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Predictors of cessation in smokers suspected of TB: secondary analysis of data from a cluster randomized controlled trial

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ABSTRACT

Objective: To identify predictors of continuous and short-term abstinence in smokers using cigarettes or hookah suspected of Tuberculosis (TB)

Design: Secondary analysis of data from a cluster randomized controlled trial of smoking cessation.

Setting: Health centers in Pakistan.

Participants: Adult daily smokers suspected of TB.

Measurements: Predictor variables of those continuously abstinent at both 5 and 25 weeks post quit-date (continuous abstinence) and those abstinent only at 5 weeks (short-term abstinence) were compared with continuous smokers and with each other. Self-reported abstinence at both time points was confirmed biochemically.

Results: Data obtained from 1,955 trial participants were analyzed. The factors that predicted continuous smoking when compared to continuous abstinence were being older RR 0.97 (0.95 to 0.98), smoking higher quantities of tobacco RR 0.975 (0.97 to 0.98) and sharing a workplace with other smokers RR 0.88 (0.77 to 0.99). Those with a confirmed TB diagnosis were more likely to remain continuously abstinent than those without RR 1.27 (1.10- 1.47).

Conclusions: Predictors of continuous smoking in Pakistan are similar to those identified in studies in high income contexts. In addition, this study shows that those diagnosed with TB are more likely to achieve continuous abstinence than those who were diagnosed with some other respiratory condition. Taking advantage of the ‘teachable moment’ that a TB diagnosis provides is an efficient means for resource-poor national TB programs in low income settings to increase tobacco cessation and improve health outcomes.

Keywords Tobacco cessation, tuberculosis, low income country, Pakistan, teachable moments, respiratory conditions.
Highlights:

- We explore the predictors of cessation among those suspected of tuberculosis in a smoking cessation trial in Pakistan.
- The trial found behavioral support, both with and without bupropion, effective in achieving smoking abstinence at 25 weeks when compared with usual care.
- The predictor variables assessed were duration, quantity and forms of smoking; gender, age, age when started smoking, income, occupation, presence and number of children at home, presence of smokers at home or workplace, and TB diagnosis.
- We found older age, more tobacco smoked, smokers in the workplace as predictive of continuous smoking and a diagnosis of TB as a predictor of quit success.
- Where resources are scarce, each contact with health workers must be optimized; contact with TB services provides a valuable teachable moment for tobacco cessation.
1. INTRODUCTION

Taking advantage of ‘teachable moments’ to support smokers to quit is a well-recognized approach to cessation [McBride et al., 2003; NICE, 2013]. These ‘teachable moments’ appear when naturally occurring health events motivate individuals to spontaneously adopt risk-reducing health behaviors [McBride et al., 2003]. Care pathways for those with tobacco-associated respiratory conditions provide opportunities for such ‘teachable moments’ to support smoking cessation. In the resource-poor contexts of low- and middle-income countries (LMICs), smoking cessation services are rare. If scarce resources for cessation are to be used effectively then taking advantage of these ‘teachable moments’ becomes a necessity. Targeting cessation activities at those suspected of TB is one such strategy.

The majority (80%) of the 8.6 million new TB cases globally (2012) are found in 22 LMICs, collectively named, high-burden countries [WHO, 2013b]. With the help of a broad coalition, known as the STOP TB Partnership, these countries have developed an extensive system to diagnose and treat TB patients [WHO, 2010]. However, only a minority of patients suspected of TB are diagnosed with the condition and the rest are found to have a variety of other respiratory illnesses.

In South and South-East Asia, all high burden countries also have high rates of tobacco use, with 20% or more men currently smoking (2012) [WHO, 2013a]. Pakistan is one such country with a high burden of TB and tobacco use. The latest estimates place TB prevalence at 376 (181 to 641) per 100,000 population and smoking prevalence at 32.4% among men and 5.7% among women [WHO, 2013a]. The high rate of male smoking is particularly important as TB commonly affects more men than women [WHO, 2013b].

