Eur Respir J 2013; 41: 727–734
DOI: 10.1183/09031936.00014012

REVIEW

Smoking cessation strategies in patients with COPD

Miriam J. Warnier*,#, Evelien E.S. van Riet*, Frans H. Rutten*, Marie Louise De Bruin# and Alfred P.E. Sachs*

ABSTRACT: Smoking cessation is the cornerstone of treatment of chronic obstructive pulmonary disease (COPD) patients. This systematic review evaluates the effectiveness of behavioural and pharmacological smoking cessation strategies in COPD patients.

MEDLINE was searched from January 2002 to October 2011. Randomised controlled trials evaluating the effect of smoking cessation interventions for COPD patients, published in English, were selected. The methodological quality of included trials was assessed using the Delphi list by two reviewers independently. The relative risks of smoking cessation due to the intervention, compared with controls, were calculated.

Eight studies met the inclusion criteria. Heterogeneity was observed for study population, the intervention strategy, the follow-up period and the outcome. According to the Delphi list methodological quality scores, five studies were considered to be of acceptable quality. Pharmacological therapy combined with behavioural counselling was more effective than each strategy separately. In COPD patients, the intensity of counselling did not seem to influence the results, nor did the choice of drug therapy make a difference.

This systematic review makes clear that in COPD patients, pharmacological therapy combined with behavioural counselling is more effective than each strategy separately. Neither the intensity of counselling nor the type of anti-smoking drug made a difference.

KEYWORDS: Behavioural therapy, chronic obstructive pulmonary disease, pharmacotherapy, smoking cessation, systematic review, tobacco use cessation

The single most common cause of chronic obstructive pulmonary disease (COPD) is cigarette smoking [1]. About 15–20% of smokers develop COPD [2, 3] and ~37% of the COPD patients are current smokers [4]. Because almost all patients with COPD smoke or have smoked in the past, they are also at increased risk for developing lung cancer [5] as well as cardiovascular diseases (*e.g.* coronary, peripheral and cerebral artery diseases) and an eventually higher cardiovascular mortality rate [6–8].

Smoking cessation [9–11], as well as pharmacological treatment of COPD [12], improves symptoms and quality of life. However, only smoking cessation substantially changes the clinical course of COPD by reducing the rate of decline of pulmonary function and all-cause mortality [9, 13, 14]. Additionally, smoking cessation reduces the risk of developing and eventually dying from lung cancer, cardiovascular disease and other tobacco-related illnesses [15, 16]. Patients with COPD therefore have a greater and more urgent need to stop smoking than the average smoker. For this, the European Respiratory Society Task Force guidelines for smoking cessation in patients with respiratory disease recommend integration of smoking cessation treatment into the management of the patients' condition [17, 18]. However, COPD patients are far more resistant to smoking cessation treatment than ''healthy'' smokers, partly because of older age, higher pack-year history and stronger physical dependence on nicotine [19]. Because COPD patients have a higher risk for depressive symptoms [20–25], smoking cessation attempts may be less successful and proportion of relapses may be higher [21, 23].

In 2002, VAN DER MEER *et al.* [21] conducted a Cochrane review to determine the effectiveness

AFFILIATIONS
*Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, and
#Division of Pharmacoepidemiology and Clinical Pharmacology, Utrecht Institute for Pharmaceutical Sciences, Utrecht, The Netherlands.

CORRESPONDENCE
M.J. Warnier
Julius Center for Health Sciences and Primary Care, and Dept of Pharmacoepidemiology and Clinical Pharmacology
Utrecht Institute for Pharmaceutical Sciences
PO-box 80082
3508 TB Utrecht
The Netherlands
E-mail: m.j.warnier@uu.nl

Received:
Jan 24 2012
Accepted after revision:
Aug 05 2012
First published online:
Aug 30 2012

European Respiratory Journal
Print ISSN 0903-1936
Online ISSN 1399-3003

This article has supplementary material available from www.erj.ersjournals.com

of smoking cessation interventions in COPD patients, concluding that a combination of psychosocial and pharmacological interventions is superior to no treatment or to psychological interventions alone. They recommended more randomised controlled trials, investigating whether tailoring interventions to the needs of COPD patients improves quit rates in these patients.

During the last decade, the attitude of physicians towards smoking has changed. More attention has been drawn to the biomedical aetiology of tobacco addiction, perceiving tobacco addiction more as a neuropsychological disease instead of simply an unhealthy lifestyle [26]. Awareness of the importance of smoking cessation medication has not only increased among health professionals, but also among responsible persons in most western governments. New laws have been introduced banning smoking from public places in Europe, Australia, Canada and the USA, and, in addition, the public opinion of smoking has shifted to regard it as something that is not socially acceptable [27–29].

The aforementioned changes might have affected the randomised controlled trials on smoking cessation intervention programmes tailored to the needs of COPD patients. In order to facilitate implementation of the newest insights in smoking cessation treatment of COPD patients, the aim of this systematic review was to investigate the efficacy and effectiveness of different behavioural and pharmacological smoking cessation strategies in COPD patients since 2002.

