REVIEW ARTICLE

A systematic review of the effectiveness of smoking cessation interventions among patients with tuberculosis

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Smoking is a significant risk factor for morbidity and mortality, particularly among patients with tuberculosis (TB). Although smoking cessation is recommended by the World Health Organization and the International Union Against Tuberculosis and Lung Disease, there has been no published evaluation of smoking cessation interventions among people with TB. The purpose of this review was to synthesize the evidence on interventions and suggest practice, research and policy implications. A systematic review of the literature identified 14 peer-reviewed studies describing 13 smoking cessation interventions between 2007 and 2017. There were five randomized controlled trials, three non-randomized interventions, and five prospective cohort studies. The primary types of interventions were brief advice (*n* = 9), behavioral counseling (*n* = 4), medication (*n* = 3), and community-based care (*n* = 3). A variety of health care workers (HCWs) implemented interventions, from physicians, nurses, clinic staff, community health workers (CHWs), as did family members. There was significant heterogeneity of design, definition of smoking and smoking abstinence, and implementation, making comparison across studies difficult. Although all smoking interventions increased smoking cessation between 15% and 82%, many studies had a high risk for bias, including six without a control group. The implementing personnel did not make a large difference in cessation results, suggesting that national TB programs may customize according to their needs and limitations. Family members may be important supporters/advocates for cessation. Future research should standardize definitions of smoking and cessation to allow comparisons across studies. Policy makers should encourage collaboration between tobacco and TB initiatives and develop smoking cessation measures to maximize results in low-resource settings.

Tuberculosis (TB) is the leading cause of death from infectious disease worldwide.[1] Smoking is a significant driver of the TB epidemic, accounting for 8% of TB cases among the 30 countries with the highest TB burden.[1,2] Smokers have increased risk for developing TB and negative treatment outcomes.[3,4] This may be due to biologic processes that impact lung health, as well as social factors associated with tobacco use, such as alcohol use.[3,5] Ongoing tobacco use increases the risk of negative TB outcomes, primarily TB relapse or recurrence.[4,6]

Of the one billion smokers worldwide, 80% reside in low- and middle-income countries (LMICs), many of which also have a high TB burden.[7] Provision of smoking cessation services during anti-tuberculosis treatment is critical to reduce the negative effects of smoking on TB treatment and lifelong health; patients are also more likely to change their smoking behavior during TB treatment, underscoring this period as a critical intervention opportunity for cessation.[8–10] In 2007, the World Health Organization (WHO) and the International Union Against Tuberculosis and Lung Disease (The Union) recommended that smoking cessation interventions be added to National TB Programs (NTPs) using the '5As' approach: 1) Ask the patient about smoking; 2) Advise about the risk of smoking; 3) Assess willingness to stop smoking; 4) Assist patient to stop smoking; and 5) Arrange for follow-up; or a modified version called the ABC approach, i.e., A, Ask about smoking; B, provide Brief advice; C, provide Cessation support.[9,11] These frameworks provide a foundation for NTPs to integrate smoking cessation interventions within TB care.

Smoking interventions have been implemented as part of NTPs since 2007 in LMICs such as Sudan, Pakistan, and South Africa, but no systematic review has explored the impact of these programs on smoking cessation among TB patients. The purpose of this systematic review was to consolidate existing evidence on smoking cessation interventions among TB patients in LMICs and summarize the practice, policy, and research implications of these findings to improve smoking cessation efforts.

METHODS

Search strategy

A systematic review of peer-reviewed literature on smoking cessation interventions among TB patients was conducted using PRISMA (Preferred reporting items for systematic reviews and meta-analyses) guidelines in May 2017.[12] The following databases were used: PubMed, the Cumulative index to Nursing and Allied Health Literature, SCOPUS, Web of Science, Cochrane, and Embase. Search criteria were developed using Medical Subject Headings (MeSH) and non-Mesh terms which were adapted to the specific database as follows:

TB: tuberculosis[Mesh] OR tuberculo* OR 'TB'

Smoking cessation: 'Tobacco Use Cessation'[Mesh] OR 'Smoking Cessation'[Mesh] OR 'Tobacco Use Cessation Products'[Mesh] OR 'Smoking/prevention and control'[Mesh] OR 'Smoking/therapy'[Mesh] OR 'Bu-
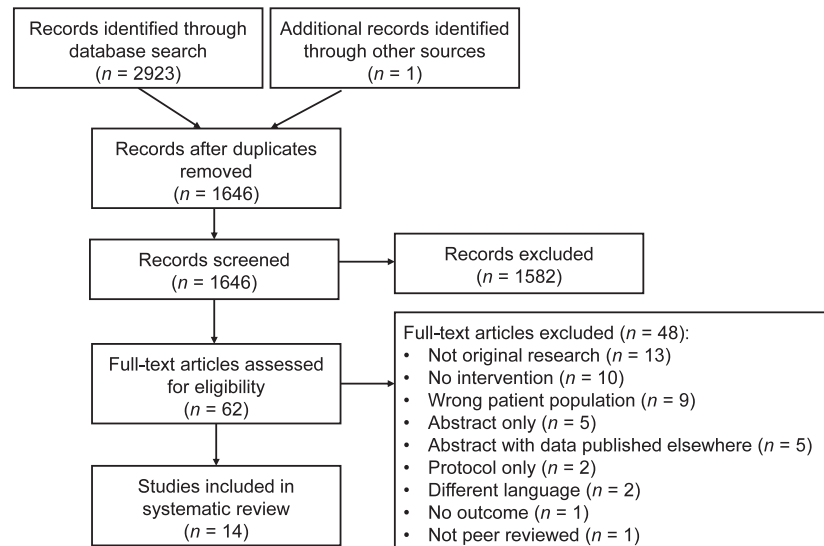
FIGURE   Literature review flowchart based on PRISMA guidelines[12]

