TITLE PAGE

A mHealth (mobile health) Intervention for Smoking Cessation in People with Tuberculosis: A Cluster Randomized Clinical Trial

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KEY POINTS

Question: What is the effectiveness of a mHealth (mobile health) intervention for achieving self-reported continuous tobacco abstinence at 6 months, supported by biochemical verification at 6 months, compared with usual care in people with TB?

Findings: In this randomized clinical trial that included 1080 patients with TB who smoked tobacco, the proportion achieving self-reported continuous tobacco abstinence at 6 months, supported by biochemical verification at 6 months, was significantly higher with mHealth (41.7%) vs with usual care (15.3%).

Meaning: In people with TB who smoke tobacco, the use of a mHealth intervention may be warranted.

ABSTRACT

Importance: Smoking worsens outcomes in people with TB, whilst quitting hastens recovery.

Objective: To assess the effectiveness of a mHealth intervention for achieving self-reported continuous tobacco abstinence at 6 months, supported by biochemical verification at 6 months compared with usual care in people with TB.

Design, Settings and Participants: In a multicenter, cluster-randomized clinical trial conducted between September 18, 2023 and January 2, 2025, 27 TB clinics in Bangladesh and Pakistan were allocated (2:1) to the mHealth or usual care groups. The follow-up was 6 months. After assessing 9,232 patients for eligibility, we enrolled 1,080 patients with TB who smoked, were willing to quit, provided written consent, and had mobile phones.

Intervention: The mHealth group (n=720) received text messages throughout TB treatment, daily for two months then monthly for four months, encouraging tobacco cessation. The usual care group (n=360) received written information on tobacco cessation.

Main Outcomes and Measures: The primary outcome was self-reported continuous abstinence at 6 months, verified biochemically using carbon monoxide breath test at 6 months. Secondary outcomes included self-reported point abstinence at 9 weeks and 6 months, TB treatment adherence (days on TB treatment), TB treatment success (cured + completed treatment), TB treatment failure, TB treatment default (interruption of TB treatment for ≥2 months), and death.

Results: Of 1080 randomized participants, most were male, (mHealth=96.9%; usual care=95.8%), and 985 were retained throughout the trial (91%). For the primary outcome, 41.7%(300/720) of participants in the mHealth group demonstrated self-reported and biochemically verified continuous abstinence at 6 months as compared with 15.3%(55/360) in the usual care group(risk ratio[RR]=3.0; 95%CI 2.0-4.9). In the mHealth vs usual care groups, respectively, mean(SD) TB treatment adherence was 174.3 ±21.5 days vs. 178.0 ±12.1 (p=0.232), and treatment success was 89.3% vs. 85.6%(RR 1.2; 95%CI 0.9-1.6). TB treatment

failure(0.1% vs. 0.5%) and default(3.1% vs. 1.9%) were uncommon. Mortality was lower with mHealth (3.5%) vs. usual care (7.5%); Hazard Ratio[HR] 0.4; 95%CI 0.2-0.9.

Conclusions and Relevance: The mHealth intervention was effective in achieving continuous abstinence in people with TB who smoked. mHealth is a feasible and effective intervention to help patients with TB quit smoking.

Trial Registration: UK's clinical study registry number, ISRCTN86971818

Tobacco consumption poses a substantial threat to global health with >8.7 million deaths, a loss of 230 million Disability-Adjusted Life Years, and >1.4 trillion USD, annually.[1,2] Despite a reduction in smoking prevalence,[3] the persistently high absolute numbers (>1.3 billion) of people who use tobacco mean intensified tobacco control efforts are required. This need is greatest in low- and middle-income countries (LMIC) where >80% of people who use tobacco live [4] and of whom approximately 90% are men.[5]

Tobacco cessation is central to global efforts to reduce tobacco-related harm. Mobile health (mHealth) interventions for tobacco cessation are promising due to their accessibility and scalability.[6] While the evidence supporting their effectiveness comes mainly from high-income countries,[7] they have potential to make tobacco cessation accessible to LMIC populations.[8] In this study, we focus on patients with tuberculosis (TB), a neglected group that may benefit from a mHealth intervention.

