Published in final edited form as:

Ann Intern Med. 2018 May 01; 168(9): 613–620. doi:10.7326/M17-2048.

Association of Electronic Cigarette Use with Smoking Cessation Among Smokers Who Plan to Quit After a Hospitalization: A Prospective Study

Nancy A. Rigotti, MD^{1,2,3,4}, Yuchiao Chang, PhD^{2,4}, Hilary A. Tindle, MD, MPH⁵, Sara M. Kalkhoran, MD, MAS^{1,2,4}, Douglas E. Levy, PhD^{1,3,4}, Susan Regan, PhD^{1,2,4}, Jennifer H. K. Kelley, RN, MA^{1,3}, Esa M. Davis, MD, MPH⁶, Daniel E. Singer, MD^{2,4}

¹Tobacco Research and Treatment Center, Massachusetts General Hospital, Boston, MA

²Division of General Internal Medicine, Department of Medicine, Massachusetts General Hospital, Boston, MA

³Mongan Institute Health Policy Center, Massachusetts General Hospital, Boston, MA

⁴Department of Medicine, Harvard Medical School, Boston, MA

⁵Vanderbilt Center for Tobacco, Addiction and Lifestyle (ViTAL), Division of Internal Medicine, Department of Medicine, Vanderbilt University School of Medicine, Nashville, TN

⁶Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA

Abstract

Background: Many smokers report using electronic cigarettes (e-cigarettes) to help them quit smoking, but whether e-cigarettes aid cessation efforts is uncertain.

Objective: To determine whether e-cigarette use after hospital discharge by cigarette smokers who plan to quit and are advised to use evidence-based treatment is associated with subsequent tobacco abstinence.

Design: Secondary data analysis of a randomized controlled trial.

Setting: 3 hospitals

Participants: 1040 hospitalized adult cigarette smokers who planned to stop smoking, received tobacco cessation counseling in hospital, and were randomly assigned at discharge to a tobacco treatment recommendation (control) or to free tobacco treatment (intervention).

Measurements: Self-reported e-cigarette use (exposure) was assessed 1 and 3 months post-discharge; biochemically-validated tobacco abstinence (outcome) was assessed 6 months post-discharge.

Corresponding Author: Nancy A. Rigotti, MD, Tobacco Research and Treatment Center, Division of General Internal Medicine, Massachusetts General Hospital, 100 Cambridge St., Floor 16, Boston, MA 02114, Phone: 617 724 3548, Fax: 617 724 6774, nrigotti@partners.org.

Current Mailing Address for Authors: Drs. Rigotti, Chang, Kalkhoran, Levy, Regan, Singer, and Ms. Kelley: Division of General Internal Medicine, Massachusetts General Hospital, 100 Cambridge St., Suite 1600, Boston, MA 02114, Dr. Tindle: Vanderbilt Division of General Internal Medicine and Public Health, 2525 West End Avenue, Suite 370, Nashville, TN 37203, Dr. Davis: University of Pittsburgh Medical Center, 230 McKee Place, Suite 600, Pittsburgh, PA 15213

Results: 28% of participants used an e-cigarette within 3 months post-discharge. In an analysis of 237 propensity-score matched pairs, e-cigarette users were less likely than non-users to abstain from tobacco at 6 months (10.1% vs. 26.6%, risk difference -16.5%, 95%CI -23.3% to -9.6%). E-cigarette use appeared to be more negatively associated with quitting among intervention patients, who were given easy access to conventional treatment (7.7% vs. 29.8%, risk difference -22.1%, 95%CI -32.3% to -11.9%), than among control patients who only received treatment recommendations (12.0% vs. 24.1%, risk difference -12.0%, 95%CI -21.2% to 2.9%, $p=0.14$ for interaction).

Limitations: Patients self-selected e-cigarette use. Unmeasured confounding is also possible in an observational study.

Conclusions: During 3 months after hospital discharge, over a quarter of smokers attempting to quit used e-cigarettes, mostly to aid cessation. Few used e-cigarettes regularly, however. This pattern of e-cigarette use was associated with less tobacco abstinence at 6 months than among smokers who did not use e-cigarettes. Whether regular use of e-cigarettes aids or detracts from smoking cessation requires additional study.

