PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Smoking cessation using preference-based tools among socially disadvantaged smokers: Study protocol for a pragmatic multicentre randomised controlled trial
AUTHORS	El-Khoury, Fabienne; El Aarbaoui, Tarik; Héron, Mégane; Hejblum, Gilles; Métadieu, Brigitte; Lefaou, Anne Laurence; Ibanez, Gladys; Melchior, Maria

VERSION 1 – REVIEW

REVIEWER	Emily Peckham University of York Department of Health Sciences, Health Sciences
REVIEW RETURNED	22-Jan-2021

GENERAL COMMENTS	This is an interesting and important study to promote smoking cessation in a deprived group. I have listed below some areas for improvement. In general the article reads well however it lacks detail particularly around recruitment and how it will take place. In some places the article is a bit vague, which may be due to uncertainty around covid-19. I think it would be better to describe how the study is planned to run with a description of changes that may need to be made in light of covid-19, Below I give some more detailed points. Please include more details about how participants will be recruited e.g. will they be invited to take part at a routine appointment, or will they be responding to a poster etc? To improve the flow of the manuscript I would recommend moving the intervention standardisation section to below the section describing the intervention. Smoking cessation is usually validated by an objective measure. I think you need to say more than 'abstinence could be validated by exhaled CO...' something like 'abstinence will be validated by exhaled CO unless this is not possible due to the ongoing covid -19 measures.' As it stands it sounds as though measuring abstinence is an option. There needs to be some acknowledgement around bias that may be introduced by participants not being honest about whether they have abstained if it is not possible for abstinence to be verified. In the sample size what does a 'total of 528 (+20%)' mean? Please explain how the intervention will be delivered i.e face to face or remotely and how the smoking aids will be provided. Please give details of how the baseline appointment and follow ups will be conducted e.g over the phone, at a clinic etc.

	SPIRIT checklist review Item 5d has been marked N/A it is good practice in a trial protocol to complete all items of a SPIRIT checklist and where an item hasn't been included include a brief explanation in the protocol as to why this item hasn't been included. In light of this please explain why a data management committee and trial steering committee haven't been convened. The page number for item 6b needs to be included. Items 11a-c need to be included in the protocol. Item 15 - it would be helpful to include more details on recruitment to the study. Item 17a - please include details on who will be blinded. Item 18b - include any information on how you will improve retention to the study Item 21 a and b need to be included (see point about item 5) Item 22 - information about how any adverse events will be reported needs to be included. Item 23 - include information on any audits that will be carried out. Item 31 - include information about dissemination.

REVIEWER	Danielle E. Mccarthy University of Wisconsin-Madison, Medicine
REVIEW RETURNED	15-Feb-2021

GENERAL COMMENTS	This manuscript describes the protocol of a pragmatic randomised clinical trial that will compare smoking reduction and abstinence rates over 6 months among socioeconomically disadvantaged adults who receive standard care from their clinician versus those who receive standard care plus adaptive offers of nicotine replacement or e-cigarettes at no cost. The protocol will assess outcomes at 10 days, 1, 3, and 6 months post-enrollment, with possible biochemical verification of abstinence via carbon monoxide testing if pandemic conditions permit such testing. The manuscript is clear and focused. Many key aspects of the trial design and analytical plan are described clearly and fully. The information presented in the manuscript is consistent with the information registered in clinicaltrials.gov. There are a few important areas in which greater clarity would be particularly helpful. These are specified below. Investigator/clinician training and fidelity checks are not adequately described. The number of sites is specified, but the number of clinicians, or an expected range for the number of clinicians that will be involved, is not specified. Plans to ensure that all clinicians who will be providing both standard care and the experimental care with no-cost medications of choice will do so with fidelity are not adequately described. The training and support procedures to promote or assess fidelity are described very briefly and without sufficient detail. Although this is a pragmatic trial, more attention to at least assessing fidelity and adaptation is warranted. Plans to promote retention in the follow-up period are not well described. Projected dates of recruitment are not clear beyond the February 2021 start date.

