

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Vaping cannabis among adolescents: prevalence and associations with tobacco use from a cross-sectional study in the United States
AUTHORS	Kowitt, Sarah; Osman, Amira; Meernik, Clare; Zarkin, Gary; Ranney, Leah; Martin, Jim; Heck, Courtney; Goldstein, A

VERSION 1 - REVIEW

REVIEWER	Stanton Glantz University of California San Francisco
REVIEW RETURNED	22-Dec-2018

GENERAL COMMENTS	<p>This paper reports the prevalence of vaping cannabis among high school students in North Carolina, a state that has not legalized cannabis use in any form. Vaping cannabis is associated with vaping tobacco and some, but not all, other forms of tobacco use.</p> <p>Page 2, line 33: Is this the same e-cigarette device as used to vape tobacco or a specialized device designed for cannabis? The authors may not be able to answer this question, but the issue needs to be addressed directly in the paper (if not the abstract).</p> <p>Page 2, line 45: Present the fact that there is not a significant association with cigarette or smokeless tobacco use. This information also needs to be added to the text of the manuscript.</p> <p>Page 5, line 8: Same comment as page 2, line 33.</p> <p>Page 5, line 19: Specify "tobacco e-cigarettes."</p> <p>Page 7, line 8: Work the material in the footnote into the text.</p> <p>Page 8, line 15: Change "that were statistically significant" to "with" to avoid arguments over whether or not 0.10 should be considered "statistically significant" when 0.05 is the traditional level. The use of 0.10 for screening variables to be included in the multivariable analysis is fine.</p> <p>Page 8, line 21: How were these "correlations" calculated, given the yes/no nature of the data. There is probably a more appropriate measure of association.</p> <p>Page 9, line 5: How was the $p < .001$ value determined?</p>
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	<p>Page 9, line 38: Include results for cigarettes and smokeless tobacco.</p> <p>Page 9, line 47: Say “high school students” rather than “adolescents,” which could include younger students. The manuscript should also give the age range at an appropriate place because BMJ Open is an international journal and “high school” could be difference age ranges in other countries.</p> <p>Page 10, line 30: What about California?</p> <p>Page 11, line 17: If the specific devices are not known, i.e., if they are tobacco e-cigarettes used for cannabis or specialized cannabis devices, that situation should be listed as a limitation.</p> <p>Table 1: Reorganize to list the percentages first. The n’s should also be there, but the percentages are the appropriate descriptive statistics.</p> <p>Page 15, line 22: Indicate that these are “tobacco e-cigarettes.”</p>
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REVIEWER	Alex Liber University of Michigan, United States
REVIEW RETURNED	08-Jan-2019

GENERAL COMMENTS	<p>General Comments:</p> <p>Overall, the paper makes a minor contribution to the literature based on a reputable data source. The findings are described in conservative language appropriate to a single cross-section of data. I cannot say that the findings are terribly interesting to me, but they merit publication in some journal.</p> <p>The authors should add a sentence in the introduction or methods section that indicates whether similar surveys have been able to verify survey reported data with observational or biological indicators. Essentially, do we know the veracity of these self-reported figures? Do they skew low, high, or some other way?</p> <p>The discussion section treats the relative risks of vaping versus smoking cannabis in a cavalier manner which does not tackle the difficult inquiries into why non-combusted cannabis products should be included or excluded as legal cannabis markets expand. Essentially, the paper identifies a co-usage pattern between products and speculates from there about health hazards and the need for tougher regulations without inquiring as to the limits of their data or why these patterns have cropped up. What we do know is that cannabis vaping is likely to be less harmful than cannabis smoking (https://www.nap.edu/catalog/24625/the-health-effects-of-cannabis-and-cannabinoids-the-current-state). The authors seem to stick to theoretical harms as justification for their concern about the implications of their data rather than considering the possibility that the diversion of youth into vaping cannabis instead of smoking it may be a public health gain if vaping does not increase overall cannabis usage rates.</p> <p>I understand that the authors wanted to utilize the dataset at hand, but is there some reason to think that the Monitoring the Future survey could have done a better job at answering their questions on a national level. That survey includes questions about smoked marijuana use and contains data from jurisdictions that have legalized marijuana in different forms. The amount of useful data</p>
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that could be extracted from that survey seems to exceed the current data used in this paper. I don't mean to mark down the current paper in reference to a potential future paper, but it seems as though that paper would have more to say to policy discussions, even though it would face more policy confounders than the current paper.

