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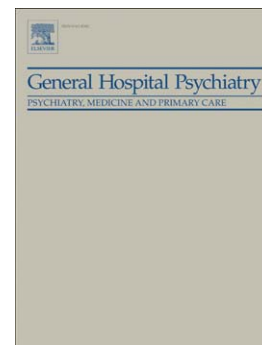
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Systematic review and meta-analysis of the impact of depression on subsequent smoking cessation in patients with chronic respiratory conditions

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Abstract**Objective:**

To systematically review the impact of depression on subsequent smoking cessation in prospective studies of chronic respiratory patients.

Method:

A systematic search of electronic databases (MEDLINE, Psychinfo, CINAHL) was conducted to identify prospective studies of chronic respiratory patients which measured depression at baseline and smoking status at follow-up, dating from 1st January 1990 to 21st February 2014. The standardised mean difference (SMD) and 95% confidence interval for the association between baseline depressive symptoms and subsequent smoking cessation was estimated from available data using random effects meta-analysis.

Results:

A total of 1314 citations were retrieved and 197 articles were further evaluated by two reviewers. Seven articles provided sufficient data to estimate the association between depressive symptoms and subsequent smoking cessation. Those with elevated depressive symptoms were significantly less likely to quit smoking at follow-up than those not reporting elevated depressive symptoms (SMD=-.31, 95%CI -.43 to -.19; $I^2=0%$, $p=.506$).

Conclusions:

The association between depression and subsequent smoking was poorly reported or omitted in most studies. However, the available evidence suggests depression decreases the likelihood that patients with chronic respiratory conditions will quit smoking. Future research is needed to determine how best to manage depression and smoking cessation in this population.

Keywords

Systematic review; meta-analysis; depression; smoking cessation; chronic respiratory disease

1. Introduction

Smoking is a leading cause of preventable death worldwide and accounts for 6 million deaths annually [1] and [2]. According to the Centres for Disease Control and Prevention, smoking causes 90% of lung cancer deaths and 80% of deaths from chronic obstructive pulmonary disease (COPD). To combat this problem, respiratory patients are encouraged to quit smoking [1]. According to guidelines, respiratory patients have greater urgency to quit smoking and smoking cessation should be integrated into the management of respiratory conditions such as COPD [5], [6]. Smoking cessation is highly cost-effective and the single most important intervention for reducing the risk of respiratory diseases such as COPD, lung cancers [7] and [8], and improving respiratory symptoms [7]. However, up to 15-43% of respiratory patients continue to smoke post-diagnosis, while approximately 20% do not attempt to quit [9]. Therefore, identification of factors that predict smoking continuation and relapse is crucial.

Depression may negatively impact on smoking cessation [1], [10], [13], [14], [15] and [16]. Depression is common among patients with chronic respiratory disease [11], with up to 40% of patients reporting elevated depressive symptoms [12], [17], [18] and [19]. In a recent systematic review, Atlantis et al. [12] described that depression was associated with increased risk of mortality in COPD patients, and it is possible that smoking continuation partially mediates this association. However, no systematic review of the effect of depression on subsequent smoking status has been conducted in chronic respiratory patients, and as such it is unclear whether depression truly impacts on smoking in this population. Such a study may have important implications for the management of such patients. We aimed to fill this gap in the literature.

2. Methods

As this is a systematic review IRB approval was not required.

2.1 Search Strategy

A systematic literature search, following recommended principles [20], of MEDLINE, Web of Science, Psycinfo, and CINAHL was performed on 21st January 2014.

Searches involved subject headings and keywords (see Appendix A for example). We included studies dating from 1st January 1990 to 21st February 2014 in the analysis. Additional articles were identified from reference lists of the included articles and we also checked citing articles.

2.2 Study Selection and Data Extraction

We included studies that met the following inclusion criteria: chronic respiratory patients (i.e. chronic obstructive pulmonary disease, asthma, lung cancer, chronic bronchitis and interstitial lung disease), published in peer-reviewed journals in 1990 or later, English language, prospective design (observational or randomized trials [control groups or full data if controls only data was unavailable]), depression measured at baseline (i.e. diagnostic interview, questionnaire, antidepressant prescription, single-item questions), and measure of smoking (self-report or objective, validated or unvalidated) at follow-up.

