PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Predictors of electronic cigarette use among Swedish teenagers – a population-based cohort study
AUTHORS	Hedman, Linnea; Backman, Helena; Stridsman, Caroline; Lundbäck, Magnus; Andersson, Martin; Rönmark, Eva

VERSION 1 – REVIEW

REVIEWER	James Sargent Geisel School of Medicine at Dartmouth
REVIEW RETURNED	08-Jul-2020

GENERAL COMMENTS	COMMENTS TO THE AUTHOR SUMMARY This is a study of predictors of e-cigarette use among 19 year olds who are members of a cohort of children recruited when they were 7-8 years old. The main aim of the study is to examine respiratory disease (asthma) so they have good data on demographics and smoking status of parents. They presumably have data on other predictors of asthma and respiratory outcomes like wheezing and maybe even lung function. However e-cigarette use was assessed only when they were 19, in 2017, and was probably uncommon at the middle assessment when they were 14-15. The study finds that multivariable risk factors for e-cigarette use include daily cigarette smoking at age 14-15, being in a vocational program of art at age 19 and having an unhealthy diet at age 19. Among never smokers at age 14, having a father that smoked was an additional risk factor. GENERAL COMMENTS This study has some strengths, being longitudinal with high retention. However, it was not developed to answer questions about onset of tobacco use, but focused instead on respiratory outcomes. It is missing individual personality predictors, like sensation seeking, and exposure to things like marketing that would be amenable to regulation. As such, it offers little to aid our understanding on why adolescents begin e-cigarette use or what to do about it. Perhaps a more useful study with this cohort would be to aid in our understanding of how personal tobacco product use affects respiratory outcomes during adolescence. MAJOR COMMENTS Factors that decrease enthusiasm: The study is overly focused on gender. It's not clear why that variable was chosen to highlight, for example in table 1. Much too much emphasis on bivariate associations, many of which disappear in the multivariable analysis.

	Two of the “predictors” in the overall sample (art student and poor diet) were measured at age 19, so represent only cross-sectional associations. What is interesting: The most interesting fact to me was that e-cigarette use was uncommon among former smokers, but this fact was buried and not at all emphasized in tables or figures. Hard to find how many former smokers there were or what a former smoker was. Could someone who was current at age 14 and non smoker at 19 be a former. Typically, one has to accumulate a set amount of smoking experience to count as a former. In the US it would be 100 cigarettes lifetime. Problem with Figure 4. Vertical line is not centered on 1.0.

REVIEWER	Jennifer Jester University of Michigan, U.S.
REVIEW RETURNED	06-Aug-2020

GENERAL COMMENTS	This is an interesting study, as understanding e-cigarette use is necessary for prevention efforts. In addition, a large sample was followed over an important time frame for nicotine use. However, there are some major issues with the presentation of the paper Primarily, Figure 1 is very difficult to understand. Actually, after my third or fourth viewing of the figure, I finally understand it. It would be helpful to have the legend read Never smokers (across ages 14-15 and 19) , etc. And make it very clear in the text that you are talking about (e.g. We define Never smokers at age 19 as those who had not smoked at age 19 and not smoked at age 14-15). Otherwise, it is more difficult to understand this data. Other issues: Snus needs to be defined, as this is not a known tobacco product for most of us in the US Physical activity - I could not find a definition of this. Healthy diet - this seems like a very strange definition of health diet (sorry I am a vegetarian so getting a point for eating fish seems odd to me). Please help us understand why these items were chosen, along with references to the literature. Missing data - please define how many were excluded due to missing data (p.7) Explain which variables were retained in the multivariate logistic regression and why they were retained. Don't use bright line cutoff for statistical analysis - see Wasserstein article https://www.tandfonline.com/doi/full/10.1080/00031305.2019.1583913 DOn't use the abbreviation HRQoL, instead use "quality of life" (defined earlier as health-related quality of life) For prediction of e-cig use among non-tobacco users, I don't find the sample size for this analysis please add In addition to the analysis of non-participants n = 153 , please look at differences in characteristics of those who were retained and those who attritted from age 14-15 to age 19

	Discussion: 'absolute number of individuals . . ." replace this with substantial portion of total sample - it's hard to make a case about how big is an absolute number of individuals. p 9 ' association seems to be bidirectional - this statement isn't very clear when you had just stated that there was 3-cig use in never smokers. Reword it please. Formers smokers - it is possible that smokers could use e-cigs as a way to quit smoking and then wean off of e-cigs, so the analysis saying that formers smokers weren't current e-cig users isn't a solid argument about the harm reduction potentioal

VERSION 1 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:

Reviewer: 1

Reviewer Name: James Sargent
Institution and Country: Geisel School of Medicine at Dartmouth Competing interests: None

SUMMARY
This is a study of predictors of e-cigarette use among 19 year olds who are members of a cohort of children recruited when they were 7-8 years old. The main aim of the study is to examine respiratory disease (asthma) so they have good data on demographics and smoking status of parents. They presumably have data on other predictors of asthma and respiratory outcomes like wheezing and maybe even lung function. However e-cigarette use was assessed only when they were 19, in 2017, and was probably uncommon at the middle assessment when they were 14-15. The study finds that multivariable risk factors for e-cigarette use include daily cigarette smoking at age 14-15, being in a vocational program of art at age 19 and having an unhealthy diet at age 19. Among never smokers at age 14, having a father that smoked was an additional risk factor.

