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Smoking Cessation Interventions for Patients with Chronic Obstructive Pulmonary Disease: A Narrative Review with Implications for Pulmonary Rehabilitation

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Abstract

Purpose: Reducing disease burden in patients with chronic obstructive pulmonary disease (COPD) focuses, in part, on helping patients become more functional through programs such as pulmonary rehabilitation (PR). Smoking cessation may be a prerequisite or component of PR, and determining which smoking interventions (e.g., behavioral, pharmacotherapy, combination) are most effective can help guide efforts to extend them to patients with COPD. The purpose of this narrative review was to summarize evidence from studies testing smoking cessation interventions in patients with COPD and discuss how these interventions may be integrated into PR programs.

Review Methods: Searches were conducted in the PubMed and Web of Science databases. Search terms included "(smoking cessation) AND (RCT OR clinical trial OR intervention) AND (pulmonary OR chronic bronchitis OR emphysema OR COPD)". Published original studies were included if they used a prospective, experimental design, tested a smoking cessation intervention, reported smoking cessation rate, and included patients with COPD or a subgroup analysis focused on smokers with COPD.

Summary: Twenty-seven distinct studies were included in the review. Most studies tested multi-treatment smoking cessation interventions involving some form of counseling in combination with pharmacotherapy and/or health education. Overall, smoking cessation interventions may help promote higher rates of smoking abstinence in patients with COPD, particularly multi-faceted interventions that include intensive counseling (e.g., individual, group, and telephone support), smoking cessation medication or nicotine replacement therapy, and health education.

Condensed Abstract

Treatment for chronic obstructive pulmonary disease (COPD) ideally would include both pulmonary rehabilitation (PR) and smoking cessation. This paper reviews the literature on smoking cessation interventions in those with COPD. Approaches combining behavioral and

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pharmacological interventions have been most successful for this population and could be integrated into PR.

Keywords

Chronic Obstructive Pulmonary Disease; COPD; pulmonary rehabilitation; smoking cessation

Chronic obstructive pulmonary disease (COPD) – characterized by irreversible airway obstruction, breathlessness, coughing, fatigue, and frequent respiratory infection constitutes a leading cause of death in the United States (US).[1] Between 2014-2015, overall prevalence of COPD was 6% among US adults and as high as 10% among former cigarette smokers and 15% among current smokers.[2] Indeed, cigarette smoking is a key risk factor for COPD onset and progression.[3] Thus, smoking cessation is critical for smokers with COPD.

Apart from efforts to promote smoking cessation in patients with COPD, reducing disease burden and improving outcomes of COPD involves helping patients become more functional through programs such as pulmonary rehabilitation (PR). PR is a patient-tailored therapeutic approach aimed at minimizing respiratory symptoms (e.g., dyspnea) and improving quality of life (e.g., fatigue, emotional functioning) and exercise capacity though exercise training and behavior change.[4] For patients with COPD, PR is strongly recommended as there is little debate over its efficacy for improving respiratory symptoms, quality of life, and exercise capacity,[5] and PR participation is associated with lower risk of rehospitalization.[6] As such, calls have urged researchers to shift focus away from determining whether PR is effective to identifying which components of PR should be considered essential.[5]

Despite the importance of smoking cessation for patients with COPD, smoking interventions appear to be inconsistently applied in PR programs.[4,7] For example, smoking cessation support is deemed a desirable but not essential component of PR,[4] and some PR programs require smoking cessation as a prerequisite.[7] Recent evidence from a US national survey indicates that < 10% of PR programs allow smokers to attend unconditionally, and one-third of PR programs disallow smokers entirely.[8] Although current smoking has been shown to predict non-attendance (i.e., not attending any session following referral), non-adherence (e.g., attending < 65% of the required sessions), and dropout among patients in PR,[9–11] research also demonstrates that people who receive smoking cessation support through PR programs may be up to 5.7 times more likely to quit smoking compared to those receiving the same support through hospital settings.[12] Furthermore, evidence suggests that PR is beneficial for patients with COPD regardless of smoking status.[13] Importantly, a multitude of empirically validated smoking interventions are available to patients with COPD,[14] and research to identify which treatment methods effectively facilitate smoking cessation in this population may help improve PR attendance and adherence, promote pre-rehabilitation smoking abstinence, and/or maintain smoking abstinence over the course of PR. Therefore, the purpose of this narrative review was to summarize evidence from studies using prospective experimental methods to test smoking interventions in patients with COPD; provide initial suggestions for ways to integrate evidence-based smoking

cessation interventions into PR; and identify gaps in the existing literature and smoking interventions for patients with COPD in need of further study.

Of note, a 2016 Cochrane Review led by van Eerd and colleagues includes a systematic review and meta-analysis of the effects of smoking interventions for people with COPD.[14] The current review was not intended to provide an exhaustive, quantitative synthesis of all available evidence on this topic. Rather, the current narrative review aimed to highlight potentially efficacious smoking cessation treatments (or components thereof) that could be practically integrated into PR, as well as treatment approaches that show initial promise for promoting smoking cessation among people with COPD. Readers should refer to van Eerd et al. (2016) for aggregated effect sizes, quantitative comparisons of smoking intervention effects, and analysis of potential moderators (e.g., COPD severity).