Clinical Trial Registration: NCT01714323 (Registration for the parent RCT)

Keywords

Inpatients; hospitalization; smoking cessation; nicotine dependence; nicotine addiction; tobacco use; electronic cigarettes

Introduction

Electronic cigarettes (e-cigarettes) are battery-operated nicotine delivery devices producing an aerosol that users inhale (1). The use of an e-cigarette is often called vaping. Because the devices do not burn tobacco, users avoid exposure to the harmful products of combustion. However, users are exposed to the heated aerosol which generally includes a humectant (e.g., propylene glycol or vegetable glycerine), nicotine, and a flavoring agent. Small amounts of potentially toxic compounds such as volatile organic compounds and heavy metals have also been measured in e-cigarette aerosol.(2) E-cigarette use has increased dramatically since 2010.(3) Among adults, the products are primarily used by cigarette smokers, most of whom report that they use them to stop smoking or to reduce their health risks.(3–5)

The health risks and benefits of e-cigarettes are uncertain,(6) but the general scientific consensus is that cigarette smokers who completely switch to e-cigarettes are likely to reduce their tobacco-related health risks.(7–9) E-cigarettes should benefit smokers if they help them to quit conventional cigarettes, but whether e-cigarettes are effective cessation aids is uncertain due to a lack of sufficient high-quality data from randomized controlled trials.(10–12)

Meanwhile, e-cigarettes are readily available consumer products that are being used by smokers who are trying to quit and who may also be using evidence-based smoking cessation medications.(13, 14) Whether e-cigarette use in this context helps or harms a

smoker's odds of succeeding in quitting smoking is a critical question. The results of observational studies done to answer this question are summarized in several systematic reviews whose methods and conclusions vary.(10–12, 15) In one meta-analysis, smokers using e-cigarettes had a 28% lower odds of quitting smoking compared to smokers not using e-cigarettes,(15) but the analysis had several limitations.(16) Three other systematic reviews found the evidence from observational studies to be insufficient to make a definitive conclusion about the relationship between e-cigarette use and tobacco cessation.(10–12)

We addressed this question in a secondary analysis of data of a large randomized controlled trial of hospitalized smokers who planned to quit smoking after discharge. The trial compared the effectiveness of free evidence-based tobacco cessation treatment to standard care after hospital discharge. The analysis reported here examined whether e-cigarette use in the 3 months after discharge was associated with more or less tobacco abstinence at 6 months. The randomized design of the parent trial also allowed us to explore how the effect of e-cigarette use on cessation success varied by smokers' access to conventional smoking cessation treatment. We hypothesized that smokers with easy access to evidence-based tobacco cessation treatment might be less likely to use e-cigarettes during a quit attempt, and that this might moderate the relationship between e-cigarettes and cessation success.

Methods

Setting

We analyzed data from Helping HAND2, a two-arm, three-site randomized controlled trial that enrolled hospitalized cigarette smokers who planned to quit smoking and compared a post-discharge smoking cessation intervention vs. standard care. A detailed study protocol and main outcomes are published.(17, 18) The study, conducted from 2012–2015 at Massachusetts General Hospital (Boston, MA), North Shore Medical Center (Salem, MA), and the University of Pittsburgh Medical Center (Pittsburgh, PA), was approved by Institutional Review Boards of Partners HealthCare and the University of Pittsburgh and registered with the National Institutes of Health Clinical Trials Registry (NCT01714323). All hospitals prohibited the use of tobacco products and e-cigarettes in the hospital.

Funding source

The project was funded by NIH/NHLBI grant #1R01-HL11821. The funding organization had no role in the study design; the collection, analysis, and interpretation of the data; or the decision to approve publication of the finished manuscript.

Subjects

Each hospital routinely identified patients' smoking status at admission. A tobacco treatment counselor visited inpatients identified as smokers to offer brief bedside counseling and encourage nicotine replacement therapy use in the hospital. Counselors did not recommend e-cigarette use to smokers. Rather, when asked, they advised that e-cigarettes' safety and efficacy were unknown, and they encouraged smokers to use tobacco cessation medications approved by the U.S. Food and Drug Administration. Adult (≥ 18 years old) daily smokers

who received the inpatient counseling session and planned to quit smoking after discharge were eligible for the study.

Interventions

Patients were randomized to Standard Care (control) or Sustained Care (intervention) for post-discharge care. Standard Care participants received advice to call a free telephone quitline and an individualized post-discharge medication recommendation. Sustained Care participants instead received an intervention that included a free 30-day supply of their choice of FDA-approved cessation medication at discharge (refillable for a total of 90 days) and 5 tailored automated telephone calls using interactive voice response technology over 90 days. At each automated call, recorded messages tailored to participants' responses encouraged participants to stay quit or make another quit attempt and offered to transfer smokers directly to a telephone quitline where they could receive counseling or refill a study medication.

Measures/Assessments

Baseline measures included demographic factors (age, gender, race/ethnicity, education), health insurance, nicotine dependence (cigarettes/day, time to first cigarette after awakening(19)), prior use of tobacco cessation treatment, perceived importance of and confidence in quitting (5-point Likert scales), post-discharge intention to quit (plan to stay quit vs. plan to try to stay quit), presence of another smoker at home, a screen for alcohol abuse (Alcohol Use Disorders Identification Test; AUDIT-C), past 30-day illicit drug use, and depression and anxiety symptoms (Patient Health Questionnaire; PHQ-4).(20, 21) Hospital records provided primary discharge diagnosis and length of stay.