propion'[Mesh] OR 'Varenicline'[Mesh] OR 'Clonidine'[Mesh] OR 'Nortriptyline'[Mesh] OR 'smoking cessation'[tiab] OR 'smoking cessations'[tiab] OR (('tobacco products'[Mesh] OR 'Tobacco Use'[Mesh] OR 'Smoking'[Mesh] OR 'vaping'[Mesh] OR 'nicotine'[mesh] OR smok*[tiab] OR 'tobacco'[tiab] OR cigar*[tiab] OR e-cig*[tiab] OR 'nicotine'[tiab] OR 'hookah'[tiab] OR 'pipe'[tiab] OR 'vaping'[tiab] OR 'vape'[tiab]) and (quit*[tiab] OR ceas*[tiab] OR cessation*[tiab] OR stop*[tiab] OR suspend*[tiab] OR desist*[tiab] OR end*[tiab] OR break*[tiab] OR cutoff*[tiab] OR termin*[tiab] OR discontinu*[tiab] OR abstin*[tiab] OR 'dehabituation'[tiab] OR 'Nicorette'[tiab] OR 'gum'[tiab] OR 'NRT'[tiab] OR patch*[tiab] OR 'bupropion'[tiab] OR 'varenicline'[tiab] OR 'nortriptyline'[tiab] OR 'clonidine'[tiab] OR 'chantix'[tiab] OR 'champix'[tiab] OR 'wellbutrin'[tiab] OR 'Zyntabac'[tiab] OR 'Quomen'[tiab] OR 'Zyban'[tiab] OR 'Amfebutamone'[tiab]))

Inclusion criteria
Peer-reviewed journal articles were included if they evaluated any smoking cessation intervention among patients with suspected or confirmed TB. Any studies that did not report on smoking cessation outcomes were excluded. The search included publications written in English, French, Spanish, Portuguese, and Korean.

Procedure
All retrieved citations were imported into Covidence® (Cochrane, Melbourne, VIC, Australia) and duplicates were removed. Two reviewers (EW, JL) independently reviewed titles and abstracts. Differences concerning full-text inclusion were resolved through consensus. The reviewers then independently extracted data on participant characteristics, intervention characteristics, smoking cessation outcome, and other qualitative or quantitative information on the implementation of the intervention. Risk of bias was assessed using the Cochrane Risk of Bias tool for intervention studies.[13] Results were compared and discrepancies were resolved through discussion. Due to the heterogeneity of comparison groups among the randomized controlled trials, the results were synthesized, but a meta-analysis was not conducted.

Ethics
Institutional review board approval was not required for this literature review.

RESULTS
After removing duplicates, the search resulted in 1646 articles for review (Figure). A total of 14 articles were included based on the inclusion/exclusion criteria for this review. Although there were no country-based exclusion criteria, all studies took place in LMICs. As two of the articles were based on the same intervention but compared outcomes for different groups, there were a total of 13 different interventions.

Study characteristics
Included studies were conducted across 11 different countries and published between 2007 and 2017. Study designs included three randomized controlled trials,[14–16] two cluster randomized controlled trials,[17,18] five prospective cohort studies,[19–23] and three non-randomized intervention studies[24–26] (Table 1). Three of the studies were intended as feasibility or pilot studies focusing on initial implementation of smoking cessation.[19,24,25]

Settings for the studies varied, with the majority (n = 7) conducted in primary health centers. All but one (Kumar et al.[17]) were conducted as multisite studies, and most (n = 11) included patients with TB on treatment. Only Kumar et al.[17] included some patients living with the human immunodeficiency virus (HIV) with no TB in addition to TB patients. Siddiqi et al. included patients with presumptive but not confirmed TB.[18] Study sample sizes ranged from 28 to 1955. The mean age of the participants, where reported, ranged from 38 to 47 years. Most participants (range 60.7–100%) were male; five studies included only male participants. Only two studies included TB outcome measures. Awaisu et al. found higher rates of successful TB treatment outcomes in the intervention group (79.5% vs. 78.3%, $P = 0.0031$),[26] whereas El Sony et al. found no differences.[24]

The operational definition of smoking ranged from any self-reported smoking to those who had smoked at least 20 packs in their lifetime (Table 2). The majority (n = 11) included patients who smoked cigarettes or tobacco only, while three included hookah as well.[18,23,27] The outcome definition of smoking cessation was highly variable (Table 2). Six of the 14 studies used exhaled carbon monoxide (CO) to define smoking cessation, some in addition to self-report and cotinine. Two studies used cotinine measurement, one in saliva and the other urine, to confirm

TABLE 1 Study and participant characteristics*

First author, year, reference	Setting	Sample size *n*	Guiding framework	Participant characteristics			Intervention components	Dosing	Service point and provider	Measurement of smoking cessation	Provider training: content and duration	Findings
				Sex (% male)	Age mean							

Randomized controlled trial design

First author, year, reference	Setting	Sample size *n*	Guiding framework	Sex (% male)	Age mean	Intervention components	Dosing	Service point and provider	Measurement of smoking cessation	Provider training: content and duration	Findings
Aryanpur, 2016[16]	Iran	210	WHO 5As; Union 2008	Control group: 90.2%; BSS: 90.3%; BSS + medication: 90.0%	Control group: 47.4 ± SD 16.3; BSS: 45.5 ± SD 16.4; BSS + medication: 45.1 ± SD 15.8	Control group: SOC; BSS group: behavioral counseling; BSS+ group: behavioral counseling plus medication	4 sessions over 2 weeks; 9 weeks of medication	6 health centers and 1 hospital; physician	Exhaled CO	Not described	Smoking abstinence at 6 months was 71.7% in the BSS + medication group, 33.9% in the BSS group and 9.8% in controls (*P* < 0.001). Behavioral counseling increased smoked cessation (OR 7.1, 95%CI 2.7–18.7) and medication increased the effect (OR 35.3, 95%CI 13.8–90.3)
Dogar, 2014[27]	Pakistan	1955	WHO 5As	Cigarette, 98.3%; hookah, 79%; both, 95%	BSS/BSS+ medication group: <40 years, 49%; 41–70 years, 43%; >70 years, 8%. Control group: <40 years, 37%; 41–70 years, 55%; >70 years, 4%	Control group: SOC (self-help leaflet); BSS group: individual counseling; BSS + medication group: counseling plus 7 weeks of bupropion	BSS/BSS + medication groups: 2 sessions and 7 weeks of medication for the BSS + medication group	33 health centers; DOT facilitator and physician (medication)	Exhaled CO	BSS/BSS+ medication: behavior change techniques; educational flipbook of 25 slides detailing smoking harms, developing a plan, triggers for smoking, and coping strategies; 1-day training	The intervention had a greater impact on cigarette smokers than hookah smokers: BSS group in cigarette smokers (OR 5.8, 95%CI 4.0–8.5) vs. BSS in hookah smokers (OR 2.2, 95%CI 1.3–3.8); BSS+ group in cigarette smokers (OR 6.6, 95%CI 4.6–9.6) vs. BSS+ in hookah smokers (OR 2.5, 95%CI 1.3–4.7). Baseline differences between hookah and cigarette smokers may have impacted this difference
Kumar, 2017[7]	India	160	WHO 5As	100%	Control group: ≤29 years, 10%; 30–40 years, 43.7%; 41–50 years, 33.8%; >50 years, 12.5% Intervention group: ≤29 years, 11.2%; 30–40 years, 56.3%; 41–50 years, 27.5%; >50 years 5%. Mix of patients with HIV, TB-HIV and TB only	Control group: brochure + counseling by a counselor; Intervention group: brochure + advice from a physician and family member involvement	Control group: 1 session with counselor; Intervention group: 1 session with physician	TB research center; physician	Self-report; exhaled CO	Use of WHO 5As; length not described	Physician advice is feasible and acceptable in people living with HIV and TB. There was no difference between MD and counselor (RR 1.2, 95%CI 0.8–1.8). Among TB patients, 40.5% of controls and 44.4% of the interventional group quit (*P* = 0.735)

