Smoking Cessation Interventions for Chronic Obstructive Pulmonary Disease - A Review of the literature

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Abstract

The aim of this systematic review is to establish the most effective stop smoking intervention approach for smokers with COPD. The search strategy included electronic databases: MEDLINE, EMBASE, AMED, PsycINFO, DARE, Cochrane Library and CINAHL between January, 2006 and January, 2010. References of the included studies were also screened for additional papers and further hand searches were conducted. The selection criteria included randomised controlled trials or quasi-randomised controlled trials with at least one group comprised of participants diagnosed with COPD. Two independent reviewers reviewed the included studies using a quality assessment form developed from the selection criteria. Divergence of quality assessment scores was resolved by the two reviewers and agreeing on a score. Four studies were selected. They indicated that psychosocial interventions combined with pharmacotherapy were effective in smoking cessation at 12 months post-intervention, although the effect was not statistically significant due to small sample size and heterogeneity between studies \( \text{OR} = 2.35, 95\% \text{CI}[0.25, 21.74] \). However, despite this medium effect size, due to a lack of universal use of pharmacotherapies in most of the studies, it makes a definitive comparison of efficacy difficult to determine. The review also shows the effectiveness of psychosocial treatment for people with or without COPD symptoms at 12 months, although the effect of disease severity is not clear. The review also highlights the difficulty of maintaining attendance at community-based locations compared to acute or research settings.

Key Words: Chronic Obstructive Pulmonary Disease, psychosocial interventions, pharmacotherapy.
Introduction

In 2007, the World Health Organization (WHO, http://www.who.int/respiratory/copd/en, Accessed November 11, 2009) estimated that Chronic Obstructive Pulmonary Disease (COPD) affected 210 million people and reported that in 2005 3 million people had died of COPD, corresponding to 5% of all global deaths. In 2002, Mannino,\(^1\) estimated that by 2020 this disease would be the 5\(^{th}\) largest contributor of disability-adjusted life-years worldwide while more recently the WHO (http://www.who.int/respiratory/copd/en, Accessed November 11, 2009) has predicted that by 2030 this disease will become the third leading cause of death worldwide; not all of these cases will be directly attributable to smoking but it is thought that smoking will play a significant factor.

In the United Kingdom (UK) nearly 900,000 people have been diagnosed with COPD, as cited by the National Health Service, 2009 (http://www.nhs.uk/Conditions/ChronicObstructivePulmonaryDisease/Pages/Introduction.aspx Accessed November 12th, 2009). However, the NHS (2009) estimates that the majority of people with COPD are unaware of their condition and that the real figure is approximately 3 million people in the UK with older people more likely to develop COPD.

Smoking Cessation and COPD

The National Institute for Health and Clinical Excellence, 2004, (www.nice.org.uk/CG012quickrefguide, Chronic obstructive pulmonary disease: Management of chronic pulmonary disease in adults in primary and secondary care. Accessed November 11\(^{th}\) 2009), recommends that all COPD patients who smoke should be encouraged to stop at every opportunity and offered pharmacotherapy combined with a behavioural support programme. However, while guidelines are set out by the Department of Health\(^2\) on supporting smokers in the general population to stop smoking no guidance is yet available as to the most effective way to support this chronic disease group in stopping smoking.

Many studies have found that this group differs from the general population in a number of ways that may affect not only their attempt to stop smoking but also the success of this attempt. Some of these differences include the type of smoker they are,\(^3\) their beliefs about how their smoking behaviour relates to their COPD condition\(^4\) as well as the effect that having a chronic disease has had on their psychological and emotional well-being.\(^5\) These factors need to be considered when designing effective stop smoking interventions.
Perception of the aetiology of the illness is an important factor playing a role in taking a decision to quit smoking. Walters and Coleman (2002) found that patients who attribute their respiratory symptoms to smoking are eight times (95% confidence interval [CI] [3.0, 23.3]) more likely to believe that their health will improve if they stop smoking and six times (95% CI [1.4, 23.3]) more likely to intend to stop smoking.

A key factor for patients with chronic diseases is adherence to treatment and long-term maintenance of the recommended behaviour changes. They attribute this to a range of factors including patients’ perception of their disease, type of treatment or medication, the quality of patient provider communication, the social environment and a raised level of anxiety and depression found in patients with COPD, although estimates of prevalence vary.

A combination of these factors has been associated with lower levels of self-efficacy and an impaired overall health status, such as dyspnoea, and loss and grief associated with the disability of COPD. Stage et al reported that depression is common in COPD patients with around 40% being affected with clinical depression. Despite these findings it is not always possible to identify the exact cause when making a diagnosis of depression in COPD patients because of common symptoms present in both COPD and depression such as fatigue and altered sleep patterns. It is difficult to quantify how many people with COPD continue to smoke after diagnosis. However, a number of clinical studies investigating the effectiveness of medications for the treatment of COPD have reported figures ranging between 38% and 43% of patients with moderately severe to severe disease levels continuing to smoke.

Attempts to identify the most effective approach for this group to stop smoking has been made in previous systematic reviews and have included a combination of behavioural support and nicotine replacement therapy (NRT) or alternative pharmacotherapies, such as bupropion, varenicline and nortriptyline as the most effective way to achieve successful cessation in this population. However, it is not clear whether, and if so how, the intervention to support an individual with COPD should differ from that offered to smokers from the general population.