Potentially relevant studies relating to depression and smoking cessation in chronic respiratory patients were yielded from multiple electronic databases. Two reviewers completed the first screening of abstracts/titles independently (SY.H., N.A.). Articles were then excluded because their titles and abstracts revealed that they were not relevant or did not fit the eligibility criteria. Studies that were considered eligible for inclusion were retrieved and evaluated in full, and suitability for inclusion was independently determined by SY. H. and N.A. Disagreements and queries were managed by consensus or discussions with a third reviewer (F.D.). Extraction of data for each study was based on setting of the study, sample type (i.e. chronic respiratory patients), follow-up duration, depression measures and smoking status. Authors were contacted to provide further information when there were insufficient data (i.e. association between depression and smoking cessation not reported) provided in the published paper.

2.3 Quality Assessment

The Crowe Critical Appraisal Tool (CCAT) [21], [22] and [23] was used to appraise study quality (D.R.), as per a similar review [16]. CCAT scores have exhibited adequate reliability and construct validity, and are provided after an objective and subjective appraisal of eight categories of study quality with a range of 0-5 each. The

total is then expressed as a percentage. As per a previous review, we considered higher quality studies to have scores $\geq 60\%$ [16].

2.4 Statistical analysis

The primary outcome was smoking status at follow-up. A priori, we used a hierarchical system to establish better depression measures: diagnostic interview, validated scale, current prescription of antidepressants, and single-item (unvalidated) measure [16]. We also used the standardised mean difference (SMD) as the primary outcome measure for two main reasons: the expected differential measurement of depression at baseline (e.g. dichotomous or continuous) and smoking status at outcome (7-day point prevalence, smoke 20 in last year, etc), and it allowed direct comparison to a similar review in patient with coronary heart disease [16]. Adjusted estimates were used where reported. The *metaeff* command in Stata 13.1 was used to estimate the SMD, and a random effects model was used to conduct the overall analysis [24], [25] and [26]. The I^2 test and Cochran's Q assessed heterogeneity. Pre-planned sensitivity analysis included examining the impact of differential depression assessment, different durations of follow-up (categorised as <1 year versus ≥ 1 year), higher quality studies ($\geq 60\%$), adjusted or unadjusted results, objective or self-report cessation [16].

3. Results

A total of 1314 articles were found (Figure 1). There were 815 articles left after removal of duplicates. Upon screening of titles and abstracts, 179 articles were selected for evaluation. A further 17 articles were added after searching citations and bibliography of the 179 articles resulting in a total of 196 articles for further evaluation. Among the 196 articles, 182 papers that did not fit the inclusion criteria were excluded, 4 papers were excluded for having too few smokers/quitters ($n < 5$), 3 papers were repeat publications. Thus, four papers reported the relevant association and three provided data on email, leaving seven studies to be included in the meta-analysis (Table 1) [32], [33], [34], [35], [36], [37] and [38]. An overview of the omitted studies is available in Appendix B.

Fig 1 about here

Table 1 about here

3.1 Study characteristics

The included studies took place across four countries, and the majority concerned patients with COPD. Sample sizes ranged from 89-372, with follow-up ranging from 6-24 months. All studies used a validated depression scale, and three had objective measures of cessation at follow-up. Study quality appraisals are available in Appendix C.

3.2 Meta-analysis

The forest plot is displayed in Fig 2.

Fig 2 about here

There is a small association between depression and subsequent smoking (SMD=-.31, 95%CI -.43 to -.19), with no heterogeneity evident ($I^2=3.1%$, 95% CI 0.0 to 71.7%, $p=.402$). The Cochran Q statistic was 6.19 (degrees of freedom = 6, $p=.402$). Egger's test did not reveal any bias ($p=0.923$; see Appendix for funnel plot).

3.3 Sensitivity analyses

Summary estimates for each sensitivity analysis are displayed in Table 2. As all studies used questionnaires, no sensitivity analyses could be conducted as per depression measurement. The SMD was unchanged for each sensitivity analysis.

Table 2 about here

4. Discussion

There are perhaps two main conclusions from this systematic review. Firstly, despite the fact that many studies were found that measured depression at baseline and smoking status at follow-up, few reported the association between depression and subsequent smoking status. The second is that, from the limited estimates we can extract from the literature, depressive symptoms are consistently associated with reduced probability of quitting smoking in those with chronic respiratory conditions.

That the depression-smoking association is largely neglected is worrying, but probably unsurprising. For example, a recent review of depression and anxiety in COPD demonstrated that these conditions are undetected and undertreated [18]. Furthermore, contrary to popular belief, cessation is associated with improved mental health [27]. Given the high prevalence of depression in respiratory patients, and the impact of depression on outcomes such as health status, health behaviours and mortality [1], [2], [3], [4], [5], [6], [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18] and [19], this underscores the need for clinicians to address the barriers to better management of depressive symptoms in such patients.

