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Effectiveness of the e-Tabac Info Service application for smoking cessation: A pragmatic randomised controlled trial

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Abstract

Objective: To compare the effectiveness of the mobile e-Tabac Info Service (e-TIS) application (app) for helping adult smokers quit smoking with current practices.

Design: Pragmatic randomised controlled trial with a 1-year follow-up (2017-2018).

Setting: France, population-wide level.

Participants: 2806 adult smokers who wished to quit smoking were recruited via the website of the French National Mandatory Health Insurance fund. Of them, 1400 were randomised to the e-TIS app arm and 1406 were randomised to the current practices arm (control).

Intervention: The app involved personalised interactive contacts that included questionnaires, advice, activities, and text messages. All contacts were individually tailored and based on each smoker's progress.

In the control group, recommended practices for quitting smoking were described on a non-interactive website.

Primary and secondary outcomes measures: The primary outcome was 7-day point prevalence abstinence (PPA) at 6 months. The secondary outcomes included continuous abstinence rates at 6 and 12 months, minimum 24-hour point abstinence at 3 months, minimum 30-day point abstinence at 12 months, and number and duration of quit attempts.

Results: There was no difference between the e-TIS and control arms for the primary outcome (12.6% vs. 13.7% for 7-day PPA at 6 months, p = 0.3949, intention-to-treat [ITT] analysis). However, e-TIS participants with high levels of exposure to the app, which was defined by the completion of at least eight activities or questionnaires, showed higher rates of smoking cessation than the control participants (17.6% vs. 12.9% for 7-day PPA at 6 months, p = 0.0169, per-protocol [PP] analysis).

Conclusion: Use of the e-TIS app was not associated with a higher rate of smoking cessation. However, high level of exposure to the e-TIS app may have been more effective than current practices. The latest result must be confirmed.

Trial registration number: NCT02841683

Keywords: Smoking cessation, e-health, internet-based intervention, prevention, mobile phone, effectiveness

Strengths and limitations of the present study

- This was a large, national, pragmatic randomised controlled trial that was conducted under 'real-life' conditions.
- This trial occurred during a time period in which there were a variety of national efforts aimed at tobacco prevention in France.
- Results contribute to improving knowledge about the effectiveness of mobile apps as tobacco control interventions.

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Data sharing statement

No additional data available

Competing interests

ALLF reports a grant and conference honoraria from Pfizer, as well as a conference honorarium from J&J that was outside the scope of the submitted work. All other authors have no competing interests to report.

The English in this document has been checked by at least two professional editors, both native speakers of English.

Authors' contributions

LC and FA managed the scientific coordination of the study, AL performed the statistical analyses, and AA prepared the first draft. Other authors were involved in the study and contributed to the interpretation of the results. All authors reviewed and contributed to the article.

Introduction

Smoking remains a leading risk factor for early death and disability (1). Thus, there is a need to strengthen support for smoking cessation. In this context, mobile phone applications (apps) are increasingly used and have several advantages in terms of their inexpensiveness, scalability to large populations, interactivity, ability to be used anywhere at any time, to be tailored to individual users, to distract smokers from cravings, and to link users with social support (2). Although several apps for smoking cessation are available only a few are theory- or evidence-based (3,4). Nonetheless, these health apps appear to be used more effectively and for longer periods of time when they offer support that extends beyond motivation maintenance and contributions to self-knowledge (5).

In France, a theory-based app for smoking cessation, the e-intervention Tabac Info Service (e-TIS), has been developed by Santé publique France and the Caisse nationale d'assurance maladie (6). This app was designed to provide support to smokers who wish to quit, including those who are not currently involved in a quit attempt, and was based on the effectiveness criteria of online programmes (7) and psychosocial and behavioural change theories (8–12). The e-TIS app provides tailored activities, self-report exercises, tips, social and/or psychological support, reassurance, and motivational text messages that are adapted to the individual characteristics of the user (13). The present study evaluated the effectiveness of the theory-based smoking cessation e-TIS app in a pragmatic randomised controlled trial conducted in France on a population-wide level.

Methods

This manuscript was written in accordance with the CONSORT Statement and the EHEALTH checklist (14).

Study design

The protocol was previously registered (NCT02841683) and published (13). Participants were randomly assigned (1:1) to either the intervention arm (invitation to use the e-TIS app) or the control arm (current practices for smoking cessation described on a non-interactive website from the French National Mandatory Health Insurance [ameli.fr]). The current practices were based on the guidelines of the Haute Autorité de Santé (15). All participants were recruited between February 2017 and April 2018, then followed up over the subsequent 1-year period.

All participants consented to inclusion in the study and an automated randomisation procedure was carried out following the receipt of all inclusion data. A minimisation software package was employed to reduce the risk of unmatched groups and to stratify the participants based on age and sex, using the following parameters: study arm (e-TIS and control, allocated 50/50), sex (male/female), and age (≤ 45 years or > 45 years).

Study population and sample

When visiting their personal account on the French Mandatory National Health Insurance website, users were invited to participate in the present study via a banner. Users who clicked on the banner were presented with an information sheet, which included a section where they could provide informed consent. The consent form contained the inclusion questionnaire, with the following criteria: 1) adult smoker; 2) completion of the online consent form; 3) agreement to participate in the study; 4) possession of a mobile phone using an iOS or Android system; 5) willingness to use the app; and 6) attempt or consideration of an attempt to quit smoking. If the user provided consent to be enrolled in the study, they were sent an email with a confirmation link. When the participants clicked the confirmation link, they were randomised and invited to fill in the entry questionnaire (T0) for the study.

Intervention arm: e-TIS app

Participants assigned to the intervention arm were invited to download the e-TIS app. In accordance with the relapse prevention model (16,17), the e-TIS app is tailored to each individual smoker based on feedback. Furthermore, the support process in the e-TIS is based on the efficacy criteria of online programmes, which include the frequency and intensity of contacts, short messages, interactivity, appeal, personalisation, credibility of content, and sharing functions (7), as well as various theoretical models that are used for withdrawal treatments (8–12,18).

The e-TIS app involves personalised interactive (push) contacts that include questionnaires, activities, and text messages which are available via mobile phone, the website platform, and tablets. In total, the intervention consists of 16 different activities, eight position questionnaires (to adapt the app content to the evolution of one's willingness to quit or attempt to quit), and a set of roughly 170 email or push-app text messages/notifications with distinct purposes. All contacts are tailored to the answers on the eight position questionnaires and an individual's progress through the four modules of the app. Each participant began the process within a module that was adapted to his/her individual stage regarding tobacco status. The content has been described in detail elsewhere (13). The present study evaluated e-TIS version 2.0.

Control arm: Current practices

Participants assigned to the control arm were invited to visit a pre-existing -website page that listed smoking cessation resources that are readily available in France and recommended by the Haute Autorité de Santé (15).

Outcomes and other data

The primary outcome in the present study was point prevalence abstinence (PPA) at the 6-month follow-up assessment. The PPA for smoking is a minimum of 7 days (19). In general, the PPA is considered to be the most appropriate measure for evaluating abstinence in intervention evaluation studies (20).

Because a large number of participants were lost to follow-up during the study, and due to the need to limit the amount of missing data, the original study protocol was modified as follows before the blinding was lifted: 1) for participants with information regarding smoking status at 12 months but not at 6 months, the 12-month smoking status was used to replace the missing data regarding smoking status at 6 months; 2) for participants with information regarding smoking status at 3 months but not at 6 or 12 months, the 3-month smoking status was used to replace the missing data regarding smoking status at 6 months. Additionally, at the 6-month follow-up assessment, participants with missing data were phoned and reminded of the study. This recalculated criterion was used as the primary outcome. Sensitivity analyses were performed with the original criterion (i.e. without imputations for missing data).

Based on previous data and recommendations (2,7,20,21), the secondary outcomes in the present study included continuous abstinence at 6 months, continuous abstinence at 12 months, minimum 24-hour point abstinence at 3 months, minimum 30-day point abstinence at 12 months, and number and duration of quit attempts. To further characterise tobacco consumption, the present study also collected data associated with the dependency and determinants of abstinence, described elsewhere (13).

Data collection

Data were collected via internet-based self-report questionnaires at inclusion (technical variables), study initiation (initial self-reporting questionnaire), and at 3, 6, and 12 months (three follow-up self-report questionnaires). Application usage data were extracted from the

application database and a match with the study data measured whether or not the persons included in both arms used the application.

Statistical analysis

Sample size calculation

The required sample size was calculated based on the hypothesis of a 10% abstinence rate at 6-month follow-up in the control group (22). Given this rate, sample sizes of 1500 participants per group were necessary to show a minimum odds ratio of 1.5 with a power of 90% ($\alpha = 0.05$, bilateral test); thus, a total sample size of 3000 individuals was necessary (23).

Statistical methods

Statistical analyses were performed for the intention-to-treat (ITT), per-protocol (PP), and as-treated (AT) populations. The ITT analysis included all participants in the arms to which they were randomised, regardless of adherence to the prescribed intervention. For the PP and AT analyses, exposure to the application was defined as the completion of at least one activity or questionnaire through the app. For the PP analysis, participants in the intervention arm were defined as those randomised to that arm who completed at least one activity or questionnaire. Participants in the control arm were defined as those randomised to that arm who did not complete any activities or questionnaires through the app. For the AT analysis, participants who completed at least one activity or questionnaire through the app, independent of their allocation arm, were regarded as those exposed to the intervention. Participants who did not complete any activities or questionnaires through the application, independent of their allocation arm, were regarded as non-exposed to the intervention.

For the main analysis, participants lost to follow-up (those who did not answer the questionnaires) were defined as smokers, as previously recommended (7,21,24), whereas the

secondary analysis only considered participants who were not lost to follow-up. Multivariate analyses, adjusted for baseline characteristics, were performed in the PP and AT populations. To compare the effects of the e-TIS app on smoking cessation in terms of low versus high levels of e-TIS use, participants were categorised based on median use in the present study: i.e., the completion of eight activities or questionnaires through the app.

Some subgroup analyses were conducted as defined in the study protocol (13). Other subgroup analyses were added to the initial protocol (before the blinding was lifted): tobacco status at inclusion and plans to have or adopt a child in the following year. Sensitivity analyses were performed using only data from participants with a smoking status at 6 months, without data recovery based on 3-month and/or 12-month smoking status. All statistical analyses were performed in 2019 using SAS 9.4 Software (SAS Institute; Cary, NC, USA).

Ethical considerations

All participants were required to provide informed consent prior to inclusion in the study and were informed that they could refuse and drop out at any time. The study protocol was reviewed by the Ethical and Deontological Institutional Review Board of the Institut National de Veille Sanitaire on 18 April 2016. All recommendations from the committee were integrated into the amended version of the protocol.

Patient and Public Involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination of our research.

Results

Recruitment and baseline characteristics

Figure 1 displays the flow chart of the randomisation and follow-up procedures. A total of 2806 participants with inclusion data were randomised for the present study; of these, 1400 were allocated to the e-TIS arm and 1406 were allocated to the control arm. Based on the recovery of missing data, 518 and 602 participants were followed up at 6 months in the e-TIS and control arms, respectively. **Figure 1** shows contamination between the groups. Specifically, of the 1400 participants in the e-TIS arm, 787 were exposed to the app, whereas 613 participants were considered to not have been exposed to the app. Of the 1406 participants in the control arm, 1127 participants were not exposed to the app, whereas 279 participants were considered to have been exposed to the app. The ITT, PP, and AT populations used to assess the primary outcome at 6 months in each arm are displayed in **Figure 1**.

The baseline characteristics of the participants and their exposure levels to the e-TIS app are presented in **Supplementary Table 1**. Of the total participants, most were women, aged 45 years or younger, and current smokers. There were no significant differences between the groups at baseline.

Primary outcome

There were no differences in PPA at 6 months between the e-TIS and control arms in the ITT, PP, and AT populations **(Table 1)**. When considering only respondents in the total population, 32.9% and 32.4% of participants were quitters in the ITT/AT and PP populations, respectively. When considering non-respondents as smokers, 13.1% and 12.9% of the participants, respectively, were quitters. There were no significant differences in the primary outcome between participants exposed to the e-TIS and participants not exposed to e-TIS in the PP and AT populations (**Table 2**).

Secondary outcomes

There were no significant differences in any of the secondary outcomes between the e-TIS and control arms in the ITT population (**Supplementary Table 2**).

High level of e-TIS use

Table 3 presents the group differences in the primary outcome in the PP and AT populations after considering exposure to the e-TIS. In the PP population when considering non-respondents as smokers, 17.6% of participants in the e-TIS high exposure group were quitters, compared to 12.9% in the control group ($p = 0.0169$). In the AT population when considering non-respondents as smokers, 18.2% of the participants in the e-TIS high exposure group were quitters, compared to 11.8% in the other group ($p < 0.0001$).

Sensitivity analysis

Sensitivity analyses were performed using participants with data at 6 months (no recovery data were used); **Supplementary Figure 1** presents the corresponding diagram flow. These results were similar to those of the main analysis (**Supplementary Table 3**).

Subgroup analyses

Supplementary Figure 2 illustrates the subgroup analyses performed using the ITT population, which considered non-respondents as smokers. There were no differences in the minimum 7-day PPA between the e-TIS and control arms in any of the identified subgroups. Similar results were obtained in the ITT population when only respondents were considered, as well as in the PP and AT populations (both cases: non-respondents were considered as smokers and only considering respondents) with the following exceptions. In the AT population and among smokers at inclusion, quitters were overrepresented among the e-TIS

participants, relative to participants who were not exposed to the e-TIS. Therefore, when considering non-respondents as smokers, 11.2% (n = 80) of the e-TIS participants were quitters, compared to 8.0% (n = 93) of the participants who were not exposed to the e-TIS (p = 0.0193; data not shown). Similar results were obtained when analyses were performed using participants with no recovery data at 6 months in the ITT, PP, and AT populations (both cases; data not shown).

Discussion

The present study evaluated the effectiveness of the theory-based smoking cessation e-TIS app. As expected, the participants were mostly young and had a high level of education (25), which is consistent with the nature of the digital intervention (26). Furthermore, more women agreed to participate. Similar rates of female participants were observed in the trials reviewed by Whittaker et al. (2) that employed similar methods of inclusion (27–29).

