Author’s response to reviews

Title: WhatsApp embedded in routine service delivery for smoking cessation: Effects on abstinence rates in a randomized controlled study

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Version: 1 Date: 27 Feb 2019

Author’s response to reviews:

Dear Editor,

We are thankful for the valuable comments on our paper. We had written an e-mail on the possibility of a delay in our reply, we apologize for this delay.

In the manuscript the changes have been highlighted. English editing has been done. Ten references have been added regarding reviewer comments and these references are also highlighted in References part.

The reviewer comments and our answers for them are below.

Kindest regards,
Seyfi Durmaz

Reviewer comments

Hayden Mcrobbie (Reviewer 1):
Line 30: You need to clarify that the intervention was added to an outpatient smoking cessation service (usual care) and compared to usual care alone.

We agree that this issue needs to be mentioned. We therefore added the following text to the Abstract and also corrections at relevant parts in Aim and Method parts have been made, too.

“... WhatsApp application added to the usual care of a university hospital cessation unit, as compared to usual care alone, on abstinence rates at first month.”

Line 34: You may wish to revise how the content was developed here. I don't think that the Transtheoretical model (TTM) is the correct theoretical basis for development (see my comments below).

We revised the parts on how the content was developed. Transtheoretical model (TTM) is the method guiding the usual care so we decided that this focus should be omitted from how the intervention content was developed. Omissions have been made in Abstract and re-write as: “Intervention content was prepared and 60 WhatsApp messages about having a plan of action and preventing relapse were developed through expert panels.”

Lines 36-37: This could be deleted.

We deleted this part.

Line 37: State what the primary outcome measure is. Based on your power calculation this is self-report abstinence rate at 1 month post target quit day (TQD). The abstinence rates at 3 and 6 months are secondary outcomes. The abstinence rates at 3 and 6 months are not really point prevalence measures, but instead sustained abstinence rates.
The primary outcome has been changed to “self-report abstinence rate at 1 month post target quit day (TQD).” 3rd and 6th month abstinence rates have been named as secondary outcomes throughout the text.

Line 44: The sentence starting "The intervention was…." needs revision. I think you mean here that when controlling for all other factors in the multivariate logistic regression, only the intervention was associated with abstinence.

This part has been changed as: “When controlled for all other factors in the multivariate logistic regression, the intervention was the only variable significantly associated with abstinence.”

Line 50: I don't think that you can claim that the intervention was equally as effective in those from lower socio-economic groups (SEGs) as those from higher SEGs. This study was not adequately powered to look at this.

We have omitted those claims.

Lines 53-55: I see that this trial is Registered online (https://clinicaltrials.gov/ct2/show/record/NCT03714971) . This should be added to the manuscript.

This is added to the Ethical approval part as: “This trial is registered online at ClinicalTrials.gov with the identifier NCT03714971.”

Line 58: Information regarding the global effect of tobacco use is not needed. Instead focus on giving the readers some background to tobacco use and tobacco cessation in Turkey.

Additions have been made at Introduction as: “In Turkey, over 65300 people are killed annually by tobacco-induced diseases [1].”

Line 63: You quote that "…1,848,462 quitting services were offered…” Do you mean the number of individuals that were provided with cessation treatment?
This part has been clarified as: “The total number of individuals admitting to cessation services in these clinics was 1,848,462 between 2009-2016 [4,5].”

Lines 65-69: I am unclear of the relevance to the TTM here. This study was undertaken in people who had enrolled in a smoking cessation services and were, presumably, already in the 'action stage' of quitting. I know that there is a 'preparation' stage in the TTM, but in this setting preparing for quitting is part of the treatment.

We have omitted the parts on TTM.

Lines 78-81: It is a little odd to cite the results of just one study in this way. There are other examples in the literature that explore smokers' preferences for cessation support.

This part has been re-written as “It was found that smokers preferred to quit by the help of a website, mobile applications, telephone line, e-mail based service, proactive telephone consultation and SMS reminders [14-16].”

Lines 84-86: It is good that you have looked at the use of WhatsApp, but it would be better if you could provide a summary of the use of WhatsApp for delivery of behavior change interventions. Are there any more studies that the one you cite? If not, you could say that you found only one published study.

This part has been enriched with the reference 18 and 19

Lines 87-89: The first sentence does not make sense to me. What studies are you referring to? Studies of text messaging or social media? Please clarify this.

This part has been clarified as: “Mobile phone based applications like WhatsApp have also been found to have positive influence on improving knowledge on diabetes or increasing access to mammography screening [18,19].......” and “Studies using social media”

Lines 89-91: I think that it would be useful if you can provide some rationale here as to why social media tools, such as WhatsApp, could add to face-to-face smoking cessation services. Then you can state what you planned and your hypotheses.
The following part has been added to Introduction. “Mobile phone based efforts for quitting tobacco offers the quitter the opportunity to be within reach in any place and in a direct manner, at a time convenient for the user and with low necessity for resources and this reach increases the continuity of motivation throughout the follow-ups. [17].”

