Relationship between tobacco and nicotine products use and clinical presentation at the Emergency Department: study protocol

Davide Campagna, Konstantinos Farsalinos, Giorgio Costantino, Giuseppe Carpinteri, Pasquale Caponnetto, Riccardo Polosa

Submitted to: JMIR Research Protocols
on: October 27, 2023

Table of Contents

Relationship between tobacco and nicotine products use and clinical presentation at the Emergency Department: study protocol

Davide Campagna[1*] MD; Konstantinos Farsalinos[2*] MD; Giorgio Costantino[3*] MD, PhD; Giuseppe Carpinteri[4] MD; Pasquale Caponnetto[5] PhD, PsyD; Riccardo Polosa[1*] MD, PhD

[1]Dep. of Clinical and Experimental Medicine University of Catania Catania IT
[2]School of Public Health, Department of Public and Community Health, University of West Attica, Athens, Greece Athen GR
[3]University of Milan 5 Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, UOC Pronto Soccorso e Medicina d'Urgenza, Milan, Italy. Milan IT
[4]Emergency Dep. – Policlinico Teaching Hospital – Catania, Italy Catania IT
[5]Department of Educational Sciences, Section of Psychology, University of Catania, Catania, Italy Catania IT
[*]these authors contributed equally

Corresponding Author:
Davide Campagna MD
Dep. of Clinical and Experimental Medicine
University of Catania
Via Santa Sofia 87
Catania
IT

Abstract

Background: In the last years several alternative to smoking nicotine products have become available. While laboratory and limited clinical studies suggest that these devices are less toxic compared to classic tobacco cigarettes, very little is still known about their epidemiological impact. Visiting the Emergency Department (ED) often represents the first or the only contact of patients with the healthcare system, so a study conducted at ED to assess the impact of these products on health is reliable and reflects the real life.

Objective: The primary endpoint of the study is to assess the association between the NEWS score and product use phenotypes. Our hypothesis is that use of ENDS may be associated with lower NEWS the score compared to cigarette smoking. If our hypothesis will be confirmed, the study will be replicated as a multicentre study in order to validate our findings.
Secondary outcomes will be hospital admissions (vs. discharge) and length of stay in the ED. Moreover, we will compare the prevalence of acute diseases known to be smoking related between the two groups, specifically stroke, acute myocardial infarction (AMI), peripheral artery diseases (PAD) chronic obstructive pulmonary disease (COPD), asthma and respiratory infections.

Methods: This is an observational study with no intervention or randomization, analysing the association between of the health condition during an ED visit as well as the outcome (hospitalization and death) and different patterns of nicotine products use. Specifically, it will explore relevant associations according to the smoking, e-cigarette use and heated tobacco product use status (current, former and never use).

Results: The study will be an observational study, with no intervention or randomization, to analyse the association between severity of clinical presentation during an ED visit as well as the outcome (hospitalization and death) and different patterns of nicotine products use. Approximately 1500-2000 people will be enrolled and categorized according to different pattern of tobacco and nicotine consumption through a specific questionnaire.
Patient recruitment will start by the end of 2023. Results will be reported within 2024.

Conclusions: There is a lot of debate about the harm reduction potential of alternative nicotine products in terms of their smoking-cessation and risk reduction potential. This study represents an opportunity to document epidemiological data on the link between different nicotine product use and disease diagnosis and severity during an ED visit, and thus evaluate the harm reduction potential claims for these products. Clinical Trial: n/a

(JMIR Preprints 27/10/2023:54041)

DOI: https://doi.org/10.2196/preprints.54041

Preprint Settings

1) Would you like to publish your submitted manuscript as preprint?

✓ **Please make my preprint PDF available to anyone at any time (recommended).**
Please make my preprint PDF available only to logged-in users; I understand that my title and abstract will remain visible to all users.
Only make the preprint title and abstract visible.
No, I do not wish to publish my submitted manuscript as a preprint.

