

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Electronic cigarettes use among the adult population: a cross-sectional study in Barcelona, Spain (2013-14)
AUTHORS	Martínez-Sánchez, Jose; Ballbè, Montse; Fu, Marcela; Martin-Sanchez, Juan Carlos; Saltó, Esteve; Gottlieb, Mark; Daynard, Richard; Connolly, Gregory; Fernandez, Esteve

VERSION 1 - REVIEW

REVIEWER	Brian King Centers for Disease Control and Prevention, United States
REVIEW RETURNED	15-Jun-2014

GENERAL COMMENTS	<p>This manuscript presents the findings of a cross-sectional study of electronic cigarette (e-cigarette) use, characteristics, purchase location, and satisfaction among adults in Barcelona, Spain during 2013-2014. The findings indicate that an estimated 6.5% of respondents reported ever using e-cigarettes, with use being strongly associated with current cigarette smoking. Additionally, nearly two-thirds of ever users indicated that they used nicotine-containing e-cigarettes, and cigarette smokers with higher dependence had lower rates of satisfaction with e-cigarettes.</p> <p>Overall, the sampling and analytic approaches employed in this study are scientifically defensible and appropriate. This study also presents findings on an important and timely issue in the field of public health that would be of interest to the readers of BMJ Open. Nonetheless, the manuscript could still benefit from some fairly straightforward revisions, including a more nuanced discussion of e-cigarettes in the Introduction and a clearer articulation of how the present findings fill an existing void in the literature, a more comprehensive discussion of study measures, consistency in the analytic approach across measures, and a more comprehensive description of the public health implications of the findings in the Discussion.</p> <p>Specific recommendations for improvement are provided below, by manuscript section.</p> <p>ABSTRACT</p> <p>1. Page 2, lines 6-8. The objective of the manuscript should be modified to reflect the broader scope of measures that were actually assessed beyond just use, including purchase location and satisfaction with the products. This is novel information that's worth highlighting.</p>
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2. Page 2, line 28. It is important to clarify the term “current smokers” with the term “cigarette”. Given the diversification of the tobacco product landscape in recent years, particularly related to flavored little cigars and cigarillos that are essentially cigarette equivalents, this distinction is important to make.

INTRODUCTION

3. Page 4, line 22. The phrase “tobacco control researchers who are concerned with their potential benefits” is inaccurate and should be modified. Researchers are not concerned with the potential benefits of these products, they’re concerned about the potential risks and cautiously optimistic about the potential benefits. Additionally, these concerns are really shared by the public health community in general, not just researchers.

4. In general, I think the Introduction could be improved with the addition of more text to help put this important public health issue in context, particularly for lay readers who may not have a nuanced understanding of e-cigarettes. In particular, it would seem reasonable to add a stronger rationale for the present study and why it fills an existing gap in the literature – the study actually assessed several previously unreported indicators, such as purchase location, nicotine content, and satisfaction. These are arguably the most novel aspects of the study, but aren’t even mentioned in the introduction and statement of objectives.

METHODS

5. Page 6, lines 14-18. Please include more information on the actual questions that were used to assess the presence of nicotine in the e-cigarettes used among ever users. The reported estimate is surprisingly low considering that the vast majority of the electronic nicotine delivery products available on the market contain nicotine. As such, it will be important to know exactly how this question was worded.

6. Page 6, lines 23-27. Further rationale needs to be provided for the decision to dichotomize satisfaction - those who reported “somewhat” satisfied are essentially considered to be not satisfied with the product. It may be more defensible to limit this category to only those who explicitly stated that they were “not satisfied”, particularly considering that this findings is highlighted so prominently in the abstract and elsewhere.

7. Page6, lines 39-41. Please include definitions in the text for the current cigarette smoking categories that were used (i.e. current, former, never).

8. If possible, it would be interesting to see what the impact including race/ethnicity in the analysis would have on the observed findings. If available and sufficient racial/ethnic diversity exists in the sample, this variable should be incorporated into the analysis.