Methods

I think that this section would benefit from some revision. Consider reorganising with the following sub-headings: Trial design; Participants; Usual care; Intervention; Sample size; Randomization; Blinding; Measures and outcomes; Analysis; and Ethical issues.

Sub-headings have been added.

Line 105: I was curious as to why you opted to use a 1:2 allocation. It's more usual, I think, to allocate more to the intervention group. Please provide the readers with some rationale here. The sentence on lines 133-134 can be included with this rationale.

The following part has been added in Methods: “Literature has provided evidence that this allocation does not have a major effect on power [23].”

Lines 105-110: I think that these should be included in a separate subsection titled 'Usual care'.

A subsection on 'Usual care' has been added.

Lines 113-124 'Participants': It would be good to make it clear in this section how participants were recruited and what the inclusion and exclusion criteria were. You should include 'ready to quit smoking' or 'wanted help in quitting smoking' as an inclusion criterion.

“Wanted help in quitting smoking” was added

Lines 136-142 should be included in at the beginning of the results section, along with Figure 1, and lines 145-151. Collectively, these lines should be re-written to clearly explain the participant flow.

Changes have been made at the beginning of Results section.
Lines 152-158 belong under the 'Randomization' sub-heading.

These lines are now under “Randomization”

Line 171: The 'Variables' section would be better labelled 'Measures and outcomes'. It should describe what was measured, and when, and then describe the primary and secondary outcomes. The label has been changed, additions have been made and the primary and secondary outcomes were described.

Lines 172-182: There should be just one primary outcome. Given that your sample size was based on 1-month abstinence rates, this would be the primary. You should also state that this was a self-reported measure. If you have CO-validated abstinence rates at this time-point then this would add strength to your study. The other measures should be included as secondary outcomes.

Primary and secondary outcomes have been re-written. The self-reported (1st, 3rd and 6th months) abstinence rates at different time points have been clearly stated.

Lines 177-179: Your description of the abstinence measure at 3 months is really a 'sustained abstinence rate', as is the 6-month abstinence measure. This makes the results a little stronger. Again, you need to clarify that these are self-reported.

The measures at 3rd and 6th months have been stated as 'Sustained abstinence rate'. Corrections have been made all through the text.

Lines 182-204: These are a mix of measures and outcomes. Consider re-organizing these sentences to describe, first, what was measured, and when, and then describe the primary and secondary outcomes. The section on 'Data Collection' (lines 205-215) could be incorporated here.

This part was incorporated with Data collection part and reorganised to clarify the measures and outcomes.
Line 196: The correct terminology for the Fagerstrom Scale is the Fagerstrom Test of Cigarette Dependence. I also noted that in Table 2 you categorized the scores, so this should also be described here.

Terminology has been corrected and the categorization of the score has been described.

Line 197: Please describe when (i.e. at which time-points) CO was measured.

We clarified this by adding the following text: “CO level was evaluated with the piCO Smokerlyzer carbon monoxide breath test monitor at first visit and at first month of abstinence.”

Line 229: It is not clear what you mean by "The advertisements occupying SMS message boxes…” I assume you don't mean paid advertisements, but the words or pictures.

We clarified this by adding the following text: “Many companies use text messages via SMS for advertisement too often and some people may get exhausted with these texts. As it does not expose the users to advertisements, WhatsApp has become a more preferable choice in personal communication.”

Lines 232-255 'Development of the message contents': As noted above in my comments regarding the abstract, the use of the TTM to guide message development does not seem correct here as all participants were ready to quit. Is this really what you based your message development on? I think that it is OK to say that you based you draft messages on the expertise of smoking cessation specialists, or whoever it was that drafted the messages. The messages may have also covered the evidence-based behavior change techniques for smoking cessation (e.g. see https://www.ncbi.nlm.nih.gov/pubmed/20478957). The important point in your development is that you tested these messages again with experts and end-users and modified these based on feedback.

We omitted TTM and the basis of the message contents development has been stated as follows: “Among 178 key messages gathered through literature review, a selection procedure was led with an expert group. These messages covered evidence based behaviour change techniques for smoking cessation behaviour. The resultant list of messages was tested again with experts and
end-users and modified according to the feedback. Similar messages were combined under two main titles: "Having a plan of action preparation" and "Preventing relapse action".

Lines 258-260: I would suggest deleting the end of the sentence from "…as non-response…” onwards.

The omission was made.

Lines265-267: What was the rationale for the two models used in logistic regression?

