

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Cannabis use among a nationally representative cross-sectional sample of smokers and non-smokers in The Netherlands: Results from the 2015 ITC Netherlands Gold Magic Survey
AUTHORS	Fix, Brian; Smith, Danielle; O'Connor, Richard; Heckman, Bryan; Willemsen, Marc; Cummings, Michael; Fong, Geoffrey

VERSION 1 – REVIEW

REVIEWER	Hannah Walsh King's College London, UK
REVIEW RETURNED	08-Aug-2018

GENERAL COMMENTS	1. The study purpose as defined in the abstract and on p4 l48 is a broad aim; the paper would benefit from additionally specified objectives, which would identify whether the intended focus is on cannabis use predictors, or patterns of cannabis (and co-use) consumption, or both. 2. The abstract is missing the study design and primary/secondary outcome measures, which in relation to point 1 would help to define the study objectives. 3. This could be addressed by defining the study objectives and design. 4. As this is secondary analysis of previously collected data, a reference to the protocol or papers published from the original Gold Magic survey would strengthen the methods section. 5. Presumably these are described in greater detail in the parent study publications, see point 4 above. 6. p5, l33 "key items" could be replaced with "outcome measures", for example. 7. Statistical analysis used for cannabis use predictors are appropriate, although the more novel data that is provided in the cannabis consumption methods paragraph (p7 l41) would benefit from more focused presentation and further analysis - I would suggest Table 1 data is presented within the text, not necessarily as table if word count does not permit this, and consumption methods, cigarette smoking status and inclusion of tobacco with cannabis in a joint is given greater emphasis by presentation in a table, expanding upon Figure 1, and analysis beyond that which is presented. The latter data has potentially more to offer in terms of original findings. 9. I suggest defining the objectives and presenting the results in line with these objectives. 10. Presentation of results is clear, but see point 7 for suggestions on presentation focus. 11. Although the conclusions align with the results, the discussion would benefit from more in-depth analysis, as described in suggested structure in "Author information" in BMJ Open. This
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	could include: summarising the results with reference to the objectives; discussing the generalisability of the results (with reference to the initial sampling frame) and a wider discussion of the implications for research as well as public health. For example, the finding that cannabis users exposed to tobacco through joints may not be identified as "tobacco users" in a survey has significant implications for questionnaire design, as well as the public health implications referenced. It is notable that the introduction is significantly longer than the discussion, the paper overall would benefit from addressing this balance. 12. To enhance the discussion, the limitations could be discussed in greater depth, with reference made to the generalisability of the findings; whether the sample was considered representative (reference the original sampling frame from the Gold Magic Survey) and to what extent the questions posed within W2 of the GM survey answered the study objectives. 13. Reference to the original parent study protocol (if published), STROBE checklist, list of author contributions could be added. An additional note on terminology: "joints" could be defined at first use, as it may refer to rolled tobacco and cannabis in some areas of the world, and to rolled cannabis only in others. Secondly, exposure to nicotine and tobacco are both referenced - it would be clearer to specify which, or to clarify "tobacco and/or nicotine" if the intention is also to refer to ENDS. Lastly, p5 l5 refers to "hard drugs", though I note this is the NL government terminology, this requires further clarification for an international audience. There are a number of typographical errors and points of clarification which require attention: p2 l17: specify "tobacco (or cigarette) smokers", same for p8 l16 p2 l33: specify whether nicotine dependence or increased tobacco use is of concern p10 l28 requires correction
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REVIEWER	Robert McMillen Mississippi State University, USA
REVIEW RETURNED	28-Aug-2018