RESULTS

9. Table 1. It’s not readily apparent why the authors used different referent categories for certain characteristics reported in Table 1. For example, for educational level, “low” is the referent for ever use, while “intermediate” is the referent for ever e-cigarette use with

	<p>nicotine. For the purposes of comparability and enhancing utility for public health practice, it is strongly recommended that the same referent be used across measures, ideally so that potential dose responses can be observed (i.e. referent = youngest age category, lowest education level, never smokers, and low-medium nicotine dependence).</p> <p>10. The term “trial e-cigarette users” is somewhat difficult to follow and may potentially confuse readers. Perhaps a more readily understood term could be used such as “experimentation”.</p> <p>DISCUSSION</p> <p>11. Page 8, line 16. The statement that “similar results were found....in the United States” is somewhat misleading considering that those data were collected two years prior to the present study (2010-2011). Use of these products has increased considerably since then, and thus, the prevalence of ever use in the present study is actually surprisingly lower than what would be expected given the surge in e-cigarette marketing and popularity in recent years.</p> <p>12. The Discussion should be enhanced to include a more robust summary of the existing peer-reviewed literature that is presently published, particularly related to the impact of e-cigarette use on cessation. There are several longitudinal studies that have been recently published, as well as special supplements in multiple journals (e.g. Tobacco Control), which include timely content that could help bolster the implications that are described in the Discussion section.</p> <p>13. There are some additional limitations that should be noted in the Discussion of the manuscript. Most importantly, the findings were collected from a limited sample of individuals in a single locality in Spain, and thus, the external validity of these findings is limited. Additionally, it appears that the questionnaire only assessed use of e-cigarettes. Evidence from several countries suggests that the ENDS marketplace has diversified in recent years and that many users, particularly youth younger adults, do not use the term “e-cigarettes” to describe these products (e.g. hookah pens, vape pens). This is an important issue that could potentially lead to underestimation of use, particularly among younger adults, if only the term “e-cigarette” was included on the questionnaire.</p>
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REVIEWER	Rehab Auf Florida International University, Miami, FL, USA Ain Shams University, Cairo, Egypt
REVIEW RETURNED	14-Jul-2014

GENERAL COMMENTS	<p>The study is not an ideal study to report prevalence estimate, given the study modest sample size. Also, the authors did not refer to any sample size estimation and its adequacy to claim generalization of this prevalence to the general population in the city of Barcelona, Spain. The other objective was to report the correlates of NDD use. The study was not highly successful in achieving this aim, since results were not stratified by nicotine content in the used device. The no-nicotine devices are different from those with nicotine, hence characteristics and correlates for each type should have been</p>
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	<p>defined separately.</p> <p>The authors stated their sample is representative to the population in the city of Barcelona, yet they did not explain why it should be? In other words, it was desired to explain the steps they have followed to assert the generalization of their outcome.</p> <p>The authors did not mention the basic demographic characteristics for each smokers group e.g. mean age. These are basic epidemiological data that should be provided.</p> <p>In the strengths and limitations section the authors mentioned that the main limitation is attrition, which does not apply to the current study. Perhaps they meant their cross-sectional design (in this study) is subject to no participation bias secondary to attrition from the original cohort. This is problematic if there is a difference between those who participated compared to those who refused to take part i.e. differential bias. This can be of importance since they mentioned those who take part in the current study were more likely to be older. However, the attrition problem does not apply for the cross-sectional design employed for the current article.</p> <p>The authors have examined the users' satisfaction with NDD. It was important to stratify the outcome according to nicotine content, since there was a high proportion of no-nicotine vaping users. It is intuitive that those using higher nicotine content devices will be more satisfied compared to the lower levels of nicotine and no nicotine devices. Therefore, presenting the satisfaction with the NDD according to the level of dependence is inadequate and it has to be stratified according to the nicotine content/absence to have an informative outcome.</p> <p>It is interesting to know: what was the content of vapour and purpose used for the no- nicotine devices. For example, did those devices have some other types of drugs or were used as a placebo to help smokers to quit?</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer #1 (Dr. Brian King)

This manuscript presents the findings of a cross-sectional study of electronic cigarette (e-cigarette) use, characteristics, purchase location, and satisfaction among adults in Barcelona, Spain during 2013-2014. The findings indicate that an estimated 6.5% of respondents reported ever using e-cigarettes, with use being strongly associated with current cigarette smoking. Additionally, nearly two-thirds of ever users indicated that they used nicotine-containing e-cigarettes, and cigarette smokers with higher dependence had lower rates of satisfaction with e-cigarettes.