The present study also revealed a high rate of smoking cessation among all participants. Notably, the rates observed in this study were higher than those in a previous French trial that evaluated the previous TIS modality, which employed email coaching (32.9% in present study *vs.* 24.7%) (30). When considering non-respondents as smokers, 12.6% and 13.7% of participants in the e-TIS and control arms, respectively, were quitters. Previous studies have reported that 9% of intervention group populations and 5-6% of control group populations are quitters (2). It is important to note that the control arm in the present study may not have been considered a true control arm; importantly, the original e-TIS protocol submitted to the ethical committee planned to compare the e-TIS arm with a control arm (no intervention other than standard practices). However, the committee suggested that the control participants be exposed to best evidence-based practices currently in use (15). Thus, the Quitting page of the French National Mandatory Health Insurance website (Ameli) was suggested to the control

participants, and some of these participants may have used the various smoking cessation resources which are all considered to be effective. For example, at 6 months, 36.4% of participants in the control arm had used nicotine replacement therapies within the previous 3 months.

The present study also revealed a lack of differences between the e-TIS and control arms in the ITT, PP, and AT populations. In a Cochrane systematic review conducted in 2014, Whittaker et al. (2) concluded that mobile phone-based smoking cessation interventions had a beneficial impact on 6-month outcomes (relative risk [RR]: 1.67, 95% confidence interval [CI]: 1.46 to 1.90; I^2 = 59%; 12 studies included). However, most studies included in that review employed short message service text messaging-based interventions, rather than complex apps; notably, more complex apps use text messaging and other forms of contact. Therefore, direct comparisons between these results may be inappropriate.

Similar to the findings of recent studies that investigated the effectiveness of complex apps (31,32), the present results showed that the results in the intervention and control arms did not differ at 6 months. Baskerville et al. (31) compared the effectiveness of an evidence-informed self-help guide with a non-intervention arm, which may explain the absence of differences in both arms, and Garrison et al. (32). evaluated a mindfulness training app. Although there were no group differences in smoking abstinence at 6 months, the intervention app reduced the associations between craving and smoking, compared to the control app. In contrast, BinDhim et al. (33) reported that individuals exposed to a smartphone-based decision aid were significantly more likely to exhibit continuous abstinence at 6 months than those exposed to an information-only app. In that study, the intervention app was required to display information regarding quitting options, whereas the control app was not required to display this information.

Furthermore, Brown et al. (22) found that the StopAdvisor app was more effective than an information-only website for helping participants with a low socioeconomic status stop smoking; it is important to note that this study was designed with sufficient power to separately assess effectiveness within each socioeconomic status subsample. In the present study, there were no differences according to socioeconomic status, based on the reported level of education. Additionally, in the StopAdvisor study, the authors noted that the control website was used less regularly than the StopAdvisor website in terms of logins, page views, and time spent on the website. At the 6-month follow-up assessment in the present study, several of the control participants reported that they had been using other forms of smoking cessation support in the 3 previous months (e.g., use of nicotine replacement therapies and/or consultation with a healthcare professional). This could explain the high smoking cessation rate in the present control group (13.7%) versus that in the StopAdvisor study (10%).

Moreover, the effects of health apps remain controversial because they are influenced by numerous factors related to the app components, characteristics of the users (e.g., motivation, previous attempts to quit, and uniformity), and the environment of the participant (e.g., social support). As a result, some authors have advocated for the use of process evaluations to complement the effectiveness evaluations when assessing this 'black box' (5,34,35).

The present study also found that the numbers of quitters in the PP and AT populations at 6 months were higher among participants exposed to the e-TIS, compared to those not exposed to the app, when e-TIS exposure was defined as the completion of at least eight activities and/or questionnaires (i.e., the median exposure). It is tempting to conclude that the e-TIS was effective if used intensively, which would be consistent with previous results on the relationship between use frequency and efficacy (5,36). However, it is likely that the most motivated participants used the app for a longer time; this motivation, rather than the duration or frequency of use, would have improved the results. This idea is consistent with the findings

of prior studies, in which the most motivated people were those who used the apps more frequently (5,37). In the same way it is possible that it is a feed-back loop between engagement and effectiveness (38). However, in our population, there is no relationship between motivation at inclusion and subsequent use (data not shown), which is an argument for the effectiveness of exposure to the application. That remains to be confirmed.

Strengths and limitations

This study was a randomised controlled trial under pragmatic conditions, which enabled evaluation of the effectiveness of the e-TIS in real-life situations. The primary outcome was point prevalence abstinence (PPA) at 6-month. This duration of follow-up is the one recommended for cessation trials (24). We had a 12-month measure, but decided not to make it the primate outcome because the rate of loss of follow-up at one year was predictably high, especially for an e-intervention. PPA is considered to be the most appropriate measure for evaluating abstinence in intervention evaluation studies (20). In fact, the continuous abstinence, recommended in clinical trials (24) is not relevant in this context because a planned cessation date is not a criterion for inclusion and patients could stop smoking at any time during follow-up. However, we have retained it as a secondary outcome and results remained unchanged with this outcome. Similarly, our imputation procedures to account for missing data did not change the results as shown in the sensitivity analyses.

There was a high rate of attrition, that is is quite common in investigations of mHealth tools (39,40). This rate was also likely due to the pragmatic conditions of the trial, as well as the ease of enrolment in the study.

Furthermore, the present findings may have been influenced by high levels of contamination between the study arms due to the unrestricted availability of the e-TIS from app stores during

the trial. Finally, the dose-response analysis was not possible for control arm for obvious reasons.

Conclusions

In the present study, the smoking cessation rates were high and there were no differences between the arms. However, high level of exposure to the e-TIS app may have been more effective than current practices. Because the present results may be explained by multiple hypotheses, the next step consists of the performance of a process evaluation (41) using behavioural change techniques taxonomy (42,43), in order to better understand the e-TIS mechanisms and conditions involved in its efficacy.

Authors' contributions

LC and FA managed the scientific coordination of the study, AL performed the statistical analyses, and AA prepared the first draft. Other authors were involved in the study and contributed to the interpretation of the results. All authors reviewed and contributed to the article.

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Table 1: Between-group differences in the primary outcome (minimum of 7-day PPA at 6 months) in the ITT, PP, and AT analyses.

	Total n = 2806		e-TIS n = 1400 (49.9%)		Control n = 1406 (50.1%)		
	n	%	n	%	n	%	p*
ITT POPULATION							
Minimum of 7-day PPA at 6 months (n = 1120)[1]							0.4593
Smokers	752	67.1	342	66.0	410	68.1	
Quitters	368	32.9	176	34.0	192	31.9	
Minimum of 7-day PPA at 6 months (n = 2806)[2]							0.3949
Smokers	2438	86.9	1224	87.4	1214	86.3	
Quitters	368	13.1	176	12.6	192	13.7	
PP POPULATION							
	Total n = 1914		e-TIS n = 787 (41.1%)		Control n = 1127 (58.9%)		
	n	%	n	%	n	%	p*
Minimum of 7-day PPA at 6 months (n = 759)[1]							0.2196
Smokers	513	67.6	191	65.0	322	69.2	
Quitters	246	32.4	103	35.0	143	30.8	
Minimum of 7-day PPA at 6 months (n = 1914)[2]							0.7974
Smokers	1668	87.1	684	86.9	984	87.3	
Quitters	246	12.9	103	13.1	143	12.7	
AT POPULATION							
	Total n = 2806		e-TIS n = 1066 (38.0%)		Non-exposure to e-TIS n = 1740 (62.0%)		
	n	%	n	%	n	%	p*
Minimum of 7-day PPA at 6 months (n = 1120)[1]							0.1745
Smokers	752	67.1	279	64.7	473	68.7	
Quitters	368	32.9	152	35.3	216	31.3	
Minimum of 7-day PPA at 6 months (n = 2806)[2]							0.1599
Smokers	2438	86.9	914	85.7	1524	87.6	
Quitters	368	13.1	152	14.3	216	12.4	

[1] Only respondents considered
[2] Non-respondents considered as smokers
* Chi-squared test
e-TIS, e-intervention Tabac Info Service; PPA, point prevalence abstinence

Table 2: Minimum of 7-day PPA in the PP and AT populations (multivariate analysis).

		Minimum 7-day PPA at 6 months		Multivariate regression[1]			
	n	Quitters	%	Odds ratio	CI 95%		*p*-value
					Lower	Upper	
PP POPULATION							
Only considering respondents (n = 743/759[2]) §							0.2140
Control	453	138	30.5	1			
e-TIS exposure	290	102	35.2	1.22	0.89	1.67	
Considering non-respondents as smokers (n = 1831/1914[2]) §§							0.6689
Non-exposure to e-TIS	1080	132	12.2	1			
e-TIS exposure	751	99	13.2	1.06	0.80	1.41	
AT POPULATION							
Only considering respondents (n = 1095/1120[2]) §							0.1882
Non-exposure to e-TIS	671	210	31.3	1			
e-TIS exposure	424	150	35.4	1.19	0.92	1.54	
Considering non-respondents as smokers (n = 2679/2806[2]) §§							0.1449
Non-exposure to e-TIS	1660	202	12.2	1			
e-TIS exposure	1019	146	14.3	1.19	0.94	1.49	

[1] Adjusted for baseline characteristics, with the exception of tobacco status at inclusion. The stepwise variable selection method was used with an input threshold in the model at 0.2 and an output threshold in the model at 0.05. Only factors with a significant association with the 0.2 threshold in the bivariate model were candidates in the multivariate model.

[2] Due to missing data regarding the variables considered in the multivariate model

§ retained variables: expecting a child

§§ retained variables: family situation, level of education, treatment for cardiovascular or respiratory diseases

CI, Confidence interval

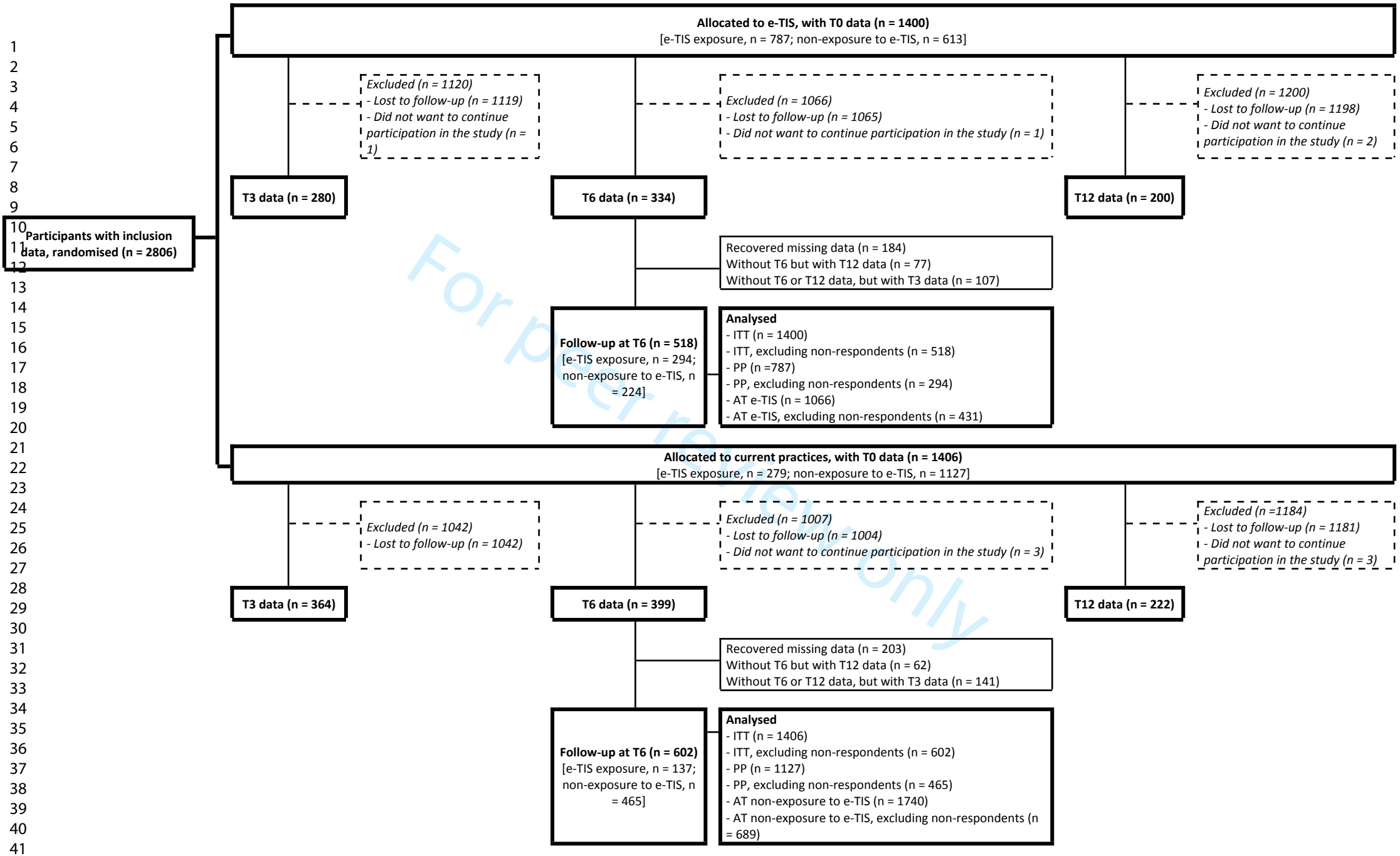
Table 3: Between-group differences in the primary outcome in the PP and AT populations, which considered exposure to be the completion of at least eight activities or questionnaires through the application.