METHODS

Literature searches were conducted in the PubMed and Web of Science databases from inception through September 27th, 2021. Search terms included the keywords “smoking cessation” AND (“RCT” OR “clinical trial” OR “intervention”) AND (“pulmonary” OR “chronic bronchitis” OR “emphysema” OR “COPD”). After limiting results to full-text articles available in English language, clinical and randomized controlled trials, and studies conducted in human adults the search yielded 1,356 records. After removing duplicates 1,215 records remained for title and abstract screening. References of relevant articles were also searched, yielding two additional articles.

Titles and abstracts of the 1,217 articles were screened and articles were advanced to full-text review if they met the following inclusion criteria: (1) published, original study, (2) used a prospective experimental design, (3) included a smoking intervention, (4) reported smoking cessation rate (e.g., point prevalence abstinence), and (5) the study population was current smokers with COPD (i.e., based on criteria from the American Thoracic Society, British Thoracic Society, GOLD, or as confirmed by a treating physician, in accordance with a recent review) [14] or contained a subgroup analysis focused on smokers with COPD. Eighty-one articles advanced to full-text review. Following full-text review, 26 articles were selected for inclusion.

RESULTS

The 26 articles in this review reported the results of 27 distinct studies.[15–40] Articles may be included in more than one table if they tested more than one type of smoking intervention. Eleven studies were designed to test a specific type of intervention for smoking cessation, such as a behavioral intervention (11.1%) (Table 1),[31,33,39] or a pharmacotherapeutic intervention (29.6%) (Table 2).[15,21,29,35–38,40] Most studies tested smoking interventions that combined treatment methods (59.3%) (e.g., behavioral interventions plus pharmacotherapy and/or health education) (Supplementary Digital Files 1, 2, 3).[15–20,22–28,30,32,34,37,40] Only two studies, presented in a single report, tested smoking interventions using a within-person study design in which each participant experienced both a control period and an intervention period;[18] the remaining studies were randomized

controlled trials in which participants were randomly assigned to an intervention or a control condition.[15–17,19–40]

Across studies, most patients had moderate to severe airflow limitation as indicated by below normal spirometry values,[15–19,21,27,29,30,32,33,35–37,39,40] or Medical Research Council dyspnea scale scores >1.[22,31] Some studies reported baseline lung function tests for the entire sample and not for subgroups of patients with COPD who smoke;[20,23–26,28,38] however, patients in these studies also tended to exhibit moderate to severe airflow limitation.[20,23–26,28] Seven studies relied solely on self-reported smoking to verify abstinence,[20,22,23,25,26,28,30] and 20 studies biochemically verified abstinence using serum carboxyhemoglobin,[32] exhaled carbon monoxide (CO),[16–19,21,24,29,31,34–37,40] urinary or salivary cotinine,[27,38] or a combination of exhaled CO and cotinine.[15,33,39] Intervention duration varied considerably, ranging from 2 wk[33] to upwards of 3 yr,[25] with some interventions involving as few as 1-4 brief consultations[20,22] and others involving intensive daily or near-daily monitoring.[18,19,33] Overall, roughly half (55.2%) of the experimental smoking interventions reviewed promoted smoking abstinence more effectively than control conditions for patients with COPD.

Behavioral Interventions

Three studies tested the effects of behavioral smoking cessation interventions (Table 1). One large trial (N=3,562) demonstrated that following a 2-yr treatment period, sustained smoking abstinence between 24-30 mo was considerably higher for patients who received intensive individualized and group counseling (46.4%) versus usual care for smoking cessation (i.e., simple smoking cessation advice and encouragement to quit plus brief education about the health effects of smoking) (3.4%).[31] In a 14-d pilot study examining the effectiveness of contingency management (CM) for smoking cessation (i.e., delivery of monetary vouchers contingent upon biochemically verified smoking abstinence), roughly 40% of patients who received CM were abstinent at 9-14 d versus approximately 10% of control patients.[33] By contrast, a 5-wk trial compared individualized counseling to group counseling for smoking cessation and found neither intervention to be more effective than usual care.[39]

Pharmacotherapy

Eight studies examined the efficacy of pharmacotherapy for smoking cessation (Table 2). In two separate studies, point prevalence smoking abstinence was approximately 2-3 times higher among patients taking bupropion sustained release (SR) versus placebo,[35,38] and one of these studies further demonstrated that there were no differences in smoking abstinence between patients taking bupropion SR versus nortriptyline.[38] One trial observed higher rates of smoking abstinence at 12-, 24- and 52-wk follow-up assessments among patients with COPD undergoing a 12-wk regimen of varenicline (42.3%, 25.8%, and 18.6%, respectively) versus placebo (8.8%, 7.2%, and 5.6%, respectively),[36] but another trial found no treatment effect of a 12-wk regimen of varenicline versus placebo at a 52-wk follow-up assessment.[29] However, the latter trial observed higher rates of abstinence among patients receiving varenicline (50%) versus placebo (27%) at wk 12.[29] Regarding nicotine replacement therapy (NRT), one trial observed higher rates of smoking abstinence among patients taking nicotine sublingual tablets versus placebo at 6-mo (23 versus 10%, respectively) and 1-yr follow-up

(17 versus 10%, respectively),[37] but a second trial examining the comparative efficacy of ad libitum nicotine gum versus smoking cessation counseling found that nicotine gum was less effective than counseling at 6- (5.3 vs 21.1%, respectively), 12- (15.3 vs 31.6%, respectively), and 29-wk assessments (21.1 vs 47.4%, respectively).[40] Another trial observed no difference between a standard (i.e., 10-wk) versus long-term (36-wk) NRT regimen.[21] One final study examined whether pharmacotherapy for lessening pulmonary symptoms helped facilitate smoking cessation and observed no differences in smoking abstinence between patients using ipratropium bromide versus placebo inhalers.[15]