Participants were called 1, 3, and 6 months after discharge to assess past 7-day abstinence from tobacco products and current use of smoking cessation treatments. Participants received \$20 per completed survey. The primary outcome was biochemically-validated past 7-day tobacco abstinence at 6 months, but the measure permitted e-cigarette only use. To verify self-reported abstinence at 6 months, patients were asked to provide a mailed saliva sample to assay for cotinine, a nicotine metabolite, and compensated \$50 for the sample.(22) Participants using nicotine-replacement therapy or e-cigarettes were asked to provide an in-person measurement of expired-air carbon monoxide and compensated \$50 for the sample. Self-reported abstinence was verified if saliva cotinine was ≤ 10 ng/ml or carbon monoxide was <9 ppm.(23)

E-cigarette use in the past 30 days was assessed at baseline ("In the 30 days before you entered the hospital, did you use an electronic cigarette [or e-cigarette]?"). At 1, 3, and 6-month follow-ups, participants were asked about any e-cigarette use since hospital discharge, past 30-day use, and past 7-day use. Additional questions about the pattern and reason for e-cigarette use were added to our assessments in August 2013, 9 months after the start of the 20-month enrollment, when it became clear that e-cigarette use in the community was increasing.(24) New questions asked about the number of days of e-cigarette use in the past 7 days and past 30 days and asked users about their primary reason for e-cigarette use.

Response options were: help me to quit smoking cigarettes, give me something to use in non-smoking area, use a less risky product than cigarettes, or other.

Analysis

The goal was to examine the association of e-cigarette use in the 3 months after discharge with tobacco abstinence at 6 months. To avoid misclassification of e-cigarette use, primary analyses were limited to the subset of study participants who completed post-discharge e-cigarette assessments. The primary dependent variable was biochemically-validated 6-month abstinence. Participants with missing or non-validated tobacco use outcomes were counted as smokers.

The independent variable of interest was e-cigarette use. Because different patterns of e-cigarette use may have different relationships with tobacco cessation, we calculated the prevalence of any e-cigarette use since discharge, past 30-day use, and past 7-day use at the 3-month follow-up. We also combined data from the 1 and 3 month follow-ups to calculate persistent use, defined as past 7-day (or past 30-day) use at both 1 and 3 months.

To adjust for baseline differences between participants who did and did not use e-cigarettes in the 3 months after discharge, we conducted a propensity score analysis, matching participants on study arm and their propensity to use e-cigarettes after discharge in a 1:1 ratio. We included baseline variables of age, sex, race, education level, cigarettes per day, time to first cigarette, e-cigarette use in the 30 days before hospital admission, importance of quitting, confidence in ability to quit, alcohol use, marijuana use in the past year, smoking-related disease as primary discharge diagnosis, baseline PHQ-4, hospital length of stay, use of medication/counseling after discharge, and study site in the propensity score models. We matched e-cigarette users (cases) to non-users (controls) on the logit scale of the propensity score and used calipers of width equal to 0.2 of the standard deviation.(29) Among all pairs of potential matches, we first calculated the number of possible matches for each case and allowed the one with the fewest match options to select first. We selected the control with the shortest distance to the case for the matched pair. We then repeated the process for all remaining cases. We reported the risk differences with 95% confidence intervals from the matched samples.

To examine whether the effect of e-cigarette use on smoking cessation varied by study arm, we repeated the analysis stratifying by study arm, and tested for an interaction between the effects of study arm and each e-cigarette measure.

In an attempt to quantify the impact of unmeasured potential confounding factors, we report the E-Value, which represents the minimum strength of association, on the risk ratio scale, that an unmeasured confounder would need to have with both the exposure (e-cigarette use) and outcome (smoking abstinence) to fully explain away exposure–outcome association, associated with each e-cigarette measure.(25)

Analyses were done using SAS version 9.4 (The SAS Institute, Cary, NC). The E-Value and 95% confidence interval were calculated using an online calculator provided by Dr. Tyler VanderWeele.(30) A two-sided p value of <.05 was considered statistically significant.

Results

The HH2 study enrolled 1357 smokers who were randomly assigned to Sustained Care (n=680) or Standard Care (n=677) after discharge. Follow-up rates were 81% (n=1100) at 1 month, 77% (n=1040) at 3 months, and 75% (n=1021) at 6 months and did not differ significantly by study arm. Participants lost to follow-up at 3 months were younger (mean age, 46 vs. 51 years; $p<0.001$) and less likely to have a smoking-related disease as primary discharge diagnosis (24% vs. 37%, $p<0.001$) but did not differ in cigarettes smoked per day. At 6 months, 69% of self-reported nonsmokers provided a sample for validation. Abstinence was confirmed in 73% of these samples (Sustained Care, 72%; Standard Care, 74%).

