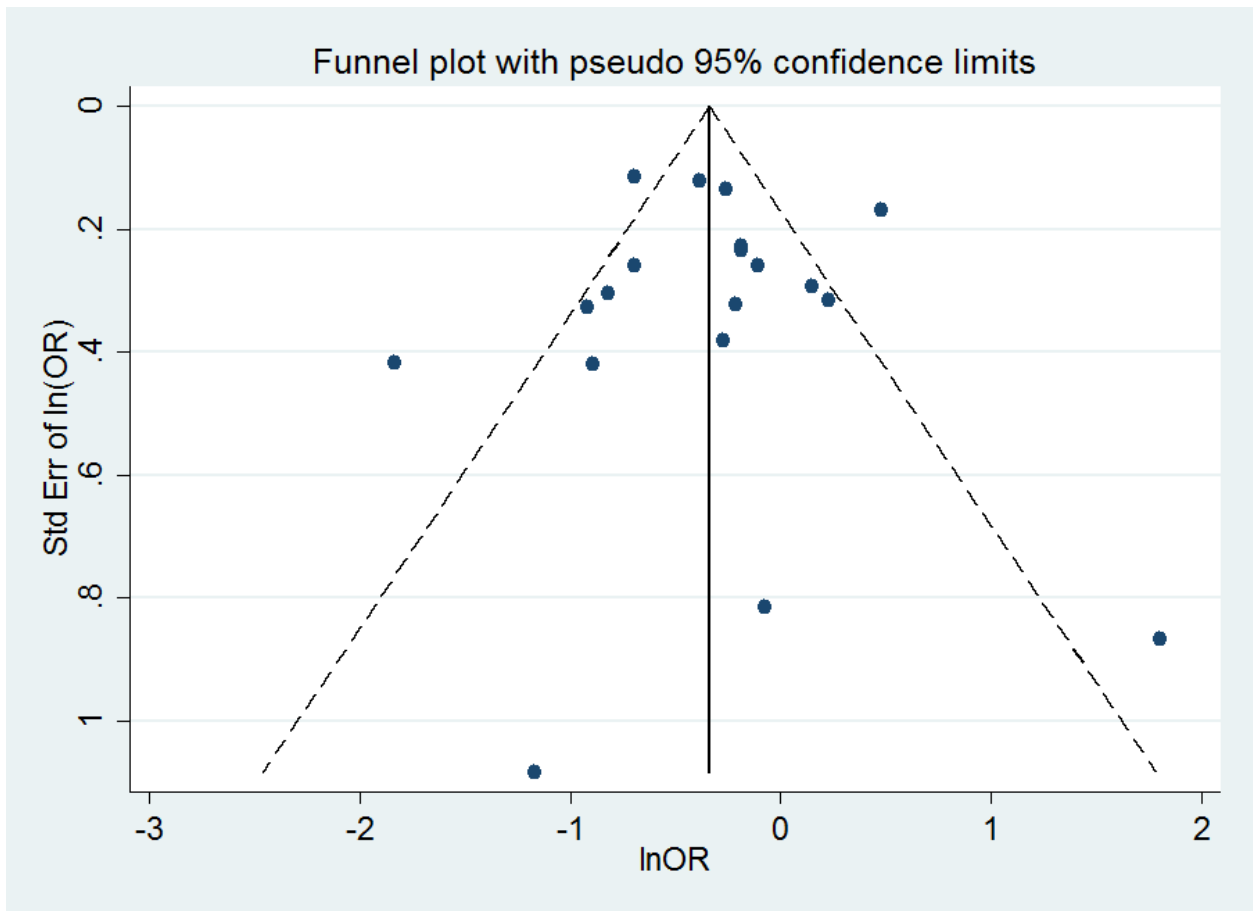


Figure A1. Funnel plot of studies included in meta-analysis

References

1. Borderud SP, Li YL, Burkhalter JE, Sheffer CE, Ostroff JS. Electronic cigarette use among patients with cancer. *Cancer* 2014; **120**(22): 3527-35.
2. Choi K, Forster JL. Authors' response. *Am J Prev Med* 2014; **46**(6): e58-9.
3. Grana RA, Popova L, Ling PM. A longitudinal analysis of electronic cigarette use and smoking cessation. *JAMA Intern Med* 2014; **174**(5): 812-3.
4. Prochaska JJ, Grana RA. E-cigarette use among smokers with serious mental illness. *PloS One* 2014; **9**(11): e113013.