Despite the fact that we could only provide estimates from seven studies, the results showed that depressive symptoms had a negative association with smoking cessation. The effect size was small, but consistent in various sensitivity analyses. Therefore, not only are depressive symptoms likely to impact on the quality of life of those with respiratory conditions, they are also stopping them achieving optimal health benefits of cessation. It is therefore possible that continued smoking is one of the mediating mechanisms behind the increased mortality rate seen in those with depressive symptoms in COPD [12] and [18], for example. The fact that depressive symptoms negatively impact on smoking cessation has also recently been demonstrated in patients with coronary heart disease, with similar effect size estimates [16].

While the effect estimates would be considered 'small' according to recommended guidelines [26], these are clinically significant effects, akin to the effects of antidepressants on depressive symptoms [28] and [29]. Also, for an addictive behaviour such as smoking, it is likely that even small effects could easily persuade patients to

re-commence smoking once they are trying to stop, or stop them from quitting in the first instance. Furthermore, even though effect estimates were similar in adjusted and unadjusted analyses, the variables accounted for were variable across studies. Hence, it is uncertain whether adjustment for other demographic factors (i.e. socioeconomic status, age, household smoking etc.), or indeed other variables which predict smoking cessation such as higher nicotine dependence, intention to quit or self-efficacy [30] would attenuate this association.

The recommended treatments for smoking cessation in respiratory conditions have recently been summarised [1] and [31]. While behavioural support is an effective treatment, and patients with depressive symptoms are likely to have less success at quitting. However, of particular relevance here is that two antidepressant therapies may be important for the depression-smoking link. Nortriptyline has only demonstrated non-significant abstinence increases in two randomized trials, and does not have FDA approval for cessation treatment. Bupropion demonstrated a significant effect on prolonged abstinence rates in COPD smokers [38] and is an approved cessation treatment, although adherence appeared to be an issue in that trial. Further research is needed for efficacious interventions in smokers with co-morbid respiratory and depressive conditions, and combination therapies have recently been advocated [1].

There were several limitations to this review. The literature in this area seems to be at an early developmental stage, and this warrants more sophisticated future research. Due to the limited literature here, the present meta-analysis will require updating once further research is conducted in this area. Secondly, we were only able to include a minority of studies in the final meta-analysis. It is unclear if the estimates from other research would match those found here. Unfortunately, having so few studies to meta-analyse increases the likelihood of an error in the mean effect estimate. Thirdly, depression in all 7 studies included in this review was measured using questionnaires instead of diagnostic interviews, and this could have led to misclassification bias. Thirdly, the follow-up duration period for the majority of the studies included ranged only from 6-24 months. Even though study duration did not seem to affect the estimates, as depression is a chronic illness with phases of relapse, studies with repeated measures and longer follow-up duration will be better able to truly measure the effect of depression on smoking cessation. It is possible that other confounders

may explain the depression-smoking link, as adjustment for confounders was heterogeneous in the current findings. However, no real differences were seen between overall adjusted and unadjusted estimates. Fourthly, as the depression measures used in this literature may not always be able to discriminate depression from anxiety or other related negative affect states [40],[41],[42] it is unclear whether the results may also be relevant to, or indeed be confounded by, other negative affect states such as anxiety. Future research using diagnostic measures should investigate this. It must also be noted that the inclusion and exclusion criteria for the studies contained within the meta-analysis could differ significantly, thereby limiting comparability. Such a limitation is typical of meta-analysis of observational studies such as this one [26]. Future research is needed to address these limitations, including repeated measures studies with adjustment for multiple confounders, and intervention studies to determine the best management methods for both depression and smoking cessation.

5. Conclusion

The association between depression and subsequent smoking was poorly reported or omitted in most studies. However, the available evidence suggests that depression decreases the likelihood that patients with chronic respiratory conditions will quit smoking. Therefore, the present paper should provide impetus for a renewed focus on the effects of depression on smoking. Future research is needed to determine how best to manage depression and smoking cessation in this population.

6. Acknowledgements

Author contributions: Dr Doyle is the guarantor of the manuscript and takes responsibility of the integrity of the data and the accuracy of the data analysis. He conceived the research idea and methods, conducted the statistical analysis, and contributed to the manuscript drafting and editing.