Combination Interventions

Behavioral interventions plus pharmacotherapy—Seven studies tested the effects of behavioral interventions in combination with pharmacotherapy (SDC 1). In one trial, roughly 35% of patients who received a 10-wk intensive counseling intervention (i.e., individualized, group, and couples) plus nicotine gum were abstinent at each of five annual follow-up assessments compared to 10-20% of patients receiving usual care.[15] Another trial demonstrated that a 5-wk guided self-change intervention (i.e., counselor-guided self-assessment of smoking risks and barriers to quitting) in combination with ad libitum nicotine gum promoted smoking cessation more effectively than ad libitum nicotine gum alone, with abstinence rates 2-7 times higher at 6-, 12-, and 29-wk follow-up assessments.[40] In a 4-wk trial, 30.2% of patients who received counseling in relation to spirometry results (i.e., discussing COPD prognosis and challenging patients' irrational beliefs about smoking in relation to COPD) plus nortriptyline were smoking abstinent at 6-mo follow-up versus 11.8% of patients receiving usual care; however, there were no differences between counseling with (30.2%) versus without abnormal spirometry results (23.2%), and no differences between conditions at 1-yr follow-up.[27] One trial observed no differences in smoking abstinence between two, 12-wk counseling conditions (i.e., 4 in-person counseling plus 6 telephone sessions vs 7 in-person counseling plus 5 telephone sessions) supplemented with nicotine sublingual tablets, but abstinence was higher for patients taking nicotine sublingual tablets versus placebo regardless of counseling conditions.[37] Additionally, one within-person study and one RCT found no effect of an 8-9-wk behavioral intervention that involved initial contingent (i.e., guaranteed) followed by variable (i.e., probabilistic) reinforcement of smoking abstinence with lottery tickets plus supplemental nicotine gum.[18,19]

Behavioral interventions plus health education—Nine studies tested the effects of behavioral interventions that incorporated health education (e.g., workshops or take-home educational materials) (SDC 2). In one trial, patients attended two, 1-hr clinic visits separated by a 12- to 20-wk interval, and during each visit they received either usual care or education-based counseling emphasizing self-care and tailored COPD management.[20] Patients who received education-based counseling were more likely to be smoking abstinent at the second visit (37.5%) compared to patients who received usual care (0%).[20] In another trial, patients who received a 24-wk telephone counseling intervention (i.e., weekly during the first mo 1, 2x/mo during mo 2, and 1x/mo during months 3, 4, and 5) plus educational materials were more likely to be abstinent at wk 24 (40.5%) compared to patients who received usual care (18.6%).[17] A third trial demonstrated that 1-4 in-person smoking

cessation counseling sessions over a 2-mo period supplemented with educational materials nearly doubled point prevalence smoking abstinence at 6-mo follow-up (16.0%) compared to usual care (8.8%).[22] One other trial demonstrated that a 24-wk counseling intervention supplemented with educational materials and personalized electronic messages encouraging smoking cessation promoted abstinence more effectively than usual care (58.8% versus 33.3%, respectively).[30]

In contrast to the four studies described above, five studies found no effect of behavioral interventions for smoking cessation that incorporated health education. Two 24-wk trials found no differences in smoking abstinence between patients receiving counseling supplemented with education versus usual care: one trial involved 3-4 family counseling sessions focused on COPD management,[24] and the second trial included ambulatory monitoring of health behavior (e.g., physical activity, smoking) to promote self-care.[23] Two additional trials found no effect of smoking interventions delivered during inpatient care: one trial provided patients with manuals to supplement smoking cessation counseling,[32] and the other trial provided educational materials that referred to COPD as either “smoker’s lung” (intervention) or chronic bronchitis or emphysema (usual care).[16] One last trial tested a 52-wk intervention and found no effect of motivational interviewing plus educational materials for smoking cessation delivered to patients with COPD in primary care settings.[28]

Behavioral plus pharmacotherapy and education—Finally, three trials tested interventions that involved smoking cessation counseling, pharmacotherapy, and health education (SDC 3). In one trial testing an individualized 3-yr (median) intervention, patients received group counseling and prescription medications for smoking cessation, tailored disease management (i.e., personalized strategies for monitoring COPD symptoms, adhering to treatment, and managing relevant lifestyle factors), and educational sessions that family members could attend.[25] More patients in the intervention (25.8%) reported smoking abstinence at their last follow-up compared to patients in the control condition (i.e., group counseling and prescription medications only) (16.9%).[25] In a 52-wk trial, patients received either usual care for smoking cessation or motivational interviewing plus referral to a hospital-based smoking cessation program, educational materials, and tailored pharmacotherapy for COPD (e.g., inhalers, antibiotics and oral corticosteroids for exacerbations).[26] Although 22.2% of patients in the intervention reported smoking abstinence at 6-mo follow-up versus only 5.3% of patients receiving usual care, the difference was not statistically significant.[26] Finally, one trial tested a 52-wk, intensive smoking cessation program that involved a 2-wk hospital stay, group counseling, educational materials, NRT, optional rehospitalization 2-3-mo post-discharge, and ongoing telephone and/or email support.[34] A higher percentage of patients in the intervention condition were smoking abstinent at 1- and 3-yr follow-up (52 and 38%, respectively) compared to patients receiving usual care (7 and 10%, respectively).[34]