METHODS

Search strategy

MEDLINE was searched from January 1, 2002 to October 20, 2011. The keywords (Medical Subject Headings and text search terms) describing the study population were ''chronic obstructive pulmonary disease'', ''chronic obstructive lung disease'', ''COLD'', ''emphysem*'', ''bronchit*'', ''COPD'', ''emphysema'' and ''chronic obstructive airway disease''. The keywords describing smoking cessation interventions were ''smoking'', ''smoking cessation'', ''tobacco'', ''tobacco use cessation'', ''tobacco use disorder'', ''nicotine'', ''cessation intervention'', ''smoking cessation program'', ''quit*'', ''smok*'' and ''cessation''. All these were combined with keywords referring to outcome ''abstain*'', ''abstin*'', ''abstinence'', ''abstination'', ''quit*'', ''stop*'', ''cessat*'' and ''ceas*''. To identify randomised controlled trials validated search terms for MEDLINE searches were used [30]. The search was limited to articles published in English or Dutch. For determining additional studies, reference lists of review articles and included studies were scrutinised [21, 31–35].

Study selection

Abstracts of identified publications were screened for eligibility. If potentially relevant abstracts did not provide enough information, full papers were retrieved. Studies were selected by applying the inclusion criteria: 1) COPD patients; 2) randomised controlled trial; 3) evaluation of smoking cessation intervention; and 4) published in English or Dutch.

Data extraction and quality assessment

A structured data extraction was performed, focussing on design, setting, type of intervention, patient characteristics, outcome measures and results. Methodological quality of included studies were rated, applying the Delphi list [36]. Items were scored ''yes'', ''no'' or ''don't know''. Only items that were assessed with ''yes'' were given a score of 1 point. A total score for overall methodological quality out of a maximum of 9 points was obtained by applying equal weights to all items. For the definition of ''acceptable methodological quality'', an arbitrary but generally accepted cut-off value of $\geqslant 5$ points was used.

If enough data were available in the original article, *i.e.* absolute numbers of smoking cessation in each treatment group, the relative risk (RR) with corresponding 95% confidence intervals were calculated by determining the rate of smoking cessation in both the treated group and the untreated group. When both point prevalence and continuous abstinence were provided, only continuous abstinence was reported.

Two reviewers (M.J. Warnier and E.E.S. van Riet) independently screened and selected the publications, as well as extracting data and assessing methodological quality. Consensus was used to resolve disagreement. If consensus could not be reached, a third reviewer (A.P.E. Sachs) was consulted.

RESULTS

Identification of studies

Results of the search strategy are presented in figure 1. In total, eight randomised controlled trials (11 publications) were included [9, 25, 37–45]. As these studies were very heterogeneous regarding study population, type of intervention, duration of follow-up and outcome measure, no pooling of data was carried out. Characteristics of the included studies and of the participants within each study are shown in tables 1 and 2, respectively.

Methodological assessment

According to the Delphi List methodological quality scores, five studies were considered to be of acceptable quality ($\geqslant 5$ points, table 1). The scores for methodological quality varied between 3 and 9 points. The study of WAGENA *et al.* [25] had a maximum score of 9 points, indicating a low probability of bias. The most prevalent methodological shortcomings were an absence of blinding of the care provider, patient and outcome assessor, and a lack of concealment of the randomisation method. All studies used biochemical validation to confirm self-reported smoking cessation (table 1). The three studies that did not have an acceptable quality score ($\geqslant 5$ points) presented the following shortcomings: none of the three studies concealed the treatment allocation or blinded the care provider, patient and outcome assessor. In addition, in the studies by CHRISTENHUSZ and co-workers [43, 44] and HILBERINK and co-workers [41, 42], the groups were not comparable at baseline. In addition, CHRISTENHUSZ and co-workers [43, 44] did not use an intention-to-treat analysis and WILSON *et al.* [37] did not provide point estimates of smoking cessation.

Behavioural intervention

BORGLYKKE *et al.* [45] showed that patients hospitalised with symptoms of acute exacerbation of COPD who participated in a smoking cessation group significantly more often stopped smoking after 1 yr (29.8%), compared with hospitalised patients who only received information on the benefits of smoking cessation (12.7%) (RR 2.3, 95% CI 1.3–4.2).