	Cost analyses seem to include research-related costs (e.g., RA time) that may not be needed for clinical implementation of the program. Costs related to procedures solely for research purposes that would not be part of clinical implementation of the program should be separated from intervention implementation costs in analyses. Analytical plans are described in very general terms, and the ways in which nesting of patients within clinicians within sites seem to vary by analysis (sometimes random clinician effects will be examined, sometimes random site effects). This could be clarified and better justified. The type(s) or generation(s) of e-cigarettes that will be offered are not specified. Adverse event monitoring is not described and may be warranted given the combinations of treatments that will be provided to people continuing to smoke. The sample postcard for collecting treatment use does not include all therapies listed as options for participants. Plans to report results in clinicaltrials.gov or other venues for dissemination are not included. There are several minor grammatical issues to be addressed in copyediting.

REVIEWER	Mette Rasmussen Bispebjerg Hospital, Who-cc
REVIEW RETURNED	05-Mar-2021

GENERAL COMMENTS	Comments to the Author This is an interesting study. It is relevant to examine any methods to increase successful quitting among disadvantaged groups. The manuscript is well written; the style is concise, understandable, clear, and transparent. My comments/questions are detailed below. Study design and participating centres: 1: Please add the research question to the manuscript. 2: I am curious, what was you rational for including 15 centres? And how did you choose which ones to include? Recruitment: 3: You state that the data collection will being in February 2021. When do you expect it to end? Outcomes: 4: The main outcome is described as “Continuous abstinence for at least 7 days”. To the best of my knowledge this is not continuous abstinence; this is a 7-day point prevalence (see Hughes et al., Measures of abstinence in clinical trials: issues and recommendations. Nicotine & Tobacco Research 2003: 5; 13-25. Doi: 10.1080/1462220031000070552). 5: A secondary outcome used is “Total number of days of abstinence”. It is unclear to me how this is measured/calculated. Is this the number of continuous smoke-free days (meaning smoke-free days from the initial quit day to the first relapse) or is it the sum of smoke-free days throughout the 6 months period? Please clarify. Sample size: 6: Taking the description of your control group into concern, you

	mention that the use of medication will be a possibility in this group also (I understand the treatment as usual can be very different depending on the clinic). I think you based your sample size calculation on a very low control quit rate (based on the effect of advice from doctor only). Please explain the rational for using this low rate. Randomisation and blinding: 7. Page 9, line 37: "Patients will be blinded to their randomisation group: …". It is unclear to me how you can make this statement. I understand that you don't inform the patients about the possible treatments as part of the protocol. But what if they ask you directly? Do you not tell them about the treatment options then? And wouldn't that be problematic regarding the ethics of the study? Also, as soon as you publish this protocol the groups will be publicly available! Other follow-up measures: 8: I would encourage you to be more specific about the assessors. Will they be blinded to the randomisation group of the participants? Statistical analyses: 9: I might be wrong here – but I wonder why you are so keen on using analysis adjusting for "socio-demographic characteristics and other potential confounders.". Isn't this unnecessary as this is a randomised controlled trial designed to deal with exactly this? 10: Page 10, lines 32-37: "Finally, we will estimate the average time it takes for a successful smoking cessation attempt using smoking aids, in order to provide decision-makers with a recommendation for how long smoking aids should be prescribed.". I suggest you rewrite the first part of the sentence. I understand why you want to do this (to recommend how long smoking cessation aid should be offered), but I don't understand how you will make this estimation.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. Emily Peckham, University of York Department of Health Sciences

Comments to the Author:
This is an interesting and important study to promote smoking cessation in a deprived group. I have listed below some areas for improvement. In general the article reads well however it lacks detail particularly around recruitment and how it will take place. In some places the article is a bit vague, which may be due to uncertainty around covid-19. I think it would be better to describe how the study is planned to run with a description of changes that may need to be made in light of covid-19, Below I give some more detailed points.

Thank you for taking the time to review our article, and for all your pertinent and thoughtful comments. We hope our replies to your comments and the consequent modifications to the manuscript are satisfactory.