2) If accepted for publication in a JMIR journal, would you like the PDF to be visible to the public?

✓ **Yes, please make my accepted manuscript PDF available to anyone at any time (Recommended).**
Yes, but please make my accepted manuscript PDF available only to logged-in users; I understand that the title and abstract will remain v
Yes, but only make the title and abstract visible (see Important note, above). I understand that if I later pay to participate in <a href="http

Original Manuscript

Relationship between tobacco and nicotine products use and clinical presentation at the Emergency Department: study protocol

D. Campagna[1,2,3], K. Farsalinos[4], G. Costantino[5,6], G. Carpinteri[3], P. Caponnetto[2,7] R. Polosa[1,2]

1 Dep. of Clinical and Experimental Medicine – University of Catania, Catania, Italy

2 Coehar - Center of Excellence for the acceleration of Harm Reduction – University of Catania, Catania, Italy

3 Emergency Dep. – Policlinico Teaching Hospital – Catania, Italy

4 School of Public Health, Department of Public and Community Health, University of West Attica, Athens, Greece

5 Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, UOC Pronto Soccorso e Medicina d'Urgenza, Milan, Italy.

6 Dipartimento di Scienze Cliniche e di Comunità, Università degli Studi di Milano, Milan, Italy.

7 Department of Educational Sciences, Section of Psychology, University of Catania, Catania, Italy

Corresponding author

Davide Campagna, MD – davide.campagna@unict.it

Version 1.0 – 29/07/2023

Abstract

Background In the last years several alternative to smoking nicotine products have become available. While laboratory and limited clinical studies suggest that these devices are less toxic compared to classic tobacco cigarettes, very little is still known about their epidemiological impact. Visiting the Emergency Department (ED) often represents the first or the only contact of patients with the healthcare system, so a study conducted at ED to assess the impact of these products on health is reliable and reflects the real life.

Methods: The study will be an observational study, with no intervention or randomization, to analyse the association between severity of clinical presentation during an ED visit as well as the outcome (hospitalization and death) and different patterns of nicotine products use. Approximately 1500-2000 people will be enrolled and categorized according to different pattern of tobacco and nicotine consumption through a specific questionnaire.

Discussion: There is a lot of debate about the harm reduction potential of alternative nicotine products in terms of their smoking-cessation and risk reduction potential. This study represents an opportunity to document epidemiological data on the link between different nicotine product use and disease diagnosis and severity during an ED visit, and thus evaluate the harm reduction potential claims for these products.

Keywords

Smoking, electronic nicotine delivery systems – ENDS, emergency department, NEWS, smoking phenotype

Introduction

Smoking related diseases are a well know group of pathologies that are responsible of 8 million deaths per year [1]. Despite numerous restrictions, taxation and communication campaigns, there are still more than 1.3 billion smokers globally. Quitting smoking remains one of the most cost-effective methods to reduce health risk. However, the success rate of smoking cessation methods remains low in the real-world setting [2-5], Additionally, a substantial proportion of smokers are unwilling to use

smoking cessation services but would prefer a less harmful alternative product [6,7]. In the last years several alternative to smoking nicotine products have become available, commonly called electronic nicotine delivery systems – ENDS), namely e-cigarettes and heated tobacco products. While laboratory and limited clinical studies suggest that these products reduce exposure to toxins and may thus reduce health risk [8-12], very little is still known about their epidemiological impact.

Several studies have demonstrated a high proportional cigarette smoking prevalence in emergency department (ED) patients, higher than the prevalence in the general population [13-19]. This is expected considering the disease burden caused by smoking, which might result in more ED visits for smokers compared to non-smokers. Current smoking as well as smoking relapse were found to be significantly associated with ED visits [20-24]. Accessing at ED often reflects the first or the only contact of patients with the healthcare system, thus, the ED visit represents an opportunity to record smoking and nicotine use patterns. However, no studies have systematically recorded use patterns for ENDS. Considering the growing popularity of these products and the limited epidemiological evidence on their health effects, a detailed recording of use patterns for all nicotine products is important in order to monitor their use prevalence, healthcare system burden and epidemiological impact.