	Total n = 1652		e-TIS exposure[1] n = 409 (24.8%)		Control n = 1243 (75.2%)		
	n	%	n	%	n	%	*p*-value*
PP POPULATION							
Minimum 7-day PPA at 6 months (n = 704)[2]							**0.0139**
Smokers	472	67.0	106	59.6	366	69.6	
Quitters	232	33.0	72	40.4	160	30.4	
Minimum 7-day PPA at 6 months (n = 1652)[2]							**0.0169**
Smokers	1420	86.0	337	82.4	1083	87.1	
Quitters	232	14.0	72	17.6	160	12.9	
AT POPULATION							
	Total n = 2806		e-TIS exposure[1] n = 572 (20.4%)		Non-exposure to e-TIS n = 2234 (79.6%)		
	n	%	n	%	n	%	*p*-value*
Minimum 7-day PPA at 6 months (n = 1120)[2]							**0.0018**
Smokers	752	67.1	150	59.1	602	69.5	
Quitters	368	32.9	104	40.9	264	30.5	
Minimum 7-day PPA at 6 months (n = 2806)3							**< 0.0001**
Smokers	2438	86.9	468	81.8	1970	88.2	
Quitters	368	13.1	104	18.2	264	11.8	

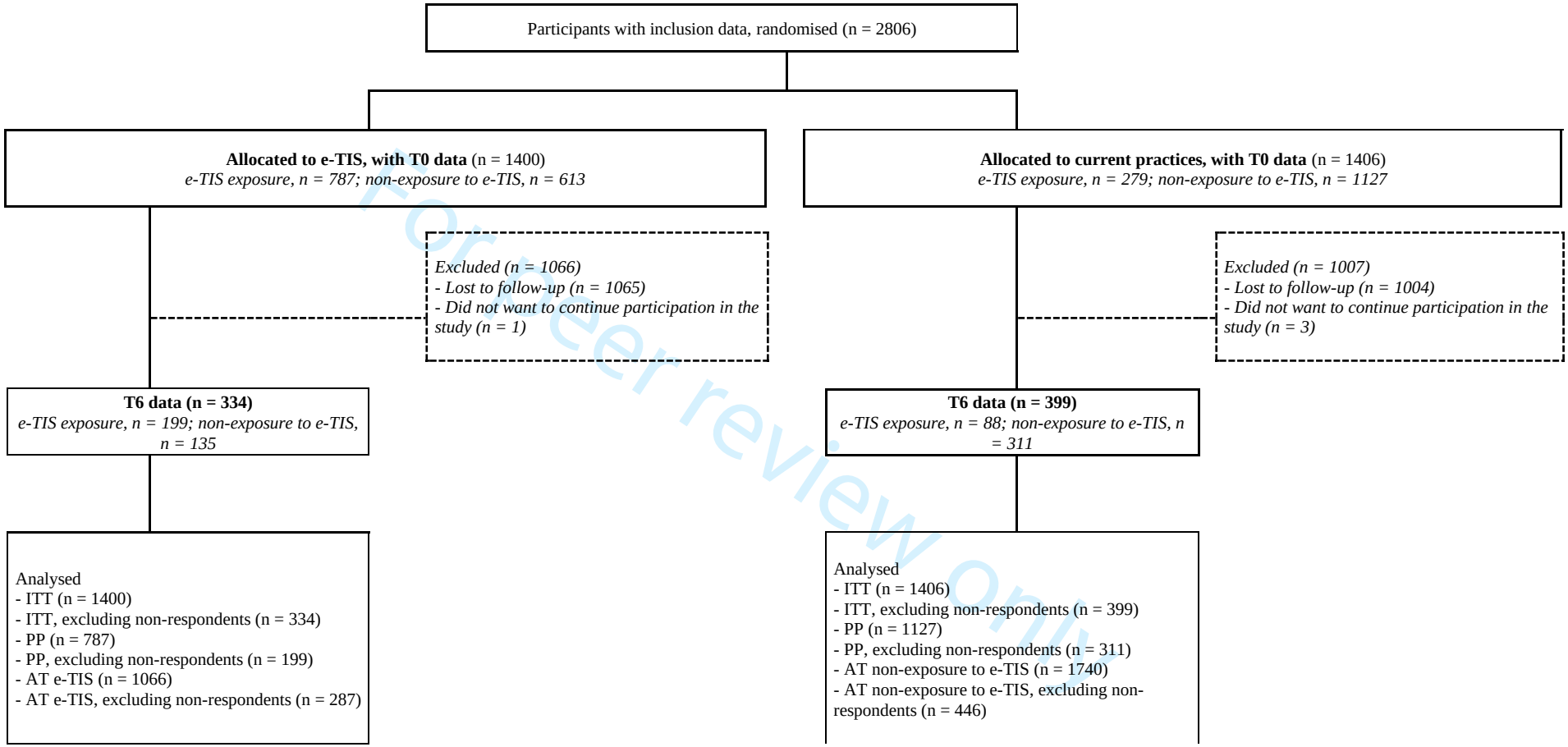
[1] Completed at least eight activities or questionnaires through the application
[2]Only respondents considered
[3] Non-respondents considered as smokers
* Chi-squared test
e-TIS, e-intervention Tabac Info Service; PPA, point prevalence abstinence

Figures legends

Figure 1: Diagram depicting the flow of participants in the study (n = 2806).

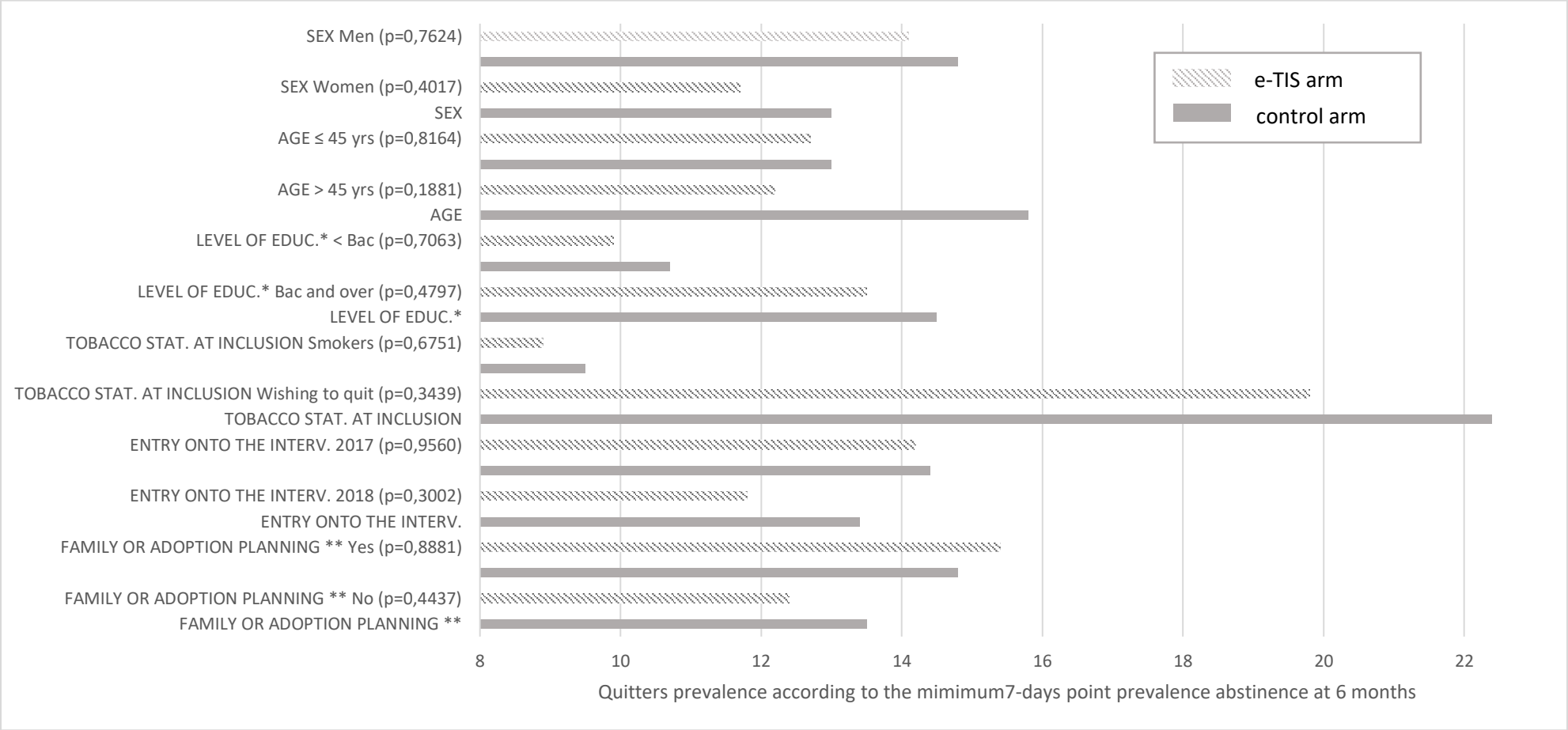


Supplementary Figure 1: Diagram flow of the study with no recovery data at T6.



e-TIS, e-intervention Tabac Info Service; ITT, Intention to Treat; PP, Per Protocol; AT, As Treated

Supplementary Figure 2: Subgroup analysis in ITT population, considering non-respondents as smokers (n=2806)



* n=2786 due to missing data
**n=2771 due to missing data
P-values are derived from Chi-2 tests

Supplementary Table 1: Baseline characteristics of the randomised patients and levels of exposure to the application during the study, according to intervention arm (n = 2806).

	Total n = 2806		e-TIS n = 1400 (49.9%)		Control n = 1406 (50.1%)		
	n	%	n	%	n	%	*p*-value*
BASELINE CHARACTERISTICS							
Sex							0.7308
Male	1033	36.8	511	36.5	522	37.1	
Female	1773	63.2	889	63.5	884	62.9	
Age							0.9418
≤ 45 years	2163	77.1	1080	77.1	1083	77.0	
< 45 years	643	22.9	320	22.9	323	23.0	
Smoking status at inclusion							0.5475
Smokers	1881	67.0	931	66.5	950	67.6	
Wishing to quit	925	33.0	469	33.5	456	32.4	
Living situation							0.9570
Single	828	29.6	414	29.7	414	29.6	
With a partner	1661	59.4	829	59.4	832	59.4	
With parents	150	5.4	71	5.1	79	5.6	
With roommates	72	2.6	38	2.7	34	2.4	
Other	85	3.0	43	3.1	42	3.0	
Missing data	10		5		5		
Living with minors							
Yes	1343	48.3	678	48.8	665	47.7	0.5344
No	1440	51.7	710	51.2	730	52.3	
Missing data	23		12		11		
Current pregnancy in the couple							0.6772
Yes	128	4.6	66	4.8	62	4.5	
No	2645	95.4	1314	95.2	1331	95.5	
Missing data	33		20		13		
Pregnancy/adoption within 1 year							0.1564
Yes	338	12.2	156	11.3	182	13.1	
No	2433	87.8	1223	88.7	1210	86.9	
Missing data	35		21		14		
Level of education							0.5847
Less than baccalaureate degree	700	25.1	355	25.6	345	24.7	
Baccalaureate degree or higher	2086	74.9	1033	74.4	1053	75.3	
Missing data	20		12		8		
Treatment for cardiovascular and/or respiratory diseases							0.0556
Yes	426	15.5	231	16.9	195	14.2	
No	2316	84.5	1139	83.1	1177	85.8	
Missing data	64		30		34		
EXPOSURE TO THE APPLICATION DURING THE STUDY							
e-TIS downloaded							**< 0.0001**
Yes	1139	40.6	843	60.2	296	21.0	
No	1667	59.6	557	39.8	1110	79.0	
e-TIS exposure (i.e., completed at least one activity or questionnaire)							**< 0.0001**
Yes	1066	38.0	787	56.2	279	19.8	
No	1740	62.0	613	43.8	1127	80.2	

* Chi-squared test for qualitative variables
e-TIS, e-intervention Tabac Info Service

Supplementary Table 2: Secondary outcomes in the ITT population, which only considered respondents.

	Total			e-TIS			Control			
	n	%/mean	SD	n	%/mean	SD	n	%/mean	SD*	*p*-value*
Continuous abstinence at 6 months (n = 733)										0.4536
No	441	60.2		196	58.7		245	61.4		
Yes	292	39.8		138	41.3		154	38.6		
Continuous abstinence at 12 months (n = 422)										0.1816
No	198	46.9		87	43.5		111	50.0		
Yes	224	53.1		113	56.5		111	50.0		
Minimum 24-hour point abstinence at 3 months (n = 644)										0.1508
No	420	65.2		174	62.1		246	67.6		
Yes	224	34.8		106	37.9		118	32.4		
Minimum 30-day point abstinence at 12 months (n = 422)										0.2914
No	258	61.1		117	58.5		141	63.5		
Yes	164	38.9		83	41.5		81	36.5		
Number of quit attempts at T3 (n = 644) ***(n miss = 409)***	235	1.7	5.7	112	1.7	6.1	123	1.6	5.4	0.9441
Duration of quit attempts at T3 (n = 644) ***(n miss = 442)***	202	58.5	45.8	95	54.8	44.8	107	61.8	46.6	0.2785
Number of quit attempts at T6 (n = 733) ***(n miss = 447)***	286	1.1	1.0	134	1.0	0.8	152	1.1	1.1	0.5654
Duration of quit attempts at T6 (n = 733) ***(n miss = 516)***	217	72.5	90.5	103	82.1	124.6	114	64.0	38.3	0.1414
Number of quit attempts at T12 (n = 422) ***(n miss = 205)***	217	1.7	6.6	112	1.0	1.2	105	2.4	9.4	0.1327
Duration of quit attempts at T12 (n = 422) ***(n miss = 262)***	160	82.9	79.8	79	87.1	87.4	81	78.9	71.8	0.5205

* Chi-squared test and Wilcoxon test

e-TIS, e-intervention Tabac Info Service; SD, standard deviation

Supplementary Table 3: Between-group differences in the primary outcome (minimum 7-day PPA at 6 months) in the ITT, PP and AT populations without considering recovery data at T6.