TABLE 1 (*continued*)

First author, year, reference	Setting	Sample size n	Guiding framework	Participant characteristics Sex (% male)	Age mean	Intervention components	Dosing	Service point and provider	Measurement of smoking cessation	Provider training: content and duration	Findings
Louwagie, 2014[15]	South Africa	409	Motivational interviewing	Control group: 88.2%; motivational interviewing group: 91.7%	Control group: 42.3 years ± SD 10.1; motivational interviewing group: 40.3 years ± SD 10.3	Control group: brief advice by TB nurse; interventional group: brief advice by TB nurse + motivational interviewing with CHW	Control group: 1 session with 3 follow-up surveys; intervention group: 1 session with three follow-up surveys	6 TB clinics; CHW and nurse	Self-report; exhaled CO	Control group: training on brief advice; interventional group: use of motivational interviewing, 1-page motivational interviewing guide form, video-taped role play with feedback; Control group: 1-day training; intervention group: 3-day training with reinforcement training every 4 months	Self-reported 6 months sustained abstinence was 21.5% in the interventional group and 9.3% in controls (RR 2.29, 95%CI 1.4–3.92). This was similar to the results for 3-month self-reported abstinence and biochemically confirmed abstinence
Nichter, 2016[14]	Indonesia	101	WHO 5As	100%	Age not reported	Intervention group-MD: brief advice from a physician; intervention group-family: physician advice + training for family members as DOT/ smoking cessation supporter	Intervention group-MD: MD advise every visit to TB clinic (~6 months) interventional group-Family: MD advice occurred at every visit during anti-tuberculosis treatment (6 months) plus family support	5 TB centers; physician and family	Self-report confirmed by family member	Physicians: use of the modified WHO 5As and educational handout; evidence-based articles on smoking and TB. Family members: educational session on TB, adherence, and smoking cessation messages; role play to teach cessation-related to communication. Physicians 1-day training; family: 3–4 h plus 1 booster training	Physician counseling and family support led to >70% smoking cessation rates. There was no difference between the two types of interventions (Intervention group-MD, 73%; Intervention group-family, 71%; χ^2 $P > 0.05$); 30–40% of patients who quit resumed smoking within 1 year at low-moderate levels (<6 cigarettes/day)
Siddiqi, 2013[18]	Pakistan	1955	WHO 5As; behavior change	Controls: 97%; BSS group: 94%; BSS + medication group, 95%	Control group, 41.7 years ± SD 13.4; BSS group, 42.8 years ± SD 13.5; BSS + medication group, 38.3 years ± SD 12.4	Control group: SOC (self-help leaflet) BSS: individual counseling BSS + medication: counseling plus 7 weeks of bupropion	BSS/BSS + medication: 2 sessions + 7 weeks of medication for the BSS + medication group	33 health centers; DOT facilitator and physician (medication)	Exhaled CO	BSS/BSS+ medication: behavior change techniques; educational flipbook of 25 slides detailing smoking harms, developing a plan, triggers for smoking, and coping strategies; 1-day training	Behavioral support with and without medications reduced smoking (BSS, RR 8.5, 95%CI 3.7–19.6; BSS + medication, RR 9.3, 95%CI 4.0–21.6). 6-month smoking abstinence was 8.5% in controls, 41.0% in the BSS group, and 41.5% in the BSS + medication group. There was no added benefit to medications for quit rates (RR 1.1, 95%CI 0.5–2.3)

TABLE 1 (continued)

First author, year, reference	Setting	Sample size n	Guiding framework	Participant characteristics		Intervention components	Dosing	Service point and provider	Measurement of smoking cessation	Provider training: content and duration	Findings
				Sex (% male)	Age mean						
Non-randomized intervention design											
Awaisu, 2011[26]	Malaysia	120	Transtheoretical model of change and WHO 5As	Control group: 97.8%; interventional group: 100%	Control group: 45.8 years ± SD 14.4 interventional group: 41.6 years ± SD 14.4	Control group: SOC; interventional group: individual behavioral counseling with or without NRT	Intervention group: 11 sessions of counseling over 6 months; 60% of interventional group patients received NRT	5 health centers; nurse (counseling) and physician (medication)	Saliva cotinine, exhaled CO	Interventional group-nurse: experiential learning of smoking cessation messaging; mentor relationship with quit smoking clinic; didactic lectures, role-plays and video shows; 3-day training	Patients were enrolled into the intervention group based on motivation to quit, which may avoid ethical challenges to not offer an intervention. The intervention increased smoking abstinence and linearly increased until month 5 (4-week abstinence at month 6: 77.5% in the intervention group vs. 8.7% in controls; $P < 0.001$)
Campbell, 2014[25]	Nepal	246	No framework	Control group: 69% intervention group: 82%	Control group: <40 years, 37%; 41–70 years, 55%; >70 years, 4%. Interventional group: <40 years, 49%; 41–70 years, 43%; >70 years, 8%	Control group: SOC; interventional group: brief advice by HCWs	3 sessions total over TB treatment (5–10 min each)	2 TB treatment centers; TB HCW	Self-report	Intervention group: training on giving brief advice and use of expired air CO machine; 1 training course initially (length not specified) and 1 refresher course after 2 years	Simple brief advice led to 39% quit rate compared to 0% in controls ($P < 0.0001$) over 6 months within the NTP using existing staff
El Sony, 2007[24]	Sudan	513 (356 smokers)	No framework	100%	Age not provided	Control group: SOC/pamphlet; intervention group: brief advice by medical assistant	4 sessions in total over 8 months of anti-tuberculosis treatment	16 health centers; medical assistant	Self-report	Intervention group: training on smoking and TB, use of protocol and questionnaires, and use of open-ended questions to increase motivation to quit; 2-day training	Implementation of smoking cessation intervention did not negatively impact TB outcomes across the centers. It was feasible to implement and increased the quit rate to 56.3% compared with 14.3% at the control centers
Prospective cohort design											
Bam, 2015[21]	Indonesia	750 (525 smokers)	Union 2010	96.7%	15–34 years, 51.9%; 35–54 years, 36.8%; >54 years, 11.3%	All smokers: establishing a smoke-free environment at health care facilities; brief advice from DOTS worker at TB visits	5–10 min at every TB visit (approximately every month)	17 health centers; TB HCW	Self-report confirmed by family member	Use of ABC guidelines; length not described	ABC is feasible in DOTS and primary health care. The intervention led to high quit rates (41.4% at month 1 and 66.8% at month 6), greater awareness of risk of secondhand smoke, and more smoke-free homes
Kaur, 2013[23]	India	2879 (1333 smokers)	WHO 5As	89.6%	No descriptive statistics	All smokers: brief advice	Initial session and then follow-up at TB visits	All DOT centers in the district; TB HCWs	Self-report	Basic counseling skills for brief advice to stop smoking based on WHO 5As; 2-day train the trainer leading to other local workshops	The intervention was feasible in existing programming with minimal financial resources and infrastructure. Among smokers, 67.3% quit tobacco, 18.2% relapsed and 14.5% were lost to follow-up at the end of treatment