Approximately 17–32% of individuals with TB currently smoke;[9] yet smoking is not adequately addressed for several reasons e.g. lack of capacity, interest and resources.[10] Due to these barriers[11] no TB high-burden country offers face-to-face tobacco cessation within TB services. Recognizing these challenges, WHO developed an mHealth tobacco cessation intervention that delivers TB-specific text messages to people with TB who smoke.[12] However, high quality evidence supporting the effectiveness of mHealth tobacco cessation interventions in patients with TB is lacking. We hypothesized that relative to usual care, patients with TB receiving a mHealth intervention would be more likely to achieve abstinence at 6 months. We report the findings of a cluster RCT, in Bangladesh and Pakistan (two high tobacco and TB-burden countries), which tested this hypothesis.

METHODS

Trial Oversight

A Trial Steering Committee met annually and reviewed the trial protocol, questionnaires, patient information sheet, consent forms, trial procedures, and progress. Ethics approvals were obtained from the respective committees at the University of Edinburgh, UK and authorized national bodies in

Bangladesh and Pakistan. The trial complied with the UK General Data Protection Regulation (GDPR) and the Data Protection Act 2018.

Trial Design and Participants

We conducted a two-group, multicenter, cluster RCT in Bangladesh (Dhaka) and Pakistan (Punjab) from September 18, 2023 to January 2, 2025. A cluster design was chosen to minimize contamination and because it was ethically simpler to implement. Twenty-seven TB clinics (clusters) were randomized in a 2:1 ratio, to the mHealth or usual care groups. In the published protocol, this trial is referred to as the 3rd phase of the project.[13]

Government approved TB clinics, registering at least 50 new patients with TB per month, were eligible. Patients aged ≥15 years, diagnosed with drug-sensitive pulmonary TB in the last four weeks, people who smoked daily (at least one puff on ≥25 days in the last month), willing to quit and having access to mobile phones, were eligible. Patients treated for multidrug resistance, miliary or extrapulmonary TB and for tobacco dependence were excluded.

Trial Procedures

An independent statistician, blinded to TB clinics, used computer-generated random-number lists to allocate clusters in a 2:1 ratio to the mHealth and usual care groups. With more clusters offering mHealth, the trial was expected to recruit faster than with equal allocation.[14] Randomization was stratified by country. While the nature of the intervention (mHealth) and the cluster design precluded us from blinding the participants and researchers, the statistician remained blinded during the analysis.

At the TB clinics, healthcare staff identified patients newly diagnosed with TB and referred them to the researchers for eligibility assessment. Those eligible provided written consent; for those <18 years, parent/guardians gave written consent. Data were collected on day 0, week-9 and month-6 from all participants, corresponding with routine TB clinic visits. If a participant missed their appointment, they were assessed within 5 days, via phone or home visit.

To monitor intervention fidelity in the mHealth group, participants were called weekly to check if they were receiving and reading the messages, or having the messages read to them. Those in the control group were also called weekly, to detect any contamination. A custom-made mobile app was used to collect the data, which was managed using a secure web platform.

Trial Intervention

The mHealth intervention was designed to deliver TB-specific text messages to people with TB.[12] These messages, together with a guide, were developed by a group of public health experts, epidemiologists and behavioral scientists, convened by WHO in 2019.[12] The messages were grounded in the behavior change technique taxonomy, a classification system of theory-informed techniques used to modify behavior.[15] The messages were translated into Bangla and Urdu using WHO's guidance,[16] then reviewed and refined with feedback from a patient group (phase 1). A pilot study involving 16 patients with TB who smoked assessed user experiences with clarity, quantity, timing, and frequency of messages (phase 2). Following trial enrollment, participants first received three welcoming messages explaining the program's purpose and schedule. While the program was not interactive, participants could opt out of receiving text messages by calling or texting the researchers.