There is an inter-relationship between respiratory disease and tobacco that can be seen both in morbidity and mortality. For TB, this association is found at every stage from initial infection [Bates et al., 2007; Yach, 2001], conversion [Slama et al., 2007] and development of disease [Bates et al., 2007] to outcomes; as smokers are less likely to adhere to TB
treatment, more likely to relapse after completing treatment or need re-treatment and have a higher chance of dying due to their tobacco use (Chiang et al., 2007) and have a higher chance of dying due to their tobacco use (Slama et al., 2007). In South East Asia, deaths attributed to tobacco accounted for 8% of all TB deaths (WHO, 2012b).

While tobacco is the leading cause for a number of respiratory illnesses, such as chronic obstructive pulmonary disease (COPD) and lung cancer, its continued use in the presence of respiratory illnesses worsens outcomes. For example, 32% of COPD deaths among women and 47% among men in LMICs (WHO, 2009) and 90% of lung cancer deaths in men and 80% in women are attributable to smoking (WHO, 2012a). Morbidity outcomes are also affected, asthma is one example where, compared to non-smokers with asthma, smokers have more severe symptoms and accelerated decline in lung function (Hedman et al., 2011; Jindal and Gupta, 2004; Lange et al., 1998) and a reduced response to corticosteroid therapy (Tomlinson et al., 2005).

There has been extensive integration of TB diagnosis and treatment within the health systems of high burden countries using the Directly Observed Treatment Short-course (DOTS) process (WHO, 2010). This offers opportunities for teachable moments to provide cessation to patients suspected of TB who also smoke (Ng et al., 2008). For example, DOTS facilitators can be trained to provide advice and counseling to patients with suspected TB (Awaisu et al., 2011; El-Sony et al., 2007).

This paper analyses data from the ASSIST trial (Siddiqi et al., 2013; Siddiqi et al., 2010) which tested a behavioral support session with (BSS+) and without bupropion (BSS), delivered by DOTS facilitators to provide smoking cessation support to patients with suspected TB. Both treatment conditions led to an eight- to nine-fold increase in continuous smoking abstinence compared to the usual care; more details can be found in the published protocol and findings of this trial (Siddiqi et al., 2013; Siddiqi et al., 2010). While the ASSIST trial shows the effectiveness of both these interventions, understanding which factors are likely to predict
smoking cessation in patients suspected of TB will aid the tailoring of such cessation interventions in future.

2. METHODS

We conducted secondary analysis of data from the ASSIST trial [Siddiqi et al., 2013] to identify predictors of continuous and short-term abstinence, and continued smoking.

2.1 ASSIST Trial Methods

The ASSIST trial was a balanced, pragmatic, cluster randomized trial with 3 groups. We estimated that a sample size of 1320 participants would be required to provide 80% power (2-sided P< 0.05) to detect a difference of at least 10% in continuous abstinence, assuming a 10% continuous smoking abstinence rate among control participants [Hughes et al., 2007; Lancaster and Stead, 2005] and adjusting for cluster effect using an intra-class correlation coefficient of 0.036 [Parker et al., 2005]. With 33 clusters (11 in each group) and assuming a 20% attrition rate, we needed 50 participants per cluster. We set a non-inferiority margin of difference of 5% between the intervention groups, which was based on a smoking cessation non-inferiority trial and has also been recognized as an acceptable effect size for any new smoking cessation intervention [Lindson et al., 2009; Walker et al., 2011; West, 2007]. Analyses were done in general accordance with the CONSORT (Consolidated Standards of Reporting Trials) statement and its extension to cluster and pragmatic trials [Campbell et al., 2004; Zwarenstein et al., 2008].

Thirty-eight primary and secondary health care centers registered as diagnostic centers by the TB program in Jhang and Sargodha districts of Pakistan were invited to participate in the ASSIST trial between 2010 and 2011; 33 centers agreed to participate. We randomly allocated health centers by using a simple stratified randomization procedure to achieve a balance of urban and rural health centers across trial groups. A researcher who was blinded to center identity used computer generated random-number lists to generate the allocation sequence.
The study enrolled 1,955 patients aged 18 years or older with suspected pulmonary TB (cough for >3 weeks without any other cause as diagnosed by a physician) who were also regular tobacco smokers (>1 cigarette/hookah session a day). TB was diagnosed by physicians as per Pakistan’s National TB Program guidelines [NTP, 2015]. Current guidelines recommend all adult patients suspected of having pulmonary TB to have at least two sputum specimens examined for Acid Fast Bacilli (AFB) smear microscopy. Based on the microscopy results, pulmonary TB cases are classified as Sputum smear positive TB patient (Bacteriological positive B+ive) and Sputum smear negative TB patient (clinical diagnosed). Smear-positivity and grade indicates relative bacterial burden and correlates with disease presentation. Clinical diagnosis of active TB is made by a clinician or other medical practitioner on the basis of X-ray abnormalities or suggestive histology and extra-pulmonary cases without laboratory confirmation [NTP, 2015].