On arrival at the ED, each patients undergoes a TRIAGE phase. A nurse is usually responsible for evaluating the severity of his health condition and the priority for clinical assessment (unless the patient enters the emergency room by ambulance in red code). The nurse usually performs this task by collecting vital signs and recording the patient’s medical history. The nurse uses this information to assign a color code representing the priority for further assessment. Then, the patient waits for the medical evaluation in a dedicated room where nurses can monitor the clinical condition of all attending patients. The National Early Warning Score (NEWS) score advocates a system to standardise the assessment and response to acute illness [24]. It is based on a simple aggregate scoring system in which a score is allocated to physiological measurements, already recorded in

routine practice, when patients present to, or are being monitored in hospital. Six simple physiological parameters form the basis of the scoring system:

1. respiration rate
2. oxygen saturation
3. systolic blood pressure
4. pulse rate
5. level of consciousness or new confusion (AVPU scale)
6. temperature.

In patients who access the Emergency Department (ED), this score helps the triage nurse to assign the correct color code to patients so that they can be examined promptly based on the severity and urgency of their disease condition.

The purpose of this study is to accurately record the smoking and nicotine product use patterns of patients visiting the ED and to determine whether the use of ENDS is associated with any measurable differences compared to tobacco smoking in disease severity and outcome among these patients.

Methods

This is an observational study with no intervention or randomization, analysing the association between of the health condition during an ED visit as well as the outcome (hospitalization and death) and different patterns of nicotine products use. Specifically, it will explore relevant associations according to the smoking, e-cigarette use and heated tobacco product use status (current, former and never use).

Study population and design

Inclusion and exclusion criteria are summarized in Table 1. Participants will be recruited among patients presenting at ED of Policlinico Teaching Hospital of Catania, Italy in one month during the diurnal shift. Only patients that access ED for non-traumatic reason will be screened, since it is unlikely that smoking or use of other nicotine products can have any causal effect on accidents. Participants who meet the inclusion criteria will be recruited and administered an electronic questionnaire (see Appendix A) about their smoking and nicotine product use habits and their medical history. This questionnaire serves to typify the patient's use phenotype and quantify exposure to each product. A dedicated website will be created for the study. This website will respect the GDPR policy. Every study's team member will access the site with personal and unique ID and password. The website will create two different databases to guarantee participants' privacy. The first database will record fiscal code of the participant and will assign a unique ID. The second database will record anonymously the data from each participant using only the participant's ID. It is necessary to create two databases so that additional information on outcomes or other missing data will be recorded at a later time.

Patients will be asked for authorization to use their clinical data in anonymous format, in accordance with the current privacy directives related to the access to the ED. The ERB approved informed consent form will be shown to potential participants who must be able to understand and sign it in order to participate in the study by a member of the study group. Each patient can withdraw his/her consent to participate in the study at any time, all data collected for that patient will be deleted. All collected informed consents will be stored at the ED of Policlinico Teaching Hospital of Catania. No financial or other incentives will be provided to the participants. Since about 70 patients per day access the ED during the diurnal shift for non-traumatic reasons, we expect to enrol about 2000 participants in one month. Besides the aforementioned questionnaire, medical data at the triage phase such as the NEWS score, heart rate, blood pressure, SpO2, respiratory rate, temperature and FiO2 will be recorded. After the assessment and management of each patient in the ED, the final diagnosis,

final disposition and colour code at discharge or admission to a ward will be recorded (see table 2). In order not to compromise the health of patients with severe disease requesting urgent medical attention, potential participants who arrive in the ED in red code (severe acute illness) will be asked to participate after they are stabilized (questionnaire, NEWS score and vital signs will be recorded later).