Electronic cigarette use

E-cigarette use in the 30 days prior to hospital admission was reported by 290 (21.4%) of 1357 participants. Pre-admission e-cigarette use did not differ significantly between intervention (20.7%) and control (22.0%) groups. Table 1 displays the prevalence of e-cigarette use among individuals who completed each follow-up survey. The rate of reporting any e-cigarette use after hospital discharge increased from 18.3% at 1 month to 28.0% at 3 months and 37.0% at 6 months ($p<0.001$), but current use at each follow-up was stable over time (16–17% for past 30-day use and 11–12% for past 7-day use), suggesting that different people were using e-cigs at different follow-ups. Persistent use, defined as e-cigarette use in the 7 or 30 days before both the current and previous follow-ups, was uncommon; only 5.6% and 9.0% of participants, respectively, did so at 1 and 3 months and only 3.6% and 5.5% of participants, respectively, did so at 1, 3 and 6 months. E-cigarette use was more frequent in the control group than the intervention group at 1 and 3 months.

At 3-month follow-up, 68% of the 178 e-cigarette users who were asked why they used an e-cigarette said that their primary reason was to quit smoking. Among the 164 participants who had used e-cigarettes in the past 30 days, 114 were asked about frequency of use, and they reported using e-cigarettes on a median of 10 days (inter-quartile range, 5–30). Among 83 of 117 participants who reported using an e-cigarette in the past 7 days at 3 months and were asked about frequency of use, the median was 5 days of the past 7 (inter-quartile range, 2–7).

Association with smoking cessation

Table 2 compares the characteristics of the participants who completed the 3-month follow-up assessment, stratified by their report of e-cigarette use in the 3 months after discharge. Among those who completed the 3-month follow-up survey, participants who did and did not use e-cigarettes differed by multiple demographic and tobacco use characteristics. These imbalances were reduced in the propensity score matched sample. Among the 286 participants reporting any e-cigarette use in the 3 months after discharge, we were able to find 237 participants who did not use e-cigarettes with a similar propensity score. Table 2 illustrates the similarity of the matched groups on baseline characteristics.

Table 3 presents the relationship between e-cigarette use at 3-month follow-up and smoking status at 6 months. In the propensity score-matched sample, participants who reported that

they had used any e-cigarette in the 3 months since hospital discharge were less likely to be biochemically abstinent at 6 months than individuals not using e-cigarettes (10.1% vs. 26.6%, risk difference -16.5%, 95% CI [-23.3%, -9.6%]). The E-Value for the observed difference was 4.7 (95% CI [2.9, 7.6]). The risk differences were consistently below 0 but were not statistically significant for alternative measures of e-cigarette use after discharge (past 30-day or past 7-day use at 3 months, past 30-day or past 7-day use at both 1 and 3 months). In contrast, there was almost no difference in cessation rates at 6-month follow-up between 223 propensity score matched pairs of participants who did or did not use an e-cigarette in the 30 days prior to hospital admission (Table 3).

Table 4 displays the analysis stratified by study arm. Participants who reported using e-cigarettes at any time in the 3 months after hospital discharge were less likely to achieve biochemically-validated tobacco cessation at 6 months if they were in the Sustained Care (intervention) group (7.7% vs. 29.8%). The risk difference (-22.1%, 95% CI [-32.3%, -11.9%]) was larger than if they were in the Standard Care (control) group (12.0% vs 24.1%, risk difference -12.0%, 95% CI [-21.2%, 2.9%]), $p=0.14$ for interaction. The same pattern of association was observed for past 7-day and past 30-day e-cigarette use measures at 3 months.

Conclusions

In this secondary analysis of a large randomized controlled trial, more than one-quarter of recently-hospitalized smokers who planned to quit smoking after discharge and were advised to use conventional tobacco cessation treatment reported using an e-cigarette in the 3 months after discharge. Although most smokers said that they used e-cigarettes to aid quitting, individuals who used an e-cigarette after discharge were less likely to be abstinent from tobacco at 6-month follow-up than smokers who did not use e-cigarettes. The negative association between e-cigarette use and smoking cessation was large and statistically significant in our propensity score matched analysis.

Because e-cigarette use was self-selected, unmeasured confounding remains possible in the observed relationship between e-cigarette use and smoking cessation, and a causal inference cannot be made. However, if the observed association were a consequence of an unmeasured confounder, sensitivity analyses to unmeasured confounding using the E-Value indicated that the observed association between any e-cigarette in the 3 months since hospital discharge and smoking cessation at 6-month follow-up could only be explained away by an unmeasured confounder that was associated with both e-cigarette use and smoking cessation by a risk ratio of 4.7-fold each, above and beyond the measured confounders. Weaker confounding could not do so. From the lower limit of the 95% confidence interval, the observed association could be moved to include the null by an unmeasured confounder that was associated with both e-cigarette use and smoking cessation by a risk ratio of 2.9-fold each, above and beyond the measured confounders, but weaker confounding could not do so. Thus, the evidence of association looks reasonably strong, because substantial unmeasured confounding would be needed to reduce the observed association or its confidence interval to null.