Patients eligible for the trial were referred by the physicians to the DOTS facilitators who are paramedics responsible for registering new patients, providing education, and supervising their treatment, at the health center. The DOTS facilitators’ followed up enrolled patients in the BSS+ and BSS groups at 1, 5, and 25 weeks after first contact and control patients at 5 and 25 weeks. The primary outcome was continuous smoking abstinence, defined as an expired carbon monoxide (CO) measurement (piCO Smokerlyzer, Bedfont Scientific, Maidstone, United Kingdom) of 9 ppm or less (Russell standard) [West, 2005] at the 5- and 25-weeks follow-up visits.

The DOT facilitators recorded and reported any adverse events, serious or otherwise, in all centers. Trial monitoring procedures included telephone calls to randomly selected participants (≥2 per center each month) to confirm whether CO tests had been done, verify data collected, and check for protocol violations.
A questionnaire was developed for collecting patient information at baseline (including demographic details, tobacco use pattern, past quit history, assessment of nicotine dependence, assessment of willingness to quit and assistance with quitting) and recording details of quit date, bupropion dispensing and CO measurements and at 1 week follow-up in case of intervention groups, where further assistance with quitting was provided in the form of behavioral support for withdrawal symptoms, recording adverse effects of bupropion (if encountered) and its additional doses. The questionnaire was originally developed in English, using standard questions like Fagerstrom Test for Nicotine Dependence and then translated to Urdu language in which it was administered to the trial participants. The Urdu translated versions of the questionnaire were pilot tested in health centers in both districts before proceeding with definitive recruitment of participants.

2.2 The ASSIST smoking cessation intervention

Those who consented to participate were randomized to three groups: patients in one group received two brief behavioral support sessions (BSS group), patients in the second group received two brief BSS plus 7 weeks of bupropion therapy (BSS+ group), and patients in the control group received usual care. Given the lack of any routine advice or educational materials in Pakistan, we provided a self-help leaflet on smoking cessation to all participants (for details, refer to the Supplement 2, available at www.annals.org; Siddiqi et al., 2013).

The support sessions consisted of two structured one-to-one consultations based on the World Health Organization’s “5 As Approach” (for details, refer to the Supplement 1, available at www.annals.org; Siddiqi et al., 2013). The aim of the first 30 minute consultation was to assist smokers who were willing to set a quit date (a week after the first contact) by encouraging them to see themselves as non-smokers, to plan for their quit day and to prepare them for the initial stages of the quit attempt. The second 10 minute one-to-one consultation was scheduled for the patient’s quit date and provided an opportunity for follow-up and review of progress. The activities within each of these consultations have
been mapped to the behavior change techniques considered effective in smoking cessation

(Michie et al., 2011).

In addition to BSS, participants in the BSS+ group also received sustained-release bupropion, 75 mg/day for the first week and 150 mg/day thereafter. The intervention was delivered by the DOTS facilitators, who received one full day of training on the intervention protocol and delivery tools.

2.3 Analysis of Cessation Predictors

Participants were classified as having achieved ‘short-term abstinence’ if they were abstinent at their week 5 appointment, but smoking at week 25. Participants abstinent at both week 5 and week 25 appointments were recorded to have ‘continuous abstinence’. Participants who were found to be smoking at both week 5 and 25 were recorded as ‘continuous smokers’. A fourth group consisting of participants found to be smoking at week 5 but not at week 25 was not included in the analysis.