The mHealth text messages supported cessation with motivational messages, and coping strategies to reduce cravings and address withdrawal symptoms. Messages to promote healthy behaviors were also included. Alongside emphasizing the importance of taking TB medications and follow-up appointments, text messages addressed the association between TB and tobacco, highlighting how smoking slows recovery and increases the risk of relapse. In total, 134 unique text messages were sent through a web-based application to participants' mobile numbers over 6 months. One hundred messages were delivered (3–4/day) in the first month, followed by 30 messages (1/day) in the second, and then four messages (1/month) over the next four months. The last four messages were reminders for attending TB clinics and collecting medications. The system reported weekly on the number of sent messages and their recipients.

Participants in both groups received TB treatment consisting of rifampicin, isoniazid, pyrazinamide and ethambutol. After two months, the regimen was reduced to rifampicin and isoniazid. In addition, written information on tobacco-related harms and quit advice were also offered to both groups. None were offered medications to help them quit as medications were neither available in the TB clinics nor accessible privately due to their prohibitive cost.

Trial Outcomes

The primary outcome was biochemically verified continuous abstinence at 6 months post-randomization. Abstinence was defined as self-report of not having used more than 5 cigarettes, bidis, or water pipe sessions since the quit date (set 5 days after enrollment), verified biochemically by a breath carbon monoxide (CO) reading of less than 10 ppm at month 6.[17] In the case of concomitant smokeless tobacco use at baseline, a COT Rapid Test Cassette (Hangzhou AllTest Biotech Co. Ltd.) was used to detect cotinine (a nicotine metabolite) in urine samples. A negative result verified abstinence.

We performed exploratory analyses of the following secondary outcomes: point abstinence, self-reported abstinence from tobacco in the previous 7 days, assessed at week-9 and month-6, adherence to TB treatment (number of days TB medication was taken), TB success rate (cured + treatment completion), TB treatment failure, TB treatment defaults (interruption of TB treatment for ≥2 months) and deaths at month-6. Outcome details are provided in Supplement 1 and the published protocol.[13]

The sample size (Phase 3 in the protocol) was estimated using 90% power, 5% significance level (two-sided), and abstinence probabilities of 18% and 8% for the mHealth and usual care groups, respectively, at six months.[18] An intracluster correlation coefficient (ICC) of 0.02 was used based on the recommendations for behavioral outcomes in cluster RCTs.[19] For a cluster size of 26 participants, we estimated a design effect of 1.5. After adjusting for this and an anticipated 20% attrition rate, we arrived at a sample size of 1,080 participants and 27 clusters (capped at 40 participants per cluster).

Statistical Analysis

We reported the analyses in accordance with CONSORT guidelines (extension for cluster RCT).[20] R version 4.4.3 and JASP Team (2024; version 0.19.3) computer software were employed for data analysis.[21]

Data normality was tested visually and by using the Shapiro-Wilk test. Categorical outcomes were summarized using frequencies and percentages, and continuous outcomes using means and standard deviations. A mixed-effects model was used to assess the effect of mHealth on abstinence outcomes, incorporating fixed-effects for the intervention, and relevant covariates selected post-hoc (age, sex, education, occupation, and smoking duration) and random effects for clusters. Logistic regression within the mixed-effects framework was used to analyze categorical outcomes, accounting for cluster-level variability and intervention effects. Additionally, a Bayesian hierarchical logistic regression model was fitted with brms package (R) to estimate cluster-level quit probabilities and 95% credible intervals. We overlaid observed proportions to compare raw data with our model-based results. For all analyses, coefficients of intraclass correlation were estimated from the variance components of a mixed effects logistic regression model using the package "lme4" in R. For comparing death rates between the two groups over 6 months, we used the Cox proportional hazards frailty model, adjusting for site-level clustering. The secondary outcomes were exploratory, and the analysis was not adjusted for multiple comparisons. A post-hoc sensitivity analysis using a CO cutoff of <6ppm was performed for the primary outcome.

Consistent with standard practice in smoking cessation trials, missing primary outcome data were treated as a negative outcome (i.e., not abstinent). The intervention effect estimates were assessed through both intention-to-treat and complete case analyses (those with missing primary outcome data were discarded).[22] A post-hoc sensitivity analysis was also carried out after excluding deaths.