We used two logistic regression models because we wanted to evaluate the crude (only adjusted for age and gender) and adjusted results. In the first model we controlled for age and gender, in the second model we controlled for age, gender and all the other associated variables in univariate analyses.

There was no information given on how weight was analyzed. Ideally you would look at change in weight in those who are abstinent only. Those who don't stop smoking are unlikely to have gained weight.

We re-analyzed the weight and only for the abstinent. The results have been changed in Table 4. An explanation about the weight evaluation has been changed as: “At first visit and at first month follow-up, weight was measured in light clothes using a high-quality digital scale. For the 3rd month, self report on weight gain was asked. Any weight change greater than or equal to 1 kilogram was considered “weight gain”.

Results

Lines 277-343, Results: I think that this section could be substantially shortened, referring readers to the tables for full results.

Results have been shortened omitting repetitions.

Lines 341-343, Table 4: Was the total N the same for all outcomes? That is, for example, did you have weights for all participants?

Total N was added to the tables
Discussion

Overall the discussion is lengthy and I think that it could be shortened substantially.

We tried to shorten the discussion as well as adding subtitles for a better understanding.

Lines 346-347: consider re-wording this part of the discussion to reflect that the results showed a benefit of providing additional support via WhatsApp, above usual care alone at all follow-up points.

This part has been changed as: “The results of this study showed a benefit of providing additional support via WhatsApp, compared to usual care alone, confirmed at all follow-up points.”

Lines 352-354: would be better placed with some of the limitations.

This part has been added to Limitations part.

Lines 355-380: this section on the determinants of quitting is a little difficult to follow. It may be better to consider each determinant in a separate paragraph.

Each determinant was dealt in a separate paragraph with a specific subtitle.

Lines 381-427: this section would benefit from re-writing to simply compare and contrast to what is known. The statement at the end of page 17 "The WhatsApp intervention in our study was found to be even more effective among these studies" is not justified. You need to be clear with what end-points you are comparing and the 95% confidence intervals overlap with those in the meta-analysis.

Changes have been made under role of intervention as: “The meta-analysis (primary outcomes assessed at <3 months) by Graham and colleagues concluded that interactive internet interventions were 2.10 (OR, 95% CI=1.25-3.52) times more effective than smoking cessation interventions with printed materials. Internet intervention was found to be 1.35 (OR, 95% CI=0.97-1.87) times more successful than face-to-face contact but this was statistically insignificant. Twenty-four studies involving different forms of internet interventions had a significant effect of 1.16 fold (OR, 95% CI=1.03-1.31) in favour of internet interventions [21].
The WhatsApp intervention in our study (for 1st month OR=3.51, 95% CI=1.30-9.44; for 3th month OR=2.50, 95% CI=1.04-5.98) was found to be even more effective than the interventions in these studies. In a meta-analysis in 2016, Whittaker and colleagues examined 12 cessation studies with outcomes for six-month follow-up. They found that mobile-phone-based interventions increased smoking cessation success rates 1.67 times (OR, 95% CI=1.46-1.90) [17]. This is in line with our study’s sixth month results (OR=2.31, 95% CI=1.03-5.16).

Lines 417-418: I don’t think that you can say too much about the elimination of the effects of gender, unemployment and mood. I think that it is OK to say that you did not find an effect of these things on abstinence in the logistic regression, but that does not mean that your intervention was responsible for eliminating the effect of these factors, which are often seen in other studies.

We agreed with this and eliminated this part from discussion. We re-worded it as: “We did not find an effect of gender, unemployment and depressive mood on abstinence in the final logistic regression.”

Lines 442-450: I think that the conclusions that you are drawing here are also not justified. It will, of course depend on how the differences in change in weight were analyzed. Comparing change in weight among abstainers will help look at this a little closer. As you have more smokers in the control arm, there are likely to be fewer people to have gained weight.

We re-analyzed the weight and only for the abstinent. The results have been changed in Table 4. An explanation about the weight evaluation has been changed as: “At first visit and at first month follow-up, weight was measured in light clothes using a high-quality digital scale. For the 3rd month, self report on weight gain was asked. Any weight change greater than or equal to 1 kilogram was considered “weight gain”.

We made omissions and changed this part as: “There was no significant difference in terms of weight gain among the quitters between the intervention and control groups. Weight gain is a common problem regarding smoking cessation [46]. Messages for promoting healthy life styles regarding dietary habits and physical activity were amongst the intervention content in this study. However we did not achieve any specific advantage of this content.”

Lines 455 and 457: The percentages of those continuing therapy are around the wrong way.

We are sorry for this mistake. We have corrected them.
Lines 480 - 495; Limitations: these should be moved up before the conclusions, I think. You should also acknowledge that the control group did not receive any messages, so there may be some subject-expectancy effect.