5. Al-Delaimy WK, Myers MG, Leas EC, Strong DR, Hofstetter CR. E-Cigarette use in the past and quitting behavior in the future: a population-based study. *Am J Public Health* 2015; **105**(6): 1213-9.
6. Harrington KF, Cheong J, Hendricks S, Kohler C, Bailey WC. E-cigarette and traditional cigarette use among smokers during hospitalization and 6 months later. *Cancer Epidemiol Biomarkers Prev* 2015; **24**(4): 762.
7. Hitchman SC, Brose LS, Brown J, Robson D, McNeill A. Associations between e-cigarette type, frequency of use, and quitting smoking: findings from a longitudinal online panel survey in Great Britain. *Nicotine Tob Res* 2015; **17**(10):1187-94.
8. Brose LS, Hitchman SC, Brown J, West R, McNeill A. Is the use of electronic cigarettes while smoking associated with smoking cessation attempts, cessation and reduced cigarette consumption? A survey with a 1-year follow-up. *Addiction* 2015; **110**(7):1160-8.
9. Manzoli L, Flacco ME, Fiore M, et al. Electronic cigarettes efficacy and safety at 12 months: cohort study. *PloS One* 2015; **10**(6): e0129443.
10. Pavlov D, Ivanonva A, Hussain S, Selby P, Zawertailo L. Adoption of e-cigarettes during tobacco dependence treatment is associated with poorer quit outcomes. Presented at: Society for Research on Nicotine and Tobacco Annual Meeting 2015 February 25-28; Philadelphia, PA.
11. Sutfin EL, Reboussin BA, Debinski B, Wagoner KG, Spangler J, Wolfson M. The impact of trying electronic cigarettes on cigarette smoking by college students: a prospective analysis. *Am J Public Health* 2015: e1-e7.
12. Adkison SE, O'Connor RJ, Bansal-Travers M, et al. Electronic Nicotine Delivery Systems International Tobacco Control Four-Country Survey. *Am J Prev Med* 2013; **44**(3): 207-15.
13. Vickerman KA, Carpenter KM, Altman T, Nash CM, Zbikowski SM. Use of electronic cigarettes among state tobacco cessation quitline callers. *Nicotine Tob Res* 2013; **15**(10): 1787-93.
14. Pearson JL, Stanton CA, Cha S, Niaura RS, Luta G, Graham AL. E-Cigarettes and smoking cessation: insights and cautions from a secondary analysis of data from a study of online treatment-seeking smokers. *Nicotine Tob Res* 2015; **17**(10):1219-27.
15. Biener L, Hargraves JL. A longitudinal study of electronic cigarette use among a population-based sample of adult smokers: association with smoking cessation and motivation to quit. *Nicotine Tob Res* 2015; **17**(2): 127-33.
16. Shi Y, Pierce J, White M, et al. E-cigarette use, smoking cessation, and change in smoking intensity in 2010/2011 TUS-CPS Longitudinal Cohort. Presented at: Society for Research on Nicotine and Tobacco Annual Meeting 2015 February 25-28; Philadelphia, PA.
17. Berg CJ, Barr DB, Stratton E, Escoffery C, Kegler M. Attitudes toward e-cigarettes, reasons for initiating e-cigarette use, and changes in smoking behavior after initiation: a pilot longitudinal study of regular cigarette smokers. *Open J Prev Med* 2014; **4**(10): 789-800.
18. Etter JF, Bullen C. A longitudinal study of electronic cigarette users. *Addict Behav* 2014; **39**(2): 491-4.
19. Polosa R, Caponnetto P, Cibella F, Le-Houezec J. Quit and smoking reduction rates in vape shop consumers: a prospective 12-month survey. *Int J Environ Res Public Health* 2015; **12**(4): 3428-38.
20. Brown J, Beard E, Kotz D, Michie S, West R. Real-world effectiveness of e-cigarettes when used to aid smoking cessation: a cross-sectional population study. *Addiction* 2014; **109**(9): 1531-40.
21. Christensen T, Welsh E, Faseru B. Profile of e-cigarette use and its relationship with cigarette quit attempts and abstinence in Kansas adults. *Prev Med* 2014; **69**: 90-4.
22. Siegel MB, Tanwar KL, Wood KS. Electronic cigarettes as a smoking-cessation tool results from an online survey. *Am J Prev Med* 2011; **40**(4): 472-5.