We recorded the number and reasons for ineligibility and calculated cluster-level recruitment, abstinence, TB success and death rates. Using multilevel modelling, we also explored associations between cluster characteristics and the primary outcome. We adjusted for relevant sociodemographic covariates (selected

post-hoc) in the primary analysis. We compared the primary outcome between the following pre-specified subgroups: age (<40 years and ≥40 years); education (no formal education, primary, secondary or higher); employment (active, dependent, retired); and smoking duration (<24 years and ≥24 years)). All statistical tests were 2-sided and only P values less than 0.05 were considered statistically significant.

RESULTS

Participants

We assessed 9,232 patients for eligibility and enrolled 1,080 (mHealth=720, usual care=360) participants (Figure 1). Six patients refused to participate; the remainder (8,146) did not meet inclusion criteria (eTable 1 in Supplement 2); the main reasons for exclusion were not smoking, non-pulmonary TB, and TB diagnosis more than 4 weeks ago.

Baseline characteristics of the clusters and participants are available in Table 1. Compared with the usual care group, the mHealth group had more people who smoked cigarettes (94.3% vs. 90.6%) and used smokeless tobacco (6.9% vs. 2.2%). The mHealth group consumed a lower average number of cigarettes/day (5 vs. 7), and bidis/day (8 vs. 15) than the usual care group. More participants in the mHealth than the usual care group made previous quit attempts (24.7% vs. 9.2%). The imbalance in prior quit attempts across groups was driven by a relatively few number of intervention clusters; eTable 2 in Supplement 2 shows the site-level distribution of prior quit attempts.

All participants in the mHealth group confirmed receiving text messages. At month 6, 8.8% of participants did not provide a primary outcome: 4.8% had died, 1.5% withdrew, and 2.5% lost contact. Except for deaths, attrition rates were comparable between groups (Figure 1). There was no missing data on outcomes, other than for these participants. No participant reported using medications for tobacco cessation. There were also no incidents of contamination based on system generated reports and calls to participants.

Primary Outcome

Based on self-report only, 47.5% of participants remained abstinent in the mHealth group, as compared with 19.4% in the usual care group. On biochemical verification (CO cutoff <10ppm) and as per intention to treat analysis, 41.7% (95%CI 38.0-45.4) of participants demonstrated continuous abstinence in the mHealth group as compared with 15.3% (95%CI 11.7-19.4) in the usual care group (RR=3.0; 95%CI 2.0-4.9) (Table 2). The association persisted after adjustments for baseline covariates, selected post-hoc, (age, sex, education, occupation, and smoking duration) –adjusted risk ratio (aRR) 3.2 (95%CI: 2.2–5.2). In those who achieved biochemically-verified continuous abstinence, the mean CO levels (mHealth=3.54ppm; SD=2.1 and usual care=4.38ppm; SD=2.8) were similar in both groups. The post-hoc analysis using a CO cutoff of <6ppm was also consistent with the primary analysis (RR =3.7, 95%CI: 2.4-5.8), confirming the robustness of the intervention effect. The Bayesian hierarchical model (Figure 2) showed heterogeneity of probabilities of quitting among clusters. Overall, clusters in the m-Health group had higher fitted rates than those in the usual care group.

Secondary Outcomes

The self-reported point-abstinence at week-9 and month-6 was also higher in the mHealth than the usual care group (Table 2). Mean (SD) treatment adherence was similar between groups (mHealth: 174.3 ± 21.5 days vs. usual care: 178.0 ± 12.1 days; p =0.232). (eTable 3 in Supplement 2). Treatment success occurred in 89.3% (643/720) of mHealth and 85.6% (308/360) of usual care participants (RR 1.2; 95% CI 0.9–1.6). Treatment failure was rare; 0.1% (1/720) in the m-health group vs. 0.5% (2/360) in the usual care group and treatment default occurred in 3.1% (22/720) vs. 1.9% (7/360) participants, respectively (Table 2). There were fewer deaths in the mHealth than in the usual care group (3.5% vs 7.5%; HR 0.4; 95% CI 0.2-0.9) (Table 2). TB disease (61.5% [32/52]) was the most common cause of death (eTable 4 in Supplement 2). The Kaplan-Meier plot showed higher probability of survival over time in the mHealth compared with the usual care group (eFigure 1 in Supplement 2).

