PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	A brief mindfulness-based intervention of “STOP (Stop, Take a Breath, Observe, Proceed) touching your face”: a study protocol of a randomized controlled trial
AUTHORS	Liao, Yanhui; Wang, Ling; Luo, Tao; Wu, Shiyou; Wu, Zhenzhen; Chen, Jianhua; Pan, Chen; Wang, Yunfei; Liu, Yueheng; Luo, Qinghua; Guo, Xin; Xie, Liqin; Zhou, Jun; Chen, Wei; Tang, Jinsong

VERSION 1 – REVIEW

REVIEWER	Alexander Bäuerle University of Duisburg-Essen, Germany
REVIEW RETURNED	07-Jul-2020

GENERAL COMMENTS	Thank you for letting me review this manuscript. I think it is a clear written and easy to understand study protocol. Publishing study protocols is important to prevent data-driven analyses and help the scientific community to reproduce trials. I completely support this and think publishing study protocols is part of good scientific practice. The research question and protocol are timely, as there is an urgent need to develop safe and effective interventions for this purpose. Regardless, I have some major concerns which leads to my decision to recommend Major Revision of the submitted manuscript. First of all, I would like to ask the authors at what point the recruitment phase is at the moment. In the trial registration (WHO) you mentioned that you are currently recruiting. The proposed timeline in manuscript is different: "We expect all trial results to be available by the end of June 2020." I think this manuscript lacks the exact status of recruitment. This should always be mentioned when publishing study protocols. The Abstracts lacks the description of the statistical methods under the section "methods and analysis" In addition, please mention under this section the time window the participants assessed the frequency of face touching One eligibility criteria is to read and write in Chinese, but is it not necessary to be able to hear/ understand Chinese, too. Sample size calculation:

	"stop smoking behavior interventions" are not appropriate reference. In my opinion smoking and face touching are not comparable. Following this issue your argumentation regarding the high drop-outs is inappropriate. I think it is clear that stop smoking interventions show high dropout rates. Please refer to literature regarding addictive behavior. Please refer to standard literature regarding dropout rates in online interventions. Please refer to this guideline for reporting RCT protocols in the text. Your figure is not clear enough. You should add the time when the follow up assessment takes place (how many weeks after). For the sake of completeness your figure should include the phase where the control group gets access to the intervention. Outcomes: You need to describe this more appropriate, please mention the time window the participants assessed the frequency of face touching here. Recruitment: Please provide an example of the informed consent form in English language. Page 16: Layout should be corrected. The self-reported times of face touching is a major concern in my opinion. The danger of over or underestimating is present. Especially for the intervention group. This study would be more accurate under lab conditions. I think this issue should be discussed more honestly. Of course, mental health is often surveyed through self-reports, but in contrast to your outcomes, validated instruments are used.

REVIEWER	Julieta Galante University of Cambridge, United Kingdom
REVIEW RETURNED	12-Jul-2020

GENERAL COMMENTS	Thank you for the opportunity to review this manuscript. My comments are listed below. The study is interesting and timely, but the methods are unclear in some places, and some extra limitations need to be acknowledged. The standard of written English is good but needs to be checked in detail for minor typos and mistakes. - Abstract Authors need to say whether the control group is active or passive, and if possible briefly describe it. The time point of the primary outcome is unclear: what does “short term” mean? Authors need to be more specific, both in the abstract and in the methods section. Many of the secondary outcomes are not comparing trial arms. This is ok but could be summarised more succinctly in order to describe the primary outcome and control group more in detail. The protocol registration number is important information; please mention it in the abstract. - Methods Authors need to describe whether/how allocation of intervention is being concealed (this is not the same as blinding participants or researchers). More detail is needed on what participants receive when they "receive the stop programme". Is this the recording, or something