Please include more details about how participants will be recruited e.g. will they be invited to take part at a routine appointment, or will they be responding to a poster etc?

Both options are possible. We added more info about how participants will be included in the revised "recruitment" paragraph (pages 7-8).
"Physicians are therefore asked to present the study to their patients who might be eligible to

participate in the study. Posters and flyers inviting smokers who wish to quit to talk to their physician about smoking cessation are also supplied to participating centres.

Physicians can also carry out a pre-inclusion questionnaire over the phone or during a remote consultation, prior to a face to face appointment. However study presentation, recruitment, and baseline measures will only be done with patients physically present at the study centre. “

To improve the flow of the manuscript I would recommend moving the intervention standardisation section to below the section describing the intervention.

Thank you for this judicious comment, we switched the paragraphs according to your suggestion.

Smoking cessation is usually validated by an objective measure.
I think you need to say more than 'abstinence could be validated by exhaled CO...' something like 'abstinence will be validated by exhaled CO unless this is not possible due to the ongoing covid -19 measures.' As it stands it sounds as though measuring abstinence is an option. There needs to be some acknowledgement around bias that may be introduced by participants not being honest about whether they have abstained if it is not possible for abstinence to be verified.

Thank you for this comment. We changed the wording as you suggested.

" This self-reported abstinence will be validated by measured exhaled carbon monoxide,[20] unless this measurement is unavailable due to the ongoing covid-19 pandemic “ (page 8).

The main outcome initially planned was abstinence validated by CO measure, and we were forced to change it before submitting the protocol because of the ongoing pandemic.

We also added this limitation in the new “strength and limitations” section (page 2).

In the sample size what does a 'total of 528 (+20%)' mean?

Thank you for pointing out this unclear sentence. We modified the paragraph in order to specify the number of participants needed before taking into account lost to follow-up (n=440), and the final number (n=528) corresponds to 440 + a rate of 20% of lost to follow-up.

“In order to account for potential drop outs, the experimental design eventually planned a total of 528 (440 + 20% lost to follow-up) participants to be enrolled in the trial..” (page 9)

Please explain how the intervention will be delivered i.e face to face or remotely and how the smoking aids will be provided.

Please give details of how the baseline appointment and follow ups will be conducted e.g over the phone, at a clinic etc.

We modified several paragraphs in order to clarify how the intervention and follow up will be carried out.
In fact, according to our protocol, recruitment and the first appointment are necessarily carried out during a face to face consultation, however follow up could be done remotely.

We added the following text to the recruitment paragraph (page 8):

“Physicians can also carry out a pre-inclusion questionnaire over the phone or during a remote consultation, prior to a face to face appointment. However study presentation, recruitment, and baseline measures are will only be done with patients physically present at the study centre.“

We also modified the intervention paragraph (page 11) by adding the following text:

“Follow-up measures after the first (baseline) appointment might take place remotely, if the participants do not require any delivery of smoking cessation tools.”

Further, we added the following paragraph in the new “promoting retention” section: (page 14):

“When a participant misses one of the follow-up visits scheduled in the protocol, the follow-up questionnaire may be completed remotely by the investigator (by telephone or remote consultation), or by phone by a research assistant. The method of follow-up (face to face or remotely) will be noted in the eCRF..”

SPIRIT checklist review Item 5d has been marked N/A it is good practice in a trial protocol to complete all items of a SPIRIT checklist and where an item hasn't been included include a brief explanation in the protocol as to why this item hasn't been included. In light of this please explain why a data management committee and trial steering committee haven't been convened.

Thank you for pointing this (unintentional) omission. We had overlooked to include information about the different committees we have in place in the original manuscript.
However we do have a steering and a scientific committees (which are required for clinical studies in the French law), and we added the corresponding following information in the revised manuscript as well as in the revised SPIRIT checklist (pages 17 and 18):
“Steering Committee and Scientific Council
The steering committee is constituted by the two principal investigators (FEK and MM), the president of the French-speaking French Society of Tabacology (ALLF), the president of the Society of Therapeutic Training of the Generalist Practitioner (study sponsor)(GI), and the project managers and research assistants.
Its role is to follow the study implementation, and to implement the recommendations of the scientific committee.
The Scientific Committee is constituted by the two principal investigators, the study’s qualitative researcher, a methodology expert, and the study’s economist.
This council was involved in the drafting of the protocol (methodology, main outcomes, analysis,…) and questionnaires, and will be responsible for drafting any possible amendments. Its role will be to validate the scientific orientations of the project, to oversee analysis, and to guarantee its medical and scientific quality.
The two committees meet regularly as required by the study’s progress, with a minimum of two meetings a year..”