Ms Shu Ying Ho: contributed to study search and selection, review of studies, data extraction and analysis, writing and editing of the manuscript.

Ms Alnashri: contributed to study search and selection, review of studies, data extraction and analysis, writing and editing of the manuscript.

Ms Rohde: conducted critical appraisals of papers using the Crowe Critical Appraisal Tool, and provided critical input to the manuscript.

Mr Murphy: contributed to the search strategy (subject headings and keywords) and provided critical input.

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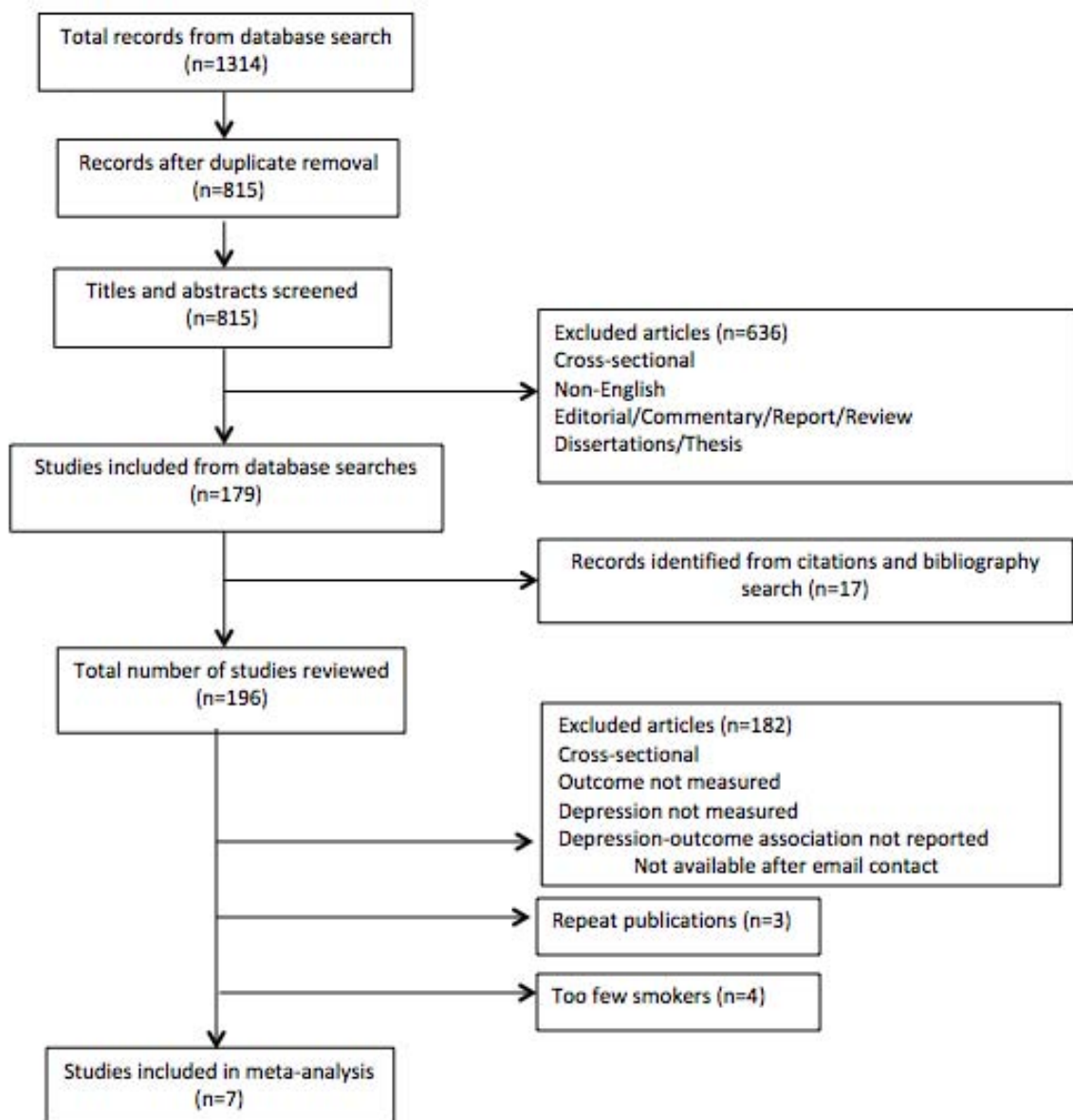


Figure 1: Flow diagram of selected articles in systematic review

Impact of depression on subsequent smoking status