Overall, the sampling and analytic approaches employed in this study are scientifically defensible and appropriate. This study also presents findings on an important and timely issue in the field of public health that would be of interest to the readers of BMJ Open. Nonetheless, the manuscript could still benefit from some fairly straightforward revisions, including a more nuanced discussion of e-cigarettes in the Introduction and a clearer articulation of how the present findings fill an existing void in the literature, a more comprehensive discussion of study measures, consistency in the analytic approach across measures, and a more comprehensive description of the public health implications of the findings in the Discussion.

Specific recommendations for improvement are provided below, by manuscript section.

Thank you very much for your kind comments.

ABSTRACT

1. Page 2, lines 6-8. The objective of the manuscript should be modified to reflect the broader scope of measures that were actually assessed beyond just use, including purchase location and satisfaction with the products. This is novel information that's worth highlighting.

As the reviewer have suggested, we have mentioned the purchase location and satisfaction with e-cigarette use in the objective of the study (in the abstract and in the main text).

2. Page 2, line 28. It is important to clarify the term "current smokers" with the term "cigarette". Given the diversification of the tobacco product landscape in recent years, particularly related to flavored little cigars and cigarillos that are essentially cigarette equivalents, this distinction is important to make.

We have clarified the type of tobacco product adding "cigarette".

INTRODUCTION

3. Page 4, line 22. The phrase "tobacco control researchers who are concerned with their potential benefits" is inaccurate and should be modified. Researchers are not concerned with the potential benefits of these products, they're concerned about the potential risks and cautiously optimistic about the potential benefits. Additionally, these concerns are really shared by the public health community in general, not just researchers.

We have modified this phrase according to the reviewer comment.

4. In general, I think the Introduction could be improved with the addition of more text to help put this important public health issue in context, particularly for lay readers who may not have a nuanced understanding of e-cigarettes. In particular, it would seem reasonable to add a stronger rationale for the present study and why it fills an existing gap in the literature – the study actually assessed several previously unreported indicators, such as purchase location, nicotine content, and satisfaction. These are arguably the most novel aspects of the study, but aren't even mentioned in the introduction and statement of objectives.

Thank you very much for the useful comment. We have added an explanatory text in the introduction section before the objective with these issues as follows:

"Moreover, to our knowledge, there is a lack of information on specific characteristics of use, such as the location of purchase, use of liquids containing nicotine, and the satisfaction with this product among users. These issues are especially relevant to characterize the use of this new product in order to implement future regulations"

METHODS

5. Page 6, lines 14-18. Please include more information on the actual questions that were used to

assess the presence of nicotine in the e-cigarettes used among ever users. The reported estimate is surprisingly low considering that the vast majority of the electronic nicotine delivery products available on the market contain nicotine. As such, it will be important to know exactly how this question was worded.

We used the question (as translated from Spanish): “Do/did you use the electronic cigarettes with nicotine? (yes/no)” We have included this question in the methods section as suggested by the reviewer.

6. Page 6, lines 23-27. Further rationale needs to be provided for the decision to dichotomize satisfaction - those who reported “somewhat” satisfied are essentially considered to be not satisfied with the product. It may be more defensible to limit this category to only those who explicitly stated that they were “not satisfied”, particularly considering that this findings is highlighted so prominently in the abstract and elsewhere.

We agree with the reviewer’s comment. We have provided the prevalence and OR of “not satisfied” across all the manuscript and in the table 1. We have also changed the text according to the new results.

7. Page6, lines 39-41. Please include definitions in the text for the current cigarette smoking categories that were used (i.e. current, former, never).

We have now included these definitions.

8. If possible, it would be interesting to see what the impact including race/ethnicity in the analysis would have on the observed findings. If available and sufficient racial/ethnic diversity exists in the sample, this variable should be incorporated into the analysis.