Conducting our study within a randomized controlled trial permitted us to make several novel observations about e-cigarette use by smokers who were trying to quit. Smokers were less likely to use e-cigarettes in the month after discharge if they were randomly assigned to the intervention group, which received immediate free access to conventional cessation treatment for 3 months, than if assigned to the control group, which received a treatment recommendation only (Table 1). Access to conventional quit aids may influence a smoker's decision about whether to use e-cigarettes when making a quit attempt.

The study arm also appeared to influence the strength of the negative association between e-cigarette use and smoking cessation success. In the propensity score matched analysis, any e-cigarette use was associated with 22% lower rate of cessation at 6 months for smokers in the intervention group but only a 12% lower rate of cessation for smokers in the control group (Table 4). One interpretation is that smokers with good access to smoking cessation aids may have initiated e-cigarettes primarily when conventional aids failed. If so, e-cigarette users in this study might represent a subgroup of smokers with more difficulty quitting. This could contribute to the negative association between e-cigarette use and cessation seen in many observational trials.(10, 11, 14, 15) To our knowledge, this is the first study to assess a treatment by e-cigarette interaction. This relationship should be tested in future studies.

This observational study had notable methodological strengths. These include a large, geographically-diverse sample of smokers who were trying to quit, a prospective design with repeated measures to permit exposure assessment prior to outcome assessment, several measures of e-cigarette exposure, biochemical validation of the tobacco abstinence, and detailed assessments of socio-demographic, clinical, and tobacco use factors to allow us to compare samples that were propensity-matched on multiple factors.

Because of the study's observational design in which e-cigarette use was self-selected, unmeasured confounding is a possible explanation for the findings, and a causal relationship cannot be made from these data. However, as noted above, the E-value calculation indicates that the effect could be explained away only by a confounder with a strong relationship (a risk ratio of at least 2.9 fold) to both e-cigarette use and smoking cessation. The analysis was also limited by a lack of data on e-cigarette type and detailed data on use frequency. Prior studies have suggested that the effect of e-cigarettes on quitting may depend on the type of product and frequency of use.(15, 26–28) We could not explore these issues. Further, detailed timing of e-cigarette use, especially in relation to use of conventional quit aids, was beyond the scope of this study. Finally, our results apply to recently-hospitalized smokers and may not apply to other groups of smokers.

In conclusion, this large prospective study of recently-hospitalized smokers who planned to quit found a negative association between the use of any e-cigarettes after discharge and subsequent tobacco abstinence. The association must be interpreted in the context in which the e-cigarettes were used—intermittently, often concomitantly with evidence-based tobacco cessation treatment, and more often by smokers without easy free access to evidence-based cessation aids. Despite the limitations inherent in its observational design, this study illustrates how e-cigarettes, which are widely-available commercial products, are being used

in a common clinical situation, a quit attempt following a hospitalization. In this setting, the use of e-cigarettes intermittently and concurrently with other quit aids did not appear to benefit and may have hampered successful quitting. It remains possible that e-cigarettes will promote tobacco cessation if they are used regularly and as a complete replacement for cigarettes, which is how conventional cessation medications are recommended for use. Future research, particularly randomized controlled trials, is needed to address this critical question.

Acknowledgments

We thank Tim Gomperts for assistance with manuscript preparation and our research staff for their assistance in conducting the study.

Disclosures

Dr. Rigotti has a research grant from and been an unpaid consultant regarding smoking cessation for Pfizer, Inc. She and Dr. Kalkhoran receive royalties from UpToDate for material on electronic cigarettes. Dr. Singer has been a paid consultant to Pfizer, Inc., on topics other than smoking cessation. No other authors have any conflicts of interest to disclose.