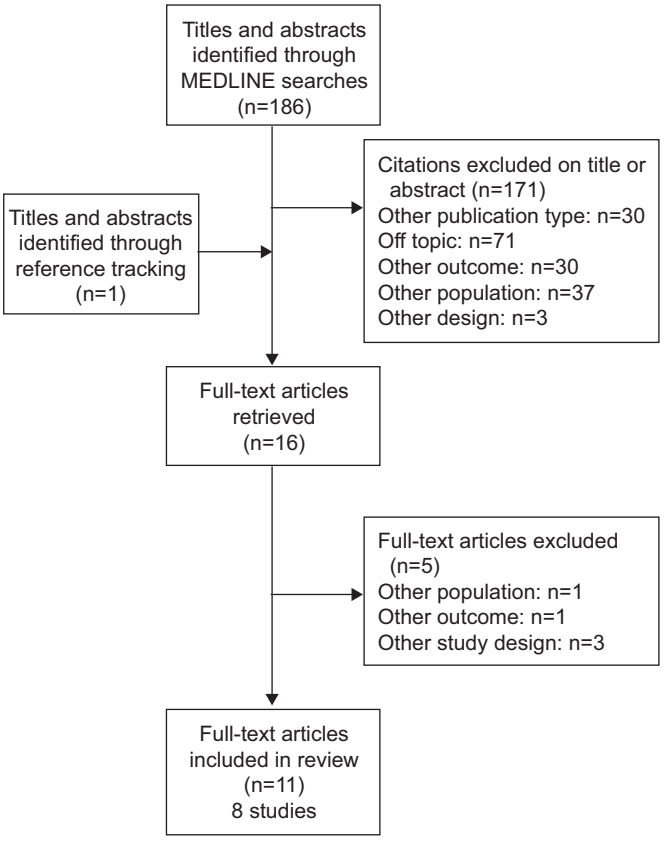

FIGURE 1. Flow chart showing results of the search strategy.

Combining a pharmacological and behavioural intervention

Added value of a pharmacological intervention

TASHKIN *et al.* [49] evaluated the effect of varenicline treatment compared with placebo. After 1 yr, the use of varenicline (18.5%) resulted in significantly higher continuous abstinence rates (RR 3.3, 95% CI 1.9–5.9) compared with placebo (5.6%).

WAGENA *et al.* [25] evaluated the smoking cessation effect of bupropion or nortriptyline. Out of the 225 participants, 44% were at risk for COPD (Global Initiative for Chronic Obstructive Lung Disease stage 0 [46]). After 6 months, the use of bupropion (28%) as well as nortriptyline (25%) resulted in higher prolonged abstinence rates compared with placebo (15%). Only the difference between bupropion and placebo reached statistical significance (RR 1.91, 95% CI 1.04–3.50). Bupropion and nortriptyline were equally effective (RR 1.12, 95% CI 0.67–1.86).

Additional value of a combined intervention

KOTZ *et al.* [39] evaluated the effect of confrontational counselling and regular counselling, both combined with nortriptyline, compared with usual care. Compared with usual care, regular counselling with nortriptyline (11.6%) as well as confrontational counselling with nortriptyline (11.2%) increased the prolonged abstinence rates after 1 year, although not statistically significant, compared to usual care (5.9%) (RR 2.1 (95% CI 0.7–5.8) and RR 1.9 (95% CI 0.7–5.6), respectively). Confrontational counselling and regular counselling plus nortriptyline were equally effective (RR 1.0, 95% CI 0.5–2.0).

HILBERINK and co-workers [41, 42, 50] evaluated the effect of a behavioural intervention combined with nicotine replacement therapy (NRT) alone or with NRT plus bupropion, compared with usual care, in patients with a clinical diagnosis of COPD. The point prevalence of abstinence after 1 yr was nonsignificantly higher in both intervention groups (NRT group, 7.4%; NRT plus bupropion group, 7.6%) than in the usual care group (3.4%) (RR 2.2 (95% CI 0.8–5.8) and RR 2.3 (95% CI 0.9–5.9), respectively).

Factorial design evaluating both a behavioural and pharmacological intervention

TØNNESEN *et al.* [9] evaluated the efficacy of nicotine sublingual tablet or placebo combined with either high or low behavioural support. After 1 yr, significantly higher quit rates were observed in the group using sublingual nicotine tablets (14%) compared with placebo (5%) (RR 2.60, 95% CI 1.29–5.24). However, no significant difference in sustained abstinence rate between the groups receiving low (9%) or high behavioural support (10%) (RR 1.12, 95% CI 0.60–2.09), was observed.

Behavioural intervention combined with free pharmacotherapy

CHRISTENHUSZ and co-workers [43, 44] evaluated the effect of SmokeStop therapy (SST) with free bupropion compared with the minimal intervention strategy. The SST group received bupropion for free while in the control group, pharmacological support was recommended but voluntary and at the patient's costs. After 12 months, the continuous abstinence rate was significantly higher in the SST group (19% *versus* 9%; RR 2.22, 95% CI 1.06–4.65).

WILSON *et al.* [37] evaluated whether an intensive individual or group behavioural intervention increased smoking cessation rates compared with usual care. As only 91 hospital outpatients participated, the number of patients in each subgroup was small. The trial failed to find a statistically significant difference between the treatment groups, as after 1 yr, none of the patients achieved complete smoking cessation.

DISCUSSION

This is the first systematic review since 2002 evaluating the efficacy and effectiveness of pharmacological and behavioural smoking cessation interventions in COPD patients. Eight studies fulfilled the inclusion criteria. The results of the included studies indicate that pharmacological therapy, combined with behavioural counselling, is still the most effective smoking cessation strategy for COPD patients. The intensity of counselling did not seem to influence the results. Neither did the choice of drug therapy make a difference. These findings are in line with the results of the Cochrane review of VAN DER MEER *et al.* [21] published in 2002.