	else? I was given access to the recording but it is in Chinese so I do not understand it unfortunately. Also, how does the practice work exactly? Do participants listen to this 5-minute recording and then practice for 15 minutes something that the recording told them to practise? Please explain in the text. I find this sentence confusing: “Later (with a one hour interval) they will be asked to self-monitor and report their one hour face-touching behaviour again" Do they do something else for an hour and then they monitor self-touching for an hour? Please explain this the text. What type of information will the participants in the control group receive? This needs to be described in more detail. I do not understand at what time points the control group participants monitor their face-touching behaviour. Do they do this before and after they get the control group information? Please clarify in the text. Is there a post-intervention measure before the follow-up measures? When do each of these happen exactly? Please describe better in the text and in Figure 1 (see comments on Figure 1 below). How does the face-touching data collection survey work? Do participants have to complete this questionnaire after the monitoring hour has passed, or do they have the questionnaire with them during the monitoring time and complete it as it happens? Please describe in the text. Authors say they will retain participants who do not respond to the questionnaires. How will they retain them? Will they impute their data? How? Please describe in the text. ITT is not a way to handle missing data. They are different things. Authors need to revise these concepts and rewrite this section. As far as I know, the analytic strategy authors are proposing is called ANCOVA, not ANACOVA. What will be the main outcome analysis? The ANCOVA of the frequency of touching? Please describe in the text. Why do authors also need to calculate a chi squared which will analyse the same data as the ANCOVA? Authors say they will encourage participants to communicate any safety issues. How will they do this? Will this be said in the STOP recording? Please describe in the text. The safety section says that even highly vulnerable participants can practice mindfulness. This is only true if they receive a mindfulness intervention that is clinically adapted to them. The STOP intervention is neither clinical nor human-facilitated, so the potential for adverse reactions among vulnerable participants exists. Please clarify this in the text. Authors encourage participants to contact a healthcare provider if they experience any issues. If they contact a healthcare provider, authors will not be able to monitor such events. How will this be handled? - Competing interests statement I would appreciate clarity on whether any of the authors are the intervention developers. If they were, I would think that this constitutes a conflict of interest, so I would advise authors to disclose it here. - Discussion The way authors measure face-touching does not differentiate between increased touching and increased awareness of touching. Mindfulness could make participants better at catching themselves touching their faces, so they may report higher

	frequency than the control group. This limitation of the tool needs to be acknowledged in the discussion. Authors need to acknowledge that they submitted this protocol to the journal after they finished recruiting and perhaps after they finished the whole trial. The trial registration is prospective, but this detailed protocol, strictly speaking, is not. High dropout rates are problematic even if you have an acceptable sample size of respondents. They are problematic because the sample of completers will be biased. What happens with those who do not complete outcome questions? They may have not found the intervention effective. There are ways to avoid high dropout rates in online interventions, like run-in periods. It is too late now to change this because the study is ongoing, but authors need to acknowledge potentially large dropout rates as a limitation. These biases arise even if the analysis is ITT. - Figure 1 Authors need to mention the baseline measurement here. In addition, the post-intervention measure is not mentioned. Are follow-up and post-intervention the same thing? These are usually different things. Authors need to clarify this; I would prefer that they use widely accepted language. Please check the CONSORT trial flow chart and try to adhere to it as much as possible.

REVIEWER	Stephen Edward Lupe The Cleveland Clinic Lerner College of Medicine of Case Western Reserve University and The Cleveland Clinic, Cleveland, Ohio, the United States of America.
REVIEW RETURNED	14-Jul-2020

GENERAL COMMENTS	An interesting study that will have wide-reaching applicability for disease prevention and health improvement, particularly in the age of COVID-19. The design was strong and I particularly enjoyed your analysis of strengths and weaknesses. I agree that self-observation will likely decrease the behavior in itself. I will be interested to see results.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Alexander Bäuerle
Institution and Country: University of Duisburg-Essen, Germany
Please state any competing interests or state ‘None declared’: None declared.

Please leave your comments for the authors below
Thank you for letting me review this manuscript. I think it is a clear written and easy to understand study protocol. Publishing study protocols is important to prevent data-driven analyses and help the scientific community to reproduce trials. I completely support this and think publishing study protocols is part of good scientific practice.

The research question and protocol are timely, as there is an urgent need to develop safe and effective interventions for this purpose.

Regardless, I have some major concerns which leads to my decision to recommend Major Revision of

the submitted manuscript.

First of all, I would like to ask the authors at what point the recruitment phase is at the moment. In the trial registration (WHO) you mentioned that you are currently recruiting.
The proposed timeline in manuscript is different: "We expect all trial results to be available by the end of June 2020."
I think this manuscript lacks the exact status of recruitment. This should always be mentioned when publishing study protocols.
Response: We drafted the protocol and submitted it to the Ethics Committee in March. The study approved by the Ethics Committee and the registration published on the same day of 1 April. Then, the study started from 2 April. We submitted the protocol in the recruitment stage. We enrolled participants from 2 April to 2 July 2020. We revised the text accordingly. We also revised the Figure1. The time-period is given in the design section.

The Abstracts lacks the description of the statistical methods under the section "methods and analysis"
Response: We now added statistical methods in the Abstract section as ”……Analysis of covariance, regression analysis, χ2 test, T-test, Pearson's correlations will be applied in data analysis.”