DISCUSSION

This review summarized evidence from 27 distinct studies using prospective experimental methods to test smoking interventions in patients with COPD. Consistent with the results of a recent Cochrane Review,[14] the current review indicates that smoking

interventions for patients with COPD are generally effective. Smoking interventions may be particularly effective when they are longer in duration,[17,30,34] intensive (e.g., more frequent and/or involving different treatment modalities such as individual and group counseling),[15,25,31] and supplemented with pharmacotherapy (e.g., NRT, bupropion SR).[35,38,40] Pharmacotherapy may help promote long-term sustained smoking abstinence (i.e., ≥6mo) for 14-27% of patients with COPD,[35–38] and potentially up to 47% of patients with COPD when combined with counseling (e.g., guided self-change).[40] Smoking interventions of shorter duration (e.g., ≤4 wk) may be effective for patients with COPD when counseling involves discussion of spirometry results[27] or financial incentives are used to reinforce biochemically verified smoking abstinence.[33] More broadly, this review highlights several smoking interventions with demonstrated efficacy for patients with COPD that could potentially be incorporated into PR programs.

Experimental smoking interventions promoted greater smoking abstinence than control conditions in more than half of the studies presently reviewed (55.2%). There was considerable heterogeneity across treatments; however, it is notable that nearly every efficacious smoking intervention involved multiple treatment methods, including studies designed to test specific interventions. For example, pharmacotherapy for smoking cessation was efficacious in six of the eight studies (75%) designed to test a specific type of pharmacotherapy (e.g., bupropion SR),[35,38] but all eight studies included counseling or educational components that may have augmented the effects of pharmacotherapy (Table 2). Although studies have demonstrated that smoking interventions for patients with COPD are likely to result in low costs per quality-adjusted life years gained regardless of differences in treatment method,[41,42] the current review suggests PR programs may benefit most from incorporating smoking interventions with multiple treatment methods. Importantly, PR programs that incorporate smoking cessation have the potential to reduce healthcare utilization, improve patient health in general, and still achieve monetary savings.[43] Despite such evidence, smoking interventions are generally not considered essential to PR programs.[4,7]

For a variety of reasons, PR should be an ideal place to incorporate multi-treatment approaches for smoking cessation. For example, clinicians are likely to be readily available to prescribe smoking cessation medications as needed. Furthermore, PR programs typically meet 2-3x/wk for a 4-12-wk period,[44] and this format may be conducive to incorporating regular smoking cessation counseling, discussion of the effects of smoking on spirometry results, and frequent abstinence monitoring (e.g., via exhaled carbon monoxide). Unfortunately, there may be barriers preventing patients who actively smoke from participating in PR. For example, some PR programs may disallow patients who smoke.[8] We reviewed sample policies from the websites of five top US health insurance companies and we were unable to locate any language specifically disallowing active smokers from PR. Additionally, it appears that in order for Medicare to cover PR, programs must include brief smoking cessation counseling at a minimum if applicable.[45] Nevertheless, it is possible that some insurance providers do not provide coverage for PR for active smokers, and in our opinion, PR programs may wish to consider contesting any such lack of coverage. That said, evidence suggests PR programs in the US are not being adequately reimbursed despite the availability of Medicare and other insurance coverage.[46]

Of course, without adequate reimbursement, it may be difficult if not impossible for some PR programs to integrate smoking interventions, particularly interventions with multiple treatment components.

For PR programs that require patients to be smoking abstinent prior to entry, CM for smoking cessation (i.e., delivery of financial incentives based on biochemical verification of smoking abstinence) may serve as a useful program prerequisite. For example, during prehabilitation, a period that aims to enhance patients' functional capacity and optimize risk profiles prior to scheduled interventions (e.g., lung volume reduction)[47], patients may be particularly motivated to quit smoking.[48] Given evidence that CM can promote initial smoking abstinence in patients with COPD in a 2-wk period,[33] prehabilitation may be an opportune time to extend CM for smoking cessation to patients with COPD. In 2022, the US Department of Health and Human Services, Office of Inspector General issued an advisory opinion to help extend CM for substance use disorders (including tobacco) to qualified patients.[49] The program, which is designed to deliver CM to patients using mobile technology, may be covered by patients' health care providers and would allow patients to earn a maximum of $200 USD/mo or $599 USD/yr for verified smoking abstinence. Although obstacles to broader dissemination of CM for smoking cessation remain, PR programs may be able to take advantage of the Office of Inspector General's advisory opinion to extend CM to their patients. However, more research is needed to establish the efficacy of CM for smoking cessation in patients with COPD, particularly mobile CM.

More generally, the findings of this review highlight several potentially effective smoking interventions that could be practically integrated into PR. Figure 1 depicts one potential minimal smoking intervention. Providers could assess smoking status at baseline (i.e., pre-rehabilitation) using expired carbon monoxide (CO) and/or cotinine in saliva – two objective, relatively quick, and minimally invasive methods for confirming use of combusted tobacco products. Next, providers could discuss patients' smoking status in relation to spirometry results to help increase their motivation to quit.[27] Discussing spirometry results with reference to the "Fletcher Curve" (i.e., COPD-related loss of lung function over time affected by smoking cessation at different ages) could highlight the benefits of quitting and the severity of COPD prognosis with continued smoking,[50] and may help improve success quitting.[51] Pre-habilitation could also be used as an opportunity to prescribe smoking medication to patients ready to make a quit attempt, and all patients could be automatically enrolled in state-funded Quitline services (e.g., free NRT, telephone counseling, and referral to individual counseling and support groups) unless they explicitly opt-out. For the remainder of PR, providers could check in with patients 1 time/wk to assess smoking status (praising verified abstinence or further encouraging cessation) and encourage the use of smoking medication and Quitline services.