Based on the responses to the questionnaire, phenotypes will be categorized as current, former and never use, separately for tobacco cigarettes, e-cigarettes and heated tobacco products. After one month, data in the eCRF will be extracted for the statistical analysis. Only the authors of this paper will have full access to stored data in eCRF.

Since the ED is usually very crowded, four study team personnel will work on the study and will screen and recruit patients during the waiting period before medical examination. The study team will interview potential participants in a dedicated room within the ED area, to guarantee privacy. Initial survey will last about 5 minutes per patient. This is a reasonable time to collect product use information from each participant. After the medical visit and final disposition, compilation of the electronic case report form (eCRF) will be completed as provided by the study protocol, with each study member collecting all necessary information about the patients' outcome (discharge, admission to a ward) by the end of their shift. Some patients can stay in the ED more than the length of diurnal shift, so data will be collected the day after. Some patient could access the ED two or more times during the study. In order to avoid double-entries, only the first visit will be included in the study. The website will reply with an error if we try to recruit for a 2nd time the same fiscal code (fiscal code is a unique identifying code ID in Italy and it is mandatory to be recorded for each patients during the triage phase in the ED).

Endpoint and outcomes

The primary endpoint of the study is to assess the association between the NEWS score and product

use phenotypes. Our hypothesis is that use of ENDS may be associated with lower NEWS the score compared to cigarette smoking. If our hypothesis will be confirmed, the study will be replicated as a multicentre study in order to validate our findings.

Secondary outcomes will be hospital admissions (vs. discharge) and length of stay in the ED. Moreover, we will compare the prevalence of acute diseases known to be smoking related between the two groups, specifically stroke, acute myocardial infarction (AMI), peripheral artery diseases (PAD) chronic obstructive pulmonary disease (COPD), asthma and respiratory infections.

Table 1. Inclusion and exclusion criteria for study participation.

Inclusion criteria	• Being an adult (age ≥ 18 years) • Ability to understand and sign informed consent
Exclusion criteria	• Access in ED for traumatic accident • Pregnancy

Table 2

Data to record in eCRF	Value
Value of NEWS score calculated at the patient's triage phase (conventionally acute patients will	From 0 up to 17

be recorded as at high risk – NEWS score >7)	
Vital signs (heart rate, blood pressure, SpO2, respiratory rate, temperature and FiO2) at the patient's triage phase	expressed in bpm, mmHg, %, rpm, °C and % respectively
Smoking questionnaire	See appendix A
Past Medical History and drugs	Textual
Length of stay in the ED	expressed in hours and minutes
Final diagnosis of discharged patients	Textual
Final disposition	Admitted/Discharged
Final diagnosis of admitted patients	ICD-9 codes

Statistical analysis

Descriptive analysis will be performed by presenting numerical data as mean (standard deviation – SD) and categorical data as number (proportion - %). Patients will be classified according to product use as current, former and never users, separately for tobacco cigarettes, e-cigarettes and heated tobacco products.

Univariate comparisons will be made using chi-square tests for categorical variables and Kruskal Wallis H test for NEWS score. Regression analyses will be performed in order to examine the association between different product use and NEWS score as well as secondary outcomes. Demographics, including age, gender and educational level, as well as past medical history will be included in as independent variables. Since the majority of ENDS users report current or past smoking, the smoking status of these users will also be recorded along with those who not report any ENDS use. Therefore, the analysis will be adjusted for the smoking status of ENDS users. Additionally, secondary analyses will be performed for never-smoking ENDS users, if a sufficient number of such participants will be available. All analyses will be performed using SPSS v.25 (IBM, Chicago, IL, USA), and a P value of < 0.05 will be considered statistically significant.