	Total n = 2806		e-TIS n = 1400 (49.9%)		Control n = 1406 (50.1%)		
	n	%	n	%	n	%	p*
ITT POPULATION							
Minimum 7-day PPA at 6 months (n = 733)[1]							0.9195
Smokers	477	65.1	218	65.3	259	64.9	
Quitters	256	34.9	116	34.7	140	35.1	
Minimum 7-day PPA at 6 months (n = 2806)[2]							0.1241
Smokers	2550	90.9	1284	91.7	1266	90.0	
Quitters	256	9.1	116	8.3	140	10.0	
PP POPULATION							
	Total n = 1914		e-TIS n = 787 (41.1%)		Control n = 1127 (58.9%)		
	n	%	n	%	n	%	p*
Minimum 7-day PPA at 6 months (n = 510)[1]							0.6570
Smokers	334	65.5	128	64.3	206	66.2	
Quitters	176	34.5	71	35.7	105	33.8	
Minimum 7-day PPA at 6 months (n = 1914)[2]							0.8260
Smokers	1738	90.8	716	91.0	1022	90.7	
Quitters	176	9.2	71	9.0	105	9.3	
AT POPULATION							
	Total n = 2806		e-TIS n = 1066 (38.0%)		Non-exposed to e-TIS n = 1740 (62.0%)		
	n	%	n	%	n	%	p*
Minimum 7-day PPA at 6 months (n = 733)[1]							0.3601
Smokers	477	65.1	181	63.1	296	66.4	
Quitters	256	34.9	106	36.9	150	33.6	
Minimum 7-day PPA at 6 months (n = 2806)[2]							0.2375
Smokers	2550	90.9	960	90.1	1590	91.4	
Quitters	256	9.1	106	9.9	150	8.6	

[1] Only respondents considered
[2] Non-respondents considered as smokers
* Chi-squared test
e-TIS, e-intervention Tabac Info Service; PPA, point prevalence abstinence

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	1
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	2
	2b	Specific objectives or hypotheses	4
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	5
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	NA
Participants	4a	Eligibility criteria for participants	6
	4b	Settings and locations where the data were collected	5
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	6
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	8
	6b	Any changes to trial outcomes after the trial commenced, with reasons	8
Sample size	7a	How sample size was determined	9
	7b	When applicable, explanation of any interim analyses and stopping guidelines	NA
Randomisation:			5
Sequence generation	8a	Method used to generate the random allocation sequence	
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	5
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	5
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	5
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	NA
	11b	If relevant, description of the similarity of interventions	NA
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	9
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	10

Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	Fig 1
	13b	For each group, losses and exclusions after randomisation, together with reasons	Fig 1
Recruitment	14a	Dates defining the periods of recruitment and follow-up	5
	14b	Why the trial ended or was stopped	NA
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Suppl
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	27
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	12
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	27
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	14
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	NA
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	19
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	21
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	15
Other information			2
Registration	23	Registration number and name of trial registry	
Protocol	24	Where the full trial protocol can be accessed, if available	5
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	3

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

BMJ Open

Effectiveness of the e-Tabac Info Service application for smoking cessation: A pragmatic randomised controlled trial

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Keywords:	PUBLIC HEALTH, PREVENTIVE MEDICINE, Clinical trials < THERAPEUTICS

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Effectiveness of the e-Tabac Info Service application for smoking cessation: A pragmatic randomised controlled trial

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Abstract

Objective: To compare the effectiveness of the mobile e-Tabac Info Service (e-TIS) application (app) for helping adult smokers quit smoking with current practices.

Design: Pragmatic randomised controlled trial with a 1-year follow-up (2017-2018).

Setting: France, population-wide level.

Participants: 2806 adult smokers who wished to quit smoking were recruited via the website of the French National Mandatory Health Insurance fund. Of them, 1400 were randomised to the e-TIS app arm and 1406 were randomised to the current practices arm (control).

Intervention: The app involved personalised interactive contacts that included questionnaires, advice, activities, and text messages. All contacts were individually tailored and based on each smoker's progress.

In the control group, recommended practices for quitting smoking were described on a non-interactive website.

Primary and secondary outcomes measures: The primary outcome was 7-day point prevalence abstinence (PPA) at 6 months. The secondary outcomes included continuous abstinence rates at 6 and 12 months, minimum 24-hour point abstinence at 3 months, minimum 30-day point abstinence at 12 months, and number and duration of quit attempts.

Results: There was no difference between the e-TIS and control arms for the primary outcome (12.6% vs. 13.7% for 7-day PPA at 6 months, p = 0.3949, intention-to-treat [ITT] analysis). However, e-TIS participants with high levels of exposure to the app, which was defined by the completion of at least eight activities or questionnaires, showed higher rates of smoking cessation than the control participants (17.6% vs. 12.9% for 7-day PPA at 6 months, p = 0.0169, per-protocol [PP] analysis).

Conclusion: Use of the e-TIS app was not associated with a higher rate of smoking cessation. However, high level of exposure to the e-TIS app may have been more effective than current practices.

Trial registration number: NCT02841683

Keywords: Smoking cessation, e-health, internet-based intervention, prevention, mobile phone, effectiveness

Strengths and limitations of the present study

- This was a large, national, randomised controlled trial
- This was a pragmatic trial that was conducted under 'real-life' conditions
- According to guidelines, the primary outcome was point prevalence abstinence (PPA) at 6-month.
- The main limitation of the study is the high attrition rate.

Findings may have been influenced by contamination between arms due to the unrestricted availability of the e-TIS from app stores during the trial.

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Data sharing statement

No additional data available

Competing interests

ALLF reports a grant and conference honoraria from Pfizer, as well as a conference honorarium from J&J that was outside the scope of the submitted work. All other authors have no competing interests to report.

The English in this document has been checked by at least two professional editors, both native speakers of English.

Authors' contributions

LC and FA managed the scientific coordination of the study. CB coordinated the data management and statistical analysis.AL performed the statistical analyses. . CB, PB, ALLF, AP, PA contributed to the design and to the interpretation of the results. AA, LC, FA wrote the draft. All authors reviewed and contributed to the article and validated its final version.

Introduction

Smoking remains a leading risk factor for early death and disability (1). Thus, there is a need to strengthen support for smoking cessation. In this context, mobile phone applications (apps) are increasingly used and have several advantages in terms of their inexpensiveness, scalability to large populations, interactivity, ability to be used anywhere at any time, to be tailored to individual users, to distract smokers from cravings, and to link users with social support (2). Although several apps for smoking cessation are available only a few are theory- or evidence-based (3,4). Nonetheless, these health apps appear to be used more effectively and for longer periods of time when they offer support that extends beyond motivation maintenance and contributions to self-knowledge (5).

In France, a theory-based app for smoking cessation, the e-intervention Tabac Info Service (e-TIS), has been developed by Santé publique France and the Caisse nationale d'assurance maladie (6). This app was designed to provide support to smokers who wish to quit, including those who are not currently involved in a quit attempt, and was based on the effectiveness criteria of online programmes (7) and psychosocial and behavioural change theories (8–12). The e-TIS app provides tailored activities, self-report exercises, tips, social and/or psychological support, reassurance, and motivational text messages that are adapted to the individual characteristics of the user (13). The present study evaluated the effectiveness of the theory-based smoking cessation e-TIS app in a pragmatic randomised controlled trial conducted in France on a population-wide level.

Methods

This manuscript was written in accordance with the CONSORT Statement and the EHEALTH checklist (14).

Study design

The protocol was previously registered (NCT02841683) and published (13). Participants were randomly assigned (1:1) to either the intervention arm (invitation to use the e-TIS app) or the control arm (current practices for smoking cessation described on a non-interactive website from the French National Mandatory Health Insurance [ameli.fr]). The current practices were based on the guidelines of the Haute Autorité de Santé (15). All participants were recruited between February 2017 and April 2018, then followed up over the subsequent 1-year period.

All participants consented to inclusion in the study and an automated randomisation procedure was carried out following the receipt of all inclusion data. A minimisation software package was employed to reduce the risk of unmatched groups and to stratify the participants based on age and sex, using the following parameters: study arm (e-TIS and control, allocated 50/50), sex (male/female), and age (≤ 45 years or > 45 years).

Study population and sample

When visiting their personal account on the French Mandatory National Health Insurance website, users were invited to participate in the present study via a banner. Users who clicked on the banner were presented with an information sheet, which included a section where they could provide informed consent. The consent form contained the inclusion questionnaire, with the following criteria: 1) adult smoker; 2) completion of the online consent form; 3) agreement to participate in the study; 4) possession of a mobile phone using an iOS or Android system; 5) willingness to use the app; and 6) attempt or consideration of an attempt to quit smoking. If the user provided consent to be enrolled in the study, they were sent an email with a confirmation link. When the participants clicked the confirmation link, they were randomised and invited to fill in the entry questionnaire (T0) for the study.

Intervention arm: e-TIS app

Participants assigned to the intervention arm were invited to download the e-TIS app. In accordance with the relapse prevention model (16,17), the e-TIS app is tailored to each individual smoker based on feedback. Furthermore, the support process in the e-TIS is based on the efficacy criteria of online programmes, which include the frequency and intensity of contacts, short messages, interactivity, appeal, personalisation, credibility of content, and sharing functions (7), as well as various theoretical models that are used for withdrawal treatments (8–12,18).

The e-TIS app involves personalised interactive (push) contacts that include questionnaires, activities, and text messages which are available via mobile phone, the website platform, and tablets. In total, the intervention consists of 16 different activities, eight position questionnaires (to adapt the app content to the evolution of one's willingness to quit or attempt to quit), and a set of roughly 170 email or push-app text messages/notifications with distinct purposes. All contacts are tailored to the answers on the eight position questionnaires and an individual's progress through the four modules of the app. Each participant began the process within a module that was adapted to his/her individual stage regarding tobacco status. The content has been described in detail elsewhere (13). The present study evaluated e-TIS version 2.0.

Control arm: Current practices

Participants assigned to the control arm were invited to visit a pre-existing -website page that listed smoking cessation resources that are readily available in France and recommended by the Haute Autorité de Santé (15).

Outcomes and other data

The primary outcome in the present study was point prevalence abstinence (PPA) at the 6-month follow-up assessment. The PPA for smoking is a minimum of 7 days (19). In general, the PPA is considered to be the most appropriate measure for evaluating abstinence in intervention evaluation studies (20).

Because a large number of participants were lost to follow-up during the study, and due to the need to limit the amount of missing data, the original study protocol was modified as follows before the blinding was lifted: 1) for participants with information regarding smoking status at 12 months but not at 6 months, the 12-month smoking status was used to replace the missing data regarding smoking status at 6 months; 2) for participants with information regarding smoking status at 3 months but not at 6 or 12 months, the 3-month smoking status was used to replace the missing data regarding smoking status at 6 months. Additionally, at the 6-month follow-up assessment, participants with missing data were phoned and reminded of the study. This recalculated criterion was used as the primary outcome. Sensitivity analyses were performed with the original criterion (i.e. without imputations for missing data).

Based on previous data and recommendations (2,7,20,21), the secondary outcomes in the present study included continuous abstinence at 6 months, continuous abstinence at 12 months, minimum 24-hour point abstinence at 3 months, minimum 30-day point abstinence at 12 months, and number and duration of quit attempts. To further characterise tobacco consumption, the present study also collected data associated with the dependency and determinants of abstinence, described elsewhere (13).

Data collection

Data were collected via internet-based self-report questionnaires at inclusion (technical variables), study initiation (initial self-reporting questionnaire), and at 3, 6, and 12 months (three follow-up self-report questionnaires). Application usage data were extracted from the

application database and a match with the study data measured whether or not the persons included in both arms used the application.

Statistical analysis

Sample size calculation

The required sample size was calculated based on the hypothesis of a 10% abstinence rate at 6-month follow-up in the control group (22). Given this rate, sample sizes of 1500 participants per group were necessary to show a minimum odds ratio of 1.5 with a power of 90% ($\alpha = 0.05$, bilateral test); thus, a total sample size of 3000 individuals was necessary (23).

Statistical methods

Statistical analyses were performed for the intention-to-treat (ITT), per-protocol (PP), and as-treated (AT) populations. The ITT analysis included all participants in the arms to which they were randomised, regardless of adherence to the prescribed intervention. For the PP and AT analyses, exposure to the application was defined as the completion of at least one activity or questionnaire through the app. For the PP analysis, participants in the intervention arm were defined as those randomised to that arm who completed at least one activity or questionnaire. Participants in the control arm were defined as those randomised to that arm who did not complete any activities or questionnaires through the app. For the AT analysis, participants who completed at least one activity or questionnaire through the app, independent of their allocation arm, were regarded as those exposed to the intervention. Participants who did not complete any activities or questionnaires through the application, independent of their allocation arm, were regarded as non-exposed to the intervention.

For the main analysis, participants lost to follow-up (those who did not answer the questionnaires) were defined as smokers, as previously recommended (7,21,24), whereas the

secondary analysis only considered participants who were not lost to follow-up. Multivariate analyses, adjusted for baseline characteristics, were performed in the PP and AT populations. To compare the effects of the e-TIS app on smoking cessation in terms of low versus high levels of e-TIS use, participants were categorised based on median use in the present study: i.e., the completion of eight activities or questionnaires through the app.

Some subgroup analyses were conducted as defined in the study protocol (13). Other subgroup analyses were added to the initial protocol (before the blinding was lifted): tobacco status at inclusion and plans to have or adopt a child in the following year. Sensitivity analyses were performed using only data from participants with a smoking status at 6 months, without data recovery based on 3-month and/or 12-month smoking status. All statistical analyses were performed in 2019 using SAS 9.4 Software (SAS Institute; Cary, NC, USA).

Ethical considerations

All participants were required to provide informed consent prior to inclusion in the study and were informed that they could refuse and drop out at any time. The study protocol was reviewed by the Ethical and Deontological Institutional Review Board of the Institut National de Veille Sanitaire on 18 April 2016. All recommendations from the committee were integrated into the amended version of the protocol.

Patient and Public Involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination of our research.

Results

Recruitment and baseline characteristics

Figure 1 displays the flow chart of the randomisation and follow-up procedures. A total of 2806 participants with inclusion data were randomised for the present study; of these, 1400 were allocated to the e-TIS arm and 1406 were allocated to the control arm. Based on the recovery of missing data, 518 and 602 participants were followed up at 6 months in the e-TIS and control arms, respectively. **Figure 1** shows contamination between the groups. Specifically, of the 1400 participants in the e-TIS arm, 787 were exposed to the app, whereas 613 participants were considered to not have been exposed to the app;, the 3-month and 6-month usage rates for the app were 10.7% and 5.7% respectively. Of the 1406 participants in the control arm, 1127 participants were not exposed to the app, whereas 279 participants were considered to have been exposed to the app. The ITT, PP, and AT populations used to assess the primary outcome at 6 months in each arm are displayed in **Figure 1**.

The baseline characteristics of the participants and their exposure levels to the e-TIS app are presented in **Supplementary Table 1**. Of the total participants, most were women, aged 45 years or younger, and current smokers. There were no significant differences between the groups at baseline.

Primary outcome

There were no differences in PPA at 6 months between the e-TIS and control arms in the ITT, PP, and AT populations **(Table 1)**. When considering only respondents in the total population, 32.9% and 32.4% of participants were quitters in the ITT/AT and PP populations, respectively. When considering non-respondents as smokers, 13.1% and 12.9% of the participants, respectively, were quitters. There were no significant differences in the primary outcome between participants exposed to the e-TIS and participants not exposed to e-TIS in the PP and AT populations (**Table 2**).