GENERAL COMMENTS	The authors address an interesting and timely issue, as more jurisdictions begin to tolerate medical and/or recreational marijuana use. Overall, the objectives are clear and the methods are appropriate to address these objectives. The paper, however, could be improved by providing more detail in several places. - The authors state that the survey was designed to provide a nationally representative sample, yet 63% of the sample were current smokers (per the abstract). That seems like a smoking rate from 1964. - The sample size numbers in the abstract do not match those in the first paragraph of the Results. I suspect that the difference is due to non-response to the cannabis use questions, but the authors should address this issue. - The results should begin with information about the response rate and sample characteristics. - The methods should provide more detail about the questions and responses used to assess cigarette smoking and cannabis use. Ideally, the authors should provide the questions, response options, and how the variable were collapsed. - There are two major limitations that need to be addressed; 1) the low sample size of past 30-day cannabis users, and 2) the very
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	low sample size of non-smoker past 30-day cannabis users. I'm not convinced that the results starting at line 41 of page 7 are justifiable when based on 16 non-smokers. - The Discussion needs to provide more detail about the importance of this study, its implications and its limitations.
REVIEWER	Lorraine Greaves PhD Centre of Excellence for Women's Health, Canada
REVIEW RETURNED	22-Oct-2018
GENERAL COMMENTS	This is a very timely and important contribution to the literature on simultaneous use of cannabis and tobacco. Not enough precise data exist on this important question. This report on survey data from the Netherlands offers a clear view of such use in the context of liberal cannabis regulations of some duration. Hence it is important for other jurisdictions to consider in further regulating or legalizing cannabis. I would suggest that where the authors found no significant differences in co use (sex, income, education), that some discussion be added to assist the readers in interpreting these results. For example, in the introduction, the authors state that being male is a key risk factor for cannabis use, but in this survey no difference is found. This bears some discussion. Is this result to be interpreted as new, specific to the Netherlands, other??? Certainly the reader will eagerly anticipate more insight into this key question, given that it makes considerable difference to both scientific and clinical measures of the effects of cannabis (sex-related factors), treatment protocols, research in nicotine/cannabis, and public health messaging. Similarly, the impact (or not) of income and education needs to be discussed, in order to render these results contextually understood and useful for future work.

VERSION 1 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:

Reviewer: 1

Reviewer Name: Hannah Walsh

Institution and Country: King's College London, UK

Please state any competing interests or state 'None declared': None

Please leave your comments for the authors below

1. The study purpose as defined in the abstract and on p4 l48 is a broad aim; the paper would benefit from additionally specified objectives, which would identify whether the intended focus is on cannabis use predictors, or patterns of cannabis (and co-use) consumption, or both.

RESPONSE: The authors agree with the need for more specific objectives. To that end, we have changed the "objectives" section of the abstract as follows:

"Objectives: Existing evidence shows that co-occurring use of tobacco and cannabis is widespread. Patterns of co-use of tobacco and cannabis may change as more jurisdictions legalize medicinal and/or recreational cannabis sales. This analysis examined predictors of current cannabis use and

characterized methods of consumption among smokers and non-smokers in a context where cannabis use is legal.”

2. The abstract is missing the study design and primary/secondary outcome measures, which in relation to point 1 would help to define the study objectives.

RESPONSE: As noted in the previous comment, we have added clearly defined study objectives to the “objectives” section of the abstract. In addition, we added the following to the “participants” section of the abstract:

“Participants (N=1,599; 1,003 current smokers, 283 former smokers, and 390 non-smokers) were asked to report their current (past 30-day) use of cigarettes and cannabis. Cigarette smokers reported whether they primarily used factory made (FM) or roll-your-own (RYO) cigarettes. Those who reported any cannabis use in the last 30 days were asked about forms of cannabis used. Chi-square and logistic regression analyses were used to assess relationships among combustible tobacco and cannabis use.”

3. This could be addressed by defining the study objectives and design.

RESPONSE: To specify the study objectives, the following paragraph was added to the end of the introduction section of the manuscript:

“This study examined co-use of cannabis and tobacco in a country where cannabis use is legal. The objectives were to examine predictors of current cannabis use and characterize methods of consumption among smokers and non-smokers.”

4. As this is secondary analysis of previously collected data, a reference to the protocol or papers published from the original Gold Magic survey would strengthen the methods section.