Grant Support: NIH/NHLBI grant R01-HL11821

Funding source: NIH/NHLBI grant 1R01-HL11821

References

1. Hajek P, Etter JF, Benowitz N, Eissenberg T, McRobbie H. Electronic cigarettes: review of use, content, safety, effects on smokers and potential for harm and benefit. *Addiction*. 2014; 109(11):1801–1810. [PubMed: 25078252]
2. Goniewicz ML, Knysak J, Gawron M, Kosmider L, Sobczak A, Kurek J, et al. Levels of selected carcinogens and toxicants in vapour from electronic cigarettes. *Tob Control*. 2014; 23(2):133–9. [PubMed: 23467656]
3. King BA, Patel R, Nguyen KH, Dube SR. Trends in awareness and use of electronic cigarettes among US adults, 2010–2013. *Nicotine Tob Res*. 2015; 17(2):219–27. [PubMed: 25239961]
4. Delnevo CD, Giovenco DP, Steinberg MB, Villanti AC, Pearson JL, Niaura RS, et al. Patterns of Electronic Cigarette Use Among Adults in the United States. *Nicotine Tob Res*. 2016; 18(5):715–9. [PubMed: 26525063]
5. Ayers JW, Leas EC, Allem JP, Benton A, Dredze M, Althouse BM, et al. Why do people use electronic nicotine delivery systems (electronic cigarettes)? A content analysis of Twitter, 2012–2015. *PLoS One*. 2017; 12(3):e0170702. [PubMed: 28248987]
6. Siu, A for the U.S. Preventive Services Task Force. Behavioral and Pharmacotherapy Interventions for Tobacco Smoking Cessation in Adults, Including Pregnant Women: U.S. Preventive Services Task Force Recommendation Statement. *Annals of Internal Medicine*. 2015; 163:622–34. [PubMed: 26389730]
7. McNeill A, Brose LS, Calder R, Hitchman SC, Hajek P, McRobbie H. E-cigarettes: an evidence update A report commissioned by Public Health England. 2015;
8. Bhatnagar A, Whitsel LP, Ribisl KM, Bullen C, Chaloupka F, Piano MR, et al. Electronic cigarettes: a policy statement from the American Heart Association. *Circulation*. 2014; 130(16):1418–36. [PubMed: 25156991]
9. Levy DT, Borland R, Lindblom EN, Goniewicz ML, Meza R, Holford TR, et al. Potential deaths averted in USA by replacing cigarettes with e-cigarettes. *Tob Control*. 2017;
10. Hartmann-Boyce J, McRobbie H, Bullen C, Begh R, Stead LF, Hajek P. Electronic cigarettes for smoking cessation. *Cochrane Database Syst Rev*. 2016; 9:CD010216. [PubMed: 27622384]

11. El Dib R, Suzumura EA, Akl EA, Gomaa H, Agarwal A, Chang Y, et al. Electronic nicotine delivery systems and/or electronic non-nicotine delivery systems for tobacco smoking cessation or reduction: a systematic review and meta-analysis. *BMJ Open*. 2017; 7(2):e012680,2016–012680.
12. Malas M, van der Tempel J, Schwartz R, Minichiello A, Lightfoot C, Noormohamed A, et al. Electronic Cigarettes for Smoking Cessation: A Systematic Review. *Nicotine Tob Res*. 2016; 18(10):1926–36. [PubMed: 27113014]
13. Fiore MC, Jaen CR, Baker TB, et al. Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline 5 2008 <http://www.ahrq.gov/professionals/clinicians-providers/guidelines-recommendations/tobacco/clinicians/references/quickref/index.html>. Accessed June 29 2016.
14. Zawertailo L, Pavlov D, Ivanova A, Ng G, Baliunas D, Selby P. Concurrent E-Cigarette Use During Tobacco Dependence Treatment in Primary Care Settings: Association With Smoking Cessation at Three and Six Months. *Nicotine Tob Res*. 2017; 19(2):183–9. [PubMed: 27613911]
15. Kalkhoran S, Glantz SA. E-cigarettes and smoking cessation in real-world and clinical settings: a systematic review and meta-analysis. *Lancet Respir Med*. 2016;
16. Hajek P, McRobbie H, Bullen C. E-cigarettes and smoking cessation. *Lancet Respir Med*. 2016; 4(6):e23,2600(16)30024–8. Epub 2016 Apr 25. [PubMed: 27133216]
17. Reid ZZ, Regan S, Kelley JH, Streck JM, Ylioja T, Tindle HA, et al. Comparative effectiveness of post-discharge strategies for hospitalized smokers: study protocol for the Helping HAND 2 randomized controlled trial. *BMC Public Health*. 2015; 15:1484,015-1484-0. Epub 2015 Feb 7.
18. Rigotti NA, Tindle HA, Regan S, Levy DE, Chang Y, Carpenter KM, et al. A Post-Discharge Smoking-Cessation Intervention for Hospital Patients: Helping Hand 2 Randomized Clinical Trial. *Am J Prev Med*. 2016; 51(4):597–608. [PubMed: 27647060]
19. Heatherton TF, Kozlowski LT, Frecker RC, Fagerstrom KO. The Fagerstrom Test for Nicotine Dependence: a revision of the Fagerstrom Tolerance Questionnaire. *Br J Addict*. 1991; 86(9):1119–27. [PubMed: 1932883]
20. Bush K, Kivlahan DR, McDonell MB, Fihn SD, Bradley KA. The AUDIT alcohol consumption questions (AUDIT-C): an effective brief screening test for problem drinking. Ambulatory Care Quality Improvement Project (ACQUIP). Alcohol Use Disorders Identification Test. *Arch Intern Med*. 1998; 158(16):1789–95. [PubMed: 9738608]
21. Melchior LA, Huba GJ, Brown VB, Reback CJ. A short depression index for women. *Educational and Psychological Measurement*. 1993; 53(4):1117–1126.
22. SRNT Subcommittee on Biochemical Verification. Biochemical verification of tobacco use and cessation. *Nicotine Tob Res*. 2002; 4(2):149–59. [PubMed: 12028847]
23. Hughes JR, Keely JP, Niaura RS, Ossip-Klein DJ, Richmond RL, Swan GE. Measures of abstinence in clinical trials: issues and recommendations. *Nicotine Tob Res*. 2003; 5(1):13–25. [PubMed: 12745503]
24. Centers for Disease Control and Prevention (CDC). Notes from the field: electronic cigarette use among middle and high school students - United States, 2011–2012. *MMWR Morb Mortal Wkly Rep*. 2013; 62(35):729–30. [PubMed: 24005229]
25. VanderWeele TJ, Ding P. Sensitivity Analysis in Observational Research: Introducing the E-Value. *Ann Intern Med*. 2017; 167(4):268–74. [PubMed: 28693043]
26. 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. [PubMed: 25301815]
27. 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. [PubMed: 25896067]
28. Zhuang YL, Cummins SE, Y Sun J, Zhu SH. Long-term e-cigarette use and smoking cessation: a longitudinal study with US population. *Tob Control*. 2016; 25(Suppl 1):i90–5. [PubMed: 27697953]
29. Austin PC. Optimal caliper widths for propensity-score matching when estimating differences in means and differences in proportions in observational studies. *Pharmaceut. Statist* 2011;10:150–161.