Secondary outcomes

There were no significant differences in any of the secondary outcomes between the e-TIS and control arms in the ITT population (**Supplementary Table 2**).

High level of e-TIS use

Table 3 presents the group differences in the primary outcome in the PP and AT populations after considering exposure to the e-TIS. In the PP population when considering non-respondents as smokers, 17.6% of participants in the e-TIS high exposure group were quitters, compared to 12.9% in the control group ($p = 0.0169$). In the AT population when considering non-respondents as smokers, 18.2% of the participants in the e-TIS high exposure group were quitters, compared to 11.8% in the other group ($p < 0.0001$).

Sensitivity analysis

Sensitivity analyses were performed using participants with data at 6 months (no recovery data were used); **Supplementary Figure 1** presents the corresponding diagram flow. These results were similar to those of the main analysis (**Supplementary Table 3**).

Subgroup analyses

Supplementary Figure 2 illustrates the subgroup analyses performed using the ITT population, which considered non-respondents as smokers. There were no differences in the minimum 7-day PPA between the e-TIS and control arms in any of the identified subgroups.

Similar results were obtained in the ITT population when only respondents were considered, as well as in the PP and AT populations (both cases: non-respondents were considered as smokers and only considering respondents) with the following exceptions (supplementary tables 4a-r). In the AT population and among smokers at inclusion, quitters were

overrepresented among the e-TIS participants, relative to participants who were not exposed to the e-TIS. Therefore, when considering non-respondents as smokers, 11.2% (n = 80) of the e-TIS participants were quitters, compared to 8.0% (n = 93) of the participants who were not exposed to the e-TIS (p = 0.0193). Similar results were obtained when analyses were performed using participants with no recovery data at 6 months in the ITT, PP, and AT populations.

Discussion

The present study evaluated the effectiveness of the theory-based smoking cessation e-TIS app. This study was a randomised controlled trial under pragmatic conditions, which enabled evaluation of the effectiveness of e-TIS in real-life situations. The pragmatic situation is particularly relevant for behaviour change interventions (25). Indeed, for these interventions, determinants of choice to participate in the trial may also be determinants of outcome (e.g., motivation). This type of intervention may thus have more favourable results within a trial than in a real-life situation (13). It is to limit this major bias that we wanted the inclusion procedure to be the lightest possible in order to recruit smokers who were not selected because of their high motivation to participate in a trial. The major disadvantage of this methodological choice is the high attrition rate we observed. Although a high rate of attrition is quite common in investigations of mHealth tools (26,27), ours is particularly high.

Moreover, the present findings may have been influenced by high levels of contamination between the study arms due to the unrestricted availability of the e-TIS from app stores during the trial. Our results according to the three types of analysis (i.e. ITT, PP, AT) are consistent, which is in favour of the robustness of our results in this regard.

The primary outcome was point prevalence abstinence (PPA) at 6-month. This is the recommended duration. It is justified by the high rate of short-term relapse during smoking

cessation. (24). PPA is considered to be the most appropriate measure for evaluating abstinence in intervention evaluation studies (20). The continuous abstinence, recommended in clinical trials (24) is not relevant in this context because a planned cessation date was not a criterion for inclusion and patients could stop smoking at any time during follow-up. However, we have retained it as a secondary outcome and results remained unchanged with this outcome. Similarly, our imputation procedures to account for missing data did not change results as shown in sensitivity analyses.

Because the trial is not conclusive given its limitations and because the present results may be explained by multiple hypotheses, the next step of our study will consist of the performance of a process evaluation (28) using behavioural change techniques taxonomy (29,30), in order to better understand the e-TIS mechanisms and conditions of efficacy. These conditions relate to the participants; the different components of e-TIS used by the participants; the psychological, social and environmental factors possibly affecting the participants during the study (13).

As expected, the participants were mostly young and had a high level of education (31), which is consistent with the nature of the digital intervention (32). Furthermore, more women agreed to participate. Similar rates of female participants were observed in the trials reviewed by Whittaker et al. (2) that employed similar methods of inclusion (33–35).

The present study also revealed a high rate of smoking cessation among all participants. Notably, the rates observed in this study were higher than those in a previous French trial that evaluated the previous TIS modality, which employed email coaching (32.9% in present study *vs.* 24.7%) (36). When considering non-respondents as smokers, 12.6% and 13.7% of participants in the e-TIS and control arms, respectively, were quitters. Previous studies have reported that 9% of intervention group populations and 5-6% of control group populations are quitters (2). It is important to note that the control arm in the present study may not have been

considered a true control arm; importantly, the original e-TIS protocol submitted to the ethical committee planned to compare the e-TIS arm with a control arm (no intervention other than standard practices). However, the committee suggested that the control participants be exposed to best evidence-based practices currently in use (15). Thus, the Quitting page of the French National Mandatory Health Insurance website (Ameli) was suggested to the control participants, and some of these participants may have used the various smoking cessation resources which are all considered to be effective. For example, at 6 months, 36.4% of participants in the control arm had used nicotine replacement therapies within the previous 3 months.

The present study also revealed a lack of differences between the e-TIS and control arms in the ITT, PP, and AT populations. In a Cochrane systematic review conducted in 2014, Whittaker et al. (2) concluded that mobile phone-based smoking cessation interventions had a beneficial impact on 6-month outcomes (relative risk [RR]: 1.67, 95% confidence interval [CI]: 1.46 to 1.90; I^2 = 59%; 12 studies included). However, most studies included in that review employed short message service text messaging-based interventions, rather than complex apps; notably, more complex apps use text messaging and other forms of contact. Therefore, direct comparisons between these results may be inappropriate.

Similar to the findings of recent studies that investigated the effectiveness of complex apps (37,38), the present results showed that the results in the intervention and control arms did not differ at 6 months. Baskerville et al. (37) compared the effectiveness of an evidence-informed self-help guide with a non-intervention arm, which may explain the absence of differences in both arms, and Garrison et al. (38). evaluated a mindfulness training app. Although there were no group differences in smoking abstinence at 6 months, the intervention app reduced the associations between craving and smoking, compared to the control app. In contrast, BinDhim et al. (39) reported that individuals exposed to a smartphone-based decision aid were

significantly more likely to exhibit continuous abstinence at 6 months than those exposed to an information-only app. In that study, the intervention app was required to display information regarding quitting options, whereas the control app was not required to display this information.

Furthermore, Brown et al. (22) found that the StopAdvisor app was more effective than an information-only website for helping participants with a low socioeconomic status stop smoking; it is important to note that this study was designed with sufficient power to separately assess effectiveness within each socioeconomic status subsample. In the present study, there were no differences according to socioeconomic status, based on the reported level of education. Additionally, in the StopAdvisor study, the authors noted that the control website was used less regularly than the StopAdvisor website in terms of logins, page views, and time spent on the website. At the 6-month follow-up assessment in the present study, several of the control participants reported that they had been using other forms of smoking cessation support in the 3 previous months (e.g., use of nicotine replacement therapies and/or consultation with a healthcare professional). This could explain the high smoking cessation rate in the present control group (13.7%) versus that in the StopAdvisor study (10%).

Moreover, the effects of health apps remain controversial because they are influenced by numerous factors related to the app components, characteristics of the users (e.g., motivation, previous attempts to quit, and uniformity), and the environment of the participant (e.g., social support). As a result, some authors have advocated for the use of process evaluations to complement the effectiveness evaluations when assessing this 'black box' (5,40,41).

The present study also found that the numbers of quitters in the PP and AT populations at 6 months were higher among participants exposed to the e-TIS, compared to those not exposed to the app, when e-TIS exposure was defined as the completion of at least eight activities and/or questionnaires (i.e., the median exposure). It is tempting to conclude that the e-TIS

was effective if used intensively, which would be consistent with previous results on the relationship between use frequency and efficacy (5,42). However, it is likely that the most motivated participants used the app for a longer time; this motivation, rather than the duration or frequency of use, would have improved the results. This idea is consistent with the findings of prior studies, in which the most motivated people were those who used the apps more frequently (5,43). In the same way it is possible that it is a feed-back loop between engagement and effectiveness (44). However, in our population, there is no relationship between motivation at inclusion and subsequent use (data not shown), which is an argument for the effectiveness of exposure to the application. That remains to be confirmed.

Conclusions

In the present study, use of the e-TIS app was not associated with a higher rate of smoking cessation. However, high level of exposure to the e-TIS app may have been more effective than current practices.

Authors' contributions

LC and FA managed the scientific coordination of the study, AL performed the statistical analyses, and AA prepared the first draft. Other authors were involved in the study and contributed to the interpretation of the results. All authors reviewed and contributed to the article.

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Table 1: Between-group differences in the primary outcome (minimum of 7-day PPA at 6 months) in the ITT, PP, and AT analyses.

	Total n = 2806		e-TIS n = 1400 (49.9%)		Control n = 1406 (50.1%)		
	n	%	n	%	n	%	p*
ITT POPULATION							
Minimum of 7-day PPA at 6 months (n = 1120)[1]							0.4593
Smokers	752	67.1	342	66.0	410	68.1	
Quitters	368	32.9	176	34.0	192	31.9	
Minimum of 7-day PPA at 6 months (n = 2806)[2]							0.3949
Smokers	2438	86.9	1224	87.4	1214	86.3	
Quitters	368	13.1	176	12.6	192	13.7	
PP POPULATION							
	Total n = 1914		e-TIS n = 787 (41.1%)		Control n = 1127 (58.9%)		
	n	%	n	%	n	%	p*
Minimum of 7-day PPA at 6 months (n = 759)[1]							0.2196
Smokers	513	67.6	191	65.0	322	69.2	
Quitters	246	32.4	103	35.0	143	30.8	
Minimum of 7-day PPA at 6 months (n = 1914)[2]							0.7974
Smokers	1668	87.1	684	86.9	984	87.3	
Quitters	246	12.9	103	13.1	143	12.7	
AT POPULATION							
	Total n = 2806		e-TIS n = 1066 (38.0%)		Non-exposure to e-TIS n = 1740 (62.0%)		
	n	%	n	%	n	%	p*
Minimum of 7-day PPA at 6 months (n = 1120)[1]							0.1745
Smokers	752	67.1	279	64.7	473	68.7	
Quitters	368	32.9	152	35.3	216	31.3	
Minimum of 7-day PPA at 6 months (n = 2806)[2]							0.1599
Smokers	2438	86.9	914	85.7	1524	87.6	
Quitters	368	13.1	152	14.3	216	12.4	

[1] Only respondents considered
[2] Non-respondents considered as smokers
* Chi-squared test
e-TIS, e-intervention Tabac Info Service; PPA, point prevalence abstinence

Table 2: Minimum of 7-day PPA in the PP and AT populations (multivariate analysis).

		Minimum 7-day PPA at 6 months		Multivariate regression[1]			
	n	Quitters	%	Odds ratio	CI 95%		*p*-value
					Lower	Upper	
PP POPULATION							
Only considering respondents (n = 743/759[2]) §							0.2140
Control	453	138	30.5	1			
e-TIS exposure	290	102	35.2	1.22	0.89 - 1.67		
Considering non-respondents as smokers (n = 1831/1914[2]) §§							0.6689
Non-exposure to e-TIS	1080	132	12.2	1			
e-TIS exposure	751	99	13.2	1.06	0.80 - 1.41		
AT POPULATION							
Only considering respondents (n = 1095/1120[2]) §							0.1882
Non-exposure to e-TIS	671	210	31.3	1			
e-TIS exposure	424	150	35.4	1.19	0.92 - 1.54		
Considering non-respondents as smokers (n = 2679/2806[2]) §§							0.1449
Non-exposure to e-TIS	1660	202	12.2	1			
e-TIS exposure	1019	146	14.3	1.19	0.94 - 1.49		

[1] Adjusted for baseline characteristics, with the exception of tobacco status at inclusion. The stepwise variable selection method was used with an input threshold in the model at 0.2 and an output threshold in the model at 0.05. Only factors with a significant association with the 0.2 threshold in the bivariate model were candidates in the multivariate model.

[2] Due to missing data regarding the variables considered in the multivariate model

§ retained variables: expecting a child

§§ retained variables: family situation, level of education, treatment for cardiovascular or respiratory diseases

CI, Confidence interval

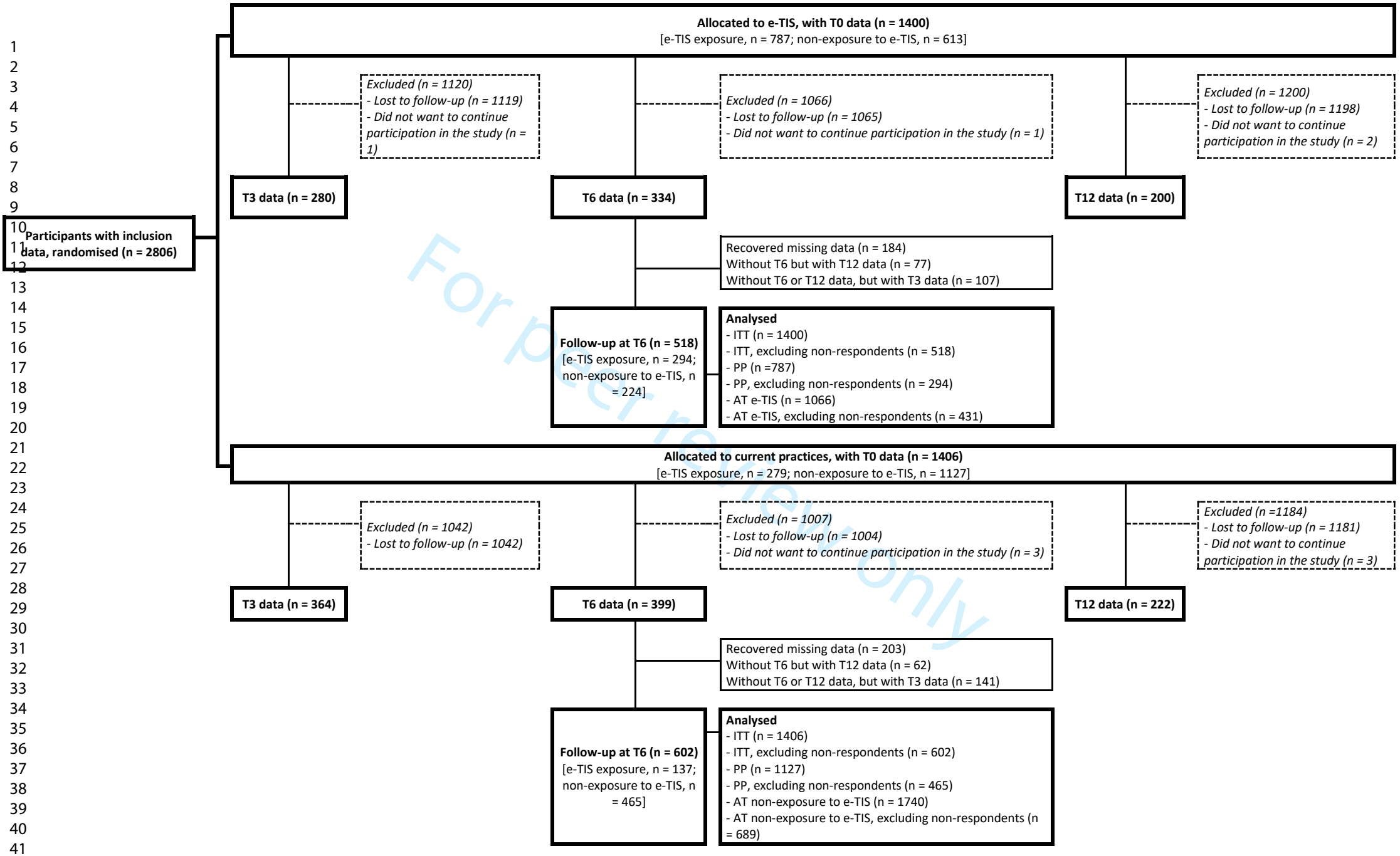
Table 3: Between-group differences in the primary outcome in the PP and AT populations, which considered exposure to be the completion of at least eight activities or questionnaires through the application.