In their review of 5 studies undertaken between 1991 and 2001, Wagena et al concluded that combining psychosocial interventions and pharmacological interventions resulted in better outcomes than either no intervention or psychosocial interventions alone. This latter finding for the lack of evidence to support the effectiveness of any psychosocial intervention alone for smokers with COPD was due to a lack of high-quality studies comparing a combination of interventions with no intervention. A later review comprising 8 studies published between 1991 and 2006 had a similar overall finding that combining psychosocial interventions and pharmacological interventions
resulted in better outcomes than either no intervention or psychosocial interventions alone. When this was investigated further there was an indication that ‘high intensity’ smoking cessation counseling (SCC) was more effective than ‘low intensity’ SCC although this was significant only when provided in combination with NRT. A similar limitation in this review was that motivation levels and the reporting of the severity of COPD of the participants were inconsistent.

The authors concluded that the success rates found with this patient group were similar to those in non-COPD trials. A major barrier also was the lack of clarity over standardization of the SCC for this group as the intervention is often individualized to the patients needs and therefore difficult to quantify and generalize these findings.

Objectives

The aim of this systematic review is to build on, update and improve the findings of the earlier reviews by Wagen et al\textsuperscript{11} and Strassman et al\textsuperscript{12} in order to identify the most effective stop smoking intervention approach for smokers with COPD. Changes were made to the search criteria in order to identify relevant studies, such as terms to identify studies with a psychological element to the intervention. To improve the quality of the included studies only those using a biochemical validation of smoking status were included.

Methods

Criteria for Considering Studies for this Review

Type of Study

Randomised controlled trials or quasi-randomised controlled trials were included.

Types of Participants

Participants were included in the studies if their diagnosis of COPD had been made as ‘mild’, ‘moderate’ or ‘severe’ after assessment using guidelines outlined by the American Thoracic Society/European Respiratory Society Task Force (ATS/ERS, http://www.thoracic.org/go/copd, Accessed January 17, 2013) or NICE guidelines (2004). Studies that also comprised non-COPD diagnosed participants in at least one comparison group were also included.
Types of Intervention

Studies investigating the effectiveness of smoking cessation interventions for smokers diagnosed with COPD with follow-up at a minimum of 12-months after the conclusion of the intervention were included. Smoking status at follow-up was required to be validated using a biochemical marker, such as CO in expired breath reading and/or saliva/urine cotinine measures. The intervention required to include a psychosocial and behavioural support element to its design with a standard stop smoking pharmacological component (nicotine replacement therapy, bupropion or varenicline) or nortriptyline.

Types of Outcome Measures

The minimum outcome measure for inclusion was point prevalence quit status at 12 months with a biochemical validation.

Search Strategy to Identify Studies

Electronic databases searched were MEDLINE, EMBASE, AMED, PsycINFO, DARE, Cochrane Library and CINAHL. The initial search dates for all databases were from January 2006 to January 2010. References of the included studies were screened for additional papers and the following journals were searched by Internet or by hand; Health Psychology, British Journal of Health Psychology, Journal of Health Psychology, Addiction and Nicotine and Tobacco Research.

Search terms

The following search terms used in the original systematic review by Wagena et al\textsuperscript{11} were used: copd*, lung-diseases-obstructive*, emphysem*, bronchit*, tobacco, nicotine, smoking, smoking-cessation, tobacco-use-disorder, tobacco-smokeless, anti-smoking, quit*, stop*, cessat*, ceas*, abstin*, abstain*, control*, smok*, giv*, tobacco*.

The search terms used in the Strassman et al\textsuperscript{12} review followed broader categories due to this being part of a larger review project on various treatments for COPD. With one exception these terms had been included in the Wagena et al\textsuperscript{11} review; the one exception was ‘treatment outcome’ which was considered by the authors to be too broad for the purposes of this review.
To identify relevant studies the following additional search terms were used: interven*, NRT, nicotine, bupropion, zyban, varenicline, champix, chantix, nortript*, anti-depress*, counsel*, behavio*, CBT and psycho*.

**Study Selection Criteria**

The search yielded 81 papers between January 2006 and January 2010. The abstracts were read and papers not meeting the full inclusion criteria were eliminated. This process resulted in 4 articles which were considered relevant for inclusion in this review.

In an attempt to expand the pool of studies for this review the same database search was repeated from March 2002 (the end of the journal search for the Wagena et al\textsuperscript{11} review) to December 2005 to identify any additional papers which may have been missed from the Strassman et al\textsuperscript{12} review. This yielded one additional study but it was excluded due to the lack of a 12-month follow up.

**Methodological Quality Assessment**

A quality assessment tool was designed for this review. In comparison to the previous two systematic reviews,\textsuperscript{11,12} this review did not use the full Delphi list\textsuperscript{13} to assess quality of the studies. The Delphi list was developed as a minimum reference standard for RCTs on many different research topics, and, rather than replace, was intended to be used alongside other criteria lists. It was felt that the subject area of this review required an active role on the part of the participant in terms of behavioural support and a degree of control over their level of engagement with behaviour change techniques. Consequently it was decided that the elements of blinding of the care provider and the participant were not valid items which, as Wagena et al\textsuperscript{11} discussed, led to internal validity difficulties for their systematic review when comparing psychosocial interventions. To overcome this, a number of quality assessment points were added which also aimed to increase the validity of the studies selected.