We added the corresponding page to the SPIRIT checklist item 5d

The page number for item 6b needs to be included.
Thank you for pointing theses omissions. We added the study page in question (referring to the control group: usual care paragraph, page 10).

Items 11a-c need to be included in the protocol.
Thank you for pointing this omission. We completed and uptdated the study pages referring to the 3 corresponding item (11a , 11b, 11c) in the checklist.

Item 15 - it would be helpful to include more details on recruitment to the study.
Following your previous comment, we added more details on study recruitment. We added the corresponding page for item 15.

Item 17a - please include details on who will be blinded.
We extended the “Randomisation and blinding” section in order to clarify that “Physicians, who will carry out the intervention, will not be blinded to treatment randomisation.”
This was also added in the SPIRIT checklist.

Item 18b - include any information on how you will improve retention to the study
Retention will be improved by calendar cards, and by phoning participants who do not show up for follow ups. We added a specific paragraph on how we plan on promoting retention (page 14), and the corresponding page in the SPIRIT checklist.

Item 21 a and b need to be included (see point about item 5)
We added a “Data monitoring” paragraph in the methods section, and a section on interim analysis (pages 14 and 16). Both are mentioned in the revised SPIRIT checklist.

Item 22 - information about how any adverse events will be reported needs to be included.
We added an “adverse events” paragraph in the methods section of the revised manuscript (page 14).
“The two principal investigators will have the responsibility to monitor adverse events which are systematically measured in all follow-up appointments, and are also monitored by two different research assistants. Every adverse event will be examined by the Steering Committee, and promptly reported to the Scientific Committee which will decide whether or not the study should continue.”

Item 23 - include information on any audits that will be carried out. Item 31 - include information about dissemination.
We added information on audits (page 14) and dissemination (page 17) in the manuscript, and added the corresponding pages in the checklist.

Reviewer: 2

Dr. Danielle E. Mccarthy, University of Wisconsin-Madison

Comments to the Author:
This manuscript describes the protocol of a pragmatic randomised clinical trial that will compare smoking reduction and abstinence rates over 6 months among socioeconomically disadvantaged adults who receive standard care from their clinician versus those who receive standard care plus adaptive offers of nicotine replacement or e-cigarettes at no cost. The protocol will assess outcomes at 10 days, 1, 3, and 6 months post-enrollment, with possible biochemical verification of abstinence via carbon monoxide testing if pandemic conditions permit such testing.

The manuscript is clear and focused. Many key aspects of the trial design and analytical plan are described clearly and fully. The information presented in the manuscript is consistent with the information registered in clinicaltrials.gov.

Thank you for taking the time to review our article and all your insightful comments.
We hope our replies to your comments, and the modifications we made to the manuscript are satisfactory.

There are a few important areas in which greater clarity would be particularly helpful. These are specified below.

Investigator/clinician training and fidelity checks are not adequately described.
The number of sites is specified, but the number of clinicians, or an expected range for the number of clinicians that will be involved, is not specified. Plans to ensure that all clinicians who will be providing

both standard care and the experimental care with no-cost medications of choice will do so with fidelity are not adequately described.
The training and support procedures to promote or assess fidelity are described very briefly and without sufficient detail. Although this is a pragmatic trial, more attention to at least assessing fidelity and adaptation is warranted.