The place of limitations has been changed in the text. Subject-expectancy effect has been added to limitations as: “The control group did not receive any messages, so there may be some subject-expectancy effect.”

Lines 484-486: I don't think that self-reported abstinence is a reliable as biochemically verified abstinence. You state that studies have proven this, yet cite none.

We have added the citation and changed the text as: “Yet studies have shown that self-reported cessation was correlated with biological measures [50].”

Table 3

Why are the effects of Social Class, Depression Score and Marital Status not assessed at 6 months? Perhaps the depression score was not collected, but data are available for the other factors

In the analysis of 6 month (Chi-square and Student’s t test), social class, depression score and marital status variables were not significant. So we did not put them in the regression model. We have added an explanation to the statistical analysis section to clarify this point: “The variables which were significant in the Chi-square and Student’s t test were put in the multivariate analysis”

Figure 3

Numbers need to be added here.

Numbers have been added.

David Buller (Reviewer 2):

1. Hypothesis 1 is based on the literature reviewed in the introduction but the authors do not provide a rationale for Hypotheses 2 or 3 either by reviewing past literature or making a coherent
arguments for long-term cessation or effect on adherence to the clinic program, medication, and weight gain. This rationale should be provided.

The following part has been added to text for providing the rationale: “Smokers who want to quit attend these services and get counseling and treatment support for their quit attempt. After a face-to-face counseling session, follow-up is initiated at the first week of quitting [6]. Adjunctions to brief counseling-like telephone counseling- are shown to increase quitting success. [7]. Drug continuity and weight change also play crucial roles throughout the quitting period. Weight gain may even impair the efforts to quit [8]. In some studies it was shown that quitting smoking and weight control efforts interact and improve the success rates for both attempts [9]. Medication, as part of a comprehensive management strategy, is integral to this service with a specified duration prescribed by the physician [10].”

2. When presenting and discussing the results on adherence to the clinic cessation visits, the authors use the term sufficiency but fail to define it. Unless there is a clear reason why a certain number of clinic visits is needed, it might be best to just describe this as a continuous measure of more or less visits.

The rationale for this classification has been defined as: “After the first visit, the first follow-up visit is recommended to be right after the quit day, preferably at the first week. A second follow-up is suggested in the second week and a third follow-up at the fourth week after quit. [6]. This has been basis to our drug continuity measure.”

3. The description of the WhatsApp messages would be improved by describing how the messages mapped onto the TTM concepts, whether they were sent in a particular order, timing, or intensity based on the TTM or practical considerations, and if the messages were tailored to personal characteristics of the smokers.

Additional File 3 has been revised and added to main text as Table 1.

4. The authors need to clarify the test statistic reported on pages 13-14 when using the term a x.xx fold increase. Is this an odds ratio? If so, report it as such.

These are odds ratios so changes have been made throughout the text.

5. Hypothesis 3 and in some points of the Discussion, the authors imply that the improvement in cessation rates may be due to the increase in adherence to clinic visits and continuity of
medication use. This should be evaluated by conducting formal statistical tests of mediation. The design with multiple follow-ups would permit a strong test of mediation by predicting cessation at 6-months based on the mediators of clinic visits and medication continuity at 1- and 3-months. This would strengthen the understanding of the mechanisms by which the WhatApps intervention improved cessation rates.

We thank the reviewer for the suggestion. We have tried several different approaches to conduct mediation analyses; however, we realized that it was not so suitable for mediation analysis. As we have explained in the discussion, people who are successful in quitting seem to have a higher tendency to attend to follow-up visits and continue their therapy. After their lapse, those who are not successful might just stop taking the medicines and stop coming to the clinic because the issue is no more in their agenda or because of their defence mechanisms. We have tried to explain this with our comment: “Another reason for the increase in face-to-face follow-ups in the intervention group may be their increased abstinence rates because those who succeed might feel more proud in attending the service and giving feedback, while the non-succeeding participants may avoid the issue and thus the visit.” As our follow-ups are like point prevalences in time and as we do not know whether they first did not succeed and then decided not to come or whether they first did not come to the visit and then could not succeed limits our approach in evaluating mediation.

To clarify, another sentence as “Another possibility is that the participants who could not continue successfully their quit attempt have also stopped taking their medication.” was added to the paragraph on drug continuity.

6. On page 16, lines 352-354, the authors repeat that the sample was predominately male but they also need to speculate how this may have affected the outcomes of the WhatsApp intervention and the generalizability of the results.

The part has been transferred to limitations as a problem of generalizability.

7. The authors should note in limitations that the individuals in the sample were experienced using WhatsApp so the findings may not generalize to smokers who are less likely to use mobile apps.

This note was added to Limitations as: “The individuals in the sample were experienced in using WhatsApp so the findings may not be generalized to smokers who are less likely to use mobile apps.”