An example of a more intensive multi-treatment smoking intervention for PR is depicted in Figure 2. For the first 4 wk of PR, a 30-40-min individual counseling session held 1 time/wk could help promote smoking abstinence for the duration of a 4-12 wk PR program, particularly if the sessions include further discussion of spirometry results in relation to smoking status.[27] In addition to assessing and encouraging the use of smoking medications and Quitline services, these sessions could also be used to discuss barriers to

quitting and relapse prevention strategies. For any remaining PR sessions (i.e., 5+ wk), the duration of counseling sessions could be shortened by removing discussion of spirometry results but continuing to follow-up on use of smoking medication and Quitline services, barriers to quitting, and relapse prevention. Importantly, research has demonstrated that people who receive smoking cessation support through PR programs are considerably more likely to quit smoking than those who receive it through other settings (e.g., hospitals),[12] underscoring the potential benefit of extending smoking interventions to patients with COPD in PR. Unfortunately, none of the reviewed studies tested a PR-based smoking intervention specifically for patients with COPD. Given long-standing calls for PR programs to include mandatory smoking interventions for patients with COPD who smoke,[7] studies examining such interventions would be immensely helpful for informing strategies to integrate smoking cessation support into PR protocols.

The present findings should be interpreted considering several limitations. First, this review identified several smoking interventions for patients with COPD in need of further study. For example, although no evidence was found to support the use of nortriptyline[38] or ipratropium bromide inhalers for smoking cessation[15] these interventions were tested in single studies. Only one, short-duration study tested CM for smoking cessation in patients with COPD, and although the results of this study were promising, there was no follow-up on patients after discontinuation of treatment.[33] Studies are needed to examine the efficacy of CM for smoking cessation among patients with COPD over longer periods of time and with follow-up assessments. Nearly all of the studies reviewed included smoking interventions with multiple treatment components, and in many cases, it was not possible to parse out the critical components of these interventions. As such, studies are needed to deconstruct smoking cessation interventions with multiple treatment components to identify which components are essential (e.g., in-person versus telephone counseling, educational materials versus in-person workshops, etc.). As noted above, none of the studies included in this review examined smoking cessation interventions delivered within the context of PR. Two studies that examined smoking interventions delivered during PR were ultimately not included in the main review: one study enrolled current smokers with and without COPD and no subgroup analysis focused on patients with COPD,[12] and the second study did not report smoking abstinence rates.[43] Research in this area would be helpful to providers developing or refining PR programs to meet the diverse needs of patients. Finally, although this study provides a detailed, narrative review of smoking interventions for patients with COPD with discussion on how such interventions may be incorporated into PR, no quantitative methods were used to evaluate aggregated effects of intervention, examine possible moderators, or assess study quality as such efforts have been reported elsewhere.[14] As studies emerge that examine the efficacy of smoking interventions for patients with COPD attending PR, systematic reviews and meta-analyses on this topic will help guide efforts to integrate smoking interventions into PR.

CONCLUSION

In conclusion, multi-treatment smoking cessation interventions are generally efficacious for patients with COPD. Whenever possible, PR programs should consider routine integration of comprehensive smoking cessation interventions to help slow COPD progression in

addition to helping patients improve their COPD symptoms, quality of life, and exercise capacity. At a minimum, PR programs may be able help facilitate success quitting smoking by incorporating an opt-out automatic referral to a state funded Quitline, and regularly following up to ensure utilization of Quitline services. Of course, smoking cessation is a universally recommended goal to improve mortality in COPD. Therefore, the need to extend effective smoking interventions to patients with COPD is broader in scope than PR, and efforts to promote smoking cessation at any point may benefit from a multi-treatment approach. More generally, future studies are needed to determine how to optimally incorporate smoking cessation interventions for patients with COPD into PR and beyond, and compare patient outcomes between PR programs with versus without smoking cessation support.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Key Perspective

What is novel?

- This review highlights smoking interventions with demonstrated efficacy for patients with chronic obstructive pulmonary disease (COPD) and provides initial suggestions on how smoking interventions could be incorporated into pulmonary rehabilitation (PR) programs.
- Smoking cessation interventions are generally effective for patients with COPD, and PR programs should consider routine integration of smoking cessation support.

What are the clinical and/or research implications?

- Smoking interventions involving multiple treatment components (e.g., behavioral support plus pharmacotherapy and health education) may be particularly effective for patients with COPD and well-suited to PR program integration.
- Smoking interventions such as contingency management (i.e., provision of incentives for biochemically confirmed smoking abstinence) can promote smoking abstinence quickly (≥2 wk) and could be a useful prerequisite for PR; however, more research is needed in this area. Trials are needed to test the efficacy of smoking interventions delivered over the course of PR.