The items in the quality assessment list and the scores attached to each were:

- **Selection bias:** How were participants randomized? Score: 2 = computer randomised, 1 = other randomisation, 0 = no explanation

- **Comparable at baseline** (did the groups appear comparable at baseline regarding the most important prognostic indicators, e.g. numbers smoked, addiction level, age?): Score: 1 = yes, 0 = no
Detection bias (Was a biomarker used to validate self-report at follow-up?): Score: 2 = used at >1 follow-up point, 1 = used at 1 follow-up point, 0 = not used/not clear

Biomarker used to validate self-report at completion of intervention: Score: 3 = >75%, 2 = 50-75%, 1 = <50%

Description of intervention procedure: Score: 3 = step by step and psychological principles, 2 = step-by-step, 1 = some description, 0 = barely any description

Suitable comparison interventions (medications): Score 2 = comparable, 1 = some comparison, 0 = no comparison

Description of stage of disease: Score: 1 = information given, 0 = no information given

Description of type of smoker (light/heavy): Score: 1 = information given, 0 = no information given

Time points of follow-up: Score: 4 = >12 months post intervention, 3 = ≥6 months ≤12 months post intervention, 2 = >end of intervention <6 months, 1 = end of intervention

Sample size justification: Score: 1 = power calculation used, 0 = power calculation not used

Drop out rate by conclusion of intervention. Score: 2 = dropout rate ≤25%, 1 = dropout rate >25% ≤50%, 0 = >50 or not known

Intention to treat analysis (non-attendees at completion classed as smokers) Score: 1 = yes, 0 = no

The selected studies were reviewed independently by two reviewers (G.A & R.K.). Divergence of quality assessment scores was resolved by the reviewers meeting to discuss differences in ratings and agreeing on a score.

**Data Analysis**

Statistical data was analysed using Statistical Package for Social Sciences version 17 (SPSS). The studies were heterogeneous with regards to: (1) The study population and its level of COPD; classified as ‘mild’ (FEV$_1$ ≥ 80%), ‘moderate’ (FEV$_1$ 50 – 79%), or ‘severe’ (FEV$_1$ 30 – 49%), as defined by the ATS/ERS (2004), (2) Format of treatment (individual, group or telephone) of behavioural/psychological support, (3) Use of pharmacological treatments (no treatment, NRT, bupropion), (4) Level of psychological assessment including motivation measures, and (5) Different levels of included study quality.

Significance levels, effect sizes, odds ratios (OR) and 95% confidence intervals (CI) have been calculated where possible and some statistical information in the primary research has been reported where it is been considered appropriate.
Description of Studies

Two studies were carried out in COPD outpatients’ clinics.\textsuperscript{14,15} One study was carried out as inpatients in an acute setting, with the control group in primary care settings,\textsuperscript{16} and one study was carried out in a respiratory outpatients clinic, with the control receiving no support after initial brief advice.\textsuperscript{17} All studies had elements of psychological intervention. One study included group, individual and telephone support\textsuperscript{14} compared to a control with individual and telephone support, one offered group support compared to a control of unspecified usual care,\textsuperscript{16} one offered group support for both experimental and control groups\textsuperscript{15} and one study comprised 2 experimental arms, one with individual support and one with group support, with a control group receiving no additional support after initial brief advice.\textsuperscript{17}

The interventions were led by a range of healthcare professionals including respiratory nurses,\textsuperscript{14} a smoking cessation nurse,\textsuperscript{16} nurse specialists trained in asthma and COPD and a researcher trained in smoking cessation in another study\textsuperscript{15} and by a respiratory nurse in the experimental groups of the final study.\textsuperscript{17} In this latter study, the control group received a brief intervention from a doctor. No information is available on usual care provided in primary care.\textsuperscript{16}

The level of COPD disease was given for all participants. All were diagnosed using the ATS/ERS (http://www.thoracic.org/go/copd, \textit{Accessed January 17, 2013}) or the NICE (2004) classification as ‘mild’, ‘moderate’ or ‘severe’. One study comprised ‘moderate’ and ‘severe’ samples,\textsuperscript{14} two studies comprised participants with three levels of diagnosis\textsuperscript{16,17} and one study compared an experimental group comprising participants with an average ‘mild’ diagnosis with a control group of asymptomatic participants.\textsuperscript{15}

The reviewers concluded that one study gave little description of the intervention,\textsuperscript{14} one study gave a step by step description\textsuperscript{16} and two studies gave a step by step description and the psychological principles.\textsuperscript{15,17}

The smoking status of participants was measured using a number of tools in all studies; cigarettes smoked ranged from 17.5–24.1;\textsuperscript{14,15,17} nicotine dependence measured using the Fagerstrom Test for Nicotine Dependence (FTND, 1991) ranged from 4.7–4.8,\textsuperscript{16} and pack years (calculated as number of cigarettes smoked x number of years smoked / 20) ranged from 25–45.5.\textsuperscript{15–17}

Characteristics of studies can be found on table 2 on the online supplementary materials.
Methodological Quality

The quality scores of the studies range from 11 to 20.

One study used computer-generated list of random numbers, one study was randomized according to other criteria, e.g., the level of COPD and two studies gave no explanation. Biomarker validation was used for more than 75% of outcomes in three studies using a range of measures; salivary cotinine test (<20ng/ml), urinary cotinine measure with a cut off set at <25 ng/ml and in one of these studies two measures were used; expired breath carbon monoxide (CO) with a cut off at ≤ 10 parts per million (PPM) and salivary cotinine with a cut off level of ≤ 10 ng/ml and less than 50% in one study using expired breath CO monitoring with a cut off set at <8ppm. Two studies used biomarkers on more than one follow-up, one study used biomarkers on one follow-up and one study did not use a biomarker until the end of the study.