Compared with the review of VAN DER MEER *et al.* [21], the studies included in our review were of higher methodological quality; in the review of VAN DER MEER *et al.* [21], only two (40%) of the five included studies had five or more ''yes'' scores on the Delphi list, compared with 63% (five out of eight) in this review. Studies included in the review of VAN DER MEER *et al.* [21] only determined the effectiveness of NRT and bupropion, while this review also included studies investigating the newer drugs varenicline and nortriptyline. Another difference is that the behavioural interventions in this review are more tailored to the

TABLE 1 Characteristics of studies

First author [ref.]	Methods#	Duration of exposure/follow-up	Intervention	Participants n	Primary end-point/ biochemical validation technique	Results		Delphi list [36] score
						Subjects meeting end-point n/N (%)	RR (95% CI)	
Wagena [25]	Population based the Netherlands RCT, double blind, placebo controlled	12 weeks/ 6 months	I1: bupropion I2: nortriptyline C: placebo All groups: individual face-to-face counselling + supportive telephone calls	255	Prolonged abstinence, week 4 to 26/urinary cotinine <60 ng·mL^{-1}	I1: 24/86 (27.9) I2: 20/80 (25.0) C3: 13/89 (14.6)	I1 *versus* C: 1.9 (1.0–3.5) I2 *versus* C: 1.7 (0.9–3.2) I1 *versus* I2: 1.1 (0.7–1.9)	9
Tønnesen [9]	Hospital outpatients Denmark RCT, placebo controlled	1 yr/1 yr	I1: nicotine sublingual tablet + low support I2: nicotine sublingual tablet + high support I3: placebo sublingual tablet + high support C: placebo sublingual tablet + low support	370	Sustained abstinence, week 2 to 52/CO <10 ppm	NRT *versus* placebo: NRT 26/185 (14.1) Placebo 10/185 (5.4) High *versus* low support: high 19/187 (10.2) low 17/183 (9.3)	NRT *versus* placebo: 2.6 (1.3–5.2) High *versus* low support: 1.1 (0.6–2.0)	5
Christenhusz [43, 44]	Hospital outpatients the Netherlands RCT	3 months/1 yr	I: SST C: MIS for lung patients	225	Continuous abstinence, 1 yr/salivary cotinine <20 ng·mL^{-1}	I: 20/114 (17.5) C: 9/111 (8.1)	2.2 (1.0–4.5)	3
Wilson [37]	Hospital outpatients Ireland RCT	5 weeks/1 yr	I1: individual support, 5 individual sessions with nurse + free NRT offered I2: group support, brief advice to stop smoking, 5 group sessions with nurse + free NRT offered C: usual care, brief advice to stop smoking	91	Complete cessation, 1 yr/CO measurement ⩽10 ppm + salivary cotinine ⩽10 ng·mL^{-1}	C: 0 I1: 0 I2: 0	NS	4
Borglykke [45]	Hospitalised patients Denmark RCT	5 weeks/1 yr	C: no additional intervention I: participation in smoking cessation group, weekly 2-h sessions, 5 weeks All groups: information on benefit of smoking cessation at admission	223	Point abstinence, 1 yr/COHb <2%	C: 13/102 (12.7) I: 36/121 (29.8)	2.3 (1.3–4.2)	5
Kotz [39]	Population based the Netherlands RCT	4 weeks/1 yr	C: usual care I1: confrontational counselling by nurse + nortriptyline I2: health education and promotion by nurse + nortriptyline	296	Prolonged abstinence, week 5 to 52/urinary cotinine <50 ng·mL^{-1}	C: 4/68 (5.9) I1: 13/116 (11.2) I2: 13/112 (11.6)	I1 *versus* I2: 1.0 (0.5–2.0) I1 *versus* C: 1.9 (0.7–5.6) I2 *versus* C: 2.0 (0.7–5.8)	7

TABLE 1 Continued

First author [ref.]	Methods#	Duration of exposure/follow-up	Intervention	Participants n	Primary end-point/ biochemical validation technique	Results		Delphi list [36] score
						Subjects meeting end-point n/N (%)	RR (95% CI)	
TASHKIN [38]	Hospital outpatients USA, Spain, France, Italy RCT	12 weeks/1 yr	C: placebo I: varenicline All groups: educational booklet, brief counselling sessions at telephone call (n=6) and clinic visits (n=19)	499	Continuous abstinence, 1 yr/ CO ⩽10 ppm	I: 46/248 (18.5) C: 14/251 (5.6)	3.3 (1.9–5.9)	6
HILBERINK [41, 42]	General practices the Netherlands Cluster RCT	Depending on motivational stage/1 yr	I1: counseling strategy + NRT I2: counseling strategy + NRT + bupropion C: usual care Counselling strategy: intensified MIS according to motivational stage	667	Point prevalence, 1 yr/urinary cotinine lever <50 ng·mL^{-1}	I1: 18/243 (7.4) I2: 21/276 (7.6) C: 5/148 (3.4)	I2 *versus* I1: 1.0 (0.6–1.9) I1 *versus* C: 2.2 (0.8–5.8) I2 *versus* C: 2.3 (0.9–5.9)	4

RR: relative risk; RCT: randomised controlled trial; I: intervention group; C: control group; CO: carbon monoxide; NRT: nicotine replacement therapy; SST: SmokeStop therapy (group and individual counselling, telephone contacts, free bupropion); MIS: minimal intervention strategy; NS: nonsignificant; COHb: carboxyhaemoglobin. #: setting, country and design.

needs of the COPD patient compared with the behavioural interventions included in the review of VAN DER MEER *et al.* [21].