Ethics and dissemination

The study will be conducted according to the principles of Good Clinical Practice and the

Declaration of Helsinki. The institute ethics committee “Comitato Etico Catania 1” - Policlinico Teaching Hospital of Catania, Catania, Italy reviewed and approved the study. If any amendments to this protocol are required, the chief investigator will be responsible for the decision to amend the protocol and for deciding whether an amendment is substantial or non-substantial. Any substantial amendments will be submitted to the research ethics committee for approval before implementation. The informed consent from trial participants will be obtained by the investigators through relevant forms. All study members are independent and have no conflict of interest. The intention of the authors is to disseminate the results of the study through journal articles in high quality peer-reviewed journals and through conference abstracts.

Results

Patient recruitment will start by the end of 2023. Results will be reported within 2024.

Discussion

There is a lot of debate about the harm reduction potential of ENDS. Recently, some studies have shown that they may help smokers quit.

ECLAT, which was conducted by our study group ten years ago, assessed the efficacy and the safety of first-generation e-cigarettes (which are now considered obsolete) when given as smoking substitutes [25]. Since then, newer generation, more effective in nicotine delivery and more appealing, were developed, which have shown positive results in both clinical and real-world settings [26-33]. Therefore, they may represent a reasonable option for those unable or unwilling to quit smoking with currently-approved methods. Still, it is important to understand and document the risk-reduction potential of these products in the clinical setting.

Little epidemiological evidence exists on the harm reduction potential of ENDS. This study represents an opportunity to document epidemiological data on the link between different nicotine

product use and illness severity during an ED visit, as well as clinical outcome and associations with specific, smoking-related diseases, and at the same time it may document the need for routinely recording nicotine use habits for all ED patients, besides the current norm of recording smoking status only.

Declarations

Ethics approval and consent to participate

The study will be conducted according to the principles of Good Clinical Practice and the Declaration of Helsinki. The institute ethics committee “Comitato Etico Catania 1” - Policlinico Teaching Hospital of Catania, Catania, Italy reviewed and approved the study. If any amendments to this protocol are required, the chief investigator will be responsible for the decision to amend the protocol and for deciding whether an amendment is substantial or non-substantial. Any substantial amendments will be submitted to the research ethics committee for approval before implementation. The informed consent from trial participants will be obtained by the investigators through relevant forms.

Competing interests

The authors declare that they have no competing interests related to this research.

Funding

This work is supported through the ministerial grant PON REACT-EU 2021 GREEN- Bando 3411/2021 by Ministero dell Università e della Ricerca (**MUR**) – PNRR EU Community

Authors' contributions

All authors, DC, KF, GC, GC, PC and RP equally contributed to write the first draft of this paper, and contributed to subsequent reviews and revisions. All authors read and approved the final manuscript. DC co-ordinated the submission process.

Acknowledgements

The authors thank the Policlinico Teaching Hospital of Catania, Italy, for the availability to carry out the study and the ED residents for their future contribution.

REFERENCES

1. World Health Organization. Fact Sheets: Tobacco. Available at: https://www.who.int/news-room/fact-sheets/detail/tobacco (accessed on February 10, 2023).
2. Moore, D.; Aveyard, P.; Connock, M.; Wang, D.; Fry-Smith, A.; Barton, P. Effectiveness and safety of nicotine replacement therapy assisted reduction to stop smoking: Systematic review and meta-analysis. *BMJ* **2009**, *338*, b1024.
3. Kotz D, Brown J, West R. 'Real-world' effectiveness of smoking cessation treatments: a population study. Addiction. 2013 (Published online: December 20, 2013).
4. Rigotti, N.A.; Pipe, A.L.; Benowitz, N.L.; Arteaga, C.; Garza, D.; Tonstad, S. Efficacy and safety of varenicline for smoking cessation in patients with cardiovascular disease: A randomized trial. *Circulation* **2009**, *121*, 221–229.
5. Casella, G.; Caponnetto, P.; Polosa R. Therapeutic advances in the treatment of nicotine addiction: present and future. *Ther Adv Chronic Dis* **2010**, *1*, 95–106.
6. Britton, J.; Edwards, R. Tobacco smoking, harm reduction, and nicotine product regulation. Lancet 2008, 371, 441-445.