Only one study included a sample size justification or power analysis, yet failed to achieve the sample size required. Two studies had over 100 participants in each group and two studies had less than 40 participants per group. Two studies had a dropout rate of less than 25%, while two studies had dropout rates of 25–50%. Explanations for these drop outs were not consistently reported. Please find a quality assessment table 3 on the online supplementary materials.

Results

The primary aim of the four studies identified for this review was the effect of the interventions on smoking cessation. Table 1 shows the outcomes of the studies included in this review (online supplementary material). A Meta-analyses were also conducted (online supplementary report – forest plot figure 1.

All four measured abstinence 12 months post-intervention. Just one reported follow-up outcomes at points before this, while one reported follow-up outcomes 24 months after this point. The results for the 12 months will be reported and the results at 36 months follow-up will be discussed in the context of that study. The overall difference in the effectiveness of all the studies at 12 months between the experimental groups and the control groups was significant (Chi-squared test for heterogeneity $\chi^2_2 = 39.7, P < 0.001$) with a total of 35.5% of participants quitting smoking in the experimental groups and 10% quitting smoking in the control groups (pooled random-effects OR 2.35, 95% CI [0.25, 21.74]). A by-studies comparison showed: in Sundblad there were similar numbers of participants in the experimental and control groups (n = 204 and 219, respectively); in Christenhusz there were more
participants in the experimental group (n = 96 compared to n = 67 in the control group); in Willemse there were more patients in the experimental group (n = 38 compared to n = 25 in the control group). Different psychosocial interventions with pharmacotherapy.

a. Christenhusz et al\(^{14}\) compared two interventions with participants diagnosed with either moderate or severe COPD. One group received 595 minutes of support (high intensity), although the number of sessions was not stated. Delivered in group, individual and telephone format, 100% were prescribed bupropion free of charge, with 6% also reported using NRT. The control group received 180 minutes (medium intensity) of individual and telephone support, although again it is not reported over how many sessions. 28% used bupropion and 14% used NRT although these were not free of charge. Respiratory nurses delivered both interventions. At 12 month follow-up 19% were abstinent in the experimental group and 9% were abstinent in the control group (OR 2.35, 95% CI [0.88, 6.27]). The high intensity group had a higher nicotine addiction score measured by Fagerstrom (59% compared to 42% scoring ≥ 6). Other independent variables measured included attitude to smoking cessation, self efficacy and quality of life although changes in these were non-significant (\(P = 0.08\)) in the experimental group. For the control group a higher cotinine value at baseline led the authors to indicate that each rise of 100ng/ml doubled the likelihood of quitting and that a positive attitude towards stopping success increased by 12 times; both variables \(P = 0.003\). However, a large confidence interval of the odds ratio was reported (OR 22.52, 95% CI [1.55, 327.97]) and indicates low precision in this estimate.

b. Sundblad et al\(^{16}\) compared a high intensity in-patient intervention with usual care provided in primary care health centres. A smoking cessation nurse delivered the experimental arm for 1 hour per day in groups of 4-8 people over 11 days as part of a wider lifestyle intervention with additional input from a doctor, a physiotherapist, a dietician, a laboratory technician, a psychologist and occupational therapist and a nurse. NRT was recommended and used by 28% in the experimental group and 14% in the control group. There were also regular follow-up telephone calls for 2-3 months after discharge and the participant and their spouse then returned for 2-4 days as in-patients, followed by additional telephone support follow-up until 12 months post intervention. No information is given on the usual care offered for the control group although just 20% (46) accessed this. At 1 year, point prevalence abstinence (in the previous 6 months) was significant (\(\chi^2 = 105.2, P < 0.001\)) with 52% in the intervention group and 7% in the control stopping (OR 14.71, 95% CI [8.14, 26.59]). At 3 years, these figures had reduced to 38% and 10% respectively but the treatment difference was still significant (\(\chi^2 = 44.0, P < 0.001\). There
was no difference in outcome based on the severity of the disease. There were no differences reported in nicotine
dependence between the groups at baseline although the authors acknowledge that which part of the intervention is
effective is difficult to deduce given the mixed use of pharmacotherapy and the extensive format of the wider
intervention.

c. Wilson et al\textsuperscript{17} compared a high intensity individual intervention and a high intensity group intervention (5
sessions of one hour each) provided by one respiratory nurse and two respiratory nurses respectively (including an
initial 5-10 minute brief intervention) with an individual usual care, brief intervention (5-10 minutes) only, delivered
by a doctor, in an outpatient department. The experimental arms also offered 12 weeks of NRT while no information
is available for the control group. No quitters were reported in either group at 12 month follow up so no effect size
has been calculated. However it was reported that all groups had a significant reduction in nicotine addiction over
this period with values reported between the control and group intervention $P = 0.006$ and between the control and
individual support $P = 0.03$

**Comparison by disease presence**

Willemse et al\textsuperscript{15} compared a group intervention (8-10 per group) in an outpatient setting. The experimental
group had been diagnosed with mild COPD and the control group was asymptomatic. A respiratory nurse specialist
and a researcher trained in smoking cessation delivered the same intervention. Nine 2-hour sessions were initially
offered over 6 weeks. Based on programmes developed in the Netherlands, they incorporated CBT techniques to
build motivation, self-efficacy and coping skills. Additional telephone support was offered in between sessions, and
6 additional group sessions were offered, ad hoc, over the remaining time to 12 months, provided by the same
facilitators. No pharmacotherapy was recommended. At 12 months continual abstinence was significant $\chi^2 = 4.05$, $P
< 0.05$) although with 42\% in the intervention group and 68\% in the control group the control group was more
successful (OR 0.342, 95\% CI 0.119–0.987).