Pharmacological interventions

Four of the included studies mainly evaluated the effect of pharmacological treatments. Pharmacological support with bupropion, nortriptyline, NRT or varenicline results in higher smoking cessation rates compared with placebo, an effect also seen in non-COPD smokers [9, 25, 38, 41, 42, 49]. Importantly, none of the RCTs showed a significant difference in smoking cessation rates between different drugs. This is in contrast to studies in smokers without COPD. Studies comparing drugs and a meta-analysis suggest that varenicline would be more effective for smoking cessation than the antidepressants nortriptyline and bupropion and NRT [51, 52], while bupropion, nortriptyline and NRT were equally effective [53]. Interestingly, a recent meta-analysis by SHAH *et al.* [54] showed that combining NRT with one of the other agents resulted in significantly higher abstinence rates if compared with any of the monotherapies in non-COPD smokers.

Behavioural interventions

Four of the included studies evaluated the effect of a behavioural intervention. TØNNESEN *et al.* [9] found no significant difference in abstinence rates between low or high behavioural support, possibly because of too much similarity of the two regimens. CHRISTENHUSZ and co-workers [43, 44] and BORGLYKKE *et al.* [45] showed that group therapy increases smoking cessation rates in COPD patients. Counselling combined with pharmacotherapy was more effective than usual care in the studies of HILBERINK and co-workers [41, 42] and KOTZ *et al.* [39]. However, these results were not statistically significant, which may be due to the high treatment standard of usual care and low statistical power of the studies.

In non COPD smokers, the results of different studies and meta-analyses suggest that all behavioural interventions are more effective when combined with pharmacotherapy to accomplish smoking cessation. A recent study by HOOGENDOORN *et al.* [34] compared the costs of intensive counselling and pharmacotherapy. They showed that compared with usual care, intensive counselling and pharmacotherapy resulted in low costs per quality adjusted life-year gained, and pharmacotherapy was cost saving compared with intensive counselling.

Limitations

Interpretation of the results of the studies was challenging. First, only five out of eight studies were of acceptable methodological quality, applying a well-accepted cut-off value of ⩾5 points to the Delphi list. Next, the numbers of patients included in the studies were small, resulting in broad confidence intervals. Furthermore, different types of outcome measures were used, making it impossible to directly compare study results. Besides, the majority of the studies failed to detect a statistically significant difference between the various smoking cessation strategies and usual care stop smoking guidance; this may be due to the high standard of usual care nowadays. Lastly, no clear uniform definition of COPD was provided.

TABLE 2 Characteristics of participants

First author [ref.]	Patients n	Age yrs	Males n (%)	Definition of COPD	FEV_1 % pred
Wagena [25]	I1: 86	I1: 51.1±8.3	I1: 34 (40)	GOLD criteria, stage 0 (at risk for)	I1: 86.3±21.0
	I2: 80	I2: 51.2±9.1	I2: 44 (55)	included [46]	I2: 83.1±21.7
	C: 89	C: 51.3±8.4	C: 46 (52)		C: 87.4±23.0
Tønnesen [9]	I1: 95	I1: 59.2±10.3	I1: 45 (47)	Post-bronchodilator	I1: 55.1±15.4
	I2: 90	I2: 61.3±9.6	I2: 46 (51)	FEV_1/FVC <70%	I2: 53.4±19.4
	I3: 97	I3: 61.2±9.4	I3: 46 (47)	FEV_1 <90% pred	I3: 58.2±17.8
	C: 88	C: 62.5±9.3	C: 40 (46)		C: 56.0±19.1
Christenhusz [43, 44]	I: 114	I: 57.0±8.4	I: 55 (48)	FEV_1 <69% pred[#]	I: 65.6±27.4
	C: 111	C: 59.6±8.5	C: 63 (57)		C: 62.8±25.7
Wilson [37]	I1: 27	I1: 61.0±8	I1: 14 (52)	FEV_1/FVC <70%	I1: 52.1±20
	I2: 29	I2: 60.4±9	I2: 12 (41)	FEV_1 <80% pred[¶]	I2: 54.6±23
	C: 35	C: 61.4±8	C: 18 (51)		C: 54.3±20
Borglykke [45]	I: 121	I: 65	I: 42 (35)	Patients having symptoms of	Not available
	C: 102	C: 67	C: 37 (36)	COPD	
Kotz [39]	I1: 116	I1: 53.8±7.0	I1: 71 (61)	Post-bronchodilator	I1: 80.5±14.7
	I2: 112	I2: 54.9±8.0	I2: 74 (66)	FEV_1/FVC <70%	I2: 83.7±16.8
	C: 68	C: 53.0±7.6	C: 40 (59)	FEV_1 ⩾50% pred	C: 79.7±14.0
Tashkin [38]	I: 248	I: 57.2±9.1	I: 155 (63)	Post-bronchodilator	I: 70.8±17.0
	C: 251	C: 57.1±9.0	C: 156 (62)	FEV_1/FVC <70%	C 69.1±16.9
				FEV_1 ⩾50% pred	
Hilberink [41, 42]	I1: 243	I1: 58.0±12.2	I1: 113 (47)	Clinical criteria by GP	Not available
	I2: 276	I2: 60.7±11.2	I2: 132 (48)		
	C: 148	C: 60.1±11.5	C: 82 (55)		