All clusters were of similar size; however, variations were observed in the recruitment, abstinence, successful TB treatment and death rates (eTable 5 in Supplement 2 and eTable 6 in Supplement 2). The main cluster characteristics that modified the primary outcome included shorter smoking duration and higher educational status (eTable 7 in Supplement 2). Subgroup analyses demonstrated that the treatment effect remained consistent across age, education, employment, ability to read SMS messages and smoking duration categories (eTable 8 in Supplement 2). Post-hoc sensitivity analysis after excluding deaths was also consistent with the primary intention-to-treat analysis (eTable 9 in Supplement 2)

Adverse Events

Minor events reported included nausea (mHealth=23.0% vs. usual care=22.3%), diarrhea (mHealth=7.5% vs. usual care=7.5%), dry mouth (mHealth=62.7% vs. usual care=55.7%), epigastric pain (mHealth=27.7% vs. usual care=40.4%), headache (mHealth=45.1% vs. usual care=49.1%), insomnia (mHealth=35.3% vs. usual care=33.5%), abnormal dreams (mHealth=10% vs. usual care=13.2%), irritability (mHealth=40.5% vs. usual care=43.4%), anxiety (mHealth=33.3% vs. usual care=36.8%), palpitations (mHealth=31% vs. usual care=28.4%), and musculoskeletal pain (mHealth=61.4% vs. usual care=60.8%). Of these, dry mouth, irritability and anxiety were more common in the mHealth group (eTable 10 in Supplement 2).

DISCUSSION

In people with TB who smoke, an mHealth intervention led to increased self-reported continuous abstinence supported by biochemical verification at month 6 compared with usual care. A similar difference was observed between groups for self-reported point abstinence at week 9 and month 6. While TB treatment adherence and TB success rates did not differ between groups, there were fewer deaths in the mHealth than in the usual care group.

While mHealth interventions have been tested in people with TB,[23] outcomes have been limited to treatment adherence [24] and TB treatment outcomes.[25,26] In a trial testing the effectiveness of a mHealth

intervention on TB treatment outcomes, no significant difference was reported in smoking abstinence (a secondary outcome) between those receiving automated text messaging and those receiving usual care.[27] To our knowledge, this is the first trial assessing the effectiveness of a mHealth intervention in people with TB who smoke where tobacco abstinence was biochemically verified. The mHealth text messages were delivered to all participants as intended, and all clusters and >90% of participants were retained throughout the trial. Our findings are consistent with studies of face-to-face behavioral support in achieving tobacco abstinence in patients with TB. A recent systematic review with 14 studies reported that smoking cessation interventions can achieve between 15% and 82% abstinence in patients with TB.[28] A mobile-based telecounselling intervention among individuals with TB who smoked achieved higher quit rates than those receiving brief advice at 6-months (67.5% vs. 42%; RR 1.60, 95% CI 1.19-2.16).[29] We observed a higher effect size for tobacco abstinence in people with TB as compared with the aforementioned review[7] findings based on 13 studies conducted in the general population, mostly in high-income countries. In prior studies, behavioral support was associated with a higher abstinence rate in people with TB who smoke as compared with the general population.[30,31] Access to tobacco cessation interventions (such as quit lines, behavioral support, and medications) is virtually non-existent in both Bangladesh and Pakistan.[32] For most participants, this was likely their first exposure to any cessation intervention, which makes the observed effect more plausible.