**Discussion**

The heterogeneity between studies with respect to populations and interventions, combined with few studies
with relatively few participants, meant that any estimation of an effect size was bound to be uncertain. So that
although the intervention looked promising it’s not possible on current evidence neither to quantify the effect, nor to
confirm that the promising results observed are not the result of chance. Further to that, odds ratios, whilst widespread, are problematic as effect size measures when the frequency of the outcome is high.

**Disease severity**

Participants with different COPD severity within and between each study make clear conclusions difficult. Therefore, as was also recommended in the Wagena et al\textsuperscript{18} review, sub-analysis would be preferable wherever possible, e.g., as in Sundblad et al.\textsuperscript{6}

The time since diagnosis was not reported which could impact on the participant’s perception of their smoking behaviour and its impact on their illness and development of coping strategies to live with and manage exacerbations. A future study could therefore investigate the effect of time from diagnosis on smoking cessation outcomes as another inclusion criterion.

It is important to highlight that given one of the studies contained a control group with non-COPD patients, estimated effect sizes may not be generalisable.

**Levels of addiction and intensity of intervention**

Consistent reporting according to disease severity would help clarify the effects of level of addiction and intensity of interventions as illustrated by two of the studies. Higher cotinine levels resulted in a better outcome, contrary to popular assumptions regarding level of addiction and successful quitting\textsuperscript{14} leading to the suggestion that the higher intensity compensates for higher addiction in one group while a higher favourable attitude score to cessation found in the less intense control could compensate for the higher addiction. One hypothesis by the authors is that smokers with a high cotinine level may have a more internal motivation as they may experience worse symptoms whereas those with a lower cotinine level may have a more external, less stable motivation, e.g. being advised to stop by a practitioner. In another study,\textsuperscript{15} the intervention group had mild COPD but higher pack years than the control group. The high quit rate in both groups was thought to be possibly due to high contact time and intense baseline and follow up measures with frequent and intensive motivational support being proposed to account for high cessation rates, suggesting flexible approach to cessation with interventions designed depending on initial findings of screening.
Effect of healthcare professional

As found by the Strassman et al\textsuperscript{12} review there were a number of points in the studies in this review where the person delivering the intervention could have affected the intervention, for example during ad hoc telephone support. This additional support could offer an opportunity for relapse prevention but its lack of measurement can make it more difficult to generalise the findings.

Attendance

Poor attendance was an issue for usual care conditions.\textsuperscript{16,17} Wilson et al\textsuperscript{17} recommend that research investigates more acceptable interventions or that their study is repeated in a community setting. In comparison, Willemse et al\textsuperscript{15} found that a medical setting may have had an effect on their study, hypothesizing that the medical research environment may have made the participants feel more responsible for the outcome. This may have made participants more serious towards the intervention, questioning the balance between ‘medicalising’ an intervention and ease of access in a community setting. The effect of exacerbations during the studies was not measured. These could affect attendance and compliance with the use of stop smoking medications and it could be hypothesized that they may be more likely to attend a medical setting during such episodes. Additional information on the health of the participants during the course of the studies would be useful.

Social support and motivation

Social circumstances should also be considered. Wilson et al\textsuperscript{17} reported that 42\% lived with a smoker and this may have affected their perception of the importance of cessation or they may not have received the peer support that could have effected a successful outcome. Similarly, motivation of participants to take part was not measured consistently and varied from a measured ‘stage of change’ identification to being estimated by their attendance at an information session and the signing of an informed consent form as a proxy measure for motivation.\textsuperscript{14,16} Poorer outcomes could possibly be a function of the participant selection; at recruitment a number of the studies indicated that a high proportion of the patients had already quit smoking, leaving a potential sub-group who could be described as ‘recalcitrant’ smokers.

Follow-up and biomarkers
It is acknowledged that a large percentage of the general population relapse within the first 12 months post-quitting. For a complex group such as COPD patients this could therefore be considered too long a period as a measure and also indicate that the level of initial support, or follow-up relapse prevention support, is not sufficient as the aim of stop smoking interventions is to provide smokers with the skills to maintain abstinence.

Three out of the four studies used continuous abstinence as a measure while one study used a long duration point prevalence marker of six months. Van der meer et al\textsuperscript{19} recognised that based on the findings of Velicer et al\textsuperscript{20} a combination of continuous abstinence and point prevalence measures should be used to assess outcomes to reach a clearer picture of the quitting process. Although not used by the studies under review, this would illustrate the dynamic nature of smoking cessation; point prevalence would raise quit rates in the short term, increasing self-efficacy that they can stop rather than being labeled a ‘failure’ for not achieving continuous abstinence status while continuous abstinence would help to identify better assessment of the longer-term effects of an intervention.

**Conclusions**

The primary aim of the studies identified in this review was to establish the effectiveness of psychosocial interventions, with the effect of pharmacotherapy being a secondary outcome. It has been difficult to establish the most effective approach to smoking cessation to take with a COPD population. Despite stricter inclusion criteria there were still many differences in the composition and level of intensity of interventions and the participants themselves. The outcome of quit/not quit does not appear to allow sufficient scope for measuring the effect of the constituent parts of a psychosocial intervention. Without this better measurement, biomedical approaches may appear more effective, e.g. Bittoun\textsuperscript{21} found that more NRT use without explicit psychosocial intervention can be very effective at achieving a non-smoking status for this group. In this review there was no consistent use of, or access to stop smoking pharamcotherapies which could obscure the effects of the psychological components of the interventions under review.