	Total n = 1652		e-TIS exposure[1] n = 409 (24.8%)		Control n = 1243 (75.2%)		
PP POPULATION	n	%	n	%	n	%	*p*-value*
Minimum 7-day PPA at 6 months (n = 704)[2]							**0.0139**
Smokers	472	67.0	106	59.6	366	69.6	
Quitters	232	33.0	72	40.4	160	30.4	
Minimum 7-day PPA at 6 months (n = 1652)[2]							**0.0169**
Smokers	1420	86.0	337	82.4	1083	87.1	
Quitters	232	14.0	72	17.6	160	12.9	
AT POPULATION	Total n = 2806		e-TIS exposure[1] n = 572 (20.4%)		Non-exposure to e-TIS n = 2234 (79.6%)		
	n	%	n	%	n	%	*p*-value*
Minimum 7-day PPA at 6 months (n = 1120)[2]							**0.0018**
Smokers	752	67.1	150	59.1	602	69.5	
Quitters	368	32.9	104	40.9	264	30.5	
Minimum 7-day PPA at 6 months (n = 2806)3							**< 0.0001**
Smokers	2438	86.9	468	81.8	1970	88.2	
Quitters	368	13.1	104	18.2	264	11.8	

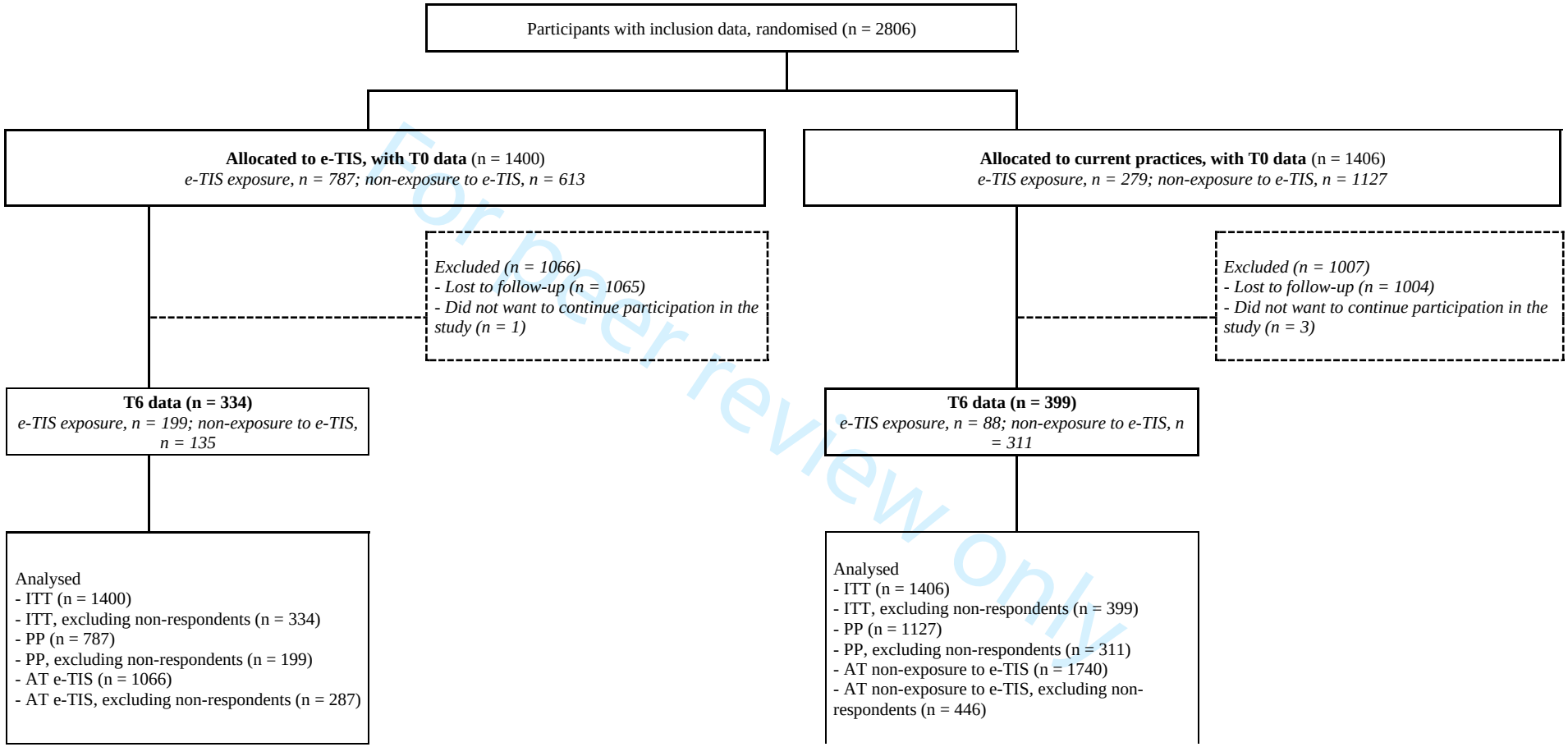
[1] Completed at least eight activities or questionnaires through the application
[2]Only respondents considered
[3] Non-respondents considered as smokers
* Chi-squared test
e-TIS, e-intervention Tabac Info Service; PPA, point prevalence abstinence

Figures legends

Figure 1: Diagram depicting the flow of participants in the study (n = 2806).

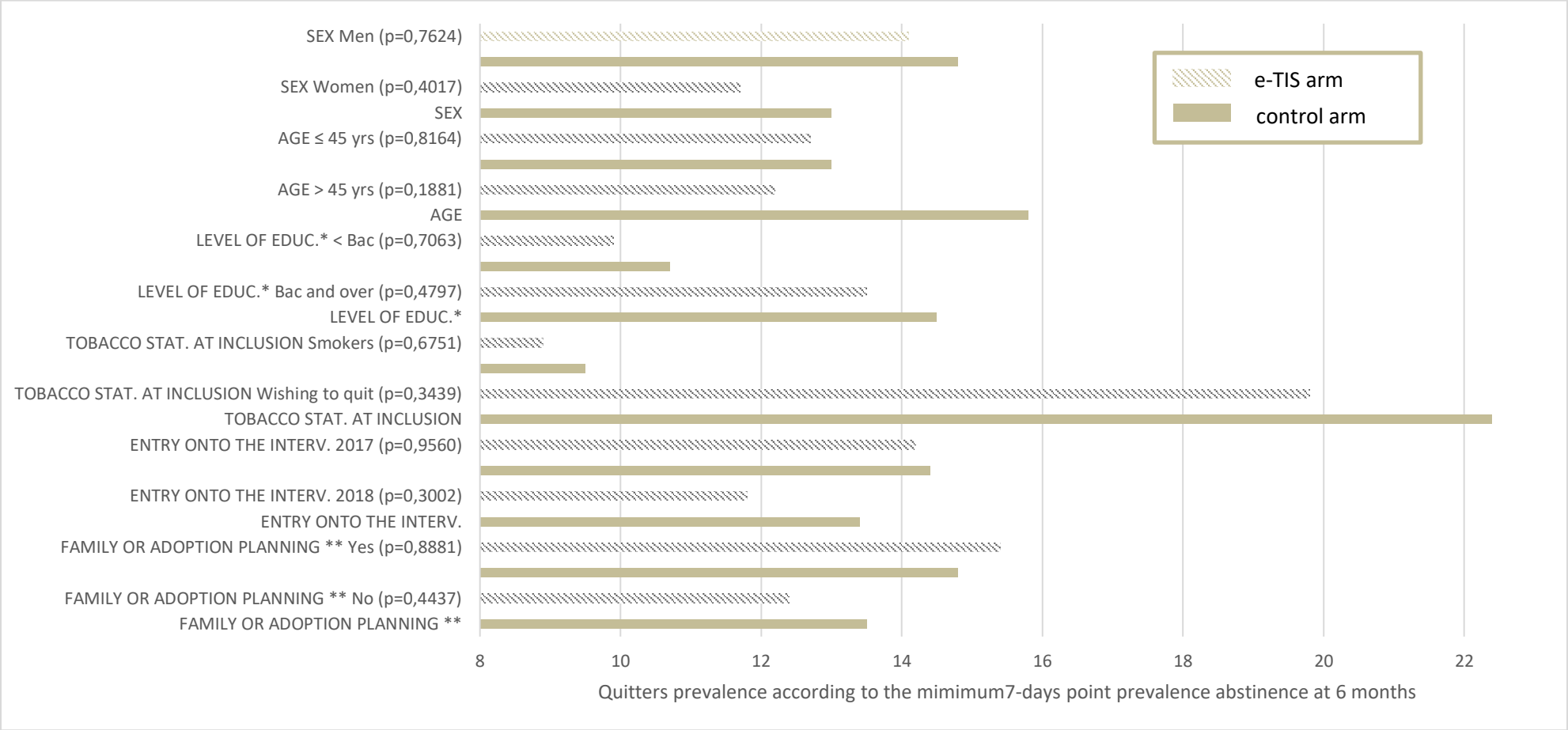


Supplementary Figure 1: Diagram flow of the study with no recovery data at T6.



e-TIS, e-intervention Tabac Info Service; ITT, Intention to Treat; PP, Per Protocol; AT, As Treated

Supplementary Figure 2: Subgroup analysis in ITT population, considering non-respondents as smokers (n=2806)



* n=2786 due to missing data
**n=2771 due to missing data
P-values are derived from Chi-2 tests

Supplementary Table 1: Baseline characteristics of the randomised patients and levels of exposure to the application during the study, according to intervention arm (n = 2806).

	Total n = 2806		e-TIS n = 1400 (49.9%)		Control n = 1406 (50.1%)		
	n	%	n	%	n	%	*p*-value*
BASELINE CHARACTERISTICS							
Sex							0.7308
Male	1033	36.8	511	36.5	522	37.1	
Female	1773	63.2	889	63.5	884	62.9	
Age							0.9418
≤ 45 years	2163	77.1	1080	77.1	1083	77.0	
< 45 years	643	22.9	320	22.9	323	23.0	
Smoking status at inclusion							0.5475
Smokers	1881	67.0	931	66.5	950	67.6	
Wishing to quit	925	33.0	469	33.5	456	32.4	
Living situation							0.9570
Single	828	29.6	414	29.7	414	29.6	
With a partner	1661	59.4	829	59.4	832	59.4	
With parents	150	5.4	71	5.1	79	5.6	
With roommates	72	2.6	38	2.7	34	2.4	
Other	85	3.0	43	3.1	42	3.0	
Missing data	10		5		5		
Living with minors							
Yes	1343	48.3	678	48.8	665	47.7	0.5344
No	1440	51.7	710	51.2	730	52.3	
Missing data	23		12		11		
Current pregnancy in the couple							0.6772
Yes	128	4.6	66	4.8	62	4.5	
No	2645	95.4	1314	95.2	1331	95.5	
Missing data	33		20		13		
Pregnancy/adoption within 1 year							0.1564
Yes	338	12.2	156	11.3	182	13.1	
No	2433	87.8	1223	88.7	1210	86.9	
Missing data	35		21		14		
Level of education							0.5847
Less than baccalaureate degree	700	25.1	355	25.6	345	24.7	
Baccalaureate degree or higher	2086	74.9	1033	74.4	1053	75.3	
Missing data	20		12		8		
Treatment for cardiovascular and/or respiratory diseases							0.0556
Yes	426	15.5	231	16.9	195	14.2	
No	2316	84.5	1139	83.1	1177	85.8	
Missing data	64		30		34		
EXPOSURE TO THE APPLICATION DURING THE STUDY							
e-TIS downloaded							**< 0.0001**
Yes	1139	40.6	843	60.2	296	21.0	
No	1667	59.6	557	39.8	1110	79.0	
e-TIS exposure (i.e., completed at least one activity or questionnaire)							**< 0.0001**
Yes	1066	38.0	787	56.2	279	19.8	
No	1740	62.0	613	43.8	1127	80.2	

* Chi-squared test for qualitative variables
e-TIS, e-intervention Tabac Info Service

Supplementary Table 2: Secondary outcomes in the ITT population, which only considered respondents.