Thank you for pointing out this ambiguousness.
Actually, fidelity checkings are also assured by the structured eCRF which guides the investigators in every step of the study.
We developed the “Intervention standardisation: training of medical doctors” section in the revised manuscript in order to clarify this matter:

“the fidelity of the care delivery in the trial will be also assured by the structured eCRF throughout the study. The eCRF will automatically determine if participants are eligible, and will guide investigators in the care delivery. » (page 11)

We also added more information on how the eCRF will facilitate study fidelity, in the methods section of the revised manuscript:
“The intervention process will be guided by the eCRF which will remind investigators to list all available products, and ask them to fill the type and quantity of the delivered tools for participants in the intervention group” (page 11)

Plans to promote retention in the follow-up period are not well described.

We added a paragraph in the methods section, describing how we plan on promoting retention.

“In addition to the calendar cards, other measures will be taken to promote retention.

When a participant misses one of the follow-up visits scheduled in the protocol, the follow-up questionnaire may be completed remotely by the investigator (by telephone or remote consultation), or by phone by a research assistant. The method of follow-up (face to face or remotely) will be noted in the eCRF..” (page 14).

Projected dates of recruitment are not clear beyond the February 2021 start date.

Thank you for pointing out this ambiguousness. We detailed projected dates of recruitment in the revised manuscript.

“Recruitment period in each centre will last for up to one year, while each participant will be followed for 6 months. However, not all centers will begin recruiting at the same time, and data collection is therefore expected to last until the end of year 2023.” (page 8)

Cost analyses seem to include research-related costs (e.g., RA time) that may not be needed for clinical implementation of the program. Costs related to procedures solely for research purposes that would not be part of clinical implementation of the program should be separated from intervention implementation costs in analyses.

Thank you for this pertinent remark. We modified the section in question in order to specify that research-related costs will not be considered as an element of the intervention costs. (page 16)

Analytical plans are described in very general terms, and the ways in which nesting of patients within clinicians within sites seem to vary by analysis (sometimes random clinician effects will be examined, sometimes random site effects). This could be clarified and better justified.

Thank you for pointing out this inaccuracy. We modified the manuscript in order to specify that we intend to take into account a random effect on the investigator level and not the centre level (most centres involve only one investigator) (page 15).

The type(s) or generation(s) of e-cigarettes that will be offered are not specified.
We added a description of the available e-cigarette in the revised manuscript.

“The provided e-cigarette is the “Zlide Tube” (Shenzhen Innokin Technology Co., Shenzhen, China) an easy to use e-cigarette with a 3000mAh rechargeable battery, a 4 mL tank with sliding top refill system, provided with several spare coils, and a wall charger.” (page 11)

Adverse event monitoring is not described and may be warranted given the combinations of treatments that will be provided to people continuing to smoke.

Thank you for pointing out this omission. We added a paragraph on adverse events monitoring in the revised manuscript. (page 14).

“The two principal investigators will have the responsibility to monitor adverse events which are systematically measured in all follow-up assessments. These events will also be monitored by two different research assistants. Every adverse event will be examined by the steering committee, and promptly reported to the scientific committee which will decide whether or not the study should continue..”

The sample postcard for collecting treatment use does not include all therapies listed as options for participants.

Thank you for pointing out this error. The postcard was updated, and we’ve added the new version (the one who is being distributed to the study centres) in the revised manuscript.

Plans to report results in clinicaltrials.gov or other venues for dissemination are not included.

We added our intention to report results in clinicaltrials.gov, as well as publish our results in a peer-reviewed journal in a new “dissemination” section. (page 17)

There are several minor grammatical issues to be addressed in copyediting.

We corrected grammatical errors throughout the manuscript.

Reviewer: 3

This is an interesting study. It is relevant to examine any methods to increase successful quitting among disadvantaged groups. The manuscript is well written; the style is concise, understandable, clear, and transparent. My comments/questions are detailed below.

Thank you for taking the time to review our article and your pertinent comments.
We hope our replies to your comments and the modifications we made to the manuscript are satisfactory.

Study design and participating centres:
1: Please add the research question to the manuscript.
Thank you for pointing out this missing point. We added the objective of the study on page 5:

"The main objective of this trial is to examine the effectiveness of the STOP intervention in real life settings."