Data are presented as mean±SD, unless otherwise stated. COPD: chronic obstructive pulmonary disease; FEV_1: forced expiratory volume in 1 s; % pred: % predicted; I: intervention group; C: control group; GOLD: Global Initiative for Chronic Obstructive Lung Disease; FVC: forced vital capacity; GP: general practitioner. [#]: moderate or severe COPD according to American Thoracic Society criteria [47]; [¶]: COPD according to National Institute for Health and Clinical Excellence guidelines [48].

Recommendations

Compared with the review of van der Meer *et al*. [21], the studies included in this 2002–2011 review are of higher methodological quality, investigated more different and newer drug therapies, and the behavioural interventions studied were more tailored to the needs of the COPD patients. However, in order to be able to identify optimal smoking cessation strategies for patients with COPD, we would like to propose some recommendations. First, more high-quality, well-powered randomised controlled trials with a minimal follow up of 1-yr and continuous abstinence from target quit date as the primary outcome measure should be performed. In order to obtain high quality, randomised controlled trials should be performed according to the Consolidated Standards of Reporting Trials statements in future research [55]. Secondly, to realise uniformity between smoking cessation studies, the duration of follow-up should be ⩾1 yr and continuous abstinence from target quit date should be used as primary outcome measure. West *et al.* [56] proposed six standard criteria to realise uniformity between smoking cessation studies: the Russell Standard. We recommend the use of these criteria to enable meaningful comparison between studies.

Subsequently, we would like to recommend a meta-analysis of individual patient data (individual data analysis) of RCTs, in order to identify subgroups of patients with COPD with specific patient characteristics (*e.g.* pack-years of smoking, age, sex, comorbidities and number of quit attempts) that might benefit from various smoking cessation strategies [57]. Smoking COPD patients are known to be a difficult target for smoking cessation, being more resistant to smoking cessation therapies. In order to amplify the development of patient-tailored smoking cessation strategies, it would be very useful to identify the characteristics of smokers with COPD and to evaluate how these characteristics may affect smoking cessation strategies (*e.g.* COPD patients have a higher risk for depressive symptoms and COPD smokers who are depressed at the same time may benefit more from antidepressant smoking cessation therapy). Finally, we recommend integrating smoking cessation treatment into regular COPD care, to lower barriers for smoking cessation treatment and to advocate a proactive role of physicians in motivating COPD patients to quit smoking [18].

Conclusions

To conclude, results of this 2002–2011 systematic review of smoking cessation strategies for patients with COPD indicate that pharmacological therapy, in addition to behavioural counselling, is the most effective smoking cessation strategy for COPD patients. In contrast to non-COPD smokers, neither the intensity of counselling nor the type of anti-smoking drug made a significant difference in smoking quit results.

Patients with COPD, being more resistant to smoking cessation therapies, could benefit significantly from smoking cessation, as smoking cessation is currently the only evidenced-based

intervention to change the clinical course of the disease. Further research should focus on identifying subgroups that benefit most of patient-tailored smoking cessation strategies.

STATEMENT OF INTEREST

None declared.