Overall, there is little reason to reject the paper. It points to some concrete results of reasonable importance. I'm looking forward to reading the revision.

Specific Comments:

Page 6

Line 8: Replace "e-cigarette" with "e-cigarettes".

Page 8

Line 8: Did the authors perform any tests to determine if the choice to exclude these observations with missing data provided a threat to the findings?

Line 49: Replace "even" with "evenly".

Page 9

Line 3: "Dose response" does not seem to be the right term here. The participants are older, so they have lived more days, but that doesn't necessarily describe what a dose response relationship is. The better term might be "age response" here because the only "dose" being experienced by older students is aging. I am not an epidemiologist, but I cannot help but think that there is a better phrase to use here.

Page 10

Line 8: Please delete the word "state" and add "for any adult" after "legal". The fact that North Carolina is a state is not germane to the conclusion being made. Cannabis use is not legal for any adult, a bit different from the way in which tobacco (with the exception of a few 12th graders) is not legal for any minor to use in the state.

Lines 11-20: The discussion of relative risks is a bit clunky in that it feints at a lower relative risk then pivots to making the case of increased harm. Cross sectional studies like this one are not able to contribute evidence of whether vaping cannabis leads to more tobacco use or vice versa, so it is exactly fair to put an unexamined risk on the side against vaping cannabis while downplaying the better-established evidence of reduced harm relative to smoking marijuana.

Lines 24-26: Please delete "high" and consider adding "to the researchers" after "concerning". I do not see why 9.6% ever use is considered to be high or why the concern engendered needs to be applied broadly. We do not know enough about this prevalence figure to know if it is rising, falling, or staying steady, which in my view are the better determinants of concern. We do see in the latest Monitoring the Future Data

(<http://www.monitoringthefuture.org/data/18data/18drtbl1.pdf>) that ever vaping of cannabis did rise from 2017 to 2018. That is likely the fact I would cite to make the case of general concern, rather than this single cross section in this paper. Until more data is available, the concern should be personally held by the authors.

Line 45: On the point of Uruguay and Canada. To the best of my knowledge neither country has yet legally allowed the sale of non-combusted forms of cannabis. Canada will get there by October 2019 (<https://bit.ly/2QfgfY1>). Uruguay's law just applies to cannabis plants

(<https://legislativo.parlamento.gub.uy/temporales/leytemp9310681.htm>). So, one would need to compare health outcomes between the two places over time once Canada allow the vaping products to be sold in order to learn anything from their experiment about

	<p>health risks. Oddly enough, the state of Utah approved a more radical version of medical cannabis that only allows the sale of non-combustibles (https://bit.ly/2F6yzCE) which might prove to be a still better experiment.</p> <p>Page 11 Line 10: Add Pax to the potential cannabis vaping brand list. Line 12: The mention of not inquiring about other forms of cannabis use seems to be a serious oversight and something worth looking into in future inquiries. The including of the clause after the comma in this sentence just sounds defensive. Please remove and comment on what threat the exclusion of this question might have posed to the answers uncovered. Line 26: Insert “the” between “With” and “North Carolina”. Also please add a citation substantiating this claim. Line 40: On the Footnote: I do wonder whether the definition of e-cigarettes that centers around nicotine-containing brand names affected the rate of affirmative responses to the question about cannabis vaping. There are no cannabis vaporizers listed among the brand names so there is some possibility of not triggering a connection to the use of those devices. Mostly, this could be listed as a limitation to the survey and a place for future methodological tinkering. Line 47: Mention the lack of inclusion of Juul as a brand name as a shortcoming. In 2017, when the survey was administered, the brand experience exponential growth. I’m sure it would have been included in a 2018 survey, but its exclusion is certainly notable.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer 1: Stanton Glantz	
1. This paper reports the prevalence of vaping cannabis among high school students in North Carolina, a state that has not legalized cannabis use in any form. Vaping cannabis is associated with vaping tobacco and some, but not all, other forms of tobacco use.	Thank you for the time you spent reviewing our manuscript and providing feedback.
2. Page 2, line 33: Is this the same e-cigarette device as used to vape tobacco or a specialized device designed for cannabis? The authors may not be able to answer this question, but the issue needs to be addressed directly in the paper (if not the abstract).	The survey did not allow us to distinguish whether participants used tobacco e-cigarettes for cannabis or specialized cannabis devices. We added this as a limitation of the study (pages 12-13).
3. Page 2, line 45: Present the fact that there is not a significant association with cigarette or smokeless tobacco use. This information also needs to be added to the text of the manuscript.	We added that there was no significant association between cigarette and smokeless tobacco and odds of ever vaping cannabis (page 2 and 9). We agree that this is important information to include in the abstract and manuscript.
4. Page 5, line 8: Same comment as page 2, line 33.	Few studies have examined the prevalence of using e-cigarette devices for vaping cannabis or the prevalence of using specialized devices