In addition, please mention under this section the time window the participants assessed the frequency of face touching
Response: We added it: “All participants will be asked to monitor and record their face-touching behavior during a 60-minute period before and after the intervention.”

One eligibility criteria is to read and write in Chinese, but is it not necessary to be able to hear/ understand Chinese, too.
Response: We provided mindfulness meditation instruction of STOP (Audio, 5 min) for participants from the intervention group. We also sent it to the control group after the trial. “……Both 750-word text and 5-min audio description (see Supplementary Material) will be available.”

Sample size calculation:
"stop smoking behavior interventions" are not appropriate reference. In my opinion smoking and face touching are not comparable. Following this issue your argumentation regarding the high drop-outs is inappropriate. I think it is clear that stop smoking interventions show high dropout rates. Please refer to literature regarding addictive behavior.
Please refer to standard literature regarding dropout rates in online interventions.
Response: Thanks for your suggestion! We deleted the inappropriate reference. The effectiveness of mindfulness intervention for addiction (such as stop smoking or drinking) could be different from Stop face touching. We revised the following information:" The sample size assessment and power calculations are mainly on the basis of the results of RCTs of different types of online short-term mindfulness intervention for behavioral changes, such as for alcohol consumption(ref 16) and stopping smoking or decreasing smoking craving(ref 29), or for positive psychological changes, such as enhancing wellbeing(ref 28) and reducing perceived stress and anxiety/depression symptoms(ref 27). A single brief session of mindfulness of 11-minutes (n=34) detected a significant reduction in alcohol consumption compared with a relaxation control intervention (n=34) (ref 16). It is estimated that, for assessing stop face-touching behavior, individuals who received mindfulness intervention will at least twice likely to reduce the chance of touching T-Zone than the control group (5 to 10% vs. 2 to 4%). Thus, a total of 562 participants (281 participants in each group) are required to achieve 80% power (1-beta=0.8), as significant at the 5% level (alpha=0.05), an increase in the primary outcome measure from 4% in the control group to 10% in the intervention group…….. A web-based guided self-help intervention for preventing depression reported about 20% dropout rate at 6-month follow-up (ref 30), but a brief online mindfulness-based intervention for reducing stress, anxiety and depression

reported 30% dropout rate in the intervention group and more than a half in the waiting list control group (ref 27)……."

Please refer to this guideline for reporting RCT protocols in the text.
Your figure is not clear enough. You should add the time when the follow up assessment takes place (how many weeks after). For the sake of completeness your figure should include the phase where the control group gets access to the intervention.
Response: We revised the figure (added the time) and uploaded it separately.

Outcomes: You need to describe this more appropriate, please mention the time window the participants assessed the frequency of face touching here.
Response: We revised the outcome as:" Primary outcome: the efficacy of short-term mindfulness-based "STOP touching your face" intervention (≥ 15min) for reducing face-touching behavior, measuring by reduction of percentage of the T-Zone touching during a 60-minute period by intervention. Secondary outcomes: the reduction of the frequency of face-touching after intervention; the factors (demographic characteristics, psychological traits of mindfulness) that would be associated with reduction of frequency of face-touching; the differences of face-touching behavior between left-handers and right-handers."

Recruitment: Please provide an example of the informed consent form in English language.
Response: I translated it into English and attached as a Supplementary file.

Page 16: Layout should be corrected.
Response: Thanks for your reminder! Corrected.

The self-reported times of face touching is a major concern in my opinion. The danger of over or underestimating is present. Especially for the intervention group. This study would be more accurate under lab conditions. I think this issue should be discussed more honestly. Of course, mental health is often surveyed through self-reports, but in contrast to your outcomes, validated instruments are used.
Response: "The danger of over or underestimating is present." Yes, we totally agree with it. We plan to run a longer-term intervention under lab condition (with video record). Hope the situation will get better and we can run it after September.
Here we added the following information in the Discussion section as a limitation: "……Also, self-reported results of self-monitored times of face touching may be overestimated or underestimated. The results will be more accurate under lab conditions. In order to reduce the bias, we will invite a sub-group of participants with video record by another person to confirm the consistency of these results……."

Reviewer: 2
Reviewer Name: Julieta Galante
Institution and Country: University of Cambridge, United Kingdom
Please state any competing interests or state 'None declared': Non declared

Please leave your comments for the authors below
Thank you for the opportunity to review this manuscript. My comments are listed below. The study is interesting and timely, but the methods are unclear in some places, and some extra limitations need to be acknowledged. The standard of written English is good but needs to be checked in detail for minor typos and mistakes.
Response: We have carefully checked this.