RESPONSE: The authors agree and have added a reference to a paper containing additional methods details, as well as the ITC technical report for the survey:

Heckman BW, Cummings KM, Nahas GJ, Willemssen MC, O'Connor RJ, Borland R, Hirsch AA, Bickel WK, Carpenter MJ. Behavioral Economic Purchase Tasks to Estimate Demand for Novel Nicotine/tobacco Products and Prospectively Predict Future Use: Evidence From The Netherlands. *Nicotine & Tobacco Research*. nty042. <https://doi.org/10.1093/ntr/nty042>

ITC Project. (2016, June). ITC Gold Magic Wave 1-2 (2014-2015) Technical Report. University of Waterloo, Waterloo, Ontario, Canada, and Maastricht University, The Netherlands. https://www.itcproject.org/files/ITC_GoldMagic_Waves1-2_Technical_Report_19Oct2016.pdf. Accessed December 8, 2018.

5. Presumably these are described in greater detail in the parent study publications, see point 4 above.

RESPONSE: As noted above, a reference was added to provide greater detail regarding the survey methods.

6. p5, l33 "key items" could be replaced with "outcome measures", for example.

RESPONSE: The authors agree and have made this change.

7. Statistical analysis used for cannabis use predictors are appropriate, although the more novel data that is provided in the cannabis consumption methods paragraph (p7 l41) would benefit from more focused presentation and further analysis - I would suggest Table 1 data is presented within the text, not necessarily as table if word count does not permit this, and consumption methods, cigarette smoking status and inclusion of tobacco with cannabis in a joint is given greater emphasis by

presentation in a table, expanding upon Figure 1, and analysis beyond that which is presented. The latter data has potentially more to offer in terms of original findings.

RESPONSE: The authors agree with the point made by the reviewer. However, the sample size (n=68) used for the suggested analysis limits our ability to do more sophisticated analyses with the consumption methods data.

9. I suggest defining the objectives and presenting the results in line with these objectives.

RESPONSE: As noted elsewhere, the objectives have now been more clearly defined throughout the manuscript. The results are now in line with the objectives.

10. Presentation of results is clear, but see point 7 for suggestions on presentation focus.

RESPONSE: Please see the response to point 7.

11. Although the conclusions align with the results, the discussion would benefit from more in-depth analysis, as described in suggested structure in "Author information" in BMJ Open. This could include: summarising the results with reference to the objectives; discussing the generalisability of the results (with reference to the initial sampling frame) and a wider discussion of the implications for research as well as public health. For example, the finding that cannabis users exposed to tobacco through joints may not be identified as "tobacco users" in a survey has significant implications for questionnaire design, as well as the public health implications referenced.

RESPONSE: The authors have added the following text to the discussion:
"Although the sample size in this study was small, a high proportion of self-reported non-cigarette smokers reported always (66.7%) or sometimes (16.7%) rolling cannabis with combustible tobacco for consumption. This means that many non-cigarette smoking cannabis users are likely misclassified as to their actual tobacco/nicotine exposure in surveys. This has importance in terms of future research when considering the precision with which we measure tobacco use and cannabis use separately and together. Future studies should take into account the potential that cannabis users are being exposed to tobacco through joints but might not identify as tobacco users in a survey."

It is notable that the introduction is significantly longer than the discussion, the paper overall would benefit from addressing this balance.

12. To enhance the discussion, the limitations could be discussed in greater depth, with reference made to the generalisability of the findings; whether the sample was considered representative (reference the original sampling frame from the Gold Magic Survey) and to what extent the questions posed within W2 of the GM survey answered the study objectives.

RESPONSE: The entire "discussion" section has been re-formatted and expanded to address concerns raised by all three reviewers. Please see the updated manuscript draft.

13. Reference to the original parent study protocol (if published), STROBE checklist, list of author contributions could be added.

RESPONSE: The parent study protocol has been referenced in the manuscript, as indicated above. The statement of contributions is included between the discussion and references in the manuscript. The STROBE checklist has been completed in the submission system, but not included with this draft of the manuscript.

An additional note on terminology: "joints" could be defined at first use, as it may refer to rolled tobacco and cannabis in some areas of the world, and to rolled cannabis only in others. Secondly,

exposure to nicotine and tobacco are both referenced - it would be clearer to specify which, or to clarify "tobacco and/or nicotine" if the intention is also to refer to ENDS. Lastly, p5 l5 refers to "hard drugs", though I note this is the NL government terminology, this requires further clarification for an international audience.