In exploratory analyses, 4.8% of our trial participants died of TB within 6 months; a similar death rate was observed in a previous trial of people with TB who smoke.[18] The probability of death was significantly higher in the usual care as compared with the mHealth group. This measurable mortality reduction within a short follow-up period of six months is striking and should be confirmed in future studies. The association between smoking and TB mortality is well established;[33] and hence, a higher abstinence rate (as observed here) may have prevented deaths in the mHealth group as compared with the usual care group. A meta-analysis of 16 RCTs of psychosocial interventions in medical settings reported improved

patient survival as compared with controls, specifically when psychosocial interventions explicitly promoted healthy behaviors.[34]

Limitations

The trial had several limitations. First, participants were almost entirely male (>96%). This is not surprising given that in Bangladesh and Pakistan, 97.8% and 91.4% of all adult individuals who smoke are men, respectively. Second, the comparator group received usual care; we did not have an attention control. Third, a substantial proportion of participants had no formal education and we were not able to confirm if they understood the text messages. Fourth, we monitored mHealth fidelity by calling participants regularly, which could also act as an intervention, and hence the results must be interpreted in light of this element. Fifth, while measuring breath CO is an established method to validate self-reported abstinence, it can only verify short-term (24-48 hrs) abstinence due to its short half-life (5-6 hours).[35] Sixth, we did not follow participants beyond their TB treatment, and therefore we cannot confirm if abstinence was sustained, however, a previous smoking cessation trial in people with TB reported that 3 out of 4 people were still abstinent at one year.[18] Additionally, the observed ICC (0.19) was substantially higher than the value (0.02) assumed for sample size calculation. However, the intervention still produced a statistically significant effect, indicating robustness.

Conclusions

Among people with TB who smoke tobacco, a mHealth intervention was effective in promoting continuous abstinence. mHealth is a feasible, effective, and potentially scalable means of supporting tobacco cessation.

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Figure 1. Recruitment, randomization, follow up and analysis flow in the trial

Figure 2. Cluster-level fitted quit probabilities from the Bayesian hierarchical model for TB clinics. Dots = posterior means (fixed + random); hollow circles = observed cluster proportions.

Table 1. Baseline characteristics of the study groups

Characteristics	mHealth Group	Usual care Group
Clusters		
Total, n	18	9
Cluster size, n	40	40
Rural setting, n	11	7
Average no. of TB cases/month	142	93
Participants		
Total, n	720	360
Age, mean(SD), y	48.7(15.8)	48.7(15.9)
Sex, n(%)		
Male	698(96.9)	345(95.8)
Female	22(3.1)	15(4.2)
BMI,[a] median(IQR)	18.7(4)	18.6(4)
Education, n(%)		
No formal education	315(43.8)	155(43.1)
Primary	175(24.3)	114(31.7)
Middle	109(15.1)	43(11.9)
Secondary	89(12.4)	36(10)
Higher	32(4.4)	12(3.3)
Marital status, n(%)		
Single	83(11.5)	37(10.3)
Married	607(84.3)	304(84.4)
Separated/Divorced	30(4.2)	19(5.3)
Employment status		
Employed	560(77.8)	275(76.4)
Dependents[b]	128(17.8)	71(19.7)
Retired	32(4.4)	14(3.9)
Able to read messages, n(%)	425(59.0)	225(62.5)
TB stage,[c] n(%)		
Stage 1	629(87.4)	326(90.6)
Stage 2	45(6.3)	20(5.6)
Stage 3	46(6.4)	14(3.9)
Smoking type, n(%)		
Cigarettes	679(94.3)	326(90.6)
Bidi (hand-rolled)	21(2.9)	21(5.8)
Hookah (water pipe)	61(8.5)	35(9.7)

Concurrent smokeless tobacco use	50(6.9)	8(2.2)
Tobacco use/day, median(IQR)		
Cigarettes	5(6.0)	7(6.0)
Bidi (hand-rolled)	8(10.0)	15(14.0)
Hookah (water pipe)	3(4.0)	3(2.0)
Smoking allowed inside homes, n(%)	482(66.9)	189(52.5)
Attempted quit in past, n(%)	178(24.7)	33(9.2)
Mean smoking duration (SD), y	24.8(15.1)	24.6(15.2)
Median smoking-start age (IQR), y	20 (9.0)	20 (8.0)
Heaviness of Smoking Index,[36] low addiction, n(%)	514(75.7)	212(65.0)