REFERENCES

1 Fabbri LM, Hurd SS. Global Strategy for the Diagnosis, Management and Prevention of COPD: 2003 update. *Eur Respir J* 2003; 22: 1–2.
2 Fletcher C, Peto R. The natural history of chronic airflow obstruction. *Br Med J* 1977; 1: 1645–1648.
3 Wagena EJ, Zeegers MP, van Schayck CP, *et al.* Benefits and risks of pharmacological smoking cessation therapies in chronic obstructive pulmonary disease. *Drug Saf* 2003; 26: 381–403.
4 Shahab L, Jarvis MJ, Britton J, *et al.* Prevalence, diagnosis and relation to tobacco dependence of chronic obstructive pulmonary disease in a nationally representative population sample. *Thorax* 2006; 61: 1043–1047.
5 Doll R, Hill AB. Smoking and carcinoma of the lung preliminary report. *Br Med J* 1950; 2: 739–748.
6 Falk JA, Kadiev S, Criner GJ, *et al.* Cardiac disease in chronic obstructive pulmonary disease. *Proc Am Thorac Soc* 2008; 5: 543–548.
7 Finkelstein J, Cha E, Scharf SM. Chronic obstructive pulmonary disease as an independent risk factor for cardiovascular morbidity. *Int J Chron Obstruct Pulmon Dis* 2009; 4: 337–349.
8 Sidney S, Sorel M, Quesenberry CP Jr, *et al.* COPD and incident cardiovascular disease hospitalizations and mortality: Kaiser Permanente Medical Care Program. *Chest* 2005; 128: 2068–2075.
9 Tønnesen P, Mikkelsen K, Bremann L. Nurse-conducted smoking cessation in patients with COPD using nicotine sublingual tablets and behavioral support. *Chest* 2006; 130: 334–342.
10 Godtfredsen NS, Vestbo J, Osler M, *et al.* Risk of hospital admission for COPD following smoking cessation and reduction: a Danish population study. *Thorax* 2002; 57: 967–972.
11 Kanner RE, Connett JE, Williams DE, *et al.* Effects of randomized assignment to a smoking cessation intervention and changes in smoking habits on respiratory symptoms in smokers with early chronic obstructive pulmonary disease: the Lung Health Study. *Am J Med* 1999; 106: 410–416.
12 Pauwels RA, Buist AS, Calverley PM. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop summary. *Am J Respir Crit Care Med* 2001; 163: 1256–1276.
13 Anthonisen NR, Connett JE, Kiley JP, *et al.* Effects of smoking intervention and the use of an inhaled anticholinergic bronchodilator on the rate of decline of FEV1. The Lung Health Study. *JAMA* 1994; 272: 1497–1505.
14 Burchfiel CM, Marcus EB, Curb JD, *et al.* Effects of smoking and smoking cessation on longitudinal decline in pulmonary function. *Am J Respir Crit Care Med* 1995; 151: 1778–1785.
15 Doll R, Peto R, Boreham J, *et al.* Mortality in relation to smoking: 50 years' observations on male British doctors. *BMJ* 2004; 328: 1519–1519.
16 Anthonisen NR, Skeans MA, Wise RA. The effects of a smoking cessation intervention on 14.5-year mortality: a randomized clinical trial. *Ann Intern Med* 2005; 142: 233–239.
17 Tonnesen P, Carrozzi L, Fagerstrom KO, *et al.* Smoking cessation in patients with respiratory diseases: A high priority, integral component of therapy. *Eur Respir J* 2007; 29: 390–417.
18 Tnnesen P, Carrozzi L, Fagerstrm KO, *et al.* Smoking cessation in patients with respiratory diseases: a high priority, integral component of therapy. *Eur Respir J* 2007; 29: 390–417.
19 Jimenez-Ruiz CA, Masa F, Miravitlles M, *et al.* Smoking characteristics: differences in attitudes and dependence between healthy smokers and smokers with COPD. *Chest* 2001; 119: 1365–1370.
20 Zhang MW, Ho RC, Cheung MW, *et al.* Prevalence of depressive symptoms in patients with chronic obstructive pulmonary disease: a systematic review, meta-analysis and meta-regression. *Gen Hosp Psychiatry* 2011; 33: 217–223.
21 van der Meer RM, Wagena EJ, Ostelo RW, *et al.* Smoking cessation for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2003; 2: CD002999.
22 Wagena EJ, Arrindell WA, Wouters EF, *et al.* Are patients with COPD psychologically distressed? *Eur Respir J* 2005; 26: 242–248.
23 Glassman AH, Helzer JE, Covey LS, *et al.* Smoking, smoking cessation, and major depression. *JAMA* 1990; 264: 1546–1549.
24 Wagena EJ, Van Der Meer RM, Ostelo RJ, *et al.* The efficacy of smoking cessation strategies in people with chronic obstructive pulmonary disease: results from a systematic review. *Respir Med* 2005; 1: 29–39.
25 Wagena EJ, Knipschild PG, Huibers MJ, *et al.* Efficacy of bupropion and nortriptyline for smoking cessation among people at risk for or with chronic obstructive pulmonary disease. *Arch Intern Med* 2005; 165: 2286–2292.
26 Benowitz N. Nicotine addiction. *N Engl J Med* 2010; 362: 2295–2303.
27 Dilley J, Harris J, Boysun M, *et al.* Program, policy, and price interventions for tobacco control: quantifying the return on investment of a state tobacco control program. *Am J Public Health* 2012; 102: e22–e28.
28 Nagelhout G, de Vries H, Fong G, *et al.* Pathways of change explaining the effect of smoke-free legislation on smoking cessation in the Netherlands. An Application of the international tobacco control conceptual model. *Nicotine Tob Res* 2012; [in press DOI: 10.1093/ntr/nts081].
29 World Health Organization. WHO Report on the Global Tobacco Epidemic, 2011: Warning About the Dangers of Tobacco. Geneva, WHO, 2011.
30 Glanville JM, Lefebvre C, Miles JN, *et al.* How to identify randomized controlled trials in MEDLINE: ten years on. *J Med Libr Assoc* 2006; 94: 130–136.
31 Wagena EJ, van der Meer RM, Ostelo RJ, *et al.* The efficacy of smoking cessation strategies in people with chronic obstructive pulmonary disease: results from a systematic review. *Respir Med* 2004; 98: 805–815.
32 Strassmann R, Bausch B, Spaar A, *et al.* Smoking cessation interventions in COPD: a network meta-analysis of randomised trials. *Eur Respir J* 2009; 34: 634–640.
33 McRobbie H, Lee M, Juniper Z. Non-nicotine pharmacotherapies for smoking cessation. *Respir Med* 2005; 99: 1203–1212.
34 Hoogendoorn M, Feenstra TL, Hoogenveen RT, *et al.* Long-term effectiveness and cost-effectiveness of smoking cessation interventions in patients with COPD. *Thorax* 2010; 65: 711–718.
35 Hylkema MN, Sterk PJ, de Boer WI, *et al.* Tobacco use in relation to COPD and asthma. *Eur Respir J* 2007; 29: 438–445.
36 Verhagen AP, de Vet HC, de Bie RA, *et al.* The Delphi list: a criteria list for quality assessment of randomized clinical trials for conducting systematic reviews developed by Delphi consensus. *J Clin Epidemiol* 1998; 51: 1235–1241.
37 Wilson JS, Fitzsimons D, Bradbury I, *et al.* Does additional support by nurses enhance the effect of a brief smoking cessation intervention in people with moderate to severe chronic obstructive pulmonary disease? A randomised controlled trial. *Int J Nurs Stud* 2008; 45: 508–517.
38 Tashkin DP, Rennard S, Hays JT, *et al.* Effects of varenicline on smoking cessation in patients with mild to moderate COPD: a randomized controlled trial. *Chest* 2011; 139: 591–599.
39 Kotz D, Wesseling G, Huibers MJ, *et al.* Efficacy of confronting smokers with airflow limitation for smoking cessation. *Eur Respir J* 2009; 33: 754–762.

