

Effect of electronic cigarette device properties on composition of emission

Protocol for a systematic review

Summary

Electronic cigarettes (e-cigarettes), both with or without nicotine, comes in a wide variety of product types and contents. E-cigarettes consist of a heating element associated with a battery and a cartridge containing a liquid (e-cigarette liquid). E-cigarettes can be disposable, rechargeable with a cartridge, or manually refillable with e-cigarette liquid. When heated, the e-cigarette liquid will form an aerosol (vapour) meant to be inhaled through a mouthpiece. To do an updated risk assessment on the use of e-cigarettes, it is important to map the contributions of the different properties of the e-cigarettes on the formation of different hazardous constituents and their levels in the emission.

As part of the collaboration with Joint Action on Tobacco Control 2 (JATC2) we will systematically evaluate the effect of different device properties on the composition of emission. The evaluation will be based on scientific methods for collection, assessments and summarizing of studies on emissions from e-cigarettes.

We will conduct a systematic search for literature. Titles and abstracts will be considered according to the inclusion and exclusion criteria. References will be screened by two researchers in pairs and independently, first by title and abstract and subsequently in full text, for inclusion and exclusion.

We will assess the risk of bias of the of included studies, conduct meta-analysis if relevant and assess our confidence in the results using the GRADE-approach.

Title:

Effect of electronic cigarette device properties on the composition of emission

Protocol for a systematic review

Commissioner:

Joint Action on Tobacco Control 2

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April 2023

Due date:

October 2023

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Sammendrag

Elektroniske sigaretter (e-sigaretter) finnes i en rekke ulike typer/utforminger. E-sigaretter består av et varmeelement tilknyttet et batteri og en beholder som inneholder en væske (e-sigarettvæske). E-sigarettvæsken kan være med eller uten nikotin. E-sigaretter kan være til engangsbruk, oppladbare med ferdigfylte beholdere eller manuelt etterfyllbare. Ved oppvarming vil e-sigarettvæsken danne en aerosol (damp) som inhaleres gjennom et munnstykke. For å kunne gjøre en oppdatert risiko vurdering av bruk av e-sigaretter, er det viktig å kartlegge hvilke egenskaper ved selve e-sigarettene som bidrar til dannelsen av ulike helsefarlige substanser og deres nivå.

Som en del av samarbeidet med Joint Action on Tobacco Control 2 (JATC2) vil vi systematisk kartlegge effektene av hvordan og hvilke egenskaper ved selve e-sigarettene som påvirker sammensetningen av aerosolen. Kunnsapsoppsummeringen vil være basert på vitenskapelige metoder for innsamling, vurdering og oppsummering av studier om aerosolen fra e-sigaretter.

Vi vil gjennomføre et systematisk litteratursøk. Titler og sammendrag vil bli vurdert i henhold til inklusjons- og eksklusjonskriteriene. To forskere vil, uavhengig av hverandre, gjennomgå de identifiserte artiklene, først etter tittel og sammendrag og deretter i fulltekst, for inkludering og ekskludering.

De inkluderte studiene vil gjennomgå en vurdering av systematiske risiko for skjevheter (bias). Hvis det er relevant vil vi gjennomføre en metaanalyse og vurdere vår tillit til effektestimaterne med GRADE-systemet.

Tittel:

Effekten av e-sigarettegenskaper på sammensetningen av utslipp

Protokoll for systematisk oversikt

Bestiller:

Joint Action on Tobacco Control II

Bestillingsdato:

April 2023

Leveringsfrist:

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Commission

As a partner in the Joint Action on Tobacco Control 2, The Norwegian Institute of Public Health has committed to perform a systematic review on the effects of e-cigarette device properties on emission/aerosol composition.

In agreement with the established policy of leading scientific journals, research funded by or otherwise linked to the tobacco or e-cigarette industry should not be included. Otherwise, NIPH is free to organize the work as they find appropriate.

Acknowledgement

We thank research librarian Trude Anine Mugggerud regarding the update of the systematic literature search.

Background

Electronic cigarettes (e-cigarettes) consist of a heating element associated with a battery and a cartridge containing a liquid (e-cigarette liquid). When heated, the e-cigarette liquid will form an inhalable aerosol (vapor). E-cigarettes can be disposable, rechargeable with a cartridge, or manually refillable with e-cigarette liquid. The e-liquid is usually a mixture of propylene glycol (PG), vegetable glycerine (VG) and various flavourings, and may or may not contain nicotine. Heating of the e-liquid can lead to thermal decomposition of constituents and/or formation of new compounds, depending on the temperature, chemical composition and duration of the heating. Decomposition products and new compounds may possess altered toxicity compared with their parent compounds. Other constituents found in aerosols including metals and silicate particles may add to the toxicity of the inhaled vapor (1).

The harmful potential of nicotine has been documented from studies in cell cultures, animals and, although less, in humans (2). The health risks associated with inhalation of e-liquid aerosol with or without nicotine have not been thoroughly elucidated in human studies. However, several *in vitro* and animal studies report cellular effects that may have impact on airways, inflammation, and impairment of cardiovascular function. In addition, some of the compounds identified in aerosol from e-liquid are known or potential carcinogens. The composition of the inhaled vapor may be affected by the e-cigarette device settings and design, user pattern as well as the composition of the e-liquid.

A precise evaluation of the health risks linked to e-cigarettes use is complicated due to the large variation of products on the market and the heterogeneity of users such as puffing behavior, time of use, age of user and comorbidity. Furthermore, the potential long-term effects of e-cigarette use have so far only been scarcely investigated (3). It should also be noted that e-cigarettes may be used for vaping other liquids or additives that may be illegal or produced for other purposes, and thus not provided commercially from an e-cigarette producer. However, such unauthorized use is beyond the scope of this report.

Why it is important to conduct this systematic review?

It is important to know what people are inhaling when they use electronic cigarettes.

Aims

The aims of this systematic review are to summarize available evidence regarding electronic cigarette device properties on the composition of emission.

More specifically, we will investigate the effects of:

- properties related to changes in watt, ohm or volt
- temperature of the heating device
- different coil materials/alloys (filaments)
- different properties of the wick
- different e-cigarette types/brands

on the emission of nicotine, volatile and/or semi-volatile organic compounds, metals, polycyclic aromatic hydrocarbons (PAHs), tobacco-specific nitrosamines (TSNAs), reactive oxygen species (ROS), free radicals, particle size distribution and/composition or other constituents in the aerosol.

Methods

We will conduct this systematic review in accordance with this protocol, the NIPH methods book (4) and the Cochrane Handbook (5).

Inclusion criteria

We will use the following inclusion criteria:

Population	electronic cigarettes
Exposure 1	Properties related to changes in watt, ohm, volt, or temperature setting of the heating device.
Comparison 1	A different measure of watt, ohm, volt, or temperature of the heating device.
Exposure 2	Coil material alloy (filament)
Comparison 2	Another coil material/alloy (filament)
Exposure 3	Properties of the wick
Comparison 3	Another property of the wick
Exposure 4	One e-cigarette type/brand or component
Comparison 4	Another e-cigarette type/brand or component from another manufacturer with same e-liquid same puffing topography.
Outcome	Composition of the emission, specifically: Nicotine Volatile and/or semi volatile organic compounds including glycerol and propylene glycol. Metals PAHs and TSNAs ROS, free radicals Particle size distribution and/ composition Other constituents in the aerosol or gas phase*
Study design	Studies with a control group using the same e-liquid(s) and same puffing topography.

Publication time	No restrictions. If very heterogeneous we will perform sensitivity analysis by year.
Country/ context	No restrictions
Language	No restrictions in the searches, but we will only be able to assess in full text and include studies in Danish, English, Norwegian and Swedish

*We acknowledge that there may be other properties and other components of the aerosol or gas phase that are important to consider that we do not have full understanding of yet, so we will have an option open if we come across other properties that should be considered.

Exclusion criteria

We will exclude studies that does not have a reasonable control group. Research funded by or otherwise linked to tobacco/electronic cigarette industry will not be included.

Literature search

Searches in databases

Research librarian Trude Anine Mugggerud updated the systematic literature search that was developed in collaboration with the project group and conducted in connection with the interactive evidence and gap map on the health effects of e-cigarettes (6). The strategy was peer reviewed by another research librarian before the literature search was conducted the first time. The following databases were searched in the original and updated search:

- Ovid MEDLINE
- Embase
- Web of Science
- Cochrane central for systematic reviews

Selection of studies

Three authors from the working group (RB, HV and EM) read and assessed the reference identified in the literature searches independently and in pairs. Relevant references were selected according to our inclusion criteria. The first selection was based on the title and abstract. Selection on full-text evaluation of the publications will be conducted by (RB, HV, EM, KH and GV). Any disagreements will be resolved through discussion or contact with another researcher in the team. EPPI Reviewer 6 is used for study selection (7)

Assessing the risk of bias of included studies

We will assess the risk of bias of the included studies using the OHAT risk of tool for in vitro studies (8). The risks of bias questions are:

- Was administered dose or exposure level adequately randomized?
- Was allocation to study groups adequately concealed?
- Were experimental conditions identical across study groups?
- Were research personnel blinded to the study group during the study?
- Were outcome data complete without attrition or exclusion from analysis?
- Can we be confident in the exposure characterization?
- Can we be confident in the outcome assessment (including blinding of outcome assessors)?
- Were all measured outcomes reported?
- Were there no other potential threats to internal validity?

If we identify and include studies involving human e-cigarette smokers fulfilling the other inclusion criteria, then we will assess the risk of bias in these studies using the OHAT risk of bias tool for the appropriate study design (8). The team will conduct the risk of bias assessment for the first 10 studies together. Subsequently, authors from the team will independently and in pairs assess each study according to the OHAT questions and then meet to compare. Disagreements will be dissolved by discussion or conferring with another member of the working group.

Data collection

One author from the author working group will collect data from the studies and another author will check that the relevant information is correctly extracted. Disagreements will be solved by consensus. We will collect information on the full reference, when and where it was conducted, information on the device and liquids used, number and type of devices included, number and characteristics of comparison devices used in the studies, puffing protocol, emission outcomes measured, measuring methods (aerosol collection technique and type of chemical analysis) and the reported results.

Analysis

Each device property will be assessed separately.

Where appropriate, we will conduct meta-analyses, alternatively we will report data descriptively. We will conduct subgroup analyses for different device properties where there is enough information and heterogeneity for it to be feasible. Dichotomous outcomes will be presented as risk ratio (RR) with 95% confidence interval (CI). Continuous outcomes will be presented as mean difference between the groups (MD) with 95% CI. Where different scales are used to measure the same outcome, we will calculate standardized mean difference (SMD) with 95% CI.

We will use Review Manager to generate forest plots. We will use random effects model and evaluate statistical heterogeneity using Q test and I^2 statistics.

Assessing our confidence in the results

We will assess our confidence in the evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (10).

Peer review of protocol and publishing of the full report

Peer reviewers: Clara Neto, ANSES and Oddvar Myhre, NIPH.

The protocol will be approved by Head of Department, Air Quality and Noise, Kristine Bjerve Gützkow and Research Director Johan Øvrevik.

Final report will be published on the JATC 2 webpages. We will in addition consider publishing findings in peer-reviewed journals.

Time schedule

Start: 03.04.2023

Delivery: 27.10.2023

Related projects at NIPH

NIPH 2022. Valen H, Becher R, Vist GE, Brinchmann BC, Holme JA, Grimsrud TK, Andreassen O, Underland V, Mariussen E, Bakkeli M, Dahl JE, Carlsen KCL, Alexander J. Adverse health effects of electronic cigarette use: an umbrella review and toxicological evaluation. Norwegian Institute of Public Health, Oslo, Norway, 2022. [Helseskadelige effekter ved bruk av elektroniske sigaretter: en paraplyoversikt og toksikologisk evaluering]. Folkehelseinstituttet, Oslo, Norge, 2022.

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NIPH 2021. Valen H, Vist GE, Becher R, Brinchmann BC, Holme JA, Grimsrud TK, Ørjasæter Elvsaa I-K, Underland V, Bakkeli M, Alexander J. Health risks associated with the use of electronic cigarettes: an interactive research map. [Helserisiko ved bruk av elektroniske sigaretter: et interaktivt forskningskart] –2021. Oslo: Norwegian Institute of Public Health, 2021.

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https://www.ncbi.nlm.nih.gov/books/NBK179276/pdf/Bookshelf_NBK179276.pdf
3. NIPH 2022. Valen H, Becher R, Vist GE, Brinchmann BC, Holme JA, Grimsrud TK, Andre-assen O, Underland V, Mariussen E, Bakkeli M, Dahl JE, Carlsen KCL, Alexander J. Ad-verse health effects of electronic cigarette use: an umbrella review and toxicological evaluation. Norwegian Institute of Public Health, Oslo, Norway, 2022. [Helseskadelige effekter ved bruk av elektroniske sigaretter: en paraplyoversikt og toksikologisk eva-luering]. Folkehelseinstituttet, Oslo, Norge, 2022.
https://www.fhi.no/contentassets/5ddc2c84f7d04995bd419344cbc55628/fin-al8-adverse-health-effects-of-electronic-cigarette-use_110522.pdf
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