TABLE 1 (*continued*)

First author, year, reference	Setting	Sample size *n*	Guiding framework	Participant characteristics		Intervention components	Dosing	Service point and provider	Measurement of smoking cessation	Provider training: content and duration	Findings
				Sex (% male)	Age mean						
Lin, 2015[20]	China	800 (244 smokers)	Union 2008	100%	≤24 years, 6.3%; 25–44 years, 27.3%; 45–64 years, 42.7%; ≥65 years, 30.9%	All smokers: brief advice	One session at treatment initiation on the harm of smoking; education reinforced at TB follow-up visits	2 TB clinics; TB HCWs	Self-report	Integration of smoking cessation into TB care and brief advice; 1-day train the trainer leading to other local workshops	Smokers with TB were willing to quit (96%) with a 66.7% cessation rate at 6 months. Only 3% of patients (*n* = 7) relapsed at 6 months
Sereno, 2012[19]	Brazil	28	WHO 5As	60.7%	PHC1, 40 years; PHC2, 44 years	All smokers: brief advice and referral for additional support	Unspecified; 12/33 patients received the intervention	2 health centers; nurse	Self-report, urine cotinine	Use of WHO 5As; not described	Smoking cessation was feasible but framework modified from 5As to AAR (Ask, Advise, Refer) by providers to improve intervention; 15% (3/28 smokers) reported quitting after 3 months
Siddiquea, 2013[22]	Bangladesh	3134 (615 smokers)	Union ABCs	99%	38 years (range 16–77)	All smokers: brief advice at TB treatment initiation. Follow-up visits by community volunteers	One counseling session at TB treatment initiation (5–10 min) and weekly/bi-weekly field visits throughout anti-tuberculosis treatment	17 TB centers; TB HCWs, community volunteers	Self-report confirmed by family member	TB HCW: ABC method of smoking cessation intervention, including harmfulness of smoking, impact on TB, and cessation support techniques. Training on counseling methods and documentation. Community volunteers: brief advice on cessation and DOT support; length not described	Modified ABCs for brief advice is feasible and effective, with 82% smoking reduction by Month 6. High nicotine dependence and extra-pulmonary TB decreased likelihood of cessation. Community volunteers may have contributed to high quit rates

*Sources: WHO 5As;[8] Union 2008;[9] Union 2010.[10]
WHO = World Health Organization; BSS = behavioral support intervention; BSS+ = BSS + medication; SD = standard deviation; SOC = standard of care; CO = carbon monoxide; OR = odds ratio; CI = confidence interval; MD = Doctor of Medicine; RR = relative risk; HIV = human immunodeficiency virus; CHW = community health care worker; TB = tuberculosis; DOT = directly observed therapy; NRT = nicotine replacement therapy; HCW = health care worker; PHC = primary health care clinic.

TABLE 2 Definition of current smoker and smoking abstinence by study

Author, reference	Definition of current smoker	Definition of smoking cessation
Aryanpur[16]	Self-reported smoking based on WHO and Union (cited) guidelines, but not specifically mentioned	Exhaled CO <7 ppm at each measurement
Awaisu[26]	Self-reported cigarette use during TB diagnosis before enrollment in study	Urine cotinine levels between 0 and 10 (negative result); exhaled CO negative result (did not include cut-off)
Bam[21]	Self-reported smoking (even a puff) in the last 3 months	Self-reported abstinence from smoking for 3 months
Campbell[25]	Self-reported cigarette smoking at time of enrollment	Self-reported abstinence for 6 months confirmed using exhaled CO test
Dogar/Siddiqi[18,27]	>1 cigarette/hookah session a day	Exhaled CO <9 ppm
El Sony[24]	Not specified	Self-reported abstinence for <3 months, 3–6 months or >6 months
Kaur[23]	Self-reported use of any type of tobacco, including smokeless tobacco	Self-reported abstinence at the end of 6 months
Kumar[17]	Self-report of smoking at least 1 cigarette in past week	Self-reported as not currently smoking and exhaled CO <10 ppm
Lin[20]	Self-reported, smoked at least 20 packs of cigarettes in a lifetime or one cigarette/day for at least 1 year and was, at the time of the study, smoking daily or occasionally	Sustained abstinence: self-reported abstinence in the last 3 months (even a puff) Recent abstinence: self-reported abstinence for ≥7 days but <3 months
Louwagie[15]	Not specified	Self-reported ongoing abstinence ignoring the first 2 weeks since enrollment; verified in some patients using exhaled CO <10 ppm
Nichter[14]	Self-reported any smoking at time of TB diagnosis or enrollment in study (up to 10 weeks into treatment)	Self-reported abstinence of cigarettes; not clearly defined
Sereno[19]	Self-reported daily smoking at time of enrollment	Saliva cotinine levels at follow-ups; specific cut-off points not mentioned
Siddiquea[22]	Self-reported smoking in the last 2 weeks (even a puff)	Self-reported abstinence from tobacco for 2 weeks at each follow-up

WHO = World Health Organization; Union = International Union Against Tuberculosis and Lung Disease; CO = carbon monoxide; TB = tuberculosis.

self-reported smoking status. The remaining seven studies used patient self-report of smoking cessation, with two of those studies asking for family member confirmation of smoking status when possible.