	to vape cannabis. We have clarified this in the introduction (page 5).
5. Page 5, line 19: Specify “tobacco e-cigarettes.”	We specified tobacco e-cigarettes in this sentence (page 5).
6. Page 7, line 8: Work the material in the footnote into the text.	We now include in the text the material that was previously listed in a footnote (page 7).
7. Page 8, line 15: Change “that were statistically significant” to “with” to avoid arguments over whether or not 0.10 should be considered “statistically significant” when 0.05 is the traditional level. The use of 0.10 for screening variables to be included in the multivariable analysis is fine.	We changed this sentence and replaced “that were statistically significant” to “with” (page 8).
8. Page 8, line 21: How were these “correlations” calculated, given the yes/no nature of the data. There is probably a more appropriate measure of association.	We calculated correlations using phi coefficients, which is a measure of association between dichotomous variables. We now state this in the methods section (page 8).
9. Page 9, line 5: How was the $p < .001$ value determined?	We calculated this p-value using bivariate chi-square tests and qualitatively determined that increasing grade was associated with increasing prevalence of ever vaping cannabis. We rephrased this sentence to make this clearer that we did not conduct a trend analysis (page 9).
10. Page 9, line 38: Include results for cigarettes and smokeless tobacco.	We added that there was no significant association between cigarette and smokeless tobacco and odds of ever vaping cannabis (page 9).
11. Page 9, line 47: Say “high school students” rather than “adolescents,” which could include younger students. The manuscript should also give the age range at an appropriate place because BMJ Open is an international journal and “high school” could be different age ranges in other countries.	We left the word “adolescents” in this sentence but clarified to which group of students each previous prevalence estimate referred. We also clarified the age range for high school students in the US and provided age ranges for the other studies when they were stated in the respective papers (page 10).
12. Page 10, line 30: What about California?	In California, you cannot consume, smoke, eat, or vape cannabis in public places and vaping marijuana is not allowed anywhere where tobacco smoking is not allowed. https://www.cdph.ca.gov/Programs/DO/letstalkcannabis/Pages/legal.aspx http://uknowledgeshare.com/wp-content/uploads/Smoke-and-Tobacco-Free-Part-1.pdf (see last slide)
13. Page 11, line 17: If the specific devices are not known, i.e., if they are tobacco e-cigarettes used for cannabis or specialized cannabis devices, that situation should be listed as a limitation.	We added as a limitation that we were unable to assess whether participants used tobacco e-cigarettes for cannabis or specialized cannabis devices (pages 12-13).