GENERAL COMMENTS
1. This study has some strengths, being longitudinal with high retention. However, it was not developed to answer questions about onset of tobacco use, but focused instead on respiratory outcomes. It is missing individual personality predictors, like sensation seeking, and exposure to things like marketing that would be amenable to regulation. As such, it offers little to aid our understanding on why adolescents begin e-cigarette use or what to do about it. Perhaps a more useful study with this cohort would be to aid in our understanding of how personal tobacco product use affects respiratory outcomes during adolescence.

Response: We agree that it is a limitation that we did not include measures of personality traits, sensation seeking or other risk-taking behaviour, as well as exposure to marketing. However, even though this is a cohort study about asthma and allergic diseases, we included factors associated with tobacco use such as parental socioeconomic status and smoking habits, diet, health-related quality of life, and educational category. We have extended the discussion about this limitation in the discussion, page 12. We thank the reviewer for the suggestion to study tobacco product use in relation to respiratory outcomes. This research question is included in a planned paper from the cohort.

MAJOR COMMENTS
Factors that decrease enthusiasm:
2. The study is overly focused on gender. It's not clear why that variable was chosen to highlight, for example in table 1.

Response: Thank you for the opportunity to clarify why differences in smoking, snus and e-cigarette use by sex were included. In Sweden, smoking is more common among women while the use of snus and e-cigarettes is more common among men. Other than a national report, there are no epidemiological studies on sex differences in e-cigarette use among Swedish teenagers. This information has been added to the introduction. As suggested we have toned down the non-significant gender differences in the Result, page 6.

3. Much too much emphasis on bivariate associations, many of which disappear in the multivariable analysis.

Response: In order to meet the requests of both this suggestion and point 12 and 13 by Reviewer 2, we chose to move the presentation of the unadjusted analyses to an online supplement. That way we can shorten the text about the bivariate associations and refer to the table instead, and also be transparent of which variables were included in the adjusted analysis.

4. Two of the "predictors" in the overall sample (art student and poor diet) were measured at age 19, so represent only cross-sectional associations.

Response: We agree that it is unfortunate that we only asked about diet and physical activity at age 19 years. This limitation of the study has been added to the section about strengths and limitations, page 12. Regarding the upper secondary education, at age 15 years Swedish teenagers choose a vocational or preparatory educational program which they attend for three years until graduation at age 19 years. Thus, even though data on education was based on the questionnaire at 19 years, they had attended the same program for the last three years. We have clarified that the program is chosen at age 15 years in the definition section of the Methods, page 5.

What is interesting:
5. The most interesting fact to me was that e-cigarette use was uncommon among former smokers, but this fact was buried and not at all emphasized in tables or figures. Hard to find how many former smokers there were or what a former smoker was. Could someone who was current at age 14 and non smoker at 19 be a former. Typically, one has to accumulate a set amount of smoking experience to count as a former. In the US it would be 100 cigarettes lifetime.

Response: We thank the reviewer for the suggestion to emphasize this result. Former smokers were defined as either self-reported former smoker in the questionnaire at age 19 years, or being an occasional or daily smoker at age 14-15 years and non-smoker at age 19 years. We have added this definition of former smokers in Methods, page 5. The number of former smokers (n=29) is presented in table 1, and among them, seven individuals had ever tried e-cigarettes and one was a current user. This information has been clarified in Results, page 7. Further, we have added the category 'Former smoker' in Figure 1.

6. Problem with Figure 4. Vertical line is not centered on 1.0.

Response: Thank you for noticing this error, the line in the figure has been corrected.

Reviewer: 2

Reviewer Name: Jennifer Jester
Institution and Country: University of Michigan, U.S.
Competing interests: None declared

Please leave your comments for the authors below
This is an interesting study, as understanding e-cigarette use is necessary for prevention efforts. In addition, a large sample was followed over an important time frame for nicotine use.

7. However, there are some major issues with the presentation of the paper Primarily, Figure 1 is very difficult to understand. Actually, after my third or fourth viewing of the figure, I finally understand it. It would be helpful to have the legend read Never smokers (across ages 14-15 and 19) , etc. And make it very clear in the text that you are talking about (e.g. We define Never smokers at age 19 as those who had not smoked at age 19 and not smoked at age 14-15). Otherwise, it is more difficult to understand this data.