7. Bell, K. Tobacco control, harm reduction and the problem of pleasure. Drug Alc Today 2013, 13, 111-118.
8. Farsalinos KE, Polosa R. Safety evaluation and risk assessment of electronic cigarettes as tobacco cigarette substitutes: a systematic review. Ther Adv Drug Saf. 2014 Apr;5(2):67-86. doi: 10.1177/2042098614524430.
9. Glasser AM, Collins L, Pearson JL, Abudayyeh H, Niaura RS, Abrams DB, Villanti AC. Overview of Electronic Nicotine Delivery Systems: A Systematic Review. Am J Prev Med. 2017 Feb;52(2):e33-e66. doi: 10.1016/j.amepre.2016.10.036.
10. Marques P, Piqueras L, Sanz MJ. An updated overview of e-cigarette impact on human health. Respir Res. 2021 May 18;22(1):151. doi: 10.1186/s12931-021-01737-5.
11. Mallock N, Pieper E, Hutzler C, Henkler-Stephani F, Luch A. Heated Tobacco Products: A Review of Current Knowledge and Initial Assessments. Front Public Health. 2019 Oct 10;7:287. doi: 10.3389/fpubh.2019.00287.
12. Akiyama Y, Sherwood N. Systematic review of biomarker findings from clinical studies of electronic cigarettes and heated tobacco products. Toxicol Rep. 2021 Jan 27;8:282-294. doi: 10.1016/j.toxrep.2021.01.014.
13. Bernstein SL, Boudreaux ED, Cydulka RK, et al. Tobacco control interventions in the emergency department: a joint statement of emergency medicine organizations. J Emerg Nurs. 2006;32(5):370-81.6.
14. Boudreaux ED, Kim S, Hohrmann JL, et al. Interest in smoking cessation among emergency department patients. Heal Psychol. 2005;24(2):220-4. 7.
15. Weiland T, Jelinek G, Taylor S, et al. Tobacco smoking by adult emergency department patients in Australia: a point-prevalence study. Public Heal Res Pract. 2016;26(3):1-10. 8.
16. Lynch A and Quigley P. ExHALED study: Prevalence of smoking and harm levels in an emergency department cohort: original research. Emerg Med Australas. 2010;22(4):287-95.

17. Lowenstein SR, Tomlinson D, Koziol-McLain J, et al. Smoking habits of emergency department patients: an opportunity for disease prevention. Acad Emerg Med. 1995;2(3):165-71.
18. Richman PB, Dinowitz S, Nashed A, et al. Prevalence of smokers and nicotine-addicted patients in a suburban emergency department. Acad Emerg Med. 1999;6(8):807-10.
19. Smith PM. Tobacco use among emergency department patients. Int J Environ Res Public Health. 2011;8(1):253-63.
20. Park J, Yeo Y, Ji Y, Kim B, Han K, Cha W, Son M, Jeon H, Park J, Shin D. Factors Associated with Emergency Department Visits and Consequent Hospitalization and Death in Korea Using a Population-Based National Health Database. Healthcare (Basel). 2022 Jul 17;10(7):1324. doi: 10.3390/healthcare10071324.
21. Agarwal P, Bias TK, Madhavan S, Sambamoorthi N, Frisbee S, Sambamoorthi U. Factors Associated With Emergency Department Visits: A Multistate Analysis of Adult Fee-for-Service Medicaid Beneficiaries. Health Serv Res Manag Epidemiol. 2016 Apr 27;3(3):2333392816648549. doi: 10.1177/2333392816648549.
22. Kao YH, Celestin MD Jr, Walker CD, Yu Q, Couk J, Moody-Thomas S, Zhang H, Tseng TS. Smoking Relapse and Type 2 Diabetes Mellitus-Related Emergency Department Visits Among Senior Patients with Diabetes. Prev Chronic Dis. 2019 Dec 19;16:E164. doi: 10.5888/pcd16.190027.
23. Selya A, Johnson EL, Weber TL, Russo J, Stansbury C, Anshutz D, Griese E, Hsu B. Smoking is associated with a higher risk of unplanned medical visits among adult patients with diabetes, using retrospective electronic medical record data from 2014 to 2016. BMC Health Serv Res. 2020 May 6;20(1):383. doi: 10.1186/s12913-020-05277-4.
24. Smith GB, Prytherch DR, Meredith P, Schmidt PE, Featherstone PI. The ability of the National Early Warning Score (NEWS) to discriminate patients at risk of early cardiac arrest,