We analyzed data from the ASSIST trial to identify the factors that predicted patients’ quitting behavior in three circumstances; firstly identifying the factors that predict continued abstinence compared to those who continue smoking; secondly those who are able to at least achieve short-term abstinence compared to those that continue smoking and thirdly identifying factors that predict continuous abstinence compared to those only able to achieve short term abstinence. All analyses were performed using SAS, version 9.4 (SAS Institute, Cary, North Carolina).

Generalized estimating equations (GEE in SAS PROC procedure GENMOD) were used to derive the estimates, using a log link and repeated statement (to account for clustering effects within health centers). Multiple Poisson regression analyses with full stepwise elimination procedures were performed to identify the predictors of continuous and short-term abstinence when compared to continued smoking and the predictors of continuous abstinence compared to short-term abstinence.
A number of self-reported variables were measured at baseline. Social and demographic measures included in the analysis as potential predictors were age, gender, monthly household income, occupation, other smokers at home or workplace, the presence and number of children at home. Manual occupation included farming and unskilled labor; non-manual included business and office work and a third ‘other’ category, which was unspecified. Smoking related measures included duration, quantity and form of tobacco smoking. In the setting in Pakistan the form of smoking was hookah, cigarettes or both. Patient’s TB diagnosis status was also included in this analysis.

Baseline data for the categorical variables were summarized by frequencies and percentages while continuous variables were summarized by means/medians and standard deviations/inter-quartile ranges. Given the known effect of the behavioral support intervention (with or without bupropion vs. usual care) on continuous smoking abstinence [Siddiqi, 2013], the intervention was included in the regression model to enable accurate estimates of predictor variables over and above the effect of the intervention itself. Those lost to follow-up were not included in this analysis. Bivariate associations (after adjusting for the intervention) between the potential covariates and the outcomes were assessed for inclusion in the multivariable regression models. The potential covariates assessed were duration, quantity and forms of smoking; gender, age, age when started smoking, monthly household income, occupation, presence and number of children at home, presence of smokers at home or workplace, and TB diagnosis. Bivariate factor associations with the outcomes resulting in a p-value less than or equal to 0.1 were considered for further model building. Covariate-covariate interactions were also explored and only those with statistically significant interactions were included in the multivariable models to adjust for their influence.
The relative risks (RRs) and corresponding 95% confidence intervals (CI) were presented for the bivariate associations and the final best fit model.

3. RESULTS

The results of the main trial are reported in detail elsewhere [Siddiqi, 2013], in summary behavioral support, alone or in combination with bupropion, was effective in achieving continuous smoking abstinence at 6 months compared with usual care (RR for BSS+, 8.2 [95% CI, 3.7 to 18.2]; RR for BSS, 7.4 [CI, 3.4 to 16.4]). The association became stronger after adjustment for potential confounders, such as age, sex, income, smoking duration, and quantity smoked per day (RR for BSS+, 9.3 [CI, 4.0 to 21.6]; RR for BSS, 8.5 [CI, 3.7 to 19.6]). However, the equivalence of effect between the BSS+ and BSS groups (RR, 1.1 [CI, 0.5 to 2.3]) could not be established. Confidence intervals were wider than the predefined non-inferiority margin.

The majority of the trial participants were male, smoked cigarettes and were engaged in manual labor and farming work. As the trial recruited participants with suspected TB, only 5.6% of these had confirmed TB at baseline. Baseline characteristics of all individuals (N=1573) and of those showing continuous abstinence (n=581), short-term abstinence (n=155) or continuous smoking (n=837), are presented in Table 1. Out of 1955 participants, 268 participants who were smoking at week 5 but not at week 25 were not considered relevant to the study aims and therefore excluded from this analysis. Thus, the total number of participants for this secondary analysis was 1573. The average age and duration of smoking was lower among those achieving continuous abstinence (39.9, SD: 14.0 and 19.2, SD: 13.3) and short-term abstinence (40.6, SD: 11.8 and 20.5, SD: 11.0) groups than among the continuous smoking group (41.9, SD: 13.1 and 21.5, SD: 12.5). Those participants who were abstinent in the short-term, but did not achieve continuous abstinence, either smoked hookah (89%, 138/155) or both hookah and cigarettes (11%, 17/155); none of this group smoked only cigarettes. In contrast, the majority of those in the continuous abstinence
(65%, 377/581) and continuous smoking (62%, 516/837) groups were exclusive cigarette smokers. There were more TB patients among the continuous abstinence (9.8%, 57/581) group compared to those in the short-term abstinence (2.6%, 4/155) and continuous smoking (3.1%, 26/837) groups.
### Table 1: Baseline participant characteristics by comparison groups as analyzed in the secondary data analysis- ASSIST Pakistan trial