Response: We thank the reviewer for the suggestion and have made clarifications of the definitions accordingly. We have also added former smokers to Figure 1, as suggested by Reviewer 1 and made the suggested clarifications in the legend to Figure 1.

Other issues:
8. Snus needs to be defined, as this is not a known tobacco product for most of us in the US

Response: Swedish snus is a smokeless, moist, grounded tobacco product that is placed under the upper lip. We have added a definition of snus in the introduction, page 3.

9. Physical activity - I could not find a definition of this.

Response: Thank you for noticing that the definition of physical activity was missing. We defined physical activity as regular participation in sports or physical activity, not including physical education at school. The definition has been added, page 6.

10. Healthy diet - this seems like a very strange definition of health diet (sorry I am a vegetarian so getting a point for eating fish seems odd to me). Please help us understand why these items were chosen, along with references to the literature.

Response: The questionnaire included four questions about diet and these were chosen based on recommendations by the Swedish National Food Agency (for information in English, please see: https://www.livsmedelsverket.se/en/food-habits-health-and-environment/dietary-guidelines/naringsrekommendationer). Among other foods, they recommend plenty of vegetables, fruit and berries, regular intake of fish and limited intake of processed meat and sweet drinks. Even though some teenagers in our study may be vegetarians, if they eat an otherwise healthy diet, they would still get a high score on our scale. We have clarified the definition, page 6.

11. Missing data - please define how many were excluded due to missing data (p.7)

Response: In table 1 and table 2, the denominators for each variable is presented in order to be transparent of the numbers of individuals excluded due to missing. We have added more information about missing values in individual questions in the section of Statistical analyses, page 6.

12. Explain which variables were retained in the multivariate logistic regression and why they were retained.

Response: The variables in the analyses were manually entered into the model, we did not use the forward or backward method in SPSS. The adjusted analyses included factors significantly or borderline significantly (with a lower value of the confidence intervals at 0.9) associated with e-cigarette use in the unadjusted analyses. Of the included variables, only sex was borderline significant in the unadjusted analysis with an OR of 1.46 and 95% CI 0.95-2.24.

13. Don't use bright line cutoff for statistical analysis - see Wasserstein article https://www.tandfonline.com/doi/full/10.1080/00031305.2019.1583913

Response: We agree with the argument in the paper, which is why we have included the exact p-values in table 1 and table 2 so the reader can assess the strength of association. As mentioned in point 12 above, also variables with p-values >0.05 were included in the adjusted analyses instead of using bright line cutoff at 0.05.

14. DOn't use the abbreviation HRQoL, instead use "quality of life" (defined earlier as health-related quality of life)

Response: We have used the instrument KIDSCREEN-10 which measures health-related quality of life and well-being among children and adolescents according to the manual (see reference number 35). Therefore we wish to use the term health-related quality of life and hope that the reviewer accept our choice.

15. For prediction of e-cig use among non-tobacco users, I don't find the sample size for this analysis please add

Response: There were n=1827 non-tobacco users included in the analyses. This information has been added in Results, page 9.

16. In addition to the analysis of non-participants n = 153 , please look at differences in characteristics of those who were retained and those who attritted from age 14-15 to age 19

Response: We realize that the analysis of representativeness was unclear. We compared the n=2185 individuals in our study sample with the n=153 that were possible to invite to the follow-up at age 19 but did not participate. In the revised version we have made new analyses. In total, the cohort consists of 2819 individuals. Our study sample are the n=2185 individuals who participated in the follow-ups at age 14-15y and 19y. In the new analysis we compare the 2185 participants with the 634 individuals that did not participate in the two follow-ups. As suggested by the reviewer, we have also included a comparison between the 2185 participants with the 213 individuals that participated at age 14-15y but not at 19 years. The results of these analyses are presented on page 8.

17. Discussion:
'absolute number of individuals . . ." replace this with substantial portion of total sample - it's hard to make a case about how big is an absolute number of individuals.

Response: we agree with the reviewer that this sentence is unclear and we have removed it from the discussion.

18. p 9 ' association seems to be bidirectional - this statement isn't very clear when you had just stated that there was 3-cig use in never smokers. Reword it please.

Response: We thank the reviewer for the suggestion and have made changes in the sentence as suggested.

19. Formers smokers - it is possible that smokers could use e-cigs as a way to quit smoking and then wean off of e-cigs, so the analysis saying that formers smokers weren't current e-cig users isn't a solid argument about the harm reduction potentioal

Response: We thank the reviewer for the opportunity to clarify these associations. At age 19y, there were 13 individuals that had quit using e-cigarettes. Of them, 10 were occasional smokers, 2 daily smokers, 1 never smoker but none of them was a former smoker. We have added this result on page 8.