However, consistent with Strassman et al\textsuperscript{12}, a combination of pharmacotherapy and psychosocial support appears to be the best approach to take to stopping smoking although a lengthy intervention does not necessarily result in better outcomes. Locating the interventions in a medical setting does appear to have a positive impact on initiation of a treatment and may be a method of improving on-going engagement with support services in comparison to standard usual care services in primary care or community settings.
This review highlights the challenge for future research to develop more tailored interventions to reduce smoking prevalence in a chronic clinical population where a range of behaviour changes is essential to managing their health and improving well being.

Please note that on-line supplementary material is available.

REFERENCES


Online supplementary materials

Figure legends

Fig. 1. Forest plot showing the three trials included in the random-effects meta-analysis. The centre of the diamond represents the random-effects pooled odds ratio.

Table legends

Table 1 showing statistics on included studies
Table 2 showing characteristics of included studies
Table 3 showing quality assessment
Prisma Diagram:

*Of these 4 studies, only 3 contributed to the estimate of pooled OR because one study (Wilson) had 0 patients stopping smoking at 12 months


For more information, visit www.prisma-statement.org.
Online supplementary material: table 1 – Statistics on the included papers

<table>
<thead>
<tr>
<th>Paper</th>
<th>Intervention n stopping smoking / N in group (%) 12m</th>
<th>Control n stopping smoking / N in group (%) 12m</th>
<th>Odds Ratio</th>
<th>95% CI (lb, ub)</th>
<th>p</th>
<th>Quality score</th>
</tr>
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<tbody>
<tr>
<td>1  Christenhusz, et al. (2007)</td>
<td>18/96 (19)</td>
<td>6/67 (9)</td>
<td>2.35</td>
<td>0.88, 6.27</td>
<td>p= 0.08</td>
<td>11</td>
</tr>
<tr>
<td>2  Sundblad, et al. (2008)</td>
<td>106/204 (52) a</td>
<td>15/219 (7) a</td>
<td>14.71</td>
<td>8.14, 26.59</td>
<td>&lt;0.001</td>
<td>13</td>
</tr>
<tr>
<td>3  Willemse, et al. (2005)</td>
<td>16/38 (42)</td>
<td>17/25 (68)</td>
<td>0.34</td>
<td>0.12, 0.99</td>
<td>0.04</td>
<td>20</td>
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<tr>
<td>4a Wilson, et al. (2008)</td>
<td>0/27 (0)</td>
<td>0/35 (0)</td>
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<td>19</td>
</tr>
<tr>
<td>4b Wilson, et al. (2008)</td>
<td>0/29 (0)</td>
<td>0/35 (0)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>19</td>
</tr>
</tbody>
</table>
Online supplementary material: Figure 1 - Forest plot showing the three trials included in the random-effects meta-analysis. The centre of the diamond represents the random-effects pooled odds ratio.

<table>
<thead>
<tr>
<th>Study</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sundblad</td>
<td>14.71 (8.14, 26.59)</td>
</tr>
<tr>
<td>Christenhusz</td>
<td>2.35 (0.88, 6.27)</td>
</tr>
<tr>
<td>Willemse</td>
<td>0.34 (0.12, 0.99)</td>
</tr>
<tr>
<td>Overall (95% CI)</td>
<td>2.35 (0.25, 21.74)</td>
</tr>
</tbody>
</table>
Online Supplementary material – Table 2 - Characteristics of included studies

**Study 1 Christenhusz, Pieterse, Seydel, & van de Palen. (2007)**

| **Methods** | Setting: 3 hospitals COPD outpatients clinic in the Netherlands. 
Recruitment: Non-dutch speakers excluded. 
Randomisation: No information given. Two intervention groups between sample comparisons 
Drop-outs: reasons not given 
Intention-to-treat: No |
| **Participants** | Participant health: Clinically diagnosed moderate COPD (FEV\textsubscript{1} = 50-69%) or severe COPD (FEV\textsubscript{1} <50%), defined by ATS/ERS (2004). ‘Heavy’ smokers, experimental group 24.1 per day; control group 20.5 per day 
Age: Between 40 – 75 years 
Male: 52.4% 
Motivation: No measurement taken. |
| **Interventions** | 1. Experimental (n 114): 
Format: Group counseling, individual counseling and telephone support. 
Intensity: High 
Time: Total counseling time 595 minutes 
N session: n/a 
Pharmacotherapy: Bupropion (free of charge) 100% used this, with 6% also using NRT 
Delivered by: Respiratory nurses 
2. Control (n 111): 
Format: Individual counseling and telephone support 
Intensity: Medium 
Time: Total counseling time 180 minutes 
N session: n/a 
Pharmacotherapy: Recommended but not provided. Not free of charge. 28% used bupropion and 14% used NRT 
Delivered by: Respiratory nurses |
| **Follow-up points** | Measurements at baseline, 6 months and 12 months |
| **Outcomes** | Abstinence: Continuous abstinence 1 year after intervention. Experimental 19% Control 9%; RR = 2.22; 95% CI: 1.06-4.65 
Validation: Salivary cotinine test (<20ng/ml) |
<table>
<thead>
<tr>
<th>Difference</th>
<th>10%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality Score</td>
<td>11</td>
</tr>
<tr>
<td>Notes</td>
<td>Experimental group had higher nicotine dependence measured using Fagerstrom, (59% compared to 42% scoring ≥ 6). Other independent variables were measured in both groups, including attitude, self efficacy and quality of life.</td>
</tr>
</tbody>
</table>

**Study 2 Sundblad, Larsson, & Nathell. (2008).**

**Methods**

Setting: Hospital setting in Sweden.