30. Mathur MB, Ding P, Riddell CA, VanderWeele TJ. Website and R package for computing E-values. *Epidemiology*. [Research Letter] 2018 (in press). Accessed via website on 1/9/18: <https://mmathur.shinyapps.io/evalue/>

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 1.

Use of electronic cigarettes after hospital discharge*

Electronic cigarette use	Month 1				Month 3				Month 6			
	All	Intervention	Control	p	All	Intervention	Control	p	All	Intervention	Control	p
	N=1100	N=560	N=540		N=1040	N=518	N=522		N=1021	N=508	N=513	
Any use since discharge	%	18.3	16.2	20.6	0.06	28.0	31.1	0.026	37.0	34.3	39.6	0.085
Use in the past 30 days	%	16.6	14.0	19.3	0.019	15.8	17.8	0.069	16.9	16.2	17.6	0.55
Use in the past 7 days	%	10.7	8.3	13.2	0.008	11.3	12.7	0.15	11.9	11.8	11.9	0.97
At both 1 and 3-month follow-up												
Use in the Past 30 days	%	--	--	--	9.0	7.4	10.5	0.079	5.5	5.2	5.7	0.72
Use in the past 7 days	%	--	--	--	5.6	4.3	7.0	0.057	3.6	3.6	3.5	0.97

*The table presents data for completers: 1100 (81%), 1040 (77%) and 1021(75%) of the randomized patients with follow-up at 1, 3, and 6 months, respectively.

Table 2.
Comparison of individuals using or not using e-cigarettes within 3 months of discharge

	Any Electronic Cigarette use in the 3 months after discharge				
	Full Sample*		Propensity Score matched sample		
	Yes N=286	No N=736	Standardized difference	p	
Demographics					
Age (mean years, SD)	49 ± 12	52 ± 12	-2.0	0.005	0.76
Male sex (%)	43.4	51.9	-0.17	0.014	1.00
Race/ethnicity – Non-White (%)	21.7	30.7	-0.21	0.004	0.91
Education – <= high school grad (%)	45.8	51.1	-0.11	0.13	0.41
Tobacco use					
Cigarettes per day (mean, SD)	17 ± 9	15 ± 10	0.20	0.003	0.79
Smoke within 30 minutes of waking (%)	80.8	73.0	0.18	0.01	0.18
E-cigarette in 30 days before hospital admission (%)	46.5	12.0	0.82	<0.0001	1.00
Importance to quit now (0–4) (mean, SD)	3.9 ± 0.4	3.9 ± 0.4	-0.01	0.83	0.40
Confidence to resist urge to smoke (0–4) (mean, SD)	3.0 ± 0.9	3.2 ± 1.0	-0.18	0.009	0.61
Other Substance Use					
Alcohol (AUDIT-C) (0–12) (Median, IQR)	1 (0–4)	1 (0–4)	-0.05	0.47	0.66
Marijuana use (past year, %)	24.8	24.3	0.01	0.81	0.83
Medical History					
Smoking-related disease as primary discharge diagnosis [†] (%)	35.7	37.0	-0.03	0.70	1.00
PHQ-4 [‡] (median, IQR)	5 (2–8)	4 (2–7)	0.18	0.015	0.88
Hospital length of stay (days, median, IQR)	4 (3–6)	5 (3–7)	-0.07	0.13	0.30
Tobacco cessation treatment after discharge					
Use of medication (%)	78.7	77.4	0.03	0.67	0.91
Use of counseling (%)	33.9	29.9	0.09	0.20	0.43
Study Arm					
Control (%)	55.6	47.8	-0.16	0.026	1.00
Intervention (%)	44.4	52.2	0.16		
Study site					
MGH (%)	36.7	41.8	-0.11	0.14	0.63