23. Dawkins L, Turner J, Roberts A, Soar K. 'Vaping' profiles and preferences: an online survey of electronic cigarette users. *Addiction* 2013; **108**(6): 1115-25.
24. Gallus S, Lugo A, Pacifici R, et al. E-cigarette awareness, use, and harm perceptions in Italy: a national representative survey. *Nicotine Tob Res* 2014; **16**(12): 1541-8.

25. Tackett AP, Lechner WV, Meier E, et al. Biochemically verified smoking cessation and vaping beliefs among vape store customers. *Addiction* 2015; **110**(5): 868-74.
26. Bullen C, Howe C, Laugesen M, et al. Electronic cigarettes for smoking cessation: a randomised controlled trial. *Lancet* 2013; **382**(9905): 1629-37.
27. O'Brien B, Knight-West O, Walker N, Parag V, Bullen C. E-cigarettes versus NRT for smoking reduction or cessation in people with mental illness: secondary analysis of data from the ASCEND trial. *Tob Induc Dis* 2015; **13**(1): 5.
28. Polosa R, Caponnetto P, Morjaria JB, Papale G, Campagna D, Russo C. Effect of an electronic nicotine delivery device (e-Cigarette) on smoking reduction and cessation: a prospective 6-month pilot study. *BMC Public Health* 2011; **11**: 786.
29. Polosa R, Morjaria JB, Caponnetto P, et al. Effectiveness and tolerability of electronic cigarette in real-life: a 24-month prospective observational study. *Intern Emerg Med* 2014; **9**(5): 537-46.
30. Caponnetto P, Campagna D, Cibella F, et al. Efficiency and Safety of an eElectronic cigAreTte (ECLAT) as tobacco cigarettes substitute: a prospective 12-month randomized control design study. *PloS One* 2013; **8**(6): e66317.
31. Caponnetto P, Auditore R, Russo C, Cappello GC, Polosa R. Impact of an electronic cigarette on smoking reduction and cessation in schizophrenic smokers: a prospective 12-month pilot study. *Int J Environ Res Public Health* 2013; **10**(2): 446-61.
32. Ely J. Evaluation of the use of electric cigarettes in a rural smoking cessation program. Greeley, Colorado: University of Northern Colorado; 2013. Available from: <https://digarch.unco.edu/islandora/object/cogru%3A4161>.
33. Adriaens K, Van Gucht D, Declerck P, Baeyens F. Effectiveness of the electronic cigarette: An eight-week flemish study with six-month follow-up on smoking reduction, craving and experienced benefits and complaints. *Int J Environ Res Public Health* 2014; **11**(11): 11220-48.
34. Humair JP, Tango R. Can e-cigarette help patients to reduce or stop smoking in primary care practice? *J Gen Int Med* 2014; **29**: S480-S.
35. McRobbie H, Goniewicz M, Phillips A, Myers Smith K, West O, Hajek P. Effects of the use of electronic cigarettes with and without concurrent smoking on acrolein delivery. Presented at: Society for Research on Nicotine and Tobacco Annual Meeting 2014 February 5-8; Seattle, WA.
36. McRobbie H, Bullen C, Hartmann-Boyce J, Hajek P. Electronic cigarettes for smoking cessation and reduction. *Cochrane Database Syst Rev* 2014; **12**: Cd010216.
37. Polosa R, Caponnetto P, Maglia M, Morjaria JB, Russo C. Success rates with nicotine personal vaporizers: a prospective 6-month pilot study of smokers not intending to quit. *BMC Public Health* 2014; **14**: 1159.
38. Sterne J, Higgins J, Reeves B. on behalf of the development group for ACROBAT-NRSI. A cochrane risk of bias assessment tool: for non-randomized studies of interventions (ACROBAT-NRSI), version 1.0. 0, 24 September 2014. Available from <http://www.riskofbias.info> [accessed November 7, 2015]
39. Higgins JP, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011; **343**: d5928.
40. McQueen N, Partington EJ, Harrington KF, Rosenthal EL, Carroll WR, Schmalbach CE. Smoking Cessation and Electronic Cigarette Use among Head and Neck Cancer Patients. *Otolaryngol Head Neck Surg* 2015; Published online Oct 30. doi: 10.1177/0194599815613279
41. Hajek P, Corbin L, Ladmore D, Spearing E. Adding E-Cigarettes to Specialist Stop-Smoking Treatment: City of London Pilot Project. *J Addict Res Ther* 2015; **6**(244): 2.