We agree with the reviewer comment. However, we did not collect information about race/ethnicity because the main race in Barcelona is Caucasian and there is no a wide variability in this sense, as occur in other countries (i.e.: United States or the United Kingdom). Our questionnaire includes a variable to identify the country of birth, but this does not imply race or ethnicity (98.6% of the participants were born in Spain).

RESULTS

9. Table 1. It’s not readily apparent why the authors used different referent categories for certain characteristics reported in Table 1. For example, for educational level, “low” is the referent for ever use, while “intermediate” is the referent for ever e-cigarette use with nicotine. For the purposes of comparability and enhancing utility for public health practice, it is strongly recommended that the same referent be used across measures, ideally so that potential dose responses can be observed (i.e. referent = youngest age category, lowest education level, never smokers, and low-medium nicotine dependence).

As suggested by the reviewer, we have changed the referent categories in table 1. We have also included the changes in the main text of the manuscript, according to the new results.

10. The term “trial e-cigarette users” is somewhat difficult to follow and may potentially confuse readers. Perhaps a more readily understood term could be used such as “experimentation”.

We have changed the term “trial e-cigarette users” by “e-cigarette experimentation” and “experimentation with e-cigarettes”.

DISCUSSION

11. Page 8, line 16. The statement that “similar results were found....in the United States” is somewhat misleading considering that those data were collected two years prior to the present study (2010-2011). Use of these products has increased considerably since then, and thus, the prevalence of ever use in the present study is actually surprisingly lower than what would be expected given the surge in e-cigarette marketing and popularity in recent years.

We agree with the reviewer’s comment. We have specified the year the study was conducted and one possible explication about the lower prevalence found in our study as follows:

“Similar results were found for general population in Europe according to the Eurobarometer survey conducted in 2012 [8] and also in the United States [9] according to a study conducted in 2010-2011. Surprisingly, our prevalence of ever-use is lower to what we would expect, considering the increase of marketing and popularity of e-cigarettes in recent years. This low prevalence could be due to a potential delay in the general marketing of e-cigarettes among countries in Spain as compared to other countries, as well as the quick reaction of the tobacco control community and public health authorities to apply the precautionary principle in Spain (Xarxa Catalana d’Hospitals Sense Fum).”

12. The Discussion should be enhanced to include a more robust summary of the existing peer-reviewed literature that is presently published, particularly related to the impact of e-cigarette use on cessation. There are several longitudinal studies that have been recently published, as well as special supplements in multiple journals (e.g. Tobacco Control), which include timely content that could help bolster the implications that are described in the Discussion section.

Thank you very much for the useful comment. As suggested, we have included more literature in the discussion section as follows:

“Two longitudinal studies (Etter & Bullen 2014; Polosa et al. 2011) also found e-cigarettes may contribute to prevent relapse in former smokers and to promote smoking cessation in current smokers.”

And

“However, the evidence is still scarce according to recent reviews of the scientific literature (Pepper et al. 2013; Grana et al. 2014).”

We have also included, as suggested by the reviewer, one comment with two articles recently published in the special issue of Tobacco Control and an analysis paper from the BMJ:

“Moreover, the current advertisements and messages of e-cigarettes in the media and the social networks, such as twitter, could increase the experimentation, particularly among young and middle aged population (Pepper et al. 2014; Huang et al. 2014; Andrade et al. 2013).”

13. There are some additional limitations that should be noted in the Discussion of the manuscript. Most importantly, the findings were collected from a limited sample of individuals in a single locality in Spain, and thus, the external validity of these findings is limited. Additionally, it appears that the

questionnaire only assessed use of e-cigarettes. Evidence from several countries suggests that the ENDS marketplace has diversified in recent years and that many users, particularly youth younger adults, do not use the term “e-cigarettes” to describe these products (e.g. hookah pens, vape pens). This is an important issue that could potentially lead to underestimation of use, particularly among younger adults, if only the term “e-cigarette” was included on the questionnaire.

As suggested by the reviewer, we have discussed these two potential limitations as follows:

“Moreover, we conducted the study only in the city of Barcelona and the validity to infer the result to the rest of Spain could be limited.”