	Total			e-TIS			Control			
	n	%/mean	SD	n	%/mean	SD	n	%/mean	SD*	*p*-value*
Continuous abstinence at 6 months (n = 733)										0.4536
No	441	60.2		196	58.7		245	61.4		
Yes	292	39.8		138	41.3		154	38.6		
Continuous abstinence at 12 months (n = 422)										0.1816
No	198	46.9		87	43.5		111	50.0		
Yes	224	53.1		113	56.5		111	50.0		
Minimum 24-hour point abstinence at 3 months (n = 644)										0.1508
No	420	65.2		174	62.1		246	67.6		
Yes	224	34.8		106	37.9		118	32.4		
Minimum 30-day point abstinence at 12 months (n = 422)										0.2914
No	258	61.1		117	58.5		141	63.5		
Yes	164	38.9		83	41.5		81	36.5		
Number of quit attempts at T3 (n = 644) ***(n miss = 409)***	235	1.7	5.7	112	1.7	6.1	123	1.6	5.4	0.9441
Duration of quit attempts at T3 (n = 644) ***(n miss = 442)***	202	58.5	45.8	95	54.8	44.8	107	61.8	46.6	0.2785
Number of quit attempts at T6 (n = 733) ***(n miss = 447)***	286	1.1	1.0	134	1.0	0.8	152	1.1	1.1	0.5654
Duration of quit attempts at T6 (n = 733) ***(n miss = 516)***	217	72.5	90.5	103	82.1	124.6	114	64.0	38.3	0.1414
Number of quit attempts at T12 (n = 422) ***(n miss = 205)***	217	1.7	6.6	112	1.0	1.2	105	2.4	9.4	0.1327
Duration of quit attempts at T12 (n = 422) ***(n miss = 262)***	160	82.9	79.8	79	87.1	87.4	81	78.9	71.8	0.5205

* Chi-squared test and Wilcoxon test

e-TIS, e-intervention Tabac Info Service; SD, standard deviation

Supplementary Table 3: Between-group differences in the primary outcome (minimum 7-day PPA at 6 months) in the ITT, PP and AT populations without considering recovery data at T6.

	Total n = 2806		e-TIS n = 1400 (49.9%)		Control n = 1406 (50.1%)		
ITT POPULATION	n	%	n	%	n	%	p*
Minimum 7-day PPA at 6 months (n = 733)[1]							0.9195
Smokers	477	65.1	218	65.3	259	64.9	
Quitters	256	34.9	116	34.7	140	35.1	
Minimum 7-day PPA at 6 months (n = 2806)[2]							0.1241
Smokers	2550	90.9	1284	91.7	1266	90.0	
Quitters	256	9.1	116	8.3	140	10.0	
PP POPULATION	Total n = 1914		e-TIS n = 787 (41.1%)		Control n = 1127 (58.9%)		
	n	%	n	%	n	%	p*
Minimum 7-day PPA at 6 months (n = 510)[1]							0.6570
Smokers	334	65.5	128	64.3	206	66.2	
Quitters	176	34.5	71	35.7	105	33.8	
Minimum 7-day PPA at 6 months (n = 1914)[2]							0.8260
Smokers	1738	90.8	716	91.0	1022	90.7	
Quitters	176	9.2	71	9.0	105	9.3	
AT POPULATION	Total n = 2806		e-TIS n = 1066 (38.0%)		Non-exposed to e-TIS n = 1740 (62.0%)		
	n	%	n	%	n	%	p*
Minimum 7-day PPA at 6 months (n = 733)[1]							0.3601
Smokers	477	65.1	181	63.1	296	66.4	
Quitters	256	34.9	106	36.9	150	33.6	
Minimum 7-day PPA at 6 months (n = 2806)[2]							0.2375
Smokers	2550	90.9	960	90.1	1590	91.4	
Quitters	256	9.1	106	9.9	150	8.6	

[1] Only respondents considered
[2] Non-respondents considered as smokers
* Chi-squared test
e-TIS, e-intervention Tabac Info Service; PPA, point prevalence abstinence

Supplementary Table 4a. ITT analyses / age

	Total N= 2163		Yes N=1080 (49,9%)		No N=1083 (50,1%)		
	N	%	N	%	N	%	p*
Age ≤ 45 years							
Minimum 7-day PPA at 6 months							0,6422
Smokers	349	64,6	159	63,6	190	65,5	
Quitters	191	35,4	91	36,4	100	34,5	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,0988
Smokers	555	66,6	240	63,7	315	69,1	
Quitters	278	33,4	137	36,3	141	30,9	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,5080
Smokers	1972	91,2	989	91,6	983	90,8	
Quitters	191	8,8	91	8,4	100	9,2	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,8164
Smokers	1885	87,1	943	87,3	942	87,0	
Quitters	278	12,9	137	12,7	141	13,0	
Age > 45 years							
	Total N= 643		Yes N=320 (49,8%)		No N=323 (50,2%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,3121
Smokers	128	66,3	59	70,2	69	63,3	
Quitters	65	33,7	25	29,8	40	36,7	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,1844
Smokers	197	68,6	102	72,3	95	65,1	
Quitters	90	31,4	39	27,7	51	34,9	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,0545
Smokers	578	89,9	295	92,2	283	87,6	
Quitters	65	10,1	25	7,8	40	12,4	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,1881
Smokers	553	86,0	281	87,8	272	84,2	
Quitters	90	14,0	39	12,2	51	15,8	

* Chi-square test

Supplementary Table 4b. PP analyses / Age

	Total N= 1502		Yes N=639 (42,5%)		No N=863 (57,5%)		
	N	%	N	%	N	%	p*
Age ≤ 45 years							
Minimum 7-day PPA at 6 months							0,5520
Smokers	254	65,5	102	63,8	152	66,7	
Quitters	134	34,5	58	36,3	76	33,3	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,0673
Smokers	391	67,3	144	62,9	247	70,2	
Quitters	190	32,7	85	37,1	105	29,8	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,8559
Smokers	1368	91,1	581	90,9	787	91,2	
Quitters	134	8,9	58	9,1	76	8,8	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,5129
Smokers	1312	87,4	554	86,7	758	87,8	
Quitters	190	12,6	85	13,3	105	12,2	
Age > 45 years							
	Total N= 412		Yes N=148 (35,9%)		No N=264 (64,1%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,8617
Smokers	80	65,6	26	66,7	54	65,1	
Quitters	42	34,4	13	33,3	29	34,9	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,4116
Smokers	122	68,5	47	72,3	75	66,4	
Quitters	56	31,5	18	27,7	38	33,6	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,4787
Smokers	370	89,8	135	91,2	235	89,0	
Quitters	42	10,2	13	8,8	29	11,0	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,5260
Smokers	356	86,4	130	87,8	226	85,6	
Quitters	56	13,6	18	12,2	38	14,4	

* Chi-square test

Supplementary Table 4c. As Treated analyses / Age

	Total N= 2163		Yes N=859 (39,7%)		No N=1304 (60,3%)		
	N	%	N	%	N	%	p*
Age ≤ 45 years							
Minimum 7-day PPA at 6 months							0,5247
Smokers	349	64,6	140	63,1	209	65,7	
Quitters	191	35,4	82	36,9	109	34,3	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,1389
Smokers	555	66,6	212	63,7	343	68,6	
Quitters	278	33,4	121	36,3	157	31,4	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,3411
Smokers	1972	91,2	777	90,5	1195	91,6	
Quitters	191	8,8	82	9,5	109	8,4	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,1641
Smokers	1885	87,1	738	85,9	1147	88,0	
Quitters	278	12,9	121	14,1	157	12,0	
Age > 45 years							
	Total N= 643		Yes N=207 (32,2%)		No N=436 (67,8%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,4968
Smokers	128	66,3	41	63,1	87	68,0	
Quitters	65	33,7	24	36,9	41	32,0	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,9426
Smokers	197	68,6	67	68,4	130	68,8	
Quitters	90	31,4	31	31,6	59	31,2	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,3893
Smokers	578	89,9	183	88,4	395	90,6	
Quitters	65	10,1	24	11,6	41	9,4	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,6220
Smokers	553	86,0	176	85,0	377	86,5	
Quitters	90	14,0	31	15,0	59	13,5	

* Chi-square test

Supplementary Table 4d. ITT analyses / sex

	Total N= 1033		Yes N=511 (49,5%)		No N=522 (50,5%)		
	N	%	N	%	N	%	p*
Men							
Minimum 7-day PPA at 6 months							0,3631
Smokers	178	61,8	76	58,9	102	64,2	
Quitters	110	38,2	53	41,1	57	35,8	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,3851
Smokers	271	64,5	119	62,3	152	66,4	
Quitters	149	35,5	72	37,7	77	33,6	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,7754
Smokers	923	89,4	458	89,6	465	89,1	
Quitters	110	10,6	53	10,4	57	10,9	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,7624
Smokers	884	85,6	439	85,9	445	85,2	
Quitters	149	14,4	72	14,1	77	14,8	
Women							
	Total N= 1773		Yes N=889 (50,1%)		No N=884 (49,9%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,3884
Smokers	299	67,2	142	69,3	157	65,4	
Quitters	146	32,8	63	30,7	83	34,6	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,7817
Smokers	481	68,7	223	68,2	258	69,2	
Quitters	219	31,3	104	31,8	115	30,8	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,0778
Smokers	1627	91,8	826	92,9	801	90,6	
Quitters	146	8,2	63	7,1	83	9,4	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,4017
Smokers	1554	87,6	785	88,3	769	87,0	
Quitters	219	12,4	104	11,7	115	13,0	

* Chi-square test

Supplementary Table 4e. PP analyses / sex

	Total N= 704		Yes N=278 (39,5%)		No N=426 (60,5%)		
	N	%	N	%	N	%	p*
Men							
Minimum 7-day PPA at 6 months							0,2367
Smokers	115	59,6	39	54,2	76	62,8	
Quitters	78	40,4	33	45,8	45	37,2	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,3214
Smokers	178	63,6	61	59,8	117	65,7	
Quitters	102	36,4	41	40,2	61	34,3	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,5891
Smokers	626	88,9	245	88,1	381	89,4	
Quitters	78	11,1	33	11,9	45	10,6	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,8744
Smokers	602	85,5	237	85,3	365	85,7	
Quitters	102	14,5	41	14,7	61	14,3	
Women							
	Total N= 1210		Yes N=509 (42,1%)		No N=701 (57,9%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,7543
Smokers	219	69,1	89	70,1	130	68,4	
Quitters	98	30,9	38	29,9	60	31,6	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,3842
Smokers	335	69,9	130	67,7	205	71,4	
Quitters	144	30,1	62	32,3	82	28,6	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,4912
Smokers	1112	91,9	471	92,5	641	91,4	
Quitters	98	8,1	38	7,5	60	8,6	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,7978
Smokers	1066	88,1	447	87,8	619	88,3	
Quitters	144	11,9	62	12,2	82	11,7	

* Chi-square test

Supplementary Table 4f. As Treated analyses / sex

Men	Total N= 1033		Yes N=374 (36,2%)		No N=659 (63,8%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,4560
Smokers	178	61,8	65	59,1	113	63,5	
Quitters	110	38,2	45	40,9	65	36,5	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,5641
Smokers	271	64,5	96	62,7	175	65,5	
Quitters	149	35,5	57	37,3	92	34,5	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,2775
Smokers	923	89,4	329	88,0	594	90,1	
Quitters	110	10,6	45	12,0	65	9,9	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,5736
Smokers	884	85,6	317	84,8	567	86,0	
Quitters	149	14,4	57	15,2	92	14,0	
Women	Total N= 1773		Yes N=692 (39,0%)		No N=1081 (61,0%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,5458
Smokers	299	67,2	116	65,5	183	68,3	
Quitters	146	32,8	61	34,5	85	31,7	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,1812
Smokers	481	68,7	183	65,8	298	70,6	
Quitters	219	31,3	95	34,2	124	29,4	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,4769
Smokers	1627	91,8	631	91,2	996	92,1	
Quitters	146	8,2	61	8,8	85	7,9	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,1588
Smokers	1554	87,6	597	86,3	957	88,5	
Quitters	219	12,4	95	13,7	124	11,5	

* Chi-square test

Supplementary Table 4g. ITT analyses / Family or adoption planning

Yes	Total N= 338		Yes N=156 (46,2%)		No N=182 (53,8%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,8599
Smokers	47	54,7	22	53,7	25	55,6	
Quitters	39	45,3	19	46,3	20	44,4	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,8020
Smokers	75	59,5	37	60,7	38	58,5	
Quitters	51	40,5	24	39,3	27	41,5	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,7327
Smokers	299	88,5	137	87,8	162	89,0	
Quitters	39	11,5	19	12,2	20	11,0	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,8881
Smokers	287	84,9	132	84,6	155	85,2	
Quitters	51	15,1	24	15,4	27	14,8	

No	Total N= 2433		Yes N=1223 (50,3%)		No N=1210 (49,7%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,8751
Smokers	428	66,5	195	66,8	233	66,2	
Quitters	216	33,5	97	33,2	119	33,8	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,3630
Smokers	671	68,1	303	66,6	368	69,3	
Quitters	315	31,9	152	33,4	163	30,7	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,0989
Smokers	2217	91,1	1126	92,1	1091	90,2	
Quitters	216	8,9	97	7,9	119	9,8	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,4437
Smokers	2118	87,1	1071	87,6	1047	86,5	
Quitters	315	12,9	152	12,4	163	13,5	

* Chi-square test

Supplementary Table 4h. PP analyses / Family or adoption planning

Yes	Total N= 252		Yes N=102 (40,5%)		No N=150 (59,5%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,9073
Smokers	40	58,8	18	58,1	22	59,5	
Quitters	28	41,2	13	41,9	15	40,5	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,9883
Smokers	57	63,3	26	63,4	31	63,3	
Quitters	33	36,7	15	36,6	18	36,7	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,4961
Smokers	224	88,9	89	87,3	135	90,0	
Quitters	28	11,1	13	12,7	15	10,0	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,5320
Smokers	219	86,9	87	85,3	132	88,0	
Quitters	33	13,1	15	14,7	18	12,0	

No	Total N= 1643		Yes N=677 (41,2%)		No N=966 (58,8%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,7169
Smokers	294	66,5	110	65,5	184	67,2	
Quitters	148	33,5	58	34,5	90	32,8	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,2081
Smokers	453	68,1	165	65,2	288	69,9	
Quitters	212	31,9	88	34,8	124	30,1	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,6014
Smokers	1495	91,0	619	91,4	876	90,7	
Quitters	148	9,0	58	8,6	90	9,3	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,9232
Smokers	1431	87,1	589	87,0	842	87,2	
Quitters	212	12,9	88	13,0	124	12,8	