Recruitment: Participants were recruited in the vicinity of 9 Swedish towns and cities using a questionnaire survey regarding smoking habits of current smokers on sick leave. Exclusion criteria included linguistic difficulties, presence of severe comorbidities or an inability to stay away from home for the required period of time.

Randomisation: No information given except a ‘prearranged schedule’ by a person not involved with the study.

Drop-outs: reasons not given

Intention to treat: No

**Participants**

Participant health: Of those smoking more than 8 cigarettes per day 674 were diagnosed with COPD using spirometry. Smoking status measured by Fagerstrom (experimental group score 4.7 and control group 4.8) and pack years (experimental group 35.9 per day and control group 33.9 per day). Following the European Respiratory Society guidelines the COPD was classed as ‘mild’ (71%), ‘moderate’ (23%) or ‘severe’ (6%). Of these, 196 were excluded. Of those randomized to the intervention group, 35 did not participate.

Age: Mean 53 years (Range 41-62)

Male: 220 (49.7%)

Motivation: Assessed using Stages of Change model

**Interventions**

1. Experimental (n=212)

Format: Group support face to face

Intensity: High

Time: 1 hour

N session: 11 inpatient

Pharmacotherapy: NRT recommended
Delivered by: Smoking cessation nurse

2. Control (n=231)
Format: Referral to primary care health centres for usual care
Intensity: n/a
Time: n/a
N session: n/a
Pharmacotherapy: n/a
Delivered by: n/a

Follow-up points
Weekly telephone calls lasting 5-30 minutes from a nurse for 2-3 months after initial discharge from the intervention. Participants and spouses returned for 2-4 days after 2-3 months from initial discharge. Subsequent to this the participants received 2 phone calls every month for 4 months and then 1 phone call every month for 8 months. Questionnaires on smoking habits were also completed at 1 year and 3 year follow up.

Outcomes
Abstinence: At 1 year: Point prevalence quit rate (self report) at 1 year was 52% in the intervention group and 7% in the control group. Classed as successful quitters if smokefree (self report) for the last 6 months, quit rate was 53% for ‘mild’, 46% for ‘moderate’ and 50% for ‘severe’ COPD. At 3 year follow up, 38% in the intervention group and 10% in the control group were smokefree. Validation: Expired breath CO verification at 3 year follow up in a random sample of the quitters. Of this sample of 35, 33 (94%) had a CO <8 ppm confirming smokefree status.

Difference
45

Quality Score
13

Notes
Only 46 (20%) of the control group accessed smoking cessation programme in the primary care centres. The composition of this care is not described.
The intervention also included a structured education programme led by a doctor, a physiotherapist, a dietician, a laboratory technician, a psychologist, an occupational therapist and a nurse. The aim of this was to increase knowledge of COPD and how to live with it.


<table>
<thead>
<tr>
<th><strong>Methods</strong></th>
<th>Setting: Acute respiratory outpatients department in the Netherlands</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Recruitment: Advertisements in the outpatient department</td>
</tr>
<tr>
<td></td>
<td>Randomisation: by condition – diagnosis of mild COPD or asymptomatic COPD</td>
</tr>
<tr>
<td></td>
<td>Drop-outs: None</td>
</tr>
<tr>
<td></td>
<td>Intention-to-treat: Yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Participants</strong></th>
<th>Participant health: Intervention group - COPD diagnosed according to the ATS/ERS (2004). Performed biomedical tests as well as quality of life, symptom questionnaires, cognitive dysfunction tests. No information given on tests used. Control group - asymptomatic smokers. Control group pack years 25, cigarettes smoked 21 per day; experimental group 35, cigarettes smoked 22 per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Mean 55(SD 5.8) intervention; 50 (SD 3.7) control</td>
</tr>
<tr>
<td>Male</td>
<td>49.2% (52.3 % intervention; 44% control)</td>
</tr>
<tr>
<td>Motivation</td>
<td>Not measured</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Interventions</strong></th>
<th>1. Experimental (n 33):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Format</td>
<td>Group intervention (8-10 smokers) based on smoking cessation</td>
</tr>
<tr>
<td>programme</td>
<td>Defacto used in the Netherlands. Made use of CBT, especially motivation and self-cessation. Also focused on relapse prevention, following a recognized Dutch format. Ad hoc telephone /face to face additional support offered in between sessions</td>
</tr>
<tr>
<td>Intensity</td>
<td>High</td>
</tr>
<tr>
<td>Time</td>
<td>2 hour sessions</td>
</tr>
<tr>
<td>N session</td>
<td>Initially 9 meetings over 6 weeks. Participants quit after 2nd session. Sessions 2-6 used to guide participants through cessation; sessions 7-9 used to maintain cessation and coping with side effects and difficult situations. An additional 6 sessions added throughout the year.</td>
</tr>
</tbody>
</table>
Pharmacotherapy: None
Delivered by: Nurse specialist trained in asthma and COPD and a researcher and smoking cessation

2. Control (n 27):
Format: As intervention
Intensity: As intervention
Time: As intervention
N session: As intervention
Pharmacotherapy: None
Delivered by: Nurse specialist trained in asthma and COPD and smoking cessation