14. Table 1: Reorganize to list the percentages first. The n's should also be there, but the percentages are the appropriate descriptive statistics.	We reorganized Table 1 so that the percentages appear first (page 16).
15. Page 15, line 22: Indicate that these are "tobacco e-cigarettes."	We stated that these are tobacco e-cigarettes (pages 16-17).
Reviewer 2: Alex Liber	
16. Overall, the paper makes a minor contribution to the literature based on a reputable data source. The findings are described in conservative language appropriate to a single cross-section of data. I cannot say that the findings are terribly interesting to me, but they merit publication in some journal.	Thank you for the time you spent reviewing our manuscript and providing feedback.
17. The authors should add a sentence in the introduction or methods section that indicates whether similar surveys have been able to verify survey reported data with observational or biological indicators. Essentially, do we know the veracity of these self-reported figures? Do they skew low, high, or some other way?	No studies, to our knowledge, have used observational or biological indicators to verify reports of vaping cannabis. We stated this as a limitation (pages 12-13).
18. The discussion section treats the relative risks of vaping versus smoking cannabis in a cavalier manner which does not tackle the difficult inquiries into why non-combusted cannabis products should be included or excluded as legal cannabis markets expand. Essentially, the paper identifies a co-usage pattern between products and speculates from there about health hazards and the need for tougher regulations without inquiring as to the limits of their data or why these patterns have cropped up. What we do know is that cannabis vaping is likely to be less harmful than cannabis smoking (https://www.nap.edu/catalog/24625/the-health-effects-of-cannabis-and-cannabinoids-the-current-state). The authors seem to stick to theoretical harms as justification for their concern about the implications of their data rather than considering the possibility that the diversion of youth into vaping cannabis instead of smoking it may be a public health gain if vaping does not increase overall cannabis usage rates.	<p>We agree that vaping cannabis is likely less harmful than smoking cannabis and have noted this in the paper. We, do, however, believe that there may be some concerns about youth vaping cannabis for the reasons listed in the paper: it could lead to earlier initiation of tobacco or cannabis use, increased frequency of use or misuse, increased potency of cannabis, or concomitant tobacco and cannabis use. Since we do not have data on non-combusted cannabis product use, we feel this topic while an important and interesting question, is beyond the scope of this paper.</p> <p>We amended this paragraph to state that there are some potential concerns about adolescents (specifically) vaping cannabis. We also acknowledged that more research quantifying the population-level benefits and harms of non-combustible forms of cannabis is needed (pages 10-11).</p>
19. I understand that the authors wanted to utilize the dataset at hand, but is there some reason to think that the Monitoring the Future survey could have done a better job at	We agree that the Monitoring the Future survey would be a great dataset for future explorations of vaping cannabis and correlates associated with vaping cannabis. We have noted this in the

<p>answering their questions on a national level. That survey includes questions about smoked marijuana use and contains data from jurisdictions that have legalized marijuana in different forms. The amount of useful data that could be extracted from that survey seems to exceed the current data used in this paper. I don't mean to mark down the current paper in reference to a potential future paper, but it seems as though that paper would have more to say to policy discussions, even though it would face more policy confounders than the current paper. Overall, there is little reason to reject the paper. It points to some concrete results of reasonable importance. I'm looking forward to reading the revision.</p>	<p>paper (page 12). Our data is the first examination of vaping cannabis among NC youth providing utility for baseline information, as NC approaches the idea of legalizing marijuana.</p>
<p>20. Page 6, Line 8: Replace "e-cigarette" with "e-cigarettes".</p>	<p>We replaced "e-cigarette" with "e-cigarettes" (page 6).</p>
<p>21. Page 8, Line 8: Did the authors perform any tests to determine if the choice to exclude these observations with missing data provided a threat to the findings?</p>	<p>We conducted an attrition analysis (see Supplementary Table A) and found that a higher proportion of females, non-Hispanic White adolescents, and non-current tobacco product users were included in the final sample. We now list this as a limitation (page 13).</p>
<p>22. Page 8, Line 49: Replace "even" with "evenly".</p>	<p>We replaced "even" with "evenly" (page 8).</p>
<p>23. Page 9, Line 3: Dose response" does not seem to be the right term here. The participants are older, so they have lived more days, but that doesn't necessarily describe what a dose response relationship is. The better term might be "age response" here because the only "dose" being experienced by older students is aging. I am not an epidemiologist, but I cannot help but think that there is a better phrase to use here.</p>	<p>We deleted the term "dose-response relationship". Instead, we now state that increasing grade was associated with increasing prevalence of ever vaping cannabis (page 9).</p>
<p>24. Page 10, Line 8: Please delete the word "state" and add "for any adult" after "legal". The fact that North Carolina is a state is not germane to the conclusion being made. Cannabis use is not legal for any adult, a bit different from the way in which tobacco (with the exception of a few 12th graders) is not legal for any minor to use in the state.</p>	<p>We deleted the word "state" and added "for any adult" after "legal" (page 10). Thank you for the clarification.</p>
<p>25. Page 10, Lines 11-20: The discussion of relative risks is a bit clunky in that it feints at a lower relative risk then pivots to making the case of increased harm. Cross sectional studies like this one are not able to contribute evidence of whether vaping</p>	<p>Please see our response to Comment # 21.</p>

