

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Association between vaping and health outcomes in patients with opioid use disorder: A systematic review protocol
AUTHORS	Sanger, Nitika; D'Elia, Alessia; Sanger, Stephanie; Rosic, Tea; Samaan, M. Constantine; Kapczinski, Flavio; de Souza, Russell; Thabane, Lehana; Samaan, Zainab

VERSION 1 – REVIEW

REVIEWER	Neha Batura University College London
REVIEW RETURNED	08-Jun-2020

GENERAL COMMENTS	Overall, this is clear protocol. However, there are some gaps that should be addressed before publication and further progress with this study. - Abstract, methods section: "data will be conducted according to the data extraction form..." there is a typo in this sentence that confuses the meaning. - Ethics and dissemination: would the authors not propose to submit the review results for publication in a peer-reviewed journal? - Introduction, lines 7-8: The authors mention that there is a scarcity of evidence the health impact of vaping. However, there are quite a few papers that look at the public health impact of vaping, for example: Palazzolo DL. Electronic cigarettes and vaping: a new challenge in clinical medicine and public health. A literature review. <i>Frontiers in public health</i>. 2013 Nov 18;1:56. Agustin M, Yamamoto M, Cabrera F, Eusebio R. Diffuse alveolar hemorrhage induced by vaping. <i>Case reports in pulmonology</i>. 2018;2018. Abafalvi L, Péntzes M, Urbán R, Foley KL, Kaán R, Kispélyi B, Hermann P. Perceived health effects of vaping among Hungarian adult e-cigarette-only and dual users: a cross-sectional internet survey. <i>BMC public health</i>. 2019 Dec;19(1):302. Could the authors clarify where exactly the gap in the existing evidence lies? Is it specifically for the OUD population? Is there a methodological gap? This would clarify the contribution of the proposed review. This should also be linked more clearly to the gap in the evidence for OUD population. - Objectives: the authors do not mention that they will conduct a quality appraisal of included studies. Quality appraisal is an important part of the evaluation of the evidence, that would give the reader an idea of the confidence one can place in the robustness of the included evidence or any meta analysis
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	conducted. The authors could include an appraisal based on the GRADE or other appropriate checklist. - Methods, eligibility criteria: It is not clear whether review papers, editorials, commentaries, and/or conference proceedings will be excluded. - Methods, data synthesis: The authors do not mention how they will analyse the data if a meta analysis is not possible. It would be worthwhile to include this in the methods section in case there is too much heterogeneity in the outcomes of the selected studies.
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REVIEWER	Kirsten Smith National Institute on Drug Abuse Intramural Research Program, United States
REVIEW RETURNED	09-Sep-2020

GENERAL COMMENTS	It was a pleasure to review the manuscript entitled "Associations between vaping and health outcomes in patients with opioid use disorder: A systematic review protocol". The topic of vaping is an important one, particularly in the context of the opioid crisis and within the context of high rates of comorbidities between nicotine (in all its forms; and cannabis to a lesser extent) and opioids (in all its forms). Overall, the manuscript was well conceived and written and the objectives are feasible and appropriate for where the current body of literature stands. The eligibility/inclusion criteria, outcomes and prioritization, information sources, search terms, etc. are all well thought out and appropriate. In short, the methods look solid as does the analytic plan Truly, there are only minor issues, such as proofreading again for minor issues, such as missing commas, hyphens and just small ways for improving readability and making sentences as concise as possible without losing information. However, the broad and most crucial question to both authors and editors is this: Why publish a protocol for a systematic review (and possible MA) rather than conducting the systematic review (and possible MA) and then publishing together in one paper (journals often expand total word count to accommodate the length of SRs, after all). There is indeed a place for the publication of protocols in academic journals (I am currently reformatting a protocol for a RCT for submission and am, in this respect, sympathetic to the cause of attempting to publish a protocol. However, a SR in a somewhat nascent subarea of work, while important, but that will not, it seems, include ground-breaking methods nor novel methodology doesn't necessarily warrant taking up precious journal space. In short, the question posed is what are the merits of publishing a protocol for a SR and why not just conduct the SR and publish what is written plus the findings? It is possible that what is written in this manuscript will be repackaged and added onto the findings and published again.
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	I must ultimately defer to the editors as to whether or not they wish to publish a SR protocol given that most protocols that are published are not for SRs, but rather for clinical trials. Again, what is presented here is a promising start and will doubtless add a contribution to the literature once completed.
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VERSION 1 – AUTHOR RESPONSE

Responses to Reviewer 1's Comments:

Overall, this is clear protocol. However, there are some gaps that should be addressed before publication and further progress with this study.

Reviewer's Comment: Abstract, methods section: "data will be conducted according to the data extraction form..." there is a typo in this sentence that confuses the meaning.

Authors' Response: Thank you for highlighting this typo. The sentence now reads as follows: "Data collection from eligible studies will be conducted according to the data extraction form tested prior to abstraction." (See page 2, Abstract, Methods section, line 20).

Reviewer's Comment: Ethics and dissemination: would the authors not propose to submit the review results for publication in a peer-reviewed journal?

Authors' Response: The ethics and dissemination section of the abstract has been amended to now include peer-reviewed publications: "The results for this review will be disseminated through publications in peer-reviewed journals, posters and presentations at scientific conferences." (See page 2, Ethics and Dissemination section, line 26).