* Chi-square test

Supplementary Table 4i. As Treated analyses / Family or adoption planning

Yes	Total N= 338		Yes N=134 (39,6%)		No N=204 (60,4%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,8913
Smokers	47	54,7	21	53,8	26	55,3	
Quitters	39	45,3	18	46,2	21	44,7	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,7349
Smokers	75	59,5	33	57,9	42	60,9	
Quitters	51	40,5	24	42,1	27	39,1	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,3770
Smokers	299	88,5	116	86,6	183	89,7	
Quitters	39	11,5	18	13,4	21	10,3	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,2401
Smokers	287	84,9	110	82,1	177	86,8	
Quitters	51	15,1	24	17,9	27	13,2	

No	Total N= 2433		Yes N=921 (37,9%)		No N=1512 (62,1%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,4405
Smokers	428	66,5	159	64,6	269	67,6	
Quitters	216	33,5	87	35,4	129	32,4	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,2504
Smokers	671	68,1	245	65,9	426	69,4	
Quitters	315	31,9	127	34,1	188	30,6	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,4418
Smokers	2217	91,1	834	90,6	1383	91,5	
Quitters	216	8,9	87	9,4	129	8,5	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,3341
Smokers	2118	87,1	794	86,2	1324	87,6	
Quitters	315	12,9	127	13,8	188	12,4	

* Chi-square test

Supplementary Table 4j. ITT analyses / Tobacco status at inclusion

Smokers	Total N= 1881		Yes N=931 (49,5%)		No N=950 (50,5%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,9587
Smokers	337	72,6	153	72,5	184	72,7	
Quitters	127	27,4	58	27,5	69	27,3	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,3667
Smokers	538	75,7	237	74,1	301	77,0	
Quitters	173	24,3	83	25,9	90	23,0	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,3719
Smokers	1754	93,2	873	93,8	881	92,7	
Quitters	127	6,8	58	6,2	69	7,3	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,6751
Smokers	1708	90,8	848	91,1	860	90,5	
Quitters	173	9,2	83	8,9	90	9,5	

Quitters	Total N= 925		Yes N=469 (50,7%)		No N=456 (49,3%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,8093
Smokers	140	52,0	65	52,8	75	51,4	
Quitters	129	48,0	58	47,2	71	48,6	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,7814
Smokers	214	52,3	105	53,0	109	51,7	
Quitters	195	47,7	93	47,0	102	48,3	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,1597
Smokers	796	86,1	411	87,6	385	84,4	
Quitters	129	13,9	58	12,4	71	15,6	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,3439
Smokers	730	78,9	376	80,2	354	77,6	
Quitters	195	21,1	93	19,8	102	22,4	

* Chi-square test

Supplementary Table 4k. PP analyses / Tobacco status at inclusion

Smokers	Total N= 1287		Yes N=526 (40,9%)		No N=761 (59,1%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,1905
Smokers	238	72,3	91	68,4	147	75,0	
Quitters	91	27,7	42	31,6	49	25,0	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,0476
Smokers	371	75,3	133	70,4	238	78,3	
Quitters	122	24,7	56	29,6	66	21,7	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,2875
Smokers	1196	92,9	484	92,0	712	93,6	
Quitters	91	7,1	42	8,0	49	6,4	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,2348
Smokers	1165	90,5	470	89,4	695	91,3	
Quitters	122	9,5	56	10,6	66	8,7	

Quitters	Total N= 627		Yes N=261 (41,6%)		No N=366 (58,4%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,5371
Smokers	96	53,0	37	56,1	59	51,3	
Quitters	85	47,0	29	43,9	56	48,7	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,6244
Smokers	142	53,4	58	55,2	84	52,2	
Quitters	124	46,6	47	44,8	77	47,8	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,1309
Smokers	542	86,4	232	88,9	310	84,7	
Quitters	85	13,6	29	11,1	56	15,3	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,3477
Smokers	503	80,2	214	82,0	289	79,0	
Quitters	124	19,8	47	18,0	77	21,0	

* Chi-square test

Supplementary Table 4l. As Treated analyses / Tobacco status at inclusion

Smokers	Total N= 1881		Yes N=715 (38,0%)		No N=1166 (62,0%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							**0,0343**
Smokers	337	72,6	128	67,4	209	76,3	
Quitters	127	27,4	62	32,6	65	23,7	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							**0,0213**
Smokers	538	75,7	196	71,0	342	78,6	
Quitters	173	24,3	80	29,0	93	21,4	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							**0,0094**
Smokers	1754	93,2	653	91,3	1101	94,4	
Quitters	127	6,8	62	8,7	65	5,6	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							**0,0193**
Smokers	1708	90,8	635	88,8	1073	92,0	
Quitters	173	9,2	80	11,2	93	8,0	

Quitters	Total N= 925		Yes N=351 (37,9%)		No N=574 (62,1%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,5224
Smokers	140	52,0	53	54,6	87	50,6	
Quitters	129	48,0	44	45,4	85	49,4	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,6983
Smokers	214	52,3	83	53,5	131	51,6	
Quitters	195	47,7	72	46,5	123	48,4	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,3329
Smokers	796	86,1	307	87,5	489	85,2	
Quitters	129	13,9	44	12,5	85	14,8	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,7404
Smokers	730	78,9	279	79,5	451	78,6	
Quitters	195	21,1	72	20,5	123	21,4	

* Chi-square test

Supplementary Table 4m. ITT analyses / Year of inclusion

2017	Total N= 875		Yes N=450 (51,4%)		No N=425 (48,6%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,6335
Smokers	136	60,4	64	62,1	72	59,0	
Quitters	89	39,6	39	37,9	50	41,0	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,3127
Smokers	241	65,8	110	63,2	131	68,2	
Quitters	125	34,2	64	36,8	61	31,8	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,1297
Smokers	786	89,8	411	91,3	375	88,2	
Quitters	89	10,2	39	8,7	50	11,8	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,9560
Smokers	750	85,7	386	85,8	364	85,6	
Quitters	125	14,3	64	14,2	61	14,4	

2018	Total N= 1931		Yes N=950 (49,2%)		No N=981 (50,8%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,8405
Smokers	341	67,1	154	66,7	187	67,5	
Quitters	167	32,9	77	33,3	90	32,5	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,8590
Smokers	511	67,8	232	67,4	279	68,0	
Quitters	243	32,2	112	32,6	131	32,0	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,4034
Smokers	1764	91,4	873	91,9	891	90,8	
Quitters	167	8,6	77	8,1	90	9,2	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,3002
Smokers	1688	87,4	838	88,2	850	86,6	
Quitters	243	12,6	112	11,8	131	13,4	

* Chi-square test

Supplementary Table 4n. PP analyses / Year of inclusion

2017	Total N= 574		Yes N=279 (48,6%)		No N=295 (51,4%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,7410
Smokers	91	60,3	43	58,9	48	61,5	
Quitters	60	39,7	30	41,1	30	38,5	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,1185
Smokers	158	66,1	69	61,1	89	70,6	
Quitters	81	33,9	44	38,9	37	29,4	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,8194
Smokers	514	89,5	249	89,2	265	89,8	
Quitters	60	10,5	30	10,8	30	10,2	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,2668
Smokers	493	85,9	235	84,2	258	87,5	
Quitters	81	14,1	44	15,8	37	12,5	

2018	Total N= 1340		Yes N=508 (37,9%)		No N=832 (62,1%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,9459
Smokers	243	67,7	85	67,5	158	67,8	
Quitters	116	32,3	41	32,5	75	32,2	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,7566
Smokers	355	68,3	122	67,4	233	68,7	
Quitters	165	31,7	59	32,6	106	31,3	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,5512
Smokers	1224	91,3	467	91,9	757	91,0	
Quitters	116	8,7	41	8,1	75	9,0	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,5427
Smokers	1175	87,7	449	88,4	726	87,3	
Quitters	165	12,3	59	11,6	106	12,7	

* Chi-square test

Supplementary Table 4o. As Treated analyses / Year of inclusion

2017	Total N= 875		Yes N=409 (46,7%)		No N=466 (53,3%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,3100
Smokers	136	60,4	67	57,3	69	63,9	
Quitters	89	39,6	50	42,7	39	36,1	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,1300
Smokers	241	65,8	111	62,0	130	69,5	
Quitters	125	34,2	68	38,0	57	30,5	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,0597
Smokers	786	89,8	359	87,8	427	91,6	
Quitters	89	10,2	50	12,2	39	8,4	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,0638
Smokers	750	85,7	341	83,4	409	87,8	
Quitters	125	14,3	68	16,6	57	12,2	

2018	Total N= 1931		Yes N=657 (34,0%)		No N=1274 (66,0%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,9818
Smokers	341	67,1	114	67,1	227	67,2	
Quitters	167	32,9	56	32,9	111	32,8	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,6455
Smokers	511	67,8	168	66,7	343	68,3	
Quitters	243	32,2	84	33,3	159	31,7	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,8886
Smokers	1764	91,4	601	91,5	1163	91,3	
Quitters	167	8,6	56	8,5	111	8,7	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,8482
Smokers	1688	87,4	573	87,2	1115	87,5	
Quitters	243	12,6	84	12,8	159	12,5	

* Chi-square test

Supplementary Table 4p. ITT analyses / level of education

< Bac	Total N= 700		Yes N=355 (50,7%)		No N=345 (49,3%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,7256
Smokers	103	69,6	49	71,0	54	68,4	
Quitters	45	30,4	20	29,0	25	31,6	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,9826
Smokers	162	69,2	79	69,3	83	69,2	
Quitters	72	30,8	35	30,7	37	30,8	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,3845
Smokers	655	93,6	335	94,4	320	92,8	
Quitters	45	6,4	20	5,6	25	7,2	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,7063
Smokers	628	89,7	320	90,1	308	89,3	
Quitters	72	10,3	35	9,9	37	10,7	

Bac and over	Total N= 2086		Yes N=1033 (49,5%)		No N=1053 (50,5%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,9990
Smokers	374	64,3	169	64,3	205	64,3	
Quitters	208	35,7	94	35,7	114	35,7	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,3931
Smokers	588	66,8	262	65,3	326	68,1	
Quitters	292	33,2	139	34,7	153	31,9	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,1882
Smokers	1878	90,0	939	90,9	939	89,2	
Quitters	208	10,0	94	9,1	114	10,8	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,4797
Smokers	1794	86,0	894	86,5	900	85,5	
Quitters	292	14,0	139	13,5	153	14,5	

* Chi-square test

Supplementary Table 4q. PP analyses / level of education

< bac	Total N= 463		Yes N=177 (38,2%)		No N=286 (61,8%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,8258
Smokers	66	69,5	22	71,0	44	68,8	
Quitters	29	30,5	9	29,0	20	31,3	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,7238
Smokers	104	70,3	37	68,5	67	71,3	
Quitters	44	29,7	17	31,5	27	28,7	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,4102
Smokers	434	93,7	168	94,9	266	93,0	
Quitters	29	6,3	9	5,1	20	7,0	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,9534
Smokers	419	90,5	160	90,4	259	90,6	
Quitters	44	9,5	17	9,6	27	9,4	

Bac and over	Total N= 1436		Yes N=601 (41,9%)		No N=835 (58,1%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,6588
Smokers	268	64,7	106	63,5	162	65,6	
Quitters	146	35,3	61	36,5	85	34,4	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,2444
Smokers	407	67,1	153	64,3	254	68,8	
Quitters	200	32,9	85	35,7	115	31,2	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,9852
Smokers	1290	89,8	540	89,9	750	89,8	
Quitters	146	10,2	61	10,1	85	10,2	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,8414
Smokers	1236	86,1	516	85,9	720	86,2	
Quitters	200	13,9	85	14,1	115	13,8	

* Chi-square test

Supplementary Table 4r. As Treated analyses / level of education

< Bac	Total N= 700		Yes N=236 (33,7%)		No N=464 (66,3%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,9958
Smokers	103	69,6	32	69,6	71	69,6	
Quitters	45	30,4	14	30,4	31	30,4	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,4764
Smokers	162	69,2	53	66,3	109	70,8	
Quitters	72	30,8	27	33,8	45	29,2	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,7026
Smokers	655	93,6	222	94,1	433	93,3	
Quitters	45	6,4	14	5,9	31	6,7	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,4731
Smokers	628	89,7	209	88,6	419	90,3	
Quitters	72	10,3	27	11,4	45	9,7	

Bac and over	Total N= 2086		Yes N=819 (39,3%)		No N=1267 (60,7%)		
	N	%	N	%	N	%	p*
Minimum 7-day PPA at 6 months							0,4202
Smokers	374	64,3	149	62,3	225	65,6	
Quitters	208	35,7	90	37,7	118	34,4	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing)							0,2704
Smokers	588	66,8	225	64,7	363	68,2	
Quitters	292	33,2	123	35,3	169	31,8	
Minimum 7-day PPA at 6 months considering non-respondents as smokers							0,2123
Smokers	1878	90,0	729	89,0	1149	90,7	
Quitters	208	10,0	90	11,0	118	9,3	
Minimum 7-day PPA at 6 months (with the use of 12-month or 3-month smoking status if missing), considering non-respondents as smokers							0,2803
Smokers	1794	86,0	696	85,0	1098	86,7	
Quitters	292	14,0	123	15,0	169	13,3	

* Chi-square test

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	1
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	2
	2b	Specific objectives or hypotheses	4
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	5
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	NA
Participants	4a	Eligibility criteria for participants	6
	4b	Settings and locations where the data were collected	5
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	6
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	8
	6b	Any changes to trial outcomes after the trial commenced, with reasons	8
Sample size	7a	How sample size was determined	9
	7b	When applicable, explanation of any interim analyses and stopping guidelines	NA
Randomisation:			5
Sequence generation	8a	Method used to generate the random allocation sequence	
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	5
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	5
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	5
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	NA
	11b	If relevant, description of the similarity of interventions	NA
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	9
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	10

Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	Fig 1
	13b	For each group, losses and exclusions after randomisation, together with reasons	Fig 1
Recruitment	14a	Dates defining the periods of recruitment and follow-up	5
	14b	Why the trial ended or was stopped	NA
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Suppl
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	27
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	12
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	27
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	14
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	NA
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	19
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	21
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	15
Other information			2
Registration	23	Registration number and name of trial registry	
Protocol	24	Where the full trial protocol can be accessed, if available	5
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	3

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.