<table>
<thead>
<tr>
<th>Follow-up points</th>
<th>2 months, 6 months and 12 months. Baseline tests also repeated at 12 months.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcomes</td>
<td>Abstinence: 42% intervention and 68% control at 12 months</td>
</tr>
<tr>
<td></td>
<td>Validation: Urinary cotinine (&lt;25 ng/ml)</td>
</tr>
<tr>
<td>Difference</td>
<td>-26</td>
</tr>
<tr>
<td>Quality Score</td>
<td>20</td>
</tr>
<tr>
<td>Notes</td>
<td>Intervention group had higher pack years, similar number smoked per day and an average FEV₁ of 80% (SD 24), indicating mild COPD. High intensity of contact – 15 group stop smoking sessions, 7 hospital visits before programme started and 3 visits through the year for follow up.</td>
</tr>
</tbody>
</table>

Study 4 Wilson, Fitzsimons, Bradbury, & Elborn (2008).

Methods
Setting: An outpatient facility of a Regional Respiratory Centre in Northern Ireland.

Recruitment: Participants were recruited from an outpatient facility. They were excluded if they had any alcohol/drug related problems, contraindications to nicotine replacement therapy or they stated they had no intention to stop smoking

Randomisation: A sequentially sealed envelope containing computer generated list of random numbers allocated the participants to one of three treatment groups

Drop-outs: Reasons stated
Intention to treat: Yes
Participants

Participant health: Using NICE classification guidelines (2004) participants level of COPD was measured and stated as either ‘mild’ (53%), ‘moderate’ (34%) or ‘severe’ (13%). Classed as ‘heavy’ smokers, average 19 per day, control group pack years 38.9, cigarettes smoked per day 17.5; experimental group 1 pack years 45.5, cigarettes smoked per day 20.8; experimental group 2 pack years 40.8, cigarettes smoked per day 20.1.

Sample: 516 assessed for eligibility; 425 excluded as not meeting inclusion criteria, being an ex smoker or refusing to participate

Sample size justification. Power analysis discussed and estimated but the quantity was not achieved

Age: mean age 61 years (Range 38-80 years)
Male: 48%

Motivation: Stage of change assessment at recruitment

Interventions

All participants received brief advice to stop smoking, face to face, by a doctor for 5-10 minutes. This training was standardized at each medical rotation but no information is given.

1. Experimental 1 (n=27): Psychosocial and pharmacotherapy

Format: Individual support face to face
Intensity: High
Time: up to 60 minutes
N session: 5
Pharmacotherapy: 12 weeks NRT 16 hour patch; 8 weeks 15mg, 2 weeks 10mg, 2 weeks 5 mg
Delivered by: 1 experienced respiratory nurse, with 6 hours standardized training from a Health Promotion Officer and Pharmacist.

2. Experimental 2 (n=29): Psychosocial and pharmacotherapy

Format: Group support face to face
Intensity: High
Time: up to 60 minutes
N session: 5
Pharmacotherapy: 12 weeks NRT 16 hour patch; 8 weeks 15mg, 2 weeks 10mg, 2 weeks 5 mg.
Delivered by: 2 experienced respiratory nurse, with 6 hours standardized training from a Health Promotion Officer and Pharmacist.
3. Control (n 35): No additional intervention after generic brief advice to stop smoking
Format: Individual face to face
Intensity: Usual care
Time: 5-10 minutes
N session: 1
Pharmacotherapy: None
Delivered by: Doctor

<table>
<thead>
<tr>
<th>Follow-up points</th>
<th>2 months, 3 months, 6 months, 9 months and 12 months</th>
</tr>
</thead>
</table>

**Outcome**

Abstinence: two biochemical measures at each follow up point as well as 1) self report of complete cessation or 2) self report of intermittent cessation. At 1 year follow up no one had achieved complete cessation, 2 (6%) of the Control group (usual care) and 3 (10%) of the Experimental 2 (group) achieved intermittent cessation but not specified at what time point

Validation: Expired breath CO and salivary cotinine at each follow up point

**Difference**

0

**Quality Score**

19

**Notes**

NRT was not available on prescription at the beginning of the study. 50% of the intervention groups used NRT; no figure is available for the control group

Participants lost to follow up were recorded as smokers.

Other outcomes included position in stage of change, and perceived dyspnoea using the MRC Dyspnoea Scale (1996).

Non-smoking status confirmed by expired breath CO reading of ≤ 10 parts per million and salivary cotinine reading of ≤ 10 ng/ml

Attendance at sessions was poor
### Online supplementary material: Table 3 - Quality Assessment for included studies

<table>
<thead>
<tr>
<th>Paper</th>
<th>Selection bias</th>
<th>Comparable at baseline</th>
<th>Detection bias</th>
<th>Biomarker – end of intervention</th>
<th>Description of intervention</th>
<th>Suitable comparison on intervention</th>
<th>Description of disease severity</th>
<th>Descriptio of type of smoker</th>
<th>Time scale of follow up points</th>
<th>Sample size (power)</th>
<th>Drop out rate at end of intervention</th>
<th>Intention to treat analysis</th>
<th>Total Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Christenhusz et al. (2007)</td>
<td>0</td>
<td>1</td>
<td>1</td>
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<td>Sundblad et al. (2008)</td>
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<td>4</td>
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<tr>
<td>Willemse et al. (2005)</td>
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<tr>
<td>Wilson et al. (2008)</td>
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<td>1</td>
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<td>19</td>
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