40 Kotz D, Wesseling G, Huibers MJ, *et al.* Efficacy of confrontational counselling for smoking cessation in smokers with previously undiagnosed mild to moderate airflow limitation: study protocol of a randomized controlled trial. *BMC Public Health* 2007; 7: 332.

41 Hilberink SR, Jacobs JE, Bottema BJ, *et al.* Smoking cessation in patients with COPD in daily general practice (SMOCC): six months' results. *Prev Med* 2005; 41: 822–827.

42 Hilberink SR, Jacobs JE, Breteler MH, *et al.* General practice counseling for patients with chronic obstructive pulmonary disease to quit smoking: impact after 1 year of two complex interventions. *Patient Educ Couns* 2011; 83: 120–124.

43 Christenhusz L, Pieterse M, Seydel E, *et al.* Prospective determinants of smoking cessation in COPD patients within a high intensity or a brief counseling intervention. *Patient Educ Couns* 2007; 66: 162–166.

44 Christenhusz LCA. Smoking Cessation in COPD Patients: (Cost-) Effectiveness of the Smokestoptherapy and Validation of Abstinence. PhD thesis, University of Twente, 2006.

45 Borglykke A, Pisinger C, Jorgensen T, *et al.* The effectiveness of smoking cessation groups offered to hospitalised patients with symptoms of exacerbations of chronic obstructive pulmonary disease (COPD). *Clin Respir J* 2008; 2: 158–165.

46 Pauwels RA, Buist AS, Ma P. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: National Heart, Lung, and Blood Institute and World Health Organization Global Initiative for Chronic Obstructive Lung Disease (GOLD): executive summary. *Respir Care* 2001; 46: 798–825.

47 Celli BR. ATS standards for the optimal management of chronic obstructive pulmonary disease. *Respirology* 1997; 2: Suppl. 1, S1–S4.

48 Gruffydd Jones K, Loveridge C. The 2010 NICE COPD Guidelines: how do they compare with the GOLD guidelines? *Prim Care Respir J* 2011; 20: 199–204.

49 Tashkin DP, Rennard S, Hays JT. Effects of varenicline on smoking cessation in patients with mild to moderate COPD: a randomized controlled trial. *Chest* 2011; 139: 591–599.

50 Hilberink SR, Jacobs JE, Bottema BJAM, *et al.* Smoking cessation in patients with COPD in daily general practice (SMOCC): six months' results. *Prev Med* 2005; 41: 822–827.

51 Cahill K, Stead LF, Lancaster T. Nicotine receptor partial agonists for smoking cessation. *Cochrane Database Syst Rev* 2008; 4: CD006103.

52 Wu P, Wilson K, Dimoulas P, *et al.* Effectiveness of smoking cessation therapies: a systematic review and meta-analysis. *BMC Public Health* 2006; 6: 300.

53 Hughes JR, Stead LF, Lancaster T. Antidepressants for smoking cessation. *Cochrane Database Syst Rev* 2007; 1: CD000031.

54 Shah SD, Wilken LA, Winkler SR, *et al.* Systematic review and meta-analysis of combination therapy for smoking cessation. *J Am Pharm Assoc (2003)* 2008; 48: 659–665.

55 Schulz K, Altman D, Moher D. CONSORT 2010 statement: Updated guidelines for reporting parallel group randomised trials. *Int J Surg* 2011; 9: 672–677.

56 West R, Hajek P, Stead L, *et al.* Outcome criteria in smoking cessation trials: proposal for a common standard. *Addiction* 2005; 100: 299–303.

57 Rovers M, Glasziou P, Appelman C, *et al.* Antibiotics for acute otitis media: a meta-analysis with individual patient data. *Lancet* 2006; 368: 1429–1435.