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Continuous abstinence (n= 581)</th>
<th>Short-term abstinence (n= 155)</th>
<th>Continuous Smoking (n= 837)</th>
<th>Total (n= 1573)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men, n (%)</td>
<td>544 (93.6)</td>
<td>145 (93.6)</td>
<td>803 (95.9)</td>
<td>1492 (94.9)</td>
</tr>
<tr>
<td>Mean age, years (SD)</td>
<td>39.9 (14.0)</td>
<td>40.6 (11.8)</td>
<td>41.9 (13.1)</td>
<td>41.0 (13.4)</td>
</tr>
<tr>
<td>Median (monthly) household income, US $ (IQR)</td>
<td>70.9 (63.3)</td>
<td>81.1 (60.8)</td>
<td>81.1 (50.7)</td>
<td>81.1 (55.7)</td>
</tr>
<tr>
<td>Mean age when started smoking, years (SD)</td>
<td>20.8 (7.3)</td>
<td>20.1 (6.8)</td>
<td>20.3 (6.4)</td>
<td>20.4 (6.8)</td>
</tr>
<tr>
<td>Mean duration of smoking, years (SD)</td>
<td>19.2 (13.3)</td>
<td>20.5 (11.0)</td>
<td>21.5 (12.5)</td>
<td>20.6 (12.7)</td>
</tr>
<tr>
<td>Median cigarette and hookah** smoked per day, n (IQR)</td>
<td>20.0 (15.0)</td>
<td>20.0 (14.0)</td>
<td>20.0 (17.0)</td>
<td>20.0 (16.0)</td>
</tr>
<tr>
<td>Forms of smoking, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exclusive hookah smokers</td>
<td>76 (13.1)</td>
<td>16 (10.3)</td>
<td>83 (9.9)</td>
<td>175 (11.1)</td>
</tr>
<tr>
<td>Mixed (hookah + cigarette smokers)</td>
<td>128 (22.0)</td>
<td>35 (22.6)</td>
<td>238 (28.4)</td>
<td>401 (25.5)</td>
</tr>
<tr>
<td>Exclusive cigarette smokers</td>
<td>377 (64.9)</td>
<td>104 (67.1)</td>
<td>516 (61.7)</td>
<td>997 (63.4)</td>
</tr>
<tr>
<td>Presence of other smoker/s at home, n (%)</td>
<td>309 (53.2)</td>
<td>89 (57.4)</td>
<td>472 (56.4)</td>
<td>870 (55.3)</td>
</tr>
<tr>
<td>Presence of other smoker/s at workplace, n (%)</td>
<td>474 (81.6)</td>
<td>137 (88.4)</td>
<td>705 (84.2)</td>
<td>1316 (83.7)</td>
</tr>
<tr>
<td>Presence of children at home, n (%)</td>
<td>415 (71.4)</td>
<td>114 (73.6)</td>
<td>576 (68.8)</td>
<td>1105 (70.3)</td>
</tr>
<tr>
<td>Number of children at home, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>92 (15.8)</td>
<td>16 (10.3)</td>
<td>117 (14.0)</td>
<td>225 (14.3)</td>
</tr>
<tr>
<td>2</td>
<td>115 (19.8)</td>
<td>34 (21.9)</td>
<td>184 (22.0)</td>
<td>333 (21.2)</td>
</tr>
<tr>
<td>3</td>
<td>98 (16.9)</td>
<td>24 (15.5)</td>
<td>133 (15.9)</td>
<td>255 (16.2)</td>
</tr>
<tr>
<td>4</td>
<td>60 (10.3)</td>
<td>18 (11.6)</td>
<td>68 (8.1)</td>
<td>146 (9.3)</td>
</tr>
<tr>
<td>5 or more</td>
<td>50 (8.6)</td>
<td>22 (14.2)</td>
<td>75 (9.0)</td>
<td>147 (9.4)</td>
</tr>
<tr>
<td>Occupation, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manual work*</td>
<td>358 (61.6)</td>
<td>106 (68.4)</td>
<td>567 (67.7)</td>
<td>1031 (65.5)</td>
</tr>
<tr>
<td>Non-manual work</td>
<td>150 (25.8)</td>
<td>38 (24.5)</td>
<td>204 (24.4)</td>
<td>392 (24.9)</td>
</tr>
<tr>
<td>Other</td>
<td>68 (11.7)</td>
<td>9 (5.8)</td>
<td>57 (6.8)</td>
<td>134 (8.5)</td>
</tr>
<tr>
<td>Diagnosed with Tuberculosis</td>
<td>57 (9.8)</td>
<td>4 (2.6)</td>
<td>26 (3.1)</td>
<td>87 (5.5)</td>
</tr>
</tbody>
</table>