And

“Additionally, our results could slightly underestimate the real prevalence of use, because we only included the term “e-cigarette” in the questionnaire, and there are other terms associated to new products in the market. However, this effect may be limited, because the term “e-cigarettes” is the most popular in Spain, and products such as “hookah pens” or “vape pens” are scanty marketed.”

Reviewer #2 (Dr. Rehab Auf)

The study is not an ideal study to report prevalence estimate, given the study modest sample size. Also, the authors did not refer to any sample size estimation and its adequacy to claim generalization of this prevalence to the general population in the city of Barcelona, Spain. The other objective was to report the correlates of NDD use. The study was not highly successful in achieving this aim, since results were not stratified by nicotine content in the used device. The no-nicotine devices are different from those with nicotine, hence characteristics and correlates for each type should have been defined separately.

The theoretical sample size was 1291 individuals, assuming an expected prevalence of smokers of 30%, (with an alpha error of 5% and a precision of 2.5%), which was the estimated prevalence of smokers in Spain when the baseline survey was conducted. According to previous studies conducted in the US, the prevalence of ever e-cigarettes user is between 6% and 10%. If we assumed the estimated prevalence of 10%, with an alpha error of 5% and a precision of 2.5%, the sample size required to be representative of the city of Barcelona would be 554 individuals. For this reason, we believe the sample size of our study is appropriate and thus representative of the city of Barcelona in order to provide estimated prevalences of e-cigarette use.

As the reviewer suggests, for clarifying this, we have added the sample size estimation in the methods section as follows:

“The theoretical baseline sample size was 1291 individuals, assuming an expected smoking prevalence of 30% (with an alpha error of 5% and a precision of 2.5%), which was the estimated percentage of smokers in Spain when the baseline survey was conducted.”

We agree with the reviewer about the importance of stratifying the results by nicotine content used in the device. We provide in the manuscript (please see table 1) the correlates according to usage of nicotine and we did not find differences; so we would also expect no differences by nicotine content. In order to confirm this, we have also stratified the results according to the nicotine usage and we have found no differences between the usage of e-cigarettes with and without nicotine (data not shown in the manuscript).

On other hand, we think the results of satisfaction stratified by nicotine content, as the reviewer comment in other point, is the main result of this stratification. We have also found no differences in the satisfaction according to the nicotine of the device (please, see next comments and responds). We have explained and provided these results in the results sections of the manuscript as follows:

“There were no statistically significant differences in the satisfaction with the usage of e-cigarettes according to use of liquids with and without nicotine (not satisfied: 40.0% vs. 38.9%; OR=0.53, 95%CI: 0.11-2.49).”

And in the discussion section as follows:

“In addition, we found no differences in the satisfaction according to the use of the e-cigarettes with or without nicotine.”

Finally, we have decided not to provide all correlates stratified by nicotine use in a new table due to the small sample size (30 users with nicotine and 18 users without nicotine). If the Editor considers it is appropriated to provide this new table with the stratification, we are able to include it in the manuscript.

The authors stated their sample is representative to the population in the city of Barcelona, yet they did not explain why it should be? In other words, it was desired to explain the steps they have followed to assert the generalization of their outcome.

There are no differences according to sex between our final sample and the population in Barcelona in 2013. However, our final sample overestimated the older people compared with the distribution of population in Barcelona (table 1).

Table 1. Distribution of our final sample (2013-14) and population in Barcelona in 2013.

Final sample (2013-14) Barcelona in 2013

Sex

Men 45,65% 47,38%

Women 54,35% 52,62%

Age group

<= 44 years old 26,90% 40,68%

45-64 years old 36,28% 32,50%

>= 65 years old 36,82% 26,82%

We have explained in the discussion section this limitation and the potential effect in our results as follows:

“Although there are no statistically significant differences between the people who were followed up and those lost from the original study according to sex, age, and educational level, our final sample overestimated the older people compared with the distribution of population in Barcelona. For this reason, the prevalence of e-cigarette use might be underestimated in our study because young people, particularly younger smokers, are those who most used e-cigarettes.”