Any Electronic Cigarette use in the 3 months after discharge

	Full Sample [*]		Propensity Score matched sample		p
	Yes N=286	No N=736	Yes N=237	No N=237	
NSMC (%)	16.1	17.8	16.9	20.3	-0.09
UPMC (%)	47.2	40.4	46.8	44.3	0.05

^{*} 1040 randomized participants were reached at 3-month follow-up but the e-cigarette use since discharge information was not available in an additional 18 patients.

Matching was based on study arm and on participants' propensity to use e-cigarettes after discharge. Variables in the propensity score model were age, sex, race, education level, cigarettes per day, time to first cigarette, e-cigarette use in the 30 days before hospital admission, importance of quitting, confidence in ability to quit, alcohol use, marijuana use in the past year, smoking-related disease as primary discharge diagnosis, baseline PHQ-4, hospital length of stay, use of medication/counseling after discharge, and study site.

[†] Smoking-related diseases are those specified in the 2014 U.S. Surgeon General's Report. These include neoplasms (ICD-9 codes 140–151, 157, 161, 162, 180, 188, 189, 204–208), cardiovascular diseases (ICD-9 codes: 410–414, 390–398, 415–417, 420–429, 430–438, 440–448), respiratory diseases (ICD-9 480–492, 496), and perinatal conditions (ICD-9 765, 769, 798.0).

[‡] PHQ-4 = Patient Health Questionnaire (4 question version) that screens for symptoms of depression (2 questions) and anxiety (2 questions).

Table 3.

Propensity score matched analysis for biochemically-verified tobacco abstinence at 6-month follow-up by e-cigarette use

		Number of e-cigarette users		Biochemically confirmed tobacco abstinence (past 7 days)		p
		Full Sample	Matched Sample*	E cigarette use	95% CI	
N		N	N	Yes %	No %	
Prior to hospital admission						
Use in the past 30 days		224	223	19.7	18.4	1.3
3 month follow-up						
Any use since discharge		286	237	10.1	26.6	-16.5
Use in the past 30 days		164	162	11.7	18.5	-6.8
Use in the past 7 days		117	117	13.7	17.9	-4.3
At both 1 and 3 months						
Use in the past 30 days		92	91	14.3	24.2	-9.9
Use in the past 7 days		58	57	17.5	21.1	-3.5
						-21.3, 1.5
						-18.0, 11.0
						0.64

* Matching was based on study arm and on participants' propensity to use e-cigarettes after discharge. Variables in the propensity score model were age, sex, race, education level, cigarettes per day, time to first cigarette, e-cigarette use in the 30 days before hospital admission, importance of quitting, confidence in ability to quit, alcohol use, marijuana use in the past year, smoking-related disease as primary discharge diagnosis, baseline PHQ-4, hospital length of stay, use of medication/counseling after discharge, and study site.

Table 4.

Propensity score matched analysis for biochemically-verified tobacco abstinence at 6-month follow-up by e-cigarette use, stratified by study arm.

E cigarette use	N	Biochemically confirmed tobacco abstinence (past 7 days)						Interaction*	
		Standard Care (Control)			Sustained Care (Intervention)			95% CI	P
		Yes %	No %	Risk Difference	95% CI	N	Yes %	No %	Risk Difference
Prior to hospital admission									
Use in the past 30 days	117	17.9	14.5	3.4	-6.0, 12.9	106	21.7	22.6	-0.9
3 month follow-up									
Any use since discharge	113	12.0	24.1	-12.0	-21.2, 2.9	104	7.7	29.8	-22.1
Use in the past 30 days	93	14.0	18.3	-4.3	-14.9, 6.3	69	8.7	18.8	-10.1
Use in the past 7 days	66	16.7	19.7	-3.0	-16.2, 10.1	51	9.8	15.7	-5.9
At both 1 and 3 months									
Use in the past 30 days	53	15.1	26.4	-11.3	-26.6, 4.0	38	13.2	21.1	-7.9
Use in the past 7 days	33	17.1	17.1	0.0	-17.7, 17.7	22	18.2	27.3	-9.1

* Interaction between study arm and e-cigarette use measure

Number of matched pairs