- Abstract
Authors need to say whether the control group is active or passive, and if possible briefly describe it.

Response: the control group will be on a wait-list. We revised it as: "…… the wait-list control group……" We also added a note under Figure 1 as:" Note: Participants from the "control" intervention will receive "STOP touching your face" intervention (both text and audio description) immediately after completing the second self-monitoring face-touching behavior. But they will not be required to practice it or to practice it at least 15 minutes.", and in the Methods section:"……either start the intervention immediately (intervention condition) or to a wait-list control condition (who will be offered the intervention immediately after reporting the second 60-min self-monitoring face-touching behavior)……."

The time point of the primary outcome is unclear: what does "short term" mean? Authors need to be more specific, both in the abstract and in the methods section.
Response: Reviewer 1 also raised this question. We revised it as:" Primary outcome: the efficacy of short-term mindfulness-based "STOP touching your face" intervention (≥ 15min) for reducing face-touching behavior, measuring by reduction of percentage of the T-Zone touching during a 60-minute period by intervention……."

Many of the secondary outcomes are not comparing trial arms. This is ok but could be summarised more succinctly in order to describe the primary outcome and control group more in detail.
Response: We revised the secondary outcomes as:" ……Secondary outcomes: the reduction of the frequency of face-touching after intervention; the factors (demographic characteristics, psychological traits of mindfulness) that would be associated with reduction of frequency of face-touching; the differences of face-touching behavior between left-handers and right-handers."

The protocol registration number is important information; please mention it in the abstract.
Response: We mentioned it in the end of Abstract section as:"Trial registration number NCT04330352."

- Methods
Authors need to describe whether/how allocation of intervention is being concealed (this is not the same as blinding participants or researchers).
Response: we revised it as:"….. All participants will report the first self-monitoring by the same link (the same Excel file will be downloaded), and the second will be reported by two different links (two separated Excel files will be downloaded) to detect group allocation. Group allocation will not be concealed to investigators who will provide interventions. But the investigators (by Dr. J Tang and Dr. Y Liu) who will analyze the data for evaluating outcomes will be blinded to participants' treatment allocations until the entire analysis has been completed."

More detail is needed on what participants receive when they "receive the stop programme". Is this the recording, or something else? I was given access to the recording but it is in Chinese so I do not understand it unfortunately. Also, how does the practice work exactly? Do participants listen to this 5-minute recording and then practice for 15 minutes something that the recording told them to practise? Please explain in the text.
Response: Participants will receive both 750-word text and 5-min audio description by online. We revised it in the Methods section:"The details of the procedure will include the following 3 steps:….. Step 1. The first self-monitoring of face-touching behavior (before intervention)…… Step 2. Intervention …… "STOP touching your face" program (both 750-word text and 5-min audio description). Each participant will be required to read the text of the program first and then listen to the audio. ……Thus, the requirement practice time will be at least 15 minutes (excluding the time of reading the text and the first time of listening to the audio)……. Step 3. The second self-monitoring of face-touching behavior (after intervention) ……"

I find this sentence confusing: "Later (with a one hour interval) they will be asked to self-monitor and

report their one hour face-touching behaviour again" Do they do something else for an hour and then they monitor self-touching for an hour? Please explain this the text.
Response: we clarified them in the text. "……complete the second self-monitoring of face-touching behavior during a 60-minute period. The repeat measurement of the face-touching behavior will be done at least 1 hour apart from the first self-monitoring……."

What type of information will the participants in the control group receive? This needs to be described in more detail.
Response: We added the following information in the Method section:" The control group: Participants who allocate to the control group will only receive information to thank them and encourage them to complete the study. They will be reminded to receive "STOP touching your face" program after the end of this study."

I do not understand at what time points the control group participants monitor their face-touching behaviour. Do they do this before and after they get the control group information? Please clarify in the text.
Response: Yes, they do this before and after they get the control group information. We clarified in the text:" Step 1. The first self-monitoring of face-touching behavior (before intervention)…… All participants will be required to monitor their face-touching behavior during a 60-minute period,……
Step 2. ……The control group: Participants who allocate to the control group will only receive information to thank them and encourage them to complete the study. They will be reminded to receive "STOP touching your face" program after the end of this study. ……
Step 3. The second self-monitoring of face-touching behavior (after intervention) After intervention, all participants will be required to monitor their face-touching behavior during a 60-minute period again……."