Intervention characteristics

All interventions were based generally on WHO or Union smoking cessation guidelines; what varied across studies was the interventionist, the method, and the frequency. Only El Sony et al. and Nichter et al. followed patients beyond anti-tuberculosis treatment, for 12 months in total.[14,24] The other studies followed patients for 1 month (n = 1),[17] 3 months (n = 1),[19] and 6 months or to the end of anti-tuberculosis treatment (n = 10).[15,16,18,20–23,25–27] Awaisu et al. and Siddiqi et al. were the only published protocol papers that described the process of developing smoking cessation tools for the local training context and implementing a training program for staff.[27,30] A variety of HCWs delivered the interventions; many of these were directly observed therapy (DOT) providers. Physicians most often prescribed smoking cessation medications in intervention studies,[16,18,26] but two studies specifically evaluated the added effect of brief advice provided by a physician.[14,17] Of the remaining studies, the interventionists were nurses (n = 2),[19,26] trained TB staff/DOT facilitators (n = 6),[18,20,21,23–25] and community CHWs (n = 2);[15,22] one included trained family member supporters.[14]

There were four general categories of intervention: brief advice, behavioral counseling, medication, and community-based care/family support. Many of the smoking cessation services combined a number of these interventions (Table 3). Brief advice was the most common form of intervention (n = 9). This consisted typically of 5–10 min of advice on the harms of smoking, asking the person if he/she wanted to quit, and promoting cessation strategies with possible referral to smoking cessation services outside the TB clinic. The number of sessions ranged from one at the beginning of anti-tuberculosis treatment to expected brief advice sessions at every visit. Of the brief advice interventions occurring with every TB visit, only Sereno et al. reported on adherence, with 12 of 33 patients receiving any brief counseling.[19]

Behavioral counseling was the second most common form of intervention (n = 4). What differentiated behavioral counseling from brief advice was not well described, but included behavioral change training for staff, additional questions to elicit stronger patient involvement in behavior change, and longer but fewer sessions (15–30 min for typically 1–2 sessions). Awaisu et al. was the exception, with 11 behavioral counseling sessions across 6 months of anti-tuberculosis treatment.[26] There did not appear to be any correlation between the number of sessions and the success of smoking cessation, although this was difficult to evaluate given the varied study designs.

Two studies prescribed medication (bupropion) for 7 or 9 weeks as a specific intervention arm in addition to counseling,[16,18] while Awaisu et al. allowed providers to prescribe nicotine replacement therapy (NRT). Only 60% of participants received NRT.[26]

Finally, three studies involved community-based care, with either family members[14,17] or CHWs providing cessation support in the community.[22] Community-based care did not demonstrate any significant improvement in smoking cessation above routine provider advice; however, qualitative interviews suggest that family members provided sustained counseling beyond anti-tuberculosis treatment, which may have led to unmeasured improvements in quit rates.[14]

Implementation

There was a significant component of clinician training involved in the implementation of interventions (Table 1). Most training sessions lasted 1–2 days, although five of the studies did not state the

TABLE 3   Summary of components for each type of intervention

Type of intervention	Possible components	Who delivered intervention	Time required
Brief advice	Open-ended questions Information on the benefits and risk of smoking Refer to smoking cessation counselor within facility (TB or primary health care center) Advice on making homes smoke-free Encouragement to speak with their family members for understanding and support of quitting No smoking sign for home	Nurse, CHW, physician, DOT provider	Typically 5–10 min (up to 20 min) Treatment initiation Follow-up visits varied from none to every TB visit
Behavioral counseling	Motivational interview assessment and solution development Behavioral change technique based on 5 A's such as envisioning person as non-smoker Identify specific situations likely to be difficult and develop coping strategies Follow-up on the set quit date to review progress	CHW, DOT provider	15–30 min initial session Shorter follow-up sessions
Medication	Nicotine replacement therapy Bupropion (7–9 weeks)	Physician	Consult for initial prescription and follow-up to monitor for side effects
Community-based care	Information on the benefits and risk of smoking Proactive support to quit and maintain abstinence including smoke-free home	CHW, family members	With community health visits weekly or monthly Ongoing with family member, including post anti-tuberculosis treatment

TB = tuberculosis; CHW = community health care worker; DOT = directly observed therapy.

duration of training. Kaur et al. and Lin et al. used 'Train the trainer' models to enable more staff to be trained at local TB clinics.[20,23] For example, Kaur et al. trained over 1400 staff in smoking cessation messaging using this model. Training courses that involved more hands-on components, such as role-playing, appeared to last longer. However, as many of the studies did not detail how knowledge and skills regarding smoking cessation messages were taught in the training courses, it is difficult to draw any conclusions. Only Louwagie et al. provided specific follow-up training for staff to reinforce smoking cessation messages; Nichter et al. provided follow-up training for family members.[14,15] Few studies provided evidence on the effectiveness or acceptability of the training by staff. El Sony et al. noted an increase in the use of smoking abstinence messaging after the training; however, the difference between the control and intervention staff was not statistically significant.[24] Lin et al. and Sereno et al. noted challenges in implementation due to busy clinic schedules or clinicians who smoked and who did not believe smoking cessation was important.[19,20] However, three other studies reported positive responses by staff, including the fact that staff and families were not always aware of the connection between smoking and TB and appreciated the training.[14,19,21]

Effectiveness of interventions

One of the challenges of evaluating effectiveness is that six of the studies did not use a control group. In addition, studies with a control group varied greatly as regards the standard of care provided to the control group. The standard of care ranged from asking about smoking status[24,25] to receiving standard DOT care that may or may not have included smoking cessation messages,[16,26] brochures,[17,18] or even brief advice or counseling by a smoking cessation counselor.[15,17] This made comparisons across different types of intervention very difficult.