2: I am curious, what was you rational for including 15 centres? And how did you choose which ones to include?
We added a paragraph explaining how we included physicians who were invited to join our study via Newsletter emails.
"We recruited physicians to our study by sending out invitations via the newsletter of two medical societies: the SFTG" (Société de Formation Thérapeutique du Généraliste: Society for Therapeutic Training of the General Practitioner) and the SFT (Société Francophone de Tabacologie, the French-speaking Society of Tabacology). Following these invitations, around 20 doctors expressed interest in participating in our study, clustered in around 15 centres". (page 5)

Recruitment:
3: You state that the data collection will being in February 2021. When do you expect it to end?

We planned for a recruitment period in each centre for up to one year, while each participant will be followed for 6 months.
However not all centres will begin recruiting in the same time, and therefore, we expect data collection to last until the end of 2023.

We added this information in the manuscript (page 8):

"Recruitment period in each centre will last for up to one year, while each participant will be followed for 6 months. However, not all centers will begin recruiting at the same time, and data collection is therefore expected to last until the end of year 2023."

Outcomes:
4: The main outcome is described as "Continuous abstinence for at least 7 days". To the best of my knowledge this is not continuous abstinence; this is a 7-day point prevalence (see Hughes et al., Measures of abstinence in clinical trials: issues and recommendations. Nicotine & Tobacco Research 2003: 5; 13-25. Doi: 10.1080/1462220031000070552).

Thank you for pointing this out, and for the pertinent reference. We corrected the manuscript according to your comment:
"The main outcome measure of this study will be the 7-day point prevalence tobacco abstinence" (page 8).
We also used this (new) term throughout the manuscript.

5: A secondary outcome used is "Total number of days of abstinence". It is unclear to me how this is measured/calculated. Is this the number of continuous smoke-free days (meaning smoke-free days from the initial quit day to the first relapse) or is it the sum of smoke-free days throughout the 6 months period? Please clarify.

Thank you for pointing out this ambiguousness. We modified the manuscript in order to specify that we will examine the total number of smoke-free days throughout the 6 months follow-up:

- "Total number of days of abstinence (sum of the number of smoke-free days throughout the follow-up period) at 6 months after inclusion" (page 9).

Sample size:
6: Taking the description of your control group into concern, you mention that the use of medication will be a possibility in this group also (I understand the treatment as usual can be very different

depending on the clinic). I think you based your sample size calculation on a very low control quit rate (based on the effect of advice from doctor only). Please explain the rational for using this low rate.

Thank you for this pertinent comment. We had trouble finding smoking rates for smokers with low socio-economic status in the scientific literature. Therefore we adopted conservative rates, on the basis that smokers with low SEP have usually more difficulties succeeding and maintaining a smoking cessation attempt as compared to the general population.

We added this sentence in the revised manuscript :
“Therefore, adopting a conservative perspective on smoking cessation rates, we hypothesised a smoking cessation rate of 6% at 6 months in the control group”. (page 8)

This was also influenced by figures from the literature: “Smoking cessation success rates are around 3 to 5%, without the help of health professionals who usually slightly increase the chance of success (by 1-2%) at one year.»

Randomisation and blinding:
7. Page 9, line 37: “Patients will be blinded to their randomisation group: …”. It is unclear to me how you can make this statement. I understand that you don’t inform the patients about the possible treatments as part of the protocol. But what if they ask you directly? Do you not tell them about the treatment options then? And wouldn’t that be problematic regarding the ethics of the study? Also, as soon as you publish this protocol the groups will be publicly available!

Thank you for this pertinent comment.

All patients will be informed that they will be randomized in one of two groups, and that we will compare two different smoking cessation support methods, as part of the study’s presentation.
We added the consent form, validated by an ethic committee, in supplementary material.
The only thing we are omitting to say in the study presentation is the delivery of free smoking cessation tools. However participants in the control group will be able to get prescription for nicotine substitutes and information on e-cigarettes as part of usual care.

It is possible that some participants will go looking for some information online, however very few information on the study will be available in French.