Is there a post-intervention measure before the follow-up measures? When do each of these happen exactly? Please describe better in the text and in Figure 1 (see comments on Figure 1 below).
Response: We revised Figure 1. There will be only steps: 1. first monitoring, 2. intervention, 3. second monitoring. There will be no follow-up after the second monitoring.

How does the face-touching data collection survey work? Do participants have to complete this questionnaire after the monitoring hour has passed, or do they have the questionnaire with them during the monitoring time and complete it as it happens? Please describe in the text.
Response: We clarified it in the Methods section: "Step 1. The first self-monitoring of face-touching behavior (before intervention)…… All participants will be provided with the same link to complete their baseline information and the first self-monitoring of face-touching behavior, and be encouraged to complete this questionnaire immediately after completion of self-monitoring."

Authors say they will retain participants who do not respond to the questionnaires. How will they retain them? Will they impute their data? How? Please describe in the text. ITT is not a way to handle missing data. They are different things. Authors need to revise these concepts and rewrite this section.
Response: We revised it as:" Withdrawal from the Program…… However, self-monitoring itself may increase the awareness of face-touching behavior, then consequently increase or decrease the frequency of face-touching behavior in the second time of observation. Alternatively, a complete case analysis will also be performed in which any participant withdrew from the study in the second observation will be excluded."

As far as I know, the analytic strategy authors are proposing is called ANCOVA, not ANACOVA. What will be the main outcome analysis? The ANCOVA of the frequency of touching? Please describe in the text.

Response: We revised it as “ANCOVA”. We revised the following information in the Methods/analysis: “……In order to determine if the “STOP touching your face” intervention group showed a reduction of face-touching behavior than the control group, two sample T-test or Mann-Whitney U test will first be applied to compared group differences in reduction of the frequency of face-touching. Then, analysis of covariance (ANCOVA) will be applied with controlling for demographic information (such age, handedness, occupation, and prior mindfulness meditation experience). In ANCOVA model, the dependent variable will be the reduction of face-touching behavior. The pre-intervention measure of the total times of face-touching will be controlled as a covariate, and intervention will be a fix factor. This model will assess the differences in the post-intervention means after accounting for pre-intervention values;……”

Why do authors also need to calculate a chi squared which will analyse the same data as the ANCOVA?
Response: χ2 test will be applied to analyze the date of “percentage of with and without T-Zone touching”. We revised it as:”…….Percentage of touching the T-Zone participants between pre- and post- intervention in the STOP group and the control group will be compared by χ2 test…….”

Authors say they will encourage participants to communicate any safety issues. How will they do this? Will this be said in the STOP recording? Please describe in the text.
Response: This will not be said in the STOP recording, but we will send a message to ask about it. The Audio record is only for STOP practice. We just assume that if participants with anxiety or depression can be encouraged to contact with us. In general, females with mental problems, such as anxiety and depression or insomnia, are more likely to practice mindfulness (from my clinical experience). We added the following information:” ……We will send a message to each participant to check whether they have any safety issues after providing them with intervention instruction.”

The safety section says that even highly vulnerable participants can practice mindfulness. This is only true if they receive a mindfulness intervention that is clinically adapted to them. The STOP intervention is neither clinical nor human-facilitated, so the potential for adverse reactions among vulnerable participants exists. Please clarify this in the text.
Response: We added the following information in the Methods section/Safey:”…… .This study is not clinical-facilitated and may have very low risk of any safety issue. We will send a message to each participant to check……”

Authors encourage participants to contact a healthcare provider if they experience any issues. If they contact a healthcare provider, authors will not be able to monitor such events. How will this be handled?
Response: Except for three psychologist, other research investigators are all psychiatrists (including myself) in this study. I revised it as: ” ……they will be encouraged to contact with us. And if necessary, we will refer a health care provider.”

- Competing interests statement
I would appreciate clarity on whether any of the authors are the intervention developers. If they were, I would think that this constitutes a conflict of interest, so I would advise authors to disclose it here.
Response: The “STOP touching your face” program is modified from STOP, which is already available. We mentioned in the text:”…… The “STOP touching your face” training program in Chinese was already developed by Dr. Y Liao, Dr. Q Luo and Dr. C Pan.”

- Discussion
The way authors measure face-touching does not differentiate between increased touching and increased awareness of touching. Mindfulness could make participants better at catching themselves touching their faces, so they may report higher frequency than the control group. This limitation of the

tool needs to be acknowledged in the discussion.
Response: We added it as a limitation:"Last, this is a mindfulness-based intervention, and mindfulness could make participants better at catching themselves touching their faces, so participants from the intervention group may report higher frequency than the control group in the second self-monitoring of face-touching behavior."
However, although STOP is a mindfulness-based intervention, it is also a kind of behavior intervention (from my opinion).