RESPONSE: In the introduction section, we defined "spliffs/mulled cigarettes" as joints filled with some mixture of tobacco and cannabis:

"Existing evidence shows that co-occurring use of tobacco and cannabis ("co-use") is widespread, with as many as 90% of cannabis users reporting a history of tobacco smoking.⁴ Co-use of these substances can take several forms, including concurrent use of tobacco and cannabis (i.e., "dual users" of both substances). Co-administration through use of "blunts" (cigar wrappers partially or fully emptied and replaces with cannabis), "spliffs"/"mulled cigarettes" (joints filled with tobacco and cannabis), or waterpipes is commonplace, with use of mulled cigarettes being significantly more common in areas outside of the U.S."

The authors have provided examples on p5/L5 of the types of drugs considered "hard" by the NL government (such as heroin, cocaine, amphetamine, ecstasy and GHB).

There are a number of typographical errors and points of clarification which require attention:
p2 l17: specify "tobacco (or cigarette) smokers", same for p8 l16

RESPONSE: Done.

p2 l33: specify whether nicotine dependence or increased tobacco use is of concern

RESPONSE: Both nicotine dependence and increased tobacco use is of concern. We have changed this sentence as follows: "As more jurisdictions permit medicinal and/or recreational cannabis sales, examining tobacco-cannabis associations and co-use becomes particularly relevant due to the prospect of increasing cannabis use⁹ and potentially, tobacco product use and dependence."

p10 l28 requires correction

RESPONSE: The citation has been corrected as follows: Williams AR, Santaella-Tenorio J, Mauro CM, Levin FR, Martins SS. Loose regulation of medical cannabis programs associated with higher rates of adult cannabis use but not cannabis use disorder. *Addiction*. 2017 Nov;112(11):1985-1991. doi: 10.1111/add.13904. Epub 2017 Jul 17.

Reviewer: 2

Reviewer Name: Robert McMillen

Institution and Country: Mississippi State University, USA

Please state any competing interests or state 'None declared': None declared.

Please leave your comments for the authors below

The authors address an interesting and timely issue, as more jurisdictions begin to tolerate medical and/or recreational marijuana use. Overall, the objectives are clear and the methods are appropriate to address these objectives. The paper, however, could be improved by providing more detail in several places.

- The authors state that the survey was designed to provide a nationally representative sample, yet 63% of the sample were current smokers (per the abstract). That seems like a smoking rate from 1964.

RESPONSE: The sample was not truly nationally representative, as in a population cross section. Rather, within the smoker and non-smoker target groups, they were representative. We have changed the text within the manuscript to reflect this and have also added a citation for the Gold Magic Survey technical report:

ITC Project. (2016, June). ITC Gold Magic Wave 1-2 (2014-2015) Technical Report. University of Waterloo, Waterloo, Ontario, Canada, and Maastricht University, The Netherlands.
https://www.itcproject.org/files/ITC_GoldMagic_Waves1-2_Technical_Report_19Oct2016.pdf.
Accessed December 8, 2018.

- The sample size numbers in the abstract do not match those in the first paragraph of the Results. I suspect that the difference is due to non-response to the cannabis use questions, but the authors should address this issue.

RESPONSE: The authors have changed the Table 1 title to indicate that the difference in sample size is indeed due to non-response to the cannabis questions. "Predictors of Current Cannabis Use (n=1591 respondents who answered the cannabis use questions)"

- The results should begin with information about the response rate and sample characteristics.

RESPONSE: As indicated above, we have added a reference to the Gold Magic Survey technical report, which details the response rate and sample characteristic information. Given that this is formatted as a brief report, we felt adding the reference without including the information as text in the manuscript was a prudent way of providing this information to the reader.

- The methods should provide more detail about the questions and responses used to assess cigarette smoking and cannabis use. Ideally, the authors should provide the questions, response options, and how the variable were collapsed.