[a]Body-mass index: weight in kilograms divided by the square of the height in meters; [b]Participants who were unemployed, homemakers, students, or otherwise not in active employment; [c]Clinical severity based on the number of TB signs and symptoms: Stage1 = mild to moderate TB disease, Stage 2 = severe TB disease, and Stage 3 = very severe TB disease

Table 2. Comparison of primary and secondary outcomes between study groups

Outcomes	n/N[a] % (95% CI)		Ab diff. (95% CI)[b]	Crude RR[c] (95% CI)	Crude ICC[d]	Adj[e] RR/HR[f] (95% CI)	Adj[e] ICC
	mHealth	Usual Care					
Primary outcomes							
Biochemically verified abstinence at month-6, <10ppm[g] (ITT)[h]	300/720 41.7(38.0-45.4)	55/360 15.3(11.7-19.4)	26.4 (21.0-31.6)	3.0(2.0-4.9)	0.18	3.2(2.2-5.2)	0.18
Biochemically verified abstinence at month-6, <10ppm[g] (PP)[i]	300/667 45(41.2-48.8)	55/318 17.3(13.3-21.9)	27.7 (22.1-33.3)	2.9(2.0-4.7)	0.19	3.1(2.1-5.2)	0.19

Biochemically verified abstinence, <6ppm[g] (ITT)[h]	264/720 36.7(33.1-40.3)	38/360 10.6(7.6-14.2)	26.1 (21.2-30.7)	3.7(2.4-5.8)	0.16	3.9(2.4-6.9)	0.18
Biochemically verified abstinence at month-6, <6ppm[g] (PP)[i]	264/667 39.6(35.9-43.4)	38/318 11.9(8.6-16.1)	27.7 (22.5-32.8)	3.6(2.14-6.87)	0.17	3.8(2.3-7.7)	0.18
Continuous abstinence, self-reported only (ITT)	342/720 47.5(43.8-51.2)	70/360 19.4(15.5-23.9)	28.1 (22.6-33.5)	2.7(1.8 - 4.1)	0.19	2.8(1.9-42)	0.19
Secondary outcomes							
Point abstinence (last 7 days) at week-9 (ITT)	353/720 49.0 (45.3-52.7)	75/360 20.8 (16.7-25.4)	28.2 (22.6-33.8)	2.6(1.8-3.9)	0.19	2.7(1.8-4.3)	0.18
Point abstinence (last 7 days) at month-6 (ITT)	400/720 55.6(51.8-59.2)	82/360 22.8(18.5-27.5)	32.8 (27.1-38.4)	2.7(2.0-3.8)	0.19	2.7(1.9-4.0)	0.19
TB treatment success (cured + completed treatment)	643/720 89.3(86.8-91.5)	308/360 85.6(81.5-89.0)	3.8 (−0.5-8.2)	1.2(0.9-1.6)	0.16	1.2(0.9-1.5)	0.15
Death	25/720 3.5(2.2-5.0)	27/360 7.5(5.0-10.7)	4 (1.0-7.1)	-	-	0.4[i](0.2-0.9)	-
Treatment default (interruption of TB treatment for ≥2 months) [j]	22/720 3.1(1.9-4.6)	7/360 1.9(0.8-4.0)	1.1 (-0.8-3.0)	-	-	-	-
TB treatment failure[j]	1/720 0.1(0.01-0.8)	2/360 0.5(0.1-2.0)	0.4 (-0.4-1.2)	-	-	-	-

[a] Number of outcomes / total number in the group, [b] Absolute difference, [c] Relative risk, [d] Intraclass correlation coefficient (reported for RR models only), [e] Adjusted (post-hoc) for age, sex, education, occupation, smoking duration: Adjusted analyses accounted for clustering: mixed-effects models for RR and shared frailty Cox models for HR, [f] Hazard Ratio estimated from a Cox proportional hazards frailty model, [g] Carbon-monoxide breath test cut-off values, [h] Intention-to-treat analysis, [i] Per-protocol analysis, [j] Mixed-effects models could not be estimated for treatment default and treatment failure due to very low numbers of events across clusters