<p>cannabis leads to more tobacco use or vice versa, so it is exactly fair to put an unexamined risk on the side against vaping cannabis while downplaying the better-established evidence of reduced harm relative to smoking marijuana.</p>	
<p>26. Page 10, Lines 24-26: Please delete “high” and consider adding “to the researchers” after “concerning”. I do not see why 9.6% ever use is considered to be high or why the concern engendered needs to be applied broadly. We do not know enough about this prevalence figure to know if it is rising, falling, or staying steady, which in my view are the better determinants of concern. We do see in the latest Monitoring the Future Data (http://www.monitoringthefuture.org/data/18data/18drtbl1.pdf) that ever vaping of cannabis did rise from 2017 to 2018. That is likely the fact I would cite to make the case of general concern, rather than this single cross section in this paper. Until more data is available, the concern should be personally held by the authors.</p>	<p>We deleted the word “high” and added “to the researchers” after “concerning”. Thank you for providing the additional reference to MTF data. We have included it in the manuscript (page 11).</p>
<p>27. Page 10, Line 45: On the point of Uruguay and Canada. To the best of my knowledge neither country has yet legally allowed the sale of non-combusted forms of cannabis. Canada will get there by October 2019 (https://bit.ly/2QfgfY1). Uruguay’s law just applies to cannabis plants (https://legislativo.parlamento.gub.uy/temporales/leytemp9310681.htm). So, one would need to compare health outcomes between the two places over time once Canada allow the vaping products to be sold in order to learn anything from their experiment about health risks. Oddly enough, the state of Utah approved a more radical version of medical cannabis that only allows the sale of non-combustibles (https://bit.ly/2F6yzCE) which might prove to be a still better experiment.</p>	<p>Thank you for providing this information, which is both thorough and relevant for our manuscript. We have included more detailed information about Utah legalizing non-combustible forms of cannabis and noted that Uruguay and Canada do not currently allow for sale of non-combustible forms of cannabis (pages 11-12).</p>
<p>28. Page 11, Line 10: Add Pax to the potential cannabis vaping brand list.</p>	<p>We added Pax as a potential cannabis vaping brand (page 12).</p>
<p>29. Page 11, Line 12: The mention of not inquiring about other forms of cannabis use seems to be a serious oversight and something worth looking into in future inquiries. The including of the clause after the comma in this sentence just sounds defensive. Please remove and comment on</p>	<p>We have removed the clause noted after the comma and provided some potential ways the lack of cannabis-related items limited the current study (page 12).</p>

what threat the exclusion of this question might have posed to the answers uncovered.	
30. Page 11, Line 26: Insert “the” between “With” and “North Carolina”. Also, please add a citation substantiating this claim.	We added citations for the 3 bills that NC legislators considered in 2017 to make it legal for adults to possess medical cannabis. These bills were recently defeated so we have updated this sentence.
31. Page 11, Line 40: On the Footnote: I do wonder whether the definition of e-cigarettes that centers around nicotine-containing brand names affected the rate of affirmative responses to the question about cannabis vaping. There are no cannabis vaporizers listed among the brand names so there is some possibility of not triggering a connection to the use of those devices. Mostly, this could be listed as a limitation to the survey and a place for future methodological tinkering.	We added a limitation about the definition of e-cigarettes included in a previous section of the survey (page 13).
32. Page 11, Line 47: Mention the lack of inclusion of Juul as a brand name as a shortcoming. In 2017, when the survey was administered, the brand experience exponential growth. I’m sure it would have been included in a 2018 survey, but its exclusion is certainly notable.	We included in the limitations that the survey did not mention JUUL as an e-cigarette brand name (page 13).

VERSION 2 – REVIEW

REVIEWER	Stanton Glantz University of California San Francisco USA
REVIEW RETURNED	14-Mar-2019

GENERAL COMMENTS	The authors did a nice job of revising this manuscript.
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