Note: SD stands for Standard Deviation; and IQR for Inter-Quartile range

* Manual work includes occupations: farmer and laborer; non-manual work includes occupations: office worker and businessman

**1 hookah session = 2 cigarettes [Eisenberg, 2009]
3.1 Continuous abstinence compared to continued smoking

As can be seen in Table 2, over and above the intervention effect, those who were older in age and smoked higher quantities of tobacco were less likely to be continuously abstinent compared to those who were younger in age and smoked less. Participants having one or more smokers at their workplace were less likely to achieve continuous abstinence than those without smokers at their workplace. Those diagnosed with TB were more likely to achieve continuous abstinence than those who were diagnosed with some other respiratory condition.

3.2 Short-term abstinence compared to continued smoking and to continuous abstinence

Those who smoked higher quantities of tobacco were less likely to be short-term abstainers and more likely to continue smoking compared to those who smoked less, RR 0.976(0.96-0.99) p = 0.0003. None of the other factors analyzed to compare short-term abstinence with continued smoking and then with continuous abstinence achieved statistical significance.
Table 2. Variables predicting carbon monoxide verified continuous abstinence versus continued smoking - ASSIST Pakistan trial (2010-2011)

<table>
<thead>
<tr>
<th>Predictor variables</th>
<th>Bivariate model:</th>
<th>Multivariable model**:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Relative Risk (95% CI)</td>
<td>Relative Risk (95% CI)</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>p-value</td>
</tr>
<tr>
<td>Received Behavioral support plus bupropion vs. usual care</td>
<td>6.08 (2.54-14.56)</td>
<td>4.88 (2.56-9.32)</td>
</tr>
<tr>
<td></td>
<td>&lt;.0001*</td>
<td>&lt;.0001*</td>
</tr>
<tr>
<td>Received Behavioral support only vs. usual care</td>
<td>5.45 (2.27-13.09)</td>
<td>4.95 (2.62-9.38)</td>
</tr>
<tr>
<td></td>
<td>0.0002*</td>
<td>&lt;.0001*</td>
</tr>
<tr>
<td>Age (at enrolment)</td>
<td>0.993 (0.987-0.999)</td>
<td>0.97 (0.95-0.98)†</td>
</tr>
<tr>
<td></td>
<td>0.0393*</td>
<td>0.0001*</td>
</tr>
<tr>
<td>Duration of smoking</td>
<td>0.99 (0.985-0.998)</td>
<td>1.01 (0.997-1.02)†</td>
</tr>
<tr>
<td></td>
<td>0.0151*</td>
<td>0.1732</td>
</tr>
<tr>
<td>Quantity † of hookah and cigarette smoked (daily)</td>
<td>0.985 (0.98-0.99)</td>
<td>0.975 (0.97-0.98)</td>
</tr>
<tr>
<td></td>
<td>0.0003†</td>
<td>&lt;.0001†</td>
</tr>
<tr>
<td>Presence of other smoker/s at workplace</td>
<td>0.87 (0.76-0.99)</td>
<td>0.88 (0.77-0.99)</td>
</tr>
<tr>
<td></td>
<td>0.0378*</td>
<td>0.0394*</td>
</tr>
<tr>
<td>Diagnosed with Tuberculosis</td>
<td>1.25 (1.07-1.45)</td>
<td>1.27 (1.10-1.47)</td>
</tr>
<tr>
<td></td>
<td>0.0041†</td>
<td>0.0014†</td>
</tr>
</tbody>
</table>