Authors need to acknowledge that they submitted this protocol to the journal after they finished recruiting and perhaps after they finished the whole trial. The trial registration is prospective, but this detailed protocol, strictly speaking, is not.
Response: Yes, we acknowledge that we submitted this protocol to the journal during the time of recruiting. We tried another journal before.

High dropout rates are problematic even if you have an acceptable sample size of respondents. They are problematic because the sample of completers will be biased. What happens with those who do not complete outcome questions? They may have not found the intervention effective. There are ways to avoid high dropout rates in online interventions, like run-in periods. It is too late now to change this because the study is ongoing, but authors need to acknowledge potentially large dropout rates as a limitation. These biases arise even if the analysis is ITT.
Response: Yes, it does have high dropout rates. The study is completed at this moment. The dropout rates are less than 30 % in the intervention group and about 35% in the control group. We mentioned it in the limitation section. We also added the following information for handling missing data in the method/analysis section: "intention-to-treat (ITT) basis will be applied in this study to handle incomplete or missing data (assuming for no reduction of the frequency of face-touching). In addition, a complete case analysis will be performed in which any participant with missing information on the follow-up will be excluded."

- Figure 1
Authors need to mention the baseline measurement here. In addition, the post-intervention measure is not mentioned. Are follow-up and post-intervention the same thing? These are usually different things. Authors need to clarify this; I would prefer that they use widely accepted language. Please check the CONSORT trial flow chart and try to adhere to it as much as possible.
Response: We revised Figure 1 (added the time and clarified the procedures) and uploaded it separately.

Reviewer: 3
Reviewer Name: Stephen Edward Lupe
Institution and Country: The Cleveland Clinic Lerner College of Medicine of Case Western Reserve University and The Cleveland Clinic, Cleveland, Ohio, the United States of America.
Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below
An interesting study that will have wide-reaching applicability for disease prevention and health improvement, particularly in the age of COVID-19. The design was strong and I particularly enjoyed your analysis of strengths and weaknesses. I agree that self-observation will likely decrease the behavior in itself. I will be interested to see results.
Response: Thank you very much for your suggestions and support! The results are under preparation.

VERSION 2 – REVIEW

REVIEWER	Alexander Bäuerle University of Duisburg-Essen
REVIEW RETURNED	24-Aug-2020

GENERAL COMMENTS	I think the revision of the protocol is adequate. I recommend publication of the submitted manuscript.

REVIEWER	Julieta Galante University of Cambridge, United Kingdom
REVIEW RETURNED	02-Sep-2020

GENERAL COMMENTS	I wish to thank the authors for their point-by-point replies. However, I am afraid that I still need clarification on the points described below. Randomisation and group allocation Authors still need to describe if the allocation of intervention was concealed, which is different from blinding as I mentioned before. I advise the authors to familiarise themselves with the concept (explained for example in https://www.bmj.com/content/347/bmj.f5518 and in https://www.sealedenvelope.com/randomisation/blinding/) and then explain in the manuscript how this was handled in their trial. Outcomes I do not understand the primary outcome: “reduction of percentage of the T-zone touching…”. Percentage of what? Reduction of the percentage of participants who touch their face from pre- to post-intervention compared with the reduction in the control group? I assume authors do not mean frequency, because frequency of face touching is mentioned as a secondary outcome. But in their trial registration they say that the primary outcome will be frequency of face-touching, not percentage of participants touching their face. The primary outcome cannot be changed at this stage (authors will have collected all the study data by now), so I request that the authors modify this section to read exactly as it reads in the registration. In other words, that frequency of face touching is the primary outcome (not a secondary outcome) and that percentage of participants touching their faces is a secondary outcome. Measures The authors have added a second measure “Reduction of frequency of face-touching behaviour”, but as it is described currently I do not think this is a measure. This is an analysis plan using the measures described in point one “Frequency of face-touching”. Please clarify, and if it is not a measure, please delete or move from here to data analysis. Withdrawal from the program “On the basis of the intention-to-treat (ITT) principle, participants who fail to respond to follow-up assessment will be retained in the analysis and classified as those who continued the same behaviour”. This is not on the basis of the ITT principle, this is a plan for imputing missing outcome data using the last-observation-carried-forward method. The ITT principle is a different thing, as I said in my first review: it simply means that participants will be analysed according to the arm they were randomised to, irrespective of whether they did the intervention or not. Please, re-write this section clarifying: 1. whether you will follow the ITT principle, and 2. that you will impute missing outcome data using the last-observation-carried-forward method. You also need to