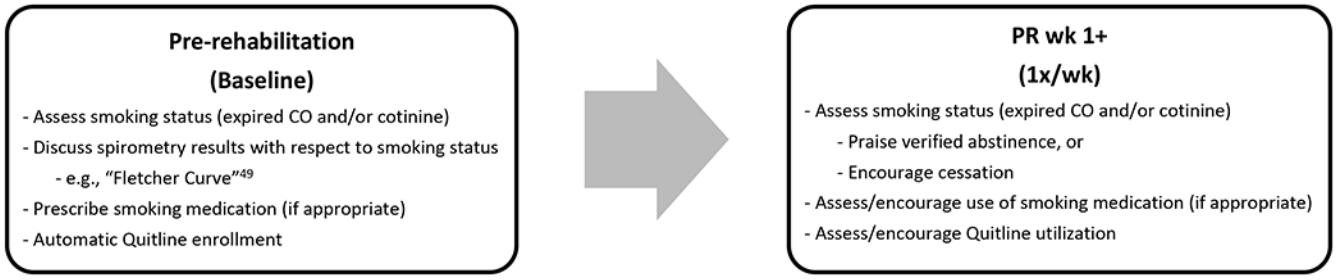

Figure 1:
Potential minimal smoking intervention for patients in pulmonary rehabilitation.
Abbreviations: CO, carbon monoxide.

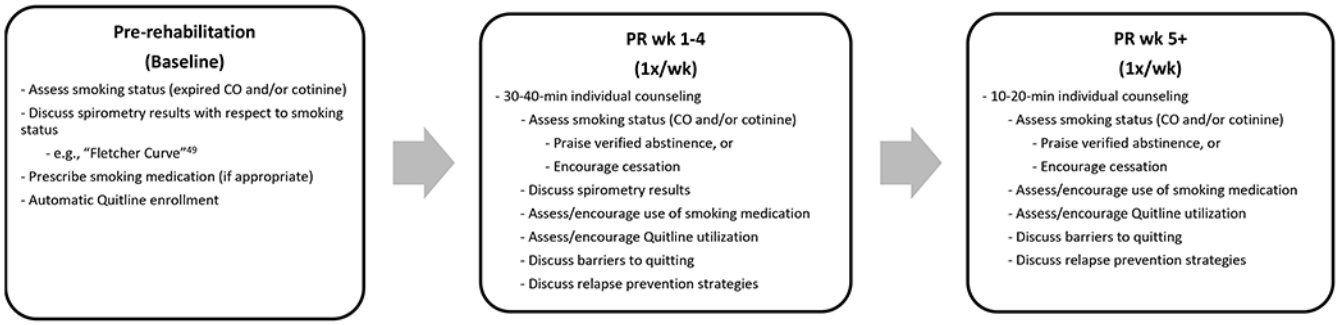

Figure 2:

Potential multi-treatment smoking intervention for patients in pulmonary rehabilitation.

Abbreviations: CO, carbon monoxide

Table 1.

Summary of studies testing behavioral interventions for smoking cessation in patients with chronic obstructive pulmonary disease.

Authors (Year)	Conditions Compared	Sample Characteristics	Baseline Lung Function	Duration of Intervention	Outcome	Results
Lou et al. (2013)	Usual care plus educational materials.	N=1,748; age range=~40-80 yr; 51.9% women; education level= 8.7% “high”, 18.5% “middle”, 72.8% “low”; household income= 8.4% “high”, 83.9% “middle”, 7.7% “low”	MRC=0 (5.1%), 1 (19.8%), 2 (28.5%), 3 (27.8%), 4 (18.8%)	2 yr	Self-reported smoking status plus biochemically confirmed sustained abstinence between 24-30 mo (breath CO ≤10 ppm)	Rate of sustained abstinence was higher for participants in the intervention (46.4%) vs. usual care (3.4%) (*P*<.001).
	Intervention: intensive individual and group counseling plus educational materials.	N=1,814; age range=~40-80 yr; 52.1% women; education level=8.8% “high”, 18.0% “middle”, 73.2% “low”; household income= 8.2% “high”, 84.3% “middle”, 7.5% “low”	MRC=0 (5.0%), 1 (19.7%), 2 (28.9%), 3 (27.7%), 4 (18.7%)			
Streck et al. (2018)	Control: non-contingent vouchers (i.e., delivery of monetary vouchers independent of smoking status).	N=16; Age 57.9 ±8.1 yr; 50% women; yr of education= 12.8 ±2.9	Postbronchodilator FEV_1/FVC 59.9 ± 11.6%	2 wk	Biochemically confirmed abstinence between 1-5 d (breath CO ≤ 6 ppm) and 6-14 d (urine cotinine ≤80 ng/mL)	Except for 12 d, abstinence rates were higher for participants in the intervention (~40%) vs. control (~10%) on 9-14 d (*P*<.05). No differences between conditions on 1-8 d.
	Intervention: contingent vouchers (delivery of vouchers dependent on biochemically verified abstinence, escalating schedule ($9.00 + 1.50 for each subsequent negative sample), temporary reset back to $0 for positive or missing samples.	N=13; Age 55.8 ±6.8 yr; 46% women; yr of education= 12.8±1.8	Postbronchodilator FEV_1/FVC 52.4 ±13.3%			
Wilson et al. (2008)	Usual care	N=35; Age 61.4 ±8 yr; 49% women; education and household income not reported	FEV_1 54.3 ±20.0%	5 wk	Biochemically confirmed abstinence at 1-yr follow-up (breath CO ≤10 ppm; saliva cotinine ≤10 ng/mL)	No difference between conditions.
	Intervention 1: individual counseling (one-to-one sessions between patient and nurse), optional NRT.	N=27; Age 61.0 ±8 yr; 48% women; education and household income not reported	FEV_1 52.1 ±20.0%			
	Intervention 2: group counseling (group of patients and 2 nurses), optional NRT.	N=29; Age 60.4 ± 9 yr; 59% women; education and household income not reported	FEV_1 54.6 ± 23.0 %			

Note: All studies summarized in Table 1 used randomized controlled trials.