We will also inform all participants about the study design at the end of their follow up, and participants in the control group will be offered an e-cigarette and/or nicotine substitutes for one month if needed and requested. Participants in the control group will also receive calendar cards during follow up so they should not feel unsupported.

Other follow-up measures:
8: I would encourage you to be more specific about the assessors. Will they be blinded to the randomization group of the participants?
Thank you for pointing out this ambiguousness. We added more detail on blinding in the revised manuscript (page 10).
We also added in the limitations sections (page 3), that our trial is not double blinded since physicians will be the ones recruiting and mainly following the participants.

Statistical analyses:
9: I might be wrong here – but I wonder why you are so keen on using analysis adjusting for “sociodemographic characteristics and other potential confounders.”. Isn’t this unnecessary as this is a randomized controlled trial designed to deal with exactly this?

Thank you for this pertinent question.
Our main analysis will be done without adjusting for covariates, however we are interested in investigating the effect of socio demographic variables and other variables on our intervention effect.
We added these precisions in the revised manuscript:

"In secondary analysis models will be adjusted for appropriate covariates (socio-demographic characteristics, and other potential confounders) in order to explore the impact of these covariates on the intervention effect. " (page 14).

10: Page 10, lines 32-37: "Finally, we will estimate the average time it takes for a successful smoking cessation attempt using smoking aids, in order to provide decision-makers with a recommendation for how long smoking aids should be prescribed.". I suggest you rewrite the first part of the sentence. I understand why you want to do this (to recommend how long smoking cessation aid should be offered), but I don't understand how you will make this estimation.

Thank you for this pertinent comment. We rephrased this sentence in order to clarify the statistical analysis intended for this question:
"Finally, if the trial results declare the intervention as successful, we will estimate the average distribution (mean, median, interquartile range,..) of the time (number of days) during which the participants in the intervention group used smoking cessation tools, in order to provide decision-makers with a recommendation for how long smoking aids should be prescribed." (page 15).

VERSION 2 – REVIEW

REVIEWER	Danielle E. Mccarthy University of Wisconsin-Madison, Medicine
REVIEW RETURNED	07-May-2021

GENERAL COMMENTS	The authors have been responsive to previous critiques and have added requested details regarding key protocol elements, including interventionist training and fidelity monitoring, adverse event monitoring, data analysis plans, the study timeline, and data monitoring and sharing plans. The postcard continues to omit lozenges/tablets for unspecified reasons. It is interesting that a refillable tank e-cigarette model will be used instead of a nicotine salt pod device. Presenting a rationale for this choice would enhance the protocol. There continue to be many minor grammatical errors that will need to be corrected in copyediting.

REVIEWER	Mette Rasmussen Bispebjerg Hospital, Who-cc
REVIEW RETURNED	29-Apr-2021

GENERAL COMMENTS	My comments have been adequately addressed. Good luck with the study, I am looking forward to seeing the study results sometime in the future.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 2
Dr. Danielle E. Mccarthy, University of Wisconsin-Madison

Comments to the Author:
The authors have been responsive to previous critiques and have added requested details regarding key protocol elements, including interventionist training and fidelity monitoring, adverse event monitoring, data analysis plans, the study timeline, and data monitoring and sharing plans. The postcard continues to omit lozenges/tablets for unspecified reasons.

Thank you for taking the time to review our article again.
We added the right figure for the calendar card which has all the available tools.

It is interesting that a refillable tank e-cigarette model will be used instead of a nicotine salt pod device. Presenting a rationale for this choice would enhance the protocol. There continue to be many minor grammatical errors that will need to be corrected in copyediting.

Thank you for this comment. We added a rationale of using refillable tanks, which are the most commonly used models in France (they are also cheaper).

“E-cigarette models with refillable tanks are the most commonly used models in France, where the use of nicotine salt pod-based models is very limited.” (page 11)

Reviewer: 3
Dr. Mette Rasmussen, Bispebjerg Hospital, Lund University

Comments to the Author:
My comments have been adequately addressed.

Good luck with the study, I am looking forward to seeing the study results sometime in the future.

Thank you for taking the time to review our article again.