Randomized controlled trials

Among the five randomized controlled trials, those that provided both advice by a health care provider and advice plus medication improved smoking cessation. Among the studies that reported a relative risk (RR) ($n = 3$), the RR for smoking abstinence ranged from 2.3 to 8.5 at the end of the follow-up period for counseling (3 studies)[15,16,18] and from 9.3 to 35.3 (odds ratio) for the combination of counseling and medication (2 studies).[16,18] In both studies where bupropion was added to counseling, there was an increase in cessation; however, this was either not evaluated statistically or was statistically non-significant. In the additional comparison of hookah smokers with cigarette smokers (1 study), smoking cessation interventions had less impact on hookah smokers; the chance of smoking abstinence in this group was nevertheless doubled (RR 2.2–2.5). Neither Kumar et al.[17] nor Nichter et al.[14] had standard of care control groups, but compared counseling or trained family support, respectively, with physician advice alone. In these two studies, quit rates were comparable between groups, suggesting that advice given specifically by a non-physician, including a family member, may be as effective as provider advice. Kumar et al. reported quit rates of 40.5–44% among TB patients,[17] while Nichter et al. reported 71–73% quit rates.[14] The intervention evaluated by Nichter et al. may have been more successful, as it continued for the entire treatment period,[14] whereas Kumar et al. had only one advice session.[17]

Non-randomized interventions

Three of the 14 interventions were non-randomized, but included a control group receiving standard of care. All three studies reported that more participants receiving the intervention quit compared with the control group, with a quit rate ranging from 39% to 82.5% compared with 0% to 14.3%, respectively.[24–26]

TABLE 4   Cochrane Risk of Bias Assessment Tool*[13]

Author, reference	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Aryanpur[16]	Low risk	Unclear*	High risk	Low risk	Low risk	Low risk	Low risk
Awaisu[26]	High risk	High risk	High risk	High risk	High risk	Low risk	High risk
Bam[21]	High risk	High risk	High risk	High risk	Low risk	Low risk	High risk
Campbell[25]	High risk	High risk	High risk	High risk	High risk	Low risk	High risk
Dogar[27]	Low risk	Low risk	High risk	High risk	Low risk	Low risk	Low risk
El Sony[24]	High risk	High risk	High risk	High risk	Unclear*	Low risk	High risk
Kaur[23]	High risk	High risk	High risk	High risk	High risk	High risk	High risk
Kumar[17]	Low risk	Low risk	High risk	Unclear*	Low risk	Low risk	Low risk
Lin[20]	High risk	High risk	High risk	High risk	High risk	Low risk	High risk
Louwagie[15]	Low risk	Low risk	High risk	High risk	Low risk	Low risk	Low risk
Nichter[14]	Low risk	High risk	High risk	Unclear*	Low risk	Low risk	High risk
Sereno[19]	High risk	High risk	Low risk	Unclear*	High risk	Low risk	High risk
Siddiqi[18]	Low risk	Low risk	High risk	High risk	Low risk	Low risk	Low risk
Siddiquea[22]	High risk	High risk	High risk	High risk	High risk	Low risk	High risk

*Due to insufficient information to permit judgment.

Awaisu et al. reported the highest level of smoking cessation compared with controls (78% vs. 9%).[26] However, the study recruited patients who were already motivated to quit (based on the transtheoretical model stages of change), whereas the control group was made up of smokers unwilling to quit. Awaisu et al. was the only study to use NRT along with counseling, but they did not analyze differences between patients who received NRT and those who did not. Campbell et al.[25] and El Sony et al.[24] both reported on pilot/feasibility studies taking place within the existing NTP structures, where TB treatment staff received training on brief smoking advice.

Prospective cohort studies
Five studies were based on the implementation of smoking cessation interventions among all smokers within existing NTPs, with no control group comparison.[19–23] The percentage of smokers who quit at the end of the follow-up period ranged from 66.8% to 82%. Most of these interventions consisted of 5–10 min of brief advice by TB center staff at initiation, with follow-up sessions intended for each return TB visit. The highest quit rate was 82%, in a study where community volunteers were trained in smoking cessation brief advice and provided weekly or bimonthly follow-up advice in the community.[22]

Quality of articles
All the studies were evaluated using the Cochrane Risk for Bias for Interventional Studies tool (Table 4).[13] Most studies had significant risk for bias, as they did not have a control group or participants who were not randomized to the intervention. Many studies did not have blinding of study participants or study personnel both in assignment of intervention and during data collection, leading to a higher risk of bias in the outcome. However, it is to be noted that the nature of this behavioral intervention makes it difficult to blind participants and clinicians to the intervention.

DISCUSSION

The addition of smoking cessation interventions to routine TB case management is feasible and effective in reducing smoking rates among patients during anti-tuberculosis treatment. While all the studies in this review reported at least some reduction in smoking, there remains a need for clearer evidence to guide the operationalization and scale-up of smoking cessation strategies within NTPs.

Practice implications
This review suggests that NTPs can implement smoking cessation interventions using existing staff for advice or counseling.[19,24] However, clinicians in LMICs are often in high demand to provide clinical care, and thus have limited time.[19,30] This review suggests that, in addition to physicians and nurses, lay counselors and HCWs can provide ongoing smoking cessation counseling.[15,17] There is some evidence that physicians may play an important role in smoking cessation messaging.[31] Physicians and nurses could incorporate short cessation messages that would be followed up with ongoing support provided by CHWs or HCWs. A combination of HCWs reinforcing smoking cessation messaging could complement a more holistic approach to health messaging around smoking and other related topics in TB care. Standardized patient education materials could make it more feasible for this messaging to be provided consistently.