Abbreviations: MRC, Medical Research Council Dyspnea Scale (higher values indicate greater dyspnea); FEV_1, Forced Expiratory Volume during 1st sec of forced expiration; FVC, Forced Vital Capacity; NRT, Nicotine Replacement Therapy.

"Usual care" for smoking cessation generally consists of low-intensity health education, simple smoking cessation advice, and encouragement to quit smoking.

Data presented as mean ± SD

Table 2.

Summary of studies testing pharmacotherapy for smoking cessation in patients with chronic obstructive pulmonary disease.

Authors (Year)	Conditions Compared	Sample Characteristics	Baseline Lung Function	Duration of Intervention	Outcome	Results
Anthonisen et al. (1994)	Usual care	N=1,964; Age 48.4 ± 6.9 yr; 36.2% women; education and household income not reported	Postbronchodilator FEV_1 2.8 ±6 L	10 wk of counseling plus an ongoing maintenance program for abstinent participants	Biochemically confirmed abstinence at five annual follow-up assessments (saliva cotinine ≤20 ng/mL and/or breath CO ≤10 ppm)	No differences between the two intervention conditions.
	Intervention 1: counseling (individual, group, and couples), nicotine gum, and *placebo inhaler*.	N=1,962; Age 48.6 ± 6.8 yr; 36% women; education and household income not reported	Postbronchodilator FEV_1 2.8 ±6 L			
	Intervention 2: counseling (individual, group, and couples), nicotine gum, and *ipratropium bromide inhaler*.	N=1,961; Age 48.4 ±6.8 yr; 39.2% women; education and household income not reported	Postbronchodilator FEV_1 2.7 ±6 L			
Ellerbeck et al. (2018)	Control: standard smoking cessation, including in-person counseling at baseline, telephone counseling at wk 1, 3, 6, and final wk, 10-wk supply of NRT (*patches plus gum and/or lozenges*) beginning on scheduled quit date.	N=198; Age 56.3, ±8.7 yr; 56.1% women; 51.0% ≤ high school education; household income not reported	% of sample with FEV1/FVC ≤ 0.70 (actual)= 62.1%	10 wk (control) vs. 9 mo supply of NRT (intervention 2)	Biochemically confirmed abstinence at 1-yr follow-up (breath CO ≤10 ppm)	No difference between conditions.
	Long-term NRT: standard smoking cessation plus 9-mo supply of NRT (*patches plus gum and/or lozenges*) beginning at baseline and replenished every 3 mo.	N=200; Age 55.6, ±9.9 yr; 63.5% women; 50.5% ≤ high school education; household income not reported	% of sample with FEV1/FVC ≤ 0.70 (actual)= 59.5%			
Le Mao et al. (2020)	Control: counseling (in-person and telephone) plus *placebo*.	N=39; Age 56.0, ±8.8 yr; 35.9% women; education and household income not reported	Postbronchodilator FEV_1 1.7 ±7 L	12 wk	Biochemically confirmed sustained abstinence at 1-yr follow-up (breath CO ≤10 ppm)	No difference between conditions at 1 yr. Compared to patients in the control condition (27%), the percentage of patients sustaining smoking abstinence was higher among patients taking varenicline (50%) at wk 12 (*P*=.03).
	Intervention: counseling (in-person and telephone) plus *varenicline*.	N=42; Age 57.6, ±8.7 yr; 42.9% women; education and household income not reported	Postbronchodilator FEV_1 1.5 ±6 L			