Reviewer's Comment:

Introduction, lines 7-8: The authors mention that there is a scarcity of evidence the health impact of vaping. However, there are quite a few papers that look at the public health impact of vaping, for example:

Palazzolo DL. Electronic cigarettes and vaping: a new challenge in clinical medicine and public health. A literature review. *Frontiers in public health*. 2013 Nov 18;1:56.

Agustin M, Yamamoto M, Cabrera F, Eusebio R. Diffuse alveolar hemorrhage induced by vaping. *Case reports in pulmonology*. 2018;2018.

Abafalvi L, Péntzes M, Urbán R, Foley KL, Kaán R, Kispélyi B, Hermann P. Perceived health effects of vaping among Hungarian adult e-cigarette-only and dual users: a cross-sectional internet survey. *BMC public health*. 2019 Dec;19(1):302.

Could the authors clarify where exactly the gap in the existing evidence lies? Is it specifically for the OUD population? Is there a methodological gap? This would clarify the contribution of the proposed review. This should also be linked more clearly to the gap in the evidence for OUD population.

Authors' Response: Thank you for your comment. The gap we propose to address through this review is referring to the research conducted related to vaping within the OUD population. In order to clarify this aim, the statement addressing the gap in the existing evidence has been amended to now read: "Vaping behaviour has increased in popularity, raising many questions about short- and long-term health outcomes in at-risk individuals given the scarcity of evidence and methodological investigations conducted within these populations." (See page 3, Rationale, line 3-5).

Reviewer's Comment:

Objectives: the authors do not mention that they will conduct a quality appraisal of included studies. Quality appraisal is an important part of the evaluation of the evidence, that would give the reader an idea of the confidence one can place in the robustness of the included evidence or any meta analysis conducted. The authors could include an appraisal based on the GRADE or other appropriate checklist.

Authors' Response: Thank you for your comment. We agree that conducting quality appraisal of the evidence is important. We have included GRADE in our protocol. (See page 7, Confidence in cumulative evidence, lines 1-2).

Reviewer's Comment:

Methods, eligibility criteria: It is not clear whether review papers, editorials, commentaries, and/or conference proceedings will be excluded.

Authors' Response: Thank you for your comment. We have added more exclusion criteria in this section to reflect that we will be excluding review papers, editorials, commentaries and conference proceedings/abstracts. (See page 4, Eligibility criteria, line 20-21).

Reviewer's Comment:

Methods, data synthesis: The authors do not mention how they will analyse the data if a meta analysis is not possible. It would be worthwhile to include this in the methods section in case there is too much heterogeneity in the outcomes of the selected studies.

Authors' Response: Thank you for your suggestion. We have included how we will analyze the data if a meta-analysis is not possible. (See page 6, Data synthesis, lines 36-38).

Responses to Reviewer 2's Comments:

It was a pleasure to review the manuscript entitled "Associations between vaping and health outcomes in patients with opioid use disorder: A systematic review protocol".

The topic of vaping is an important one, particularly in the context of the opioid crisis and within the context of high rates of comorbidities between nicotine (in all its forms; and cannabis to a lesser extent) and opioids (in all its forms).

Overall, the manuscript was well conceived and written and the objectives are feasible and appropriate for where the current body of literature stands.

The eligibility/inclusion criteria, outcomes and prioritization, information sources, search terms, etc. are all well thought out and appropriate. In short, the methods look solid as does the analytic plan

Truly, there are only minor issues, such as proofreading again for minor issues, such as missing commas, hyphens and just small ways for improving readability and making sentences as concise as possible without losing information.

Authors' Response: Thank you for your comment. We have gone through the entire manuscript to ensure that readability and conciseness has improved.

Reviewer's Comment: However, the broad and most crucial question to both authors and editors is this: Why publish a protocol for a systematic review (and possible MA) rather than conducting the

systematic review (and possible MA) and then publishing together in one paper (journals often expand total word count to accommodate the length of SRs, after all). There is indeed a place for the publication of protocols in academic journals (I am currently reformatting a protocol for a RCT for submission and am, in this respect, sympathetic to the cause of attempting to publish a protocol. However, a SR in a somewhat nascent subarea of work, while important, but that will not, it seems, include ground-breaking methods nor novel methodology doesn't necessarily warrant taking up precious journal space.

In short, the question posed is what are the merits of publishing a protocol for a SR and why not just conduct the SR and publish what is written plus the findings?

It is possible that what is written in this manuscript will be repackaged and added onto the findings and published again.

I must ultimately defer to the editors as to whether or not they wish to publish a SR protocol given that most protocols that are published are not for SRs, but rather for clinical trials.

Again, what is presented here is a promising start and will doubtless add a contribution to the literature once completed.

Authors' Response: Thank you for your comment. Publishing the protocols for systematic reviews provides transparency and peer-review of the methods before the actual review commences to improve quality of the review, avoid selective reporting of results, errors in methodology and duplication of reviews. Additionally, the Cochrane Handbook of systematic reviews provides the rationale for publishing a protocol "...publication of a protocol for a review prior to knowledge of the available studies reduces the impact of review authors' biases, promotes transparency of methods and processes, reduces the potential for duplication, and allows peer review of the planned methods". (Cochrane Handbook 2.1 Rationale for protocols).