RESPONSE: Because of the word count limit for this brief report, we chose to cite back to the Gold Magic Survey technical report to provide readers with these details.

- There are two major limitations that need to be addressed; 1) the low sample size of past 30-day cannabis users, and 2) the very low sample size of non-smoker past 30-day cannabis users. I'm not convinced that the results starting at line 41 of page 7 are justifiable when based on 16 non-smokers.

RESPONSE: The entire "discussion" section has been re-formatted and expanded to address study limitations raised by all three reviewers. Please see the updated manuscript draft.

- The Discussion needs to provide more detail about the importance of this study, its implications and its limitations.

RESPONSE: The entire "discussion" section has been re-formatted and expanded to address concerns raised by all three reviewers. Please see the updated manuscript draft.

Reviewer: 3

Reviewer Name: Lorraine Greaves PhD

Institution and Country: Centre of Excellence for Women's Health
Canada

Please state any competing interests or state 'None declared': none

Please leave your comments for the authors below

This is a very timely and important contribution to the literature on simultaneous use of cannabis and tobacco. Not enough precise data exist on this important question. This report on survey data from the Netherlands offers a clear view of such use in the context of liberal cannabis regulations of some duration. Hence it is important for other jurisdictions to consider in further regulating or legalizing cannabis.

I would suggest that where the authors found no significant differences in co use (sex, income, education), that some discussion be added to assist the readers in interpreting these results. For example, in the introduction, the authors state that being male is a key risk factor for cannabis use, but in this survey no difference is found. This bears some discussion. Is this result to be interpreted as new, specific to the Netherlands, other??? Certainly the reader will eagerly anticipate more insight into this key question, given that it makes considerable difference to both scientific and clinical measures of the effects of cannabis (sex-related factors), treatment protocols, research in nicotine/cannabis, and public health messaging.

RESPONSE: The difference in findings between this study and others that have found being male is an important risk factor for cannabis use can likely be attributed to the characteristics of the sample. Given the overall sample size used in this analysis, we are hesitant to generalize in terms of what our results mean for treatment, research, and messaging. We have addressed this limitation in the discussion section.

Similarly, the impact (or not) of income and education needs to be discussed, in order to render these results contextually understood and useful for future work.

RESPONSE: Same as above.

VERSION 2 – REVIEW

REVIEWER	Hannah Walsh King's College London, United Kingdom
REVIEW RETURNED	20-Dec-2018

GENERAL COMMENTS	Thank you for the opportunity to review this revised manuscript. I note the authors have addressed the points raised in the first review in detail, and have revised the manuscript accordingly. Points 2 and 11 relate to the same issue. The abstract (p2, line 36; p6, line 24) and the final conclusions state that these results indicate that "most cannabis users in the Netherlands" mix it with tobacco. Although the survey drew a nationally representative sample, a sample size of n=68 undoubtedly limits conclusions that can be drawn about the overall population of cannabis users in the Netherlands, a point already well made in the limitations section. I would suggest that a more bounded and provisional conclusion is made regarding the generalisability of the results.
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REVIEWER	Robert McMillen Mississippi State Univ, Social Science Research Center
REVIEW RETURNED	14-Dec-2018

GENERAL COMMENTS	The authors have addressed my concerns.
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REVIEWER	Lorraine Greaves UBC, Canada
REVIEW RETURNED	11-Jan-2019

GENERAL COMMENTS	The topic of co use of cannabis and tobacco is an extremely important issue, with implications for public health, surveillance and clinical care. This revision of this research note reporting on a survey in Netherlands is instructive, indicating that smoking status affects cannabis use and co use. This revision is much more clear and accurate, and reports the data in a more understandable manner. The implications are clear and point to need for future research, wider surveillance, revised clinical approaches and focused public health messaging, especially for young people who smoke tobacco.
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VERSION 2 – AUTHOR RESPONSE

We have revised the manuscript in accord with suggestions raised by reviewer #1. Additionally, we have changed the title and made sure to include a statement relating to the ethics approval for this study. We are submitting marked and clean copies of the revised manuscript. All authors read and approved the final revised manuscript.