Family members are a critical component of smoking cessation that could be more systematically included during smoking cessation interventions. As smoking may resume after anti-tuberculosis treatment is completed, this is particularly important for preventing relapse.[14,20,32] This review found that family members enjoyed learning more about TB and smoking cessation messages and requested additional topics for training in the future.[14] When considering who participates in the family, an intergenerational approach to engaging older and younger generations could facilitate stronger messaging.[33,34] Research on smoking cessation in non-TB-specific contexts has demonstrated the influence of both social networks and family members on smoking habits and cessation efforts.[35–37] Despite this, a review of smoking cessation interventions involving family members found few studies that directly compared individual vs. family-based interventions, limiting the ability to draw conclusions as to whether family member involvement had an additive effect.[38] In addition, all of these studies were from Europe and North America, and family dynamics may vary across countries. This review suggests that family members may have a positive influence on TB patients, but addi-

tional research is needed to identify how to maximize family support. In addition, as secondhand smoke is a serious health concern, not only for TB patients but their families, counseling TB patients and any other family members within the household who smoke may help to reduce the risk of exposure to secondhand smoke and the risk of development of TB for household members.[39,40]

Training and supervision are a key requisite for integrating smoking cessation messaging into routine NTPs.[41,42] HCWs themselves may smoke and not recognize the importance of smoking cessation messages, particularly for TB patients.[30,41] In addition, even if HCWs agree with smoking cessation, they may not have adequate knowledge to provide tailored advice for TB patients.[30,41,42] For example, one study noted that TB nurses asked patients about smoking habits and gave advice 87% of the time, but did not provide TB-specific messaging that could increase the likelihood of quitting.[15] Most interventions required a 1-day training course for providers, with some utilizing a training-of-trainers approach to increase reach. More in-depth techniques, such as motivation interviewing, could be incorporated into the training if time and resources allow. Motivational interviewing has been found to be effective in the case of counseling on a variety of topics, from medication adherence to chronic disease management to smoking cessation.[43] These techniques may help TB providers target patient barriers to smoking cessation during anti-tuberculosis treatment and at the same time increase TB treatment success rates.[15,26]

Cessation counseling may be accompanied by medications such as NRT or anti-depressants used to reduce cravings, such as bupropion. Of the three studies that included medications, only one compared the effect of advice with advice plus medication, and found no difference. A systematic review by Cochrane suggested that anti-depressants such as bupropion may not be any more effective than NRTs.[44] In addition, a separate review found that combined behavioral interventions with medication (NRTs or bupropion) worked better than usual care in the general population, but they did not explore the separate impacts of medication and intensive behavioral therapy on smoking cessation.[45] However, given that NRT and other pharmaceuticals can be costly and add to the pill and side effect burden, providers may try other methods of promoting smoking cessation before routinely prescribing medications. Further studies are needed to determine which patients may derive the greatest benefit from medications to guide prescribers. In addition, it is important for TB and tobacco control programs to be able to evaluate whether it would be beneficial to include medications in their programming choices, or whether other cessation methods provide greater benefit, and have a larger impact on community smoking norms and behaviors.

None of the studies in this review used technology to promote smoking cessation. As more people have access to mobile and smartphones, this may be a way to provide additional information and smoking cessation messages for smokers and their families. There is some evidence that mobile phone use in HIV care has improved treatment adherence, and mixed results about whether text reminders could also improve adherence to TB treatment.[46–48] In general populations, mobile technology, including short messaging service text reminders, has been effective in promoting and sustaining smoking cessation for up to 6 months, although most such studies have been conducted in high-income countries.[49,50] However, as mobile phone use increases in LMICs, technology will continue to be a possible source of cessation or medication adherence messaging.

Research implications

This review provides initial evidence that smoking cessation interventions can reduce smoking rates in TB patients. However, there were few randomized trials, and most studies did not have a control group for comparison. The risk for bias was thus high, and there is a need for additional studies such as adaptive clinical trials to evaluate the effectiveness of smoking cessation interventions in this population.[51] Both qualitative and quantitative studies of TB patients who have and those who have not successfully quit smoking would further elucidate what was most helpful about specific interventions, how interventions impact patients beyond just smoking cessation, such as improving overall quality of life, and other factors that contribute to smoking cessation, such as self-efficacy.[52,53] Nichter et al. included qualitative interviews of patients who continued smoking after the 6-month TB treatment period and intervention.[14] These interviews suggested that the smokers did not see low-level smoking as harmful and that they resumed smoking to demonstrate that they were healthy enough to smoke. This also suggests a critical need for studies that follow patients after the end of anti-tuberculosis treatment, because patients who quit may resume smoking once they have completed treatment, and such patients have been shown to be at greater risk of recurrent TB.[6,14] In this review, only two studies assessed smoking cessation after the end of anti-tuberculosis treatment. Studies with longer follow-up and using more qualitative research methods are therefore critical to facilitating and maintaining smoking abstinence.

While the recommendations for integrating smoking cessation messages into TB care are clear, the most cost-effective methods for improving cessation are not known. Only two of the studies in this review mentioned cost, and none did a cost-analysis.[18,23] Siddiqi et al. reported that behavioral support cost US$2.50 per person, while medication cost US$20.90 per person.[18] Kaur et al. reported that the entire program—training 1436 staff and counseling 1333 smokers among 2879 registered TB patients—was conducted between October 2010 and June 2011 at a cost of US$7000, and could therefore be incorporated into the NTP and smoking cessation budget.[23] Future studies should focus on the direct and indirect costs of smoking cessation interventions to assist programs in deciding how to effectively use scarce resources.

Policy implications

Both the WHO and The Union have recommended the integration of smoking cessation messages into TB care for over a decade. However, this review highlights the challenges of implementing effective smoking cessation interventions in resource-limited TB care programs. While the WHO and The Union guidelines provide broad overviews of smoking cessation techniques and messaging, additional resources based on empirical research that can be adapted to different settings are needed. In addition, encouraging standardization of tools and definitions in research and practice will allow for better comparisons of the various smoking cessation interventions. This review also highlights the richness of the data from studies outside of randomized controlled trials. Although randomized controlled trials are the standard, particularly in biomedical research, they may not be the most useful for developing effective pragmatic behavioral interventions and programming, particularly when smoking cessation messaging should be the standard of care.[54,55]

National and local TB programs should look for ways to integrate smoking cessation training and messaging into existing

programs. While smoking cessation interventions can feasibly be introduced in TB clinics, these programs do require resources—smoking cessation materials, training of personnel, changing TB protocols and forms—to include ongoing screening for smoking. As recommended by the WHO, the incorporation of smoking indicators into TB clinical documentation tools could increase the accountability of providers in implementing smoking cessation interventions. These indicators also provide important feedback on the programs' success. In addition, as reported by Kaur et al., integration of national tobacco control programming with TB programming can be successful, especially when TB clinics are located within primary health clinics.[23] National and international policy should encourage collaboration between chronic disease prevention and health promotion with TB programming to maximize the impact of messaging.