	change the part in the Data Analysis section where you mention ITT. “However, self-monitoring itself may increase the awareness of face-touching behavior, then consequently increase or decrease the frequency of face-touching behavior in the second time of observation.” I think the authors for acknowledging this, but I think it should go in the discussion section, as a limitation, not here in the methods. Data analysis I thank the authors for their reply, however it is still not clear which of all these analyses will be taken as the main result. This is crucial in an RCT, to avoid multiple testing problems and cherry-picking of positive results. The authors said in their trial registration that the main outcome is frequency of face-touching. Two of the tests they mention could be used to determine this: T test and ANCOVA. Unfortunately, by now the authors already have collected and perhaps even analysed all the trial data, so now it is not possible for them to choose one of these analyses in advance. It will be important that they report all of these analyses when they publish the results. Discussion While I appreciate that the authors acknowledge that they submitted this protocol to the journal after they started recruiting, I meant that they acknowledge it in the manuscript rather than to me privately. I think this is a limitation of the protocol and as such it should be mentioned. Competing interests statement I also thank the authors for clarifying that they have developed the intervention. In that case, I think this should be mentioned in the competing interests section, given that intervention developers could obtain potential financial gains from showing that the intervention is effective (just as pharmaceutical companies do when they develop drugs).

VERSION 2 – AUTHOR RESPONSE

Reviewer: 2

Reviewer Name: Julieta Galante

Institution and Country: University of Cambridge, United Kingdom

Please state any competing interests or state ‘None declared’: None declared

Please leave your comments for the authors below

I wish to thank the authors for their point-by-point replies. However, I am afraid that I still need clarification on the points described below.

Randomisation and group allocation

Authors still need to describe if the allocation of intervention was concealed, which is different from blinding as I mentioned before. I advise the authors to familiarise themselves with the concept

(explained for example in https://www.bmj.com/content/347/bmj.f5518 and in https://www.sealedenvelope.com/randomisation/blinding/) and then explain in the manuscript how this was handled in their trial.

Response: Thank you so much for providing relevant links! We carefully read them and learned from them. We added the following information: “In this online-based, randomized, parallel-group trial, ……. Since participants will be told that they will either receive “STOP touching your face” training program before (intervention group) or after (control group) the second 60-minute self-monitoring face-touching behavior, blinding of participants will not be possible. Blinding of the investigators (mainly Dr. Y Liao and Dr. L Wang) who are directly involved in interventions will also not be possible because of the nature differences of these two interventions (“STOP touching your face” training program intervention and control intervention). The investigators (Dr. J Tang and Dr. Y Liu) who will assess the outcomes will be blinded to participants’ allocated groups until all data have been analyzed…….”

Outcomes

I do not understand the primary outcome: “reduction of percentage of the T-zone touching…”. Percentage of what? Reduction of the percentage of participants who touch their face from pre- to post-intervention compared with the reduction in the control group? I assume authors do not mean frequency, because frequency of face touching is mentioned as a secondary outcome. But in their trial registration they say that the primary outcome will be frequency of face-touching, not percentage of participants touching their face. The primary outcome cannot be changed at this stage (authors will have collected all the study data by now), so I request that the authors modify this section to read exactly as it reads in the registration. In other words, that frequency of face touching is the primary outcome (not a secondary outcome) and that percentage of participants touching their faces is a secondary outcome.

Response: Thanks for your help to clarify them! We revised it accordingly: “Primary outcome: the efficacy of short-term mindfulness-based “STOP touching your face” intervention (≥15min) for reducing face-touching behavior, measuring by reduction of frequency of face touching behavior (this will be calculated as the total times of face-touching (including the eyes, nose, mouth, ears, cheeks, chin, neck, forehead, hair) during a 60-minute period before the intervention minus the total times of face-touching after the intervention).

Secondary outcomes: the reduction of percentage of participants touching their faces (this will be calculated as the percentage of participants touching their faces (including any of the following areas: the eyes, nose, mouth, ears, cheeks, chin, neck, forehead, hair) during a 60-minute period before the intervention - the percentage of participants touching their faces after the intervention) after intervention;……”

Measures

The authors have added a second measure “Reduction of frequency of face-touching behaviour”, but as it is described currently I do not think this is a measure. This is an analysis plan using the measures described in point one “Frequency of face-touching”. Please clarify, and if it is not a measure, please delete or move from here to data analysis.