†1 hookah session = 2 cigarettes
* P-value <0.05
** Adjusted for both interventions, age, duration of smoking, quantity smoked, the presence of other smokers at workplace and diagnosis of TB in regression model.
† Interaction between duration of smoking and quantity (of hookah and cigarette) smoked was accounted for in analysis; p-value <.0001
‡ Interaction between participant age and age of starting smoking was adjusted in analysis; p-value 0.0001
4. DISCUSSION

4.1 Summary of findings

We found that a confirmed TB diagnosis was a significant predictor of continuous abstinence at 25 weeks. Smokers who were older, smoked high quantities, were in close proximity to smokers at work were more likely to continue smoking. Factors that were not associated with either continuous or short-term abstinence were gender, form of tobacco smoked, household income and having children at home. This is the first paper to use trial data to identify the predictors of continuous and short-term abstinence among patients suspected of TB. The low-income context in which the study was set has great relevance to other low-income countries with a high TB burden.

While a detailed discussion of the results can be found in Siddiqi et al., 2013 it is important to note here the effectiveness of behavioral support, both with and without bupropion when compared with usual care in achieving smoking abstinence at 25 weeks. While we were unable to confirm the non-inferiority of behavioral support compared to behavioral support with bupropion, the estimated cost of behavioral support ($2.50 per participant) which was approximately one tenth that of behavioral support plus bupropion ($20.90 per participant) favors its consideration for adoption in the routine TB care for maximizing patient benefit. Low and middle-income countries, where access to and affordability of medicine is constrained, might favor an inexpensive non-pharmacologic intervention that can be delivered by existing staff.

4.2 Interpretation and implications of findings

The existing literature identifies a range of possible predictors of both continuous and short-term abstinence. Our findings concur with previous evidence that gender does not predict cessation Caponnetto and Polosa, 2008 Vangeli et al., 2011. Unlike previous studies Vangeli et al., 2011 we did find age to be a predictor of continuous abstinence. When considering the socio-familial context, it appears that close proximity to smokers,
particularly at work, may potentially undermine smokers’ ability to achieve continuous abstinence and again, this is also in concordance with other studies (Caponnetto and Polosa, 2008; Okechukwu et al., 2013). Similar to previous studies (Okechukwu et al., 2013; Vangeli et al., 2011), having a child in the home was not a significant predictor of abstinence. The ASSIST behavioral support included messages on the harmful effects of Second-Hand Smoke on children’s health. However, we could not confirm the fidelity to delivery of all messages (by all providers) included in the BSS resource as adherence to intervention content was not assessed. This is reflected in the main trial results (Siddiqi et al., 2013) where a wide heterogeneity in cessation rates was observed between health centers, which might be attributed to the variability in delivery of intervention content by the DOTS facilitators. Measuring fidelity to smoking cessation interventions in effectiveness studies, in future, could aid identification and replication of active ingredients of such complex interventions (Moore et al., 2015). Part of the role of DOT facilitators is to educate the patient on infection control within the home, and it may be that this provides an opportunity for emphasizing the dangers of second hand smoke within the home.

Psychological and physiological factors that have been studied include depression, anxiety and nicotine dependence. Vangeli et al’s (2011) review shows that of all these factors it is only measures of nicotine dependence, which show the strongest and most consistent association with continuous abstinence. Our study concurs with this evidence; with a lower quantity smoked predicting continuous abstinence.