We have also included more information about the sample design in the discussion section. Moreover, we have included the reference of previous articles (Fu et al. 2009; Martínez-Sánchez et al. 2009) where the readers could find more and detailed information about the sample procedures. We have added more information as follows:

“Moreover, we conducted the study only in the city of Barcelona and the validity to infer the results to the rest of Spain could be limited. Nevertheless, the baseline sample size was representative of the city of Barcelona (Fu et al. 2009; Martínez-Sánchez et al. 2009) and the final sample size for this analysis was sufficient to estimate the prevalence of e-cigarette users, due to the relatively lower prevalence of ever e-cigarette use in the general population [8-9]. According to an expected prevalence of ever e-cigarette use of 10%, the sample size would be 554 individuals, with an alpha error of 5% and a precision of 2.5%.”

The authors did not mention the basic demographic characteristics for each smokers group e.g. mean age. These are basic epidemiological data that should be provided.

As suggested by the reviewer, we have mentioned the basic demographic characteristics of smokers and e-cigarette users in the results section as follows:

“The prevalence of smokers of manufactured cigarettes was 23.3% (95%CI: 20.2-26.3) and the prevalence of ever e-cigarette use was 6.5% (95%CI: 4.7-8.3). Smokers of manufactured cigarettes had a mean age of 49.4 years, 53.8% were men, and 47.9% had intermediate educational level. The e-cigarette users had a mean age of 45.1 years, 56.2% were men, and 58.3% had intermediate educational level. There were no statistically significant differences according to demographic characteristics (sex, age, and level of education) between smokers of manufactured cigarettes and e-cigarette users.”

In the strengths and limitations section the authors mentioned that the main limitation is attrition, which does not apply to the current study. Perhaps they meant their cross-sectional design (in this study) is subject to no participation bias secondary to attrition from the original cohort. This is problematic if there is a difference between those who participated compared to those who refused to take part i.e. differential bias. This can be of importance since they mentioned those who take part in the current study were more likely to be older. However, the attrition problem does not apply for the cross-sectional design employed for the current article.

We agree with the reviewer’s comment. We have specified this potential bias derived from the use the follow-up of a cohort of individuals in the strengths and limitations of the study as follows:

“The main limitation of our study is the potential no participation bias due to the attrition of the cohort of participants.”

The authors have examined the users’ satisfaction with NDD. It was important to stratify the outcome according to nicotine content, since there was a high proportion of no-nicotine vaping users. It is intuitive that those using higher nicotine content devices will be more satisfied compared to the lower levels of nicotine and no nicotine devices. Therefore, presenting the satisfaction with the NDD according to the level of dependence is inadequate and it has to be stratified according to the nicotine content/absence to have an informative outcome.

We agree with the reviewer. Unfortunately, we did not gather information about satisfaction with e-cigarette use according to nicotine content, but to use of nicotine and, as said before, we have found no differences between both groups of users. We have added a sentence in the results section as follows:

“There were no statistically significant differences in the satisfaction with the usage of e-cigarettes

according to use of liquids with and without nicotine (not satisfied: 40.0% vs. 38.9%; OR=0.53, 95%CI: 0.11-2.49).”

And in the discussion section as follows:

“In addition, we found no differences in the satisfaction according to the usage of the e-cigarettes with or without nicotine.”

We are inclined to maintain the information according to the level of dependence. However, we are open to remove it if the Editor advises its deletion.

It is interesting to know: what was the content of vapour and purpose used for the no- nicotine devices. For example, did those devices have some other types of drugs or were used as a placebo to help smokers to quit?

We agree with the reviewer’s comment that this information would be very interesting. Unfortunately, we did not collect information about the content of the liquids without nicotine nor the purpose of use

VERSION 2 – REVIEW

REVIEWER	Brian King Centers for Disease Control and Prevention, United States
REVIEW RETURNED	03-Aug-2014

GENERAL COMMENTS	The authors have adequately and appropriately addressed the comments of both of the original reviewers and provided adequate rationale in instances where the suggested revisions could not be incorporated. This original reviewer (#1) recommends acceptance of the manuscript in its current form.
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