Response: Thanks for your reminder! We removed this part. We also added the following information in the Measures section: “Percentage of participants touching their faces: this will be the number of participants who touched any of the following areas: the eyes, nose, mouth, ears, cheeks, chin, neck,

forehead, hair, during their 60-minute self-monitoring of face-touching / the total number of participants in the intervention group or the control group."

Withdrawal from the program

"On the basis of the intention-to-treat (ITT) principle, participants who fail to respond to follow-up assessment will be retained in the analysis and classified as those who continued the same behaviour". This is not on the basis of the ITT principle, this is a plan for imputing missing outcome data using the last-observation-carried-forward method. The ITT principle is a different thing, as I said in my first review: it simply means that participants will be analysed according to the arm they were randomised to, irrespective of whether they did the intervention or not. Please, re-write this section clarifying: 1. whether you will follow the ITT principle, and 2. that you will impute missing outcome data using the last-observation-carried-forward method. You also need to change the part in the Data Analysis section where you mention ITT.

Response: Thanks for pointing them! We revised them accordingly. We revised the following information in the Withdrawal from the Program section: "……On the basis of the intention-to-treat (ITT) principle38, participants who fail to respond to the second assessment will be retained in the analysis according to the arm they were randomized to, irrespective of whether they did the intervention or not.……"

We also revised the following information in the Data analysis section: "……Intention-to-treat (ITT) basis will be applied in this study, all participants who complete the first 60-minute self-monitoring face-touching behavior will be retained in the analysis. The last-observation-carried-forward (LOCF) method will be applied to handle incomplete or missing data (assuming for no reduction of the frequency of face-touching)……."

"However, self-monitoring itself may increase the awareness of face-touching behavior, then consequently increase or decrease the frequency of face-touching behavior in the second time of observation." I think the authors for acknowledging this, but I think it should go in the discussion section, as a limitation, not here in the methods.

Response: We added it as a limitation: "Also, self-reported results of self-monitored times of face touching may be overestimated or underestimated. Furthermore, self-monitoring itself may increase the awareness of face-touching behavior, then consequently increase or decrease the frequency of face-touching behavior in the second time of observation. The results will be more accurate under lab conditions……."

Data analysis

I thank the authors for their reply, however it is still not clear which of all these analyses will be taken as the main result. This is crucial in an RCT, to avoid multiple testing problems and cherry-picking of positive results. The authors said in their trial registration that the main outcome is frequency of face-touching. Two of the tests they mention could be used to determine this: T test and ANCOVA. Unfortunately, by now the authors already have collected and perhaps even analysed all the trial data, so now it is not possible for them to choose one of these analyses in advance. It will be important that they report all of these analyses when they publish the results.

Response: We applied both methods to analyze the primary outcome (reduction of frequency of face touching behavior), we revised the following information to clarify the analysis for the main outcome: "……For assessing the primary outcome, determining if the "STOP touching your face" intervention group showed a reduction of face-touching behavior than the control group, two sample T-test or Mann-Whitney U test will first be applied to compared group differences in reduction of the frequency of face-touching. Then, analysis of covariance (ANCOVA) will be applied with controlling for demographic information (such age, handedness and prior mindfulness meditation experience). In ANCOVA model, the dependent variable will be the reduction of face-touching behavior. The pre-intervention measure of the total times of face-touching will be controlled as a covariate, and intervention will be a fix factor. This model will assess the differences in the post-intervention means after accounting for pre-intervention values……."

Discussion

While I appreciate that the authors acknowledge that they submitted this protocol to the journal after they started recruiting, I meant that they acknowledge it in the manuscript rather than to me privately. I think this is a limitation of the protocol and as such it should be mentioned.

Response: We added it in the Limitation section: "……Last, we submitted this protocol to the journal during the time of recruiting."

Competing interests statement

I also thank the authors for clarifying that they have developed the intervention. In that case, I think this should be mentioned in the competing interests section, given that intervention developers could obtain potential financial gains from showing that the intervention is effective (just as pharmaceutical companies do when they develop drugs).

Response: We revised the Competing interests statement section as: "Dr. Y Liao developed the "STOP touching your face" training program. No other potential conflicts of interest to declare." However, I believe we will not obtain potential financial gains the "STOP touching your face" training program.

VERSION 3 – REVIEW

REVIEWER	Julieta Galante University of Cambridge, UK
REVIEW RETURNED	30-Sep-2020

GENERAL COMMENTS	I thank the authors for addressing my concerns and for their patience. I think this manuscript is now fit for publication.