A key influence on continuous and short-term abstinence that is not explored in Vangeli et al’s review or many other cessation studies is the influence of ill health and disease. Significant associations have been found between continuous abstinence and being diagnosed with smoking-related cancers (Berg et al., 2013; Boudreaux et al., 2007; Eng et al., 2014; Hayran et al., 2013). Perceived severity of disease may also play a role in the continuing abstinence. Health care use, in itself, does not appear to
be associated with continuous abstinence (Beard et al., 2013). Our study highlights TB diagnosis as a predictor of continuous abstinence. Being diagnosed with TB clearly provides a valuable ‘teachable moment’ for smoking cessation. McBride et al. (McBride et al., 2003) identified three characteristics that influence the success of utilizing a teachable moment for smoking cessation success; namely the extent to which the health event 1) increases perceptions of personal risk and outcome expectancies, 2) prompts strong affective or emotional responses, and 3) redefines self-concept or social role. In the case of TB, while treatment success has improved significantly in recent years (WHO, 2013b), its diagnosis still raises concerns in terms of health outcomes, stigma and fear of transmission. The stigma associated with TB is well documented, and this often leads to changes in conceptions of self and social role (Christodoulou, 2011). This study reinforces the message from previous studies of the effectiveness of targeting TB patients in smoking cessation programs (Awaisu et al., 2011; El-Sony et al., 2007; Ng et al., 2008). McBride et al.’s (McBride et al., 2003) characteristics of ‘teachable moments’ may also explain why those with a respiratory condition other than TB were not so successful in their cessation. It is likely that patients with other respiratory conditions (such as asthma and COPD) do not face the same level of stigmatization and social affects as those with TB. These conditions do not stimulate the same level of fear for patients in terms of prognosis and infecting others. We found that while all the participants in our study had respiratory symptoms, those given the ‘all-clear’ for TB were less likely to successfully abstain from smoking. It would appear that the ‘teachable moment’ provided by this interaction with TB services is nuanced by the nature of the TB diagnosis. While it may be the case that those without TB struggle with their quit, this knowledge can be put to good use by health workers who may be able to tailor their advice to these patients reinforcing the benefits of quitting regardless of TB status. This might help to maintain abstinence among patients without a TB diagnosis.
Given that drug-sensitive TB is successfully treated among the majority of patients - in 2013 Pakistan’s National TB Program achieved a treatment success rate of 91% [NTP, 2013] - the longevity of cessation among these patients has been questioned [Ng et al., 2008]. It could be argued that once their TB is cured and these characteristics of a ‘teachable moment’ no longer apply then the patient’s motivation to maintain abstinence may dwindle. The patient may also take up social activities that they had discontinued during treatment due to stigma and the fear of infecting others. This could increase interaction with other smokers, undermining their will power to maintain abstinence. The longevity of abstinence post-TB cure is an area for exploration in future research.

4.3 Strengths and limitations

Unlike much previous work on smoking cessation predictors [Caponnetto and Polosa, 2008; Okechukwu et al., 2013; Vangeli et al., 2011] we have used trial data in which outcomes were biochemically-validated in accordance with the Russell Standard [West, 2005] and measured on more than one occasion. This allowed us to examine not only the predictors of a continuous abstinence at 5 and 25 weeks, but also the predictors of short-term abstinence at 5 weeks. The majority of previous studies identifying predictors of cessation have been conducted in high-income contexts. Given the high levels of smoking prevalence in many low-income contexts [WHO, 2013a], understanding predictors of cessation in these contexts provides valuable insights to inform interventions.

The limitations of the trial have been discussed elsewhere [Siddiqi et al., 2013]. As this paper presents a post-hoc analysis of the trial data there are several variables that would have added to this analysis but were not collected in the original trial e.g. details of the ‘other’ occupation category, classification of respiratory conditions diagnosed among the non-TB patients and the limited assessment of nicotine dependence, given that the Fagerström Tolerance Questionnaire [Fagerstrom and Schneider, 1989] was only used with participants.
in the intervention sites. However, smoking quantity and duration does provide some indication of the effects of dependence.
5. CONCLUSIONS

Predictors of cessation among smokers suspected with TB are similar to general smokers. Over and above the effects of the intervention, those with a confirmed diagnosis of TB were more likely to achieve continuous abstinence than those without. Those with other respiratory conditions may require further support in achieving smoking cessation. Our study highlights the importance of ensuring opportunities to take advantage of these ‘teachable moments’ are maximized within TB programs. This is particularly important in low- and middle-income contexts where limited resources must be targeted at cessation interventions most likely to be effective.

Declaration of interests

None
References


Hayran, M., Killickap, S., Elkiran, T., Akbulut, H., Abali, H., Yuce, D., Kilic, D., Turhal, S., 2013. Smoking habits of relatives of patients with cancer: cancer diagnosis in the family is an