Strength and limitations of the studies

Most of the studies reviewed were non-randomized or observational, with no control groups. As noted in Table 4, the risk of bias in many of the studies was high. Additional limitations were small sample size, high rates of attrition among participants, and measurement error related to self-reporting of smoking status. Furthermore, most studies followed patients only up to the end of anti-tuberculosis treatment, which fails to capture longer-term relapse and intervention impact. In addition, differing definitions of smokers and smoking cessation made it difficult to compare results across studies.

A major strength of these studies is that they were largely pragmatic interventions situated in existing NTPs. They all suggest that it is feasible to integrate smoking cessation into TB care, and that this can successfully increase the number of patients who quit smoking. In addition, half of the studies used biometric methods (exhaled CO or cotinine) to validate self-reported smoking status, increasing the validity of the results.

Strength and limitations of this review

A limitation of this review was that it included only peer-reviewed journal articles, while program reports and grey literature such as WHO or national reports were excluded. NTPs implementing smoking cessation interventions may have important findings that have not been published in peer-reviewed journals. This review specifically included a variety of study designs, making comparison of outcomes difficult. The strength of this method was the inclusion of more interventions beyond randomized controlled trials to understand the qualitative aspects of interventions that may otherwise have been excluded.

CONCLUSIONS

Smoking cessation interventions can be incorporated into TB treatment and care programs across hospitals and clinics. Increased access to smoking intervention services within NTPs can play a critical role in reducing tobacco use among patients, which could improve TB cure rates and reduce the risk of subsequent morbidity and mortality.[3] However, to facilitate the integration of behavioral smoking cessation interventions into NTPs as standard practice, greater policy and program guidance is needed. In addition to research on the effectiveness of smoking cessation strategies in TB patients, a greater focus on the feasibility and cost requirements of various intervention approaches is critically needed to guide implementation.

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Le tabac constitue un facteur de risque significatif en termes de morbidité et de mortalité, particulièrement pour les patients atteints de tuberculose (TB). L'arrêt du tabac a été recommandé par l'Organisation Mondiale de la Santé et l'Union Internationale contre la Tuberculose et les Maladies Respiratoires ; aucune évaluation n'a cependant été publiée à propos des interventions de sevrage du tabac parmi les personnes atteintes de TB. Le but de cette revue a été de synthétiser les données probantes relatives à ces interventions et de suggérer les implications en matière de pratique, de recherche et de politique. Une revue systématique de la littérature a identifié 14 études revues par des pairs, décrivant 13 interventions d'arrêt du tabac entre 2007 et 2017 : 5 essais randomisés contrôlés, 3 interventions non randomisées et 5 études prospectives de cohorte. Les types principaux d'intervention ont consisté en brefs conseils (*n* = 9), en conseil comportemental (*n* = 4), en médicaments (*n* = 3) et en prise en charge communautaire (*n* = 3). Les interventions ont été mises en œuvre par toute une gamme de personnel de santé—médecins, infirmiers, personnel des dispensaires, travailleurs de santé communautaire—et par des membres de la famille. Ces interventions ont été significativement hétérogènes en matière de schéma, de définition du tabagisme et de l'abstinence et de mise en œuvre, ce qui a rendu difficiles les comparaisons entres les études. Dans l'ensemble, toutes les interventions ont accru le taux d'arrêt du tabac de 15% à 82%, mais de nombreuses études sont très sujettes aux biais, notamment les six études dépourvues de groupe témoin. Le type de personnel de mise en œuvre n'a pas entraîné de modifications majeures en termes de résultats, ce qui suggère que les programmes nationaux TB peuvent adapter la mise en œuvre de ces interventions à leurs besoins et à leurs limites. Les membres de la famille semblent jouer un rôle important en matière de soutien et de plaidoyer. Des recherches ultérieures devraient standardiser les définitions de la consommation et de l'arrêt du tabac afin de permettre des comparaisons entre les études. Les décideurs politiques devraient encourager la collaboration entre les initiatives liées au tabac et celles liées à la TB et élaborer des mesures d'arrêt du tabac pour maximiser les résultats dans les contextes de faibles ressources.

El tabaquismo representa un importante factor de riesgo de morbilidad y mortalidad, sobre todo para los pacientes con tuberculosis (TB). La Organización Mundial de la Salud y la Unión Internacional contra la Tuberculosis y las Enfermedades Respiratorias han recomendado que se promueva la deshabituación tabáquica, pero aún no se ha publicado una evaluación de las intervenciones que favorecen el abandono del tabaquismo en las personas con diagnóstico de TB. La finalidad de la presente revisión consistió en reunir la evidencia existente sobre estas intervenciones y proponer los corolarios que se podrían aplicar en la práctica, la investigación y la formulación de políticas. En una revisión sistemática de artículos científicos se encontraron 14 estudios publicados del 2007 al 2017 en revistas con comité de lectura que describían 13 intervenciones de deshabituación tabáquica. Los artículos abordaban 5 ensayos aleatorizados, 3 intervenciones no aleatorizadas y 5 estudios de cohortes prospectivos. Los principales tipos de intervenciones consistieron en asesoramiento breve ($n = 9$), orientación conductual ($n = 4$), tratamiento médico ($n = 3$) y atención al nivel comunitario ($n = 3$). Diversos profesionales de salud participaron en la ejecución de las intervenciones como miembros del personal médico, de enfermería, auxiliares clínicos, agentes de salud comunitarios y miembros de la familia. Se observó una gran heterogeneidad con respecto al diseño de los estudios, la definición de tabaquismo y de la abstinencia de tabaco y a la ejecución, que dificultó las comparaciones entre los estudios. En general, todas las intervenciones de deshabituación tabáquica aumentaron el abandono del tabaco de 15% a 82%, pero en muchos de los artículos existía la probabilidad de sesgo como en seis estudios que no contaban con un grupo testigo. El tipo de personal que ejecutaba la intervención no tuvo un efecto notorio en los resultados de abandono, lo cual indica que los programas nacionales contra la TB pueden adaptar las iniciativas a sus necesidades y limitaciones. Los miembros de la familia pueden cumplir una función importante de apoyo o promoción del abandono del tabaco. En las investigaciones futuras es preciso normalizar las definiciones de tabaquismo y de abandono del tabaco con el fin de facilitar las comparaciones entre los estudios. Las instancias normativas deben fomentar la colaboración entre las iniciativas contra el tabaquismo y contra la TB y formular medidas encaminadas a la deshabituación tabáquica que optimicen sus resultados en los entornos con bajos recursos.