Authors (Year)	Conditions Compared	Sample Characteristics	Baseline Lung Function	Duration of Intervention	Outcome	Results
Tashkin et al. (2001)	Control: counseling (in-person and telephone), self-monitoring diaries, plus *placebo*.	N=205; Age 54.5, ±9.5 yr; 45% women; education and household income not reported	FEV_1, % predicted 69.4 ±17.3	12 wk	Self-reported sustained abstinence from wk 4 to 6-mo follow-up, biochemically confirmed at regular intervals (breath CO ≤10 ppm)	Sustained abstinence was higher for participants in the intervention (16%) vs. control condition (9%) (*P*=.04).
	Intervention: counseling (in-person and telephone), self-monitoring diaries, plus *bupropion SR*.	N=206; Age 53.2, ±9.0 yr; 45% women; education and household income not reported	FEV_1, % predicted 73.2 ±19.4			
Tashkin et al. (2011)	Control: counseling (in-person and telephone), educational booklet, plus *placebo*. Intervention: counseling (in-person and telephone), educational booklet, plus *varenicline*.	N=251; Age 51.1, ±9.0 yr; 37.8% women; education and household income not reported N=248; Age 57.2, ±9.1 yr; 37.5% women; education and household income not reported	Postbronchodilator FEV_1 2.3 ±7 L Postbronchodilator FEV_1 2.3 ±6 L	12 wk	Self-reported sustained abstinence from wk 9-12, 9-24, and 9-52, biochemically confirmed at regular intervals (breath CO ≤10 ppm)	Sustained abstinence rate was higher for participants in the intervention vs. control condition for wk 9-12 (42.3% vs. 8.8%, respectively; *P*<.0001), 9-24 (25.8% vs. 7.2%, respectively; *P*<.0001), and 9-52 (18.6% vs. 5.6%, respectively; *P*<.0001).
Tønnesen et al. (2006)	Intervention 1 (low support, placebo): individual (4 sessions) and telephone counseling (6 sessions), self-help materials, plus *placebo*.	N=88; Age 62.5, ±9.3 yr; 54.5% women; education and household income not reported	Postbronchodilator FEV_1 1.6 ±7 L	12 wk	Biochemically confirmed abstinence at 6-mo and 1-yr follow-up (breath CO <10 ppm); self-reported sustained abstinence, biochemically confirmed at assessments from wk 2 through yr 1 (breath CO <10 ppm).	Abstinence rate was higher for participants in the NRT vs. placebo condition at 6-mo (23 vs. 10%, respectively), and 1-yr follow-up (17 vs. 10%, respectively). Sustained abstinence was also higher in the NRT vs. placebo condition (14 vs. 5%, respectively) (*P* values not reported).
	Intervention 2 (low support, NRT): individual (4 sessions) and telephone counseling (6 sessions), self-help materials, plus *nicotine sublingual tablet*.	N=95; Age 59.2, ±10.3 yr; 52.6% women; education and household income not reported	Postbronchodilator FEV_1 1.6 ±7 L			
	Intervention 3: (high support, placebo): individual (7 sessions) and telephone counseling (5 sessions), self-help materials, plus *placebo*.	N=97; Age 61.2, ±9.4 yr; 52.6% women; education and household income not reported	Postbronchodilator FEV_1 1.6 ±6 L			
	Intervention 4 (high support, NRT): individual (7 sessions) and telephone counseling (5 sessions), self-help materials, plus *nicotine sublingual tablet*.	N=90; Age 61.3, ±9.6 yr; 48.9% women; education and household income not reported	Postbronchodilator FEV_1 1.5 ±7 L			

Authors (Year)	Conditions Compared	Sample Characteristics	Baseline Lung Function	Duration of Intervention	Outcome	Results
Wagena et al. (2005)	Control: counseling (in-person, telephone), plus *placebo*.	N=48 patients with COPD, demographics not reported for subgroup; group (N=89) Age 51.3, ±8.4 yr; 48.3% women; education and household income not reported	Lung function not reported for COPD subgroup; group (N=89) postbronchodilator FEV_1, % predicted 87.4 ±23.0	12 wk	Self-reported sustained abstinence from wk 4-26, biochemically confirmed at wk 4, 12, and 26 (urine cotinine ≤60 ng/mL)	Sustained abstinence was higher in the bupropion (27.3%) vs. placebo condition (8.3%) (*P*=.02). No differences between the nortriptyline and placebo or the bupropion and nortriptyline conditions.
	Intervention 1: counseling (in-person, telephone), plus *bupropion SR*.	N=44 patients with COPD, demographics not reported for subgroup; group (N=86) Age 51.1, ±8.3 yr; 60.5% women; education and household income not reported	Lung function not reported for COPD subgroup; group (N=86) postbronchodilator FEV_1, % predicted 86.3 ±21.0			
	Intervention 2: counseling (in-person, telephone), plus *nortriptyline*.	N=52 patients with COPD, demographics not reported for subgroup; group (N=80) Age 51.2, ±9.1 yr; 45.0% women; education and household income not reported	Lung function not reported for COPD subgroup; group (N=80) postbronchodilator FEV_1, % predicted 83.1 ±21.7			
Zarghami et al. (2019)	Intervention 1: Guided self-change (GSC: self-assessment of smoking risks, barriers to quitting, and personalized counselor feedback).	N=19; Age 50, ±6 yr; gender, education, and household income not reported	FEV_1 2.4 ±6 L FVC 3.7 ±7 L	5 wk	Biochemically confirmed abstinence at 6-, 12, and 29-wk follow-up assessments (breath CO, cut-off point not reported)	At wk 6, 12, and 29, abstinence rates were higher for participants who received intervention 1 (21.1, 31.6, 47.4%, respectively) or intervention 3 (36.8, 36.8, 47.4%, respectively) vs. intervention 2 (5.3, 15.3, 21.1%, respectively) (*P*=.001). No differences between interventions 1 and 3 (i.e., no added benefit of NRT).
	Intervention 2: NRT only (*ad libitum nicotine gum*).	N=19; Age 56, ±10 yr; gender, education, and household income not reported	FEV_1 1.9 ±7 L FVC 3.2 1.0 L			
	Intervention 3: GSC plus NRT (*ad libitum nicotine gum*).	N=19; Age 54, ±8 yr; gender, education, and household income not reported	FEV_1 1.9 ±7 L FVC 3.4 ± 0.8 L			

Note: All studies summarized in Table 2 used randomized controlled trials.

Abbreviations: FEV_1 = Forced Expiratory Volume during 1st sec of forced expiration; FVC = Forced Vital Capacity; NRT = Nicotine Replacement Therapy; SR = Sustained Release.

"Usual care" for smoking cessation generally consists of low-intensity health education, simple smoking cessation advice, and encouragement to quit smoking. Type of pharmacotherapy tested in each study condition is italicized.