unanticipated intensive care unit admission, and death. Resuscitation. 2013 Apr;84(4):465-70. doi: 10.1016/j.resuscitation.2012.12.016. Epub 2013 Jan 4. PMID: 23295778.

25. Caponnetto P, Campagna D, Cibella F, Morjaria JB, Caruso M, Russo C, Polosa R. EffiCiency and Safety of an eLectronic cigAreTte (ECLAT) as tobacco cigarettes substitute: a prospective 12-month randomized control design study. PLoS One. 2013 Jun 24;8(6):e66317. doi: 10.1371/journal.pone.0066317.
26. 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):1531–1540. doi: 10.1111/add.12623.
27. Cox S, Dawkins L, Doshi J, Cameron J. Effects of e-cigarettes versus nicotine replacement therapy on short-term smoking abstinence when delivered at a community pharmacy. Addict Behav Rep. 2019;10:100202. doi: 10.1016/j.abrep.2019.100202.
28. Lee SH, Ahn SH, Cheong YS. Effect of Electronic Cigarettes on Smoking Reduction and Cessation in Korean Male Smokers: A Randomized Controlled Study. J Am Board Fam Med. 2019 Jul-Aug;32(4):567-574. doi: 10.3122/jabfm.2019.04.180384.
29. Hajek P, Phillips-Waller A, Przulj D, Pesola F, Myers Smith K, Bisal N, Li J, Parrott S, Sasieni P, Dawkins L, Ross L, Goniewicz M, Wu Q, McRobbie HJ. A Randomized Trial of E-Cigarettes versus Nicotine-Replacement Therapy. N Engl J Med. 2019 Feb 14;380(7):629-637. doi: 10.1056/NEJMoa1808779.
30. Lee SM, Tenney R, Wallace AW, Arjomandi M. E-cigarettes versus nicotine patches for perioperative smoking cessation: a pilot randomized trial. PeerJ. 2018;6:e5609. doi: 10.7717/peerj.5609.
31. Hartmann-Boyce J, Lindson N, Butler AR, McRobbie H, Bullen C, Begh R, Theodoulou A, Notley C, Rigotti NA, Turner T, Fanshawe TR, Hajek P. Electronic cigarettes for smoking cessation. Cochrane Database Syst Rev. 2022 Nov 17;11(11):CD010216. doi:

10.1002/14651858.CD010216.pub7.

32. Li J, Hui X, Fu J, Ahmed MM, Yao L, Yang K. Electronic cigarettes versus nicotine-replacement therapy for smoking cessation: A systematic review and meta-analysis of randomized controlled trials. Tob Induc Dis. 2022 Oct 20;20:90. doi: 10.18332/tid/154075.
33. Li J, Hajek P, Pesola F, Wu Q, Phillips-Waller A, Przulj D, Myers Smith K, Bisal N, Sasieni P, Dawkins L, Ross L, Goniewicz ML, McRobbie H, Parrott S. Cost-effectiveness of e-cigarettes compared with nicotine replacement therapy in stop smoking services in England (TEC study): a randomized controlled trial. Addiction. 2020 Mar;115(3):507-517. doi: 10.1111/add.14829.

Abbreviations

AMI acute myocardial infarction

COPD chronic obstructive pulmonary disease

eCRF electronic case report form

ED emergency department

ENDS electronic nicotine delivery systems

NEWS National Early Warning Score

PAD peripheral artery diseases