Effective Health Care

Vaping and Insulin Levels

Results of Topic Selection Process & Next Steps

The nominator is interested in research about the effect of liquid used in vaping devices on insulin levels.

We found no relevant studies. No further activity on this nomination will be undertaken by the Effective Health Care (EHC) Program.

Topic Brief

Topic Number and Name: Vaping and Insulin Levels, #847

Nomination Date: 2/6/2019

Topic Brief Date: 5/13/2019

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Conflict of Interest: None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

Background

- E-cigarette produce an aerosol by heating a liquid that usually contains nicotine, flavorings, and other chemicals that help to make the aerosol. People inhale this aerosol into their lungs. Bystanders can also breathe in this aerosol when the user exhales into the air.[1]
- E-cigarettes are sometimes called “e-cigs,” “e-hookahs,” “mods,” “vape pens,” “vapes,” “tank systems,” and “electronic nicotine delivery systems (ENDS).”[1]
- The liquid and vapor from e-cigarettes contain glycols (propylene glycol and glycerine), nicotine, and flavorings. Flavorings that are certified as safe by the Flavor Extracts Manufacturers Association may not be safe in e-cigarettes.[2]
- It is estimated that 4.5% (or 10.8 million) American adults are e-cigarette users. The prevalence was highest among 18-24 year olds. It is also higher in former smokers and current smokers; lesbian, gay, bisexual and transgender person; and among adults with chronic health problems.[3]
- Smokers may use e-cigarettes to help with smoking cessation. However a recent systematic review found that the odds of quitting smoking were 28% lower in those who used e-cigarettes compared to those who did not. [4]
- A study of some e-cigarette products found the vapor contains known carcinogens and toxic chemicals, as well as potentially toxic metal nanoparticles from the device itself.[5]
- Information about the long-term benefits and harms is limited. [6]
- Nicotine raises blood pressure and pulse. It has a deleterious effect on insulin sensitivity by decreasing insulin sensitivity and causing or worsening diabetes.
- Nicotine can cause HbA1c levels to increase by as much as 34 percent [7]

Key Question and PICOs

The key question for this nomination are:

1. What is the effect of the flavorings and sweeteners in vaping devices on insulin levels?

To define the inclusion criteria for the key questions, we specify the population, interventions, comparators, and outcomes (PICO) of interest (Table 1).

Table 1. Key Questions and PICO

Key Questions	
Population	Adults 18 years and older
Interventions	Vaping device
Comparators	No vaping device Cigarettes
Outcomes	Blood insulin level Hemoglobin A1C Blood glucose

Methods

We assessed this nomination for priority for a systematic review or other AHRQ EHC report with a hierarchical process using established selection criteria. Assessment of each criteria determined the need to evaluate the next one. See Appendix A for detailed description of the criteria.

1. Determine the *appropriateness* of the nominated topic for inclusion in the EHC program.
2. Establish the overall *importance* of a potential topic as representing a health or healthcare issue in the United States.
3. Determine the *desirability of new evidence review* by examining whether a new systematic review or other AHRQ product would be duplicative.

4. Assess the *potential impact* a new systematic review or other AHRQ product.
5. Assess whether the *current state of the evidence* allows for a systematic review or other AHRQ product (feasibility).
6. Determine the *potential value* of a new systematic review or other AHRQ product.

Appropriateness and Importance
We assessed the nomination for appropriateness and importance.

Desirability of New Review/Duplication
We searched for high-quality, completed or in-process evidence reviews published in the last three years on the key questions of the nomination. See Appendix B for sources searched.

Impact of a New Evidence Review
The impact of a new evidence review was qualitatively assessed by analyzing the current standard of care, the existence of potential knowledge gaps, and practice variation. We considered whether it was possible for this review to influence the current state of practice through various dissemination pathways (practice recommendation, clinical guidelines, etc.).

Feasibility of New Evidence Review
We conducted a literature search in PubMed from May 2014 to May 2019. See Appendix C for the PubMed search strategy and links to the ClinicalTrials.gov search.

We reviewed all identified titles and abstracts for inclusion and classified identified studies by key question and study design to assess the size and scope of a potential evidence review.

Results

See Appendix A for detailed assessments of all EPC selection criteria.

Appropriateness and Importance
This is an appropriate and important topic.

Desirability of New Review/Duplication
A new evidence review would not be duplicative of an existing evidence review. We found no relevant reviews on this topics.

Impact of a New Evidence Review
A new systematic review may have uncertain impact. It is not clear if this is a widespread concern about e-cigarettes.

Feasibility of a New Evidence Review
A new evidence review is not feasible. We found no relevant studies.

Related Literature
We identified two completed systematic reviews and one in-process systematic review. The two completed reviews appear to have sought all harms, and the studies that they identified did not relate to insulin levels or blood glucose levels. The in-process focuses on benefits and harms of vaping devices broadly, and does not look specifically at the impact of the flavorings and sweeteners. See Table 2, Duplication column.

- Zare et al. A systematic review of consumer preference for e-cigarette attributes: flavor, nicotine strength and type. 2018.[8]

    - This review included the impact of flavor on health and harm perception. They identified seven studies about the association between flavor and health. It stated that five studies showed that the flavors and sweeteners could be of toxicological concern.
- Zulkifli et al. Electronic cigarettes: a systematic review of available studies on health risk assessment. 2018. 9
    - This review identified four articles on the health risk assessment of e-cigarettes. Three focused on specific chemicals, including nicotine, propylene glycol, glycerol and 1,2 propanediol; and one evaluated health risks by heavy metals.
- MacDonald et al. Clearing the air: a meta-narrative synthesis on the harms and benefits of electronic cigarettes and vapour devices. PROSPERO 2015 CRD42015025267 Available from: http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42015025267 10
    - The outcomes sought are any benefits or harms. Presumably if insulin levels, glucose levels or hemoglobin A1C is reported in primary studies, these would be included.

Summary of Findings

- Appropriateness and importance: The topic is both appropriate and important.
- Duplication: A new review would not be duplicative of an existing product. We found no relevant reviews.
- Impact: The impact of a new review on this topic is uncertain.
- Feasibility: A new review is not feasible. We found no relevant studies.

References

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Appendix A. Selection Criteria Assessment

Selection Criteria	Assessment
1. Appropriateness	
1a. Does the nomination represent a health care drug, intervention, device, technology, or health care system/setting available (or soon to be available) in the U.S.?	Yes, vaping devices are available.
1b. Is the nomination a request for a systematic review?	No
1c. Is the focus on effectiveness or comparative effectiveness?	No
1d. Is the nomination focus supported by a logic model or biologic plausibility? Is it consistent or coherent with what is known about the topic?	Yes
2. Importance	
2a. Represents a significant disease burden; large proportion of the population	It is estimated that 4.5% (or 10.8 million) American adults are e-cigarette users. The prevalence was highest among 18-24 year olds.
2b. Is of high public interest; affects health care decision making, outcomes, or costs for a large proportion of the US population or for a vulnerable population	yes
2c. Represents important uncertainty for decision makers	Yes, there is uncertainty about the benefits and harms of vaping devices
2d. Incorporates issues around both clinical benefits and potential clinical harms	Yes, there is uncertainty about the benefits and harms of vaping devices. It is theorized that e-cigarettes are less harmful than cigarettes.
2e. Represents high costs due to common use, high unit costs, or high associated costs to consumers, to patients, to health care systems, or to payers	Yes
3. Desirability of a New Evidence Review/Duplication	
3. Would not be redundant (i.e., the proposed topic is not already covered by available or soon-to-be available high-quality systematic review by AHRQ or others)	We identified no relevant systematic reviews.
4. Impact of a New Evidence Review	
4a. Is the standard of care unclear (guidelines not available or guidelines inconsistent, indicating an information gap that may be addressed by a new evidence review)?	Guidelines do not address the concern about the liquids in e-cigarettes impacting diabetes control.
4b. Is there practice variation (guideline inconsistent with current practice, indicating a potential implementation gap and not best addressed by a new evidence review)?	See above.
5. Primary Research	
5. Effectively utilizes existing research and knowledge by considering: - Adequacy (type and volume) of research for conducting a systematic review - Newly available evidence (particularly for updates or new technologies)	We found no studies addressing the nomination question.

Abbreviations: AHRQ=Agency for Healthcare Research and Quality

Appendix B. Search for Evidence Reviews (Duplication)

Listed below are the sources searched, hierarchically

Primary Search
AHRQ: Evidence reports and technology assessments https://effectivehealthcare.ahrq.gov/; https://www.ahrq.gov/research/findings/ta/index.html; https://www.ahrq.gov/research/findings/evidence-based-reports/search.html
VA Products: PBM, and HSR&D (ESP) publications, and VA/DoD EBCPG Program https://www.hsrd.research.va.gov/publications/esp/
Cochrane Systematic Reviews http://www.cochranelibrary.com/
PubMed Health http://www.ncbi.nlm.nih.gov/pubmedhealth/
PROSPERO Database (international prospective register of systematic reviews and protocols) http://www.crd.york.ac.uk/prospero/
Epistemonikos
Health Systems Evidence
PDQ Evidence
HTA

Appendix C. Search for Primary Studies (Feasibility)

Feasibility	
MEDLINE(PubMed) searched on: May 16, 2019	
Concept	
Electronic Cigarettes	(((((vaping[Title/Abstract] OR vaporizing[Title/Abstract] OR inhale[Title/Abstract] OR inhaled[Title/Abstract] OR inhaler[Title/Abstract] OR aerosol[Title/Abstract]))) OR ((((("Electronic Nicotine Delivery Systems"[Mesh]) OR "Vaping"[Mesh])) OR ("Nebulizers and Vaporizers"[Mesh]))
AND	
Flavorings and sweeteners	(((((((("Flavoring Agents"[Mesh] OR "Flavoring Agents" [Pharmacological Action] OR "Vanilla"[Mesh] OR "Mentha"[Mesh] OR "Cinnamomum"[Mesh] OR "Eucalyptus"[Mesh] OR "Benzaldehydes"[Mesh] OR "vanillin" [Supplementary Concept]) OR "Diacetyl"[Mesh]) OR "2,3-pentanedione" [Supplementary Concept]) OR "Furaldehyde"[Mesh]) OR "Glucose"[Mesh]) OR "Sorbitol"[Mesh]) OR ("Sucrose"[Mesh] OR "sucrose synthase" [Supplementary Concept]))) OR ((flavor*[Title] OR flavour*[Title] OR sweetener*[Title]))
AND	
Insulin Levels	((("Diabetes Complications"[Mesh] OR "Diabetes Insipidus"[Mesh] OR "Diabetes Mellitus"[Mesh]) OR "Insulin"[Mesh]) OR ("Glycated Hemoglobin A"[Mesh] OR "hemoglobin A1c protein, human" [Supplementary Concept])) OR "Blood Glucose"[Mesh]
AND	
Limits: 5 years, English N=30	published in the last 5 years; English
SR N=0	systematic[sb]
RCT N=20	(((((((groups[tiab])) OR (trial[tiab])) OR (randomly[tiab])) OR (drug therapy[sh])) OR (placebo[tiab])) OR (randomized[tiab])) OR (controlled clinical trial[pt])) OR (randomized controlled trial[pt])
Other N=30	
clinicalTrials.gov	[again, noting related to eCigarettes, only inhaled insulin]

https://clinicaltrials.gov/ct2/results?cond=e-cigarette&term=diabetes&cntry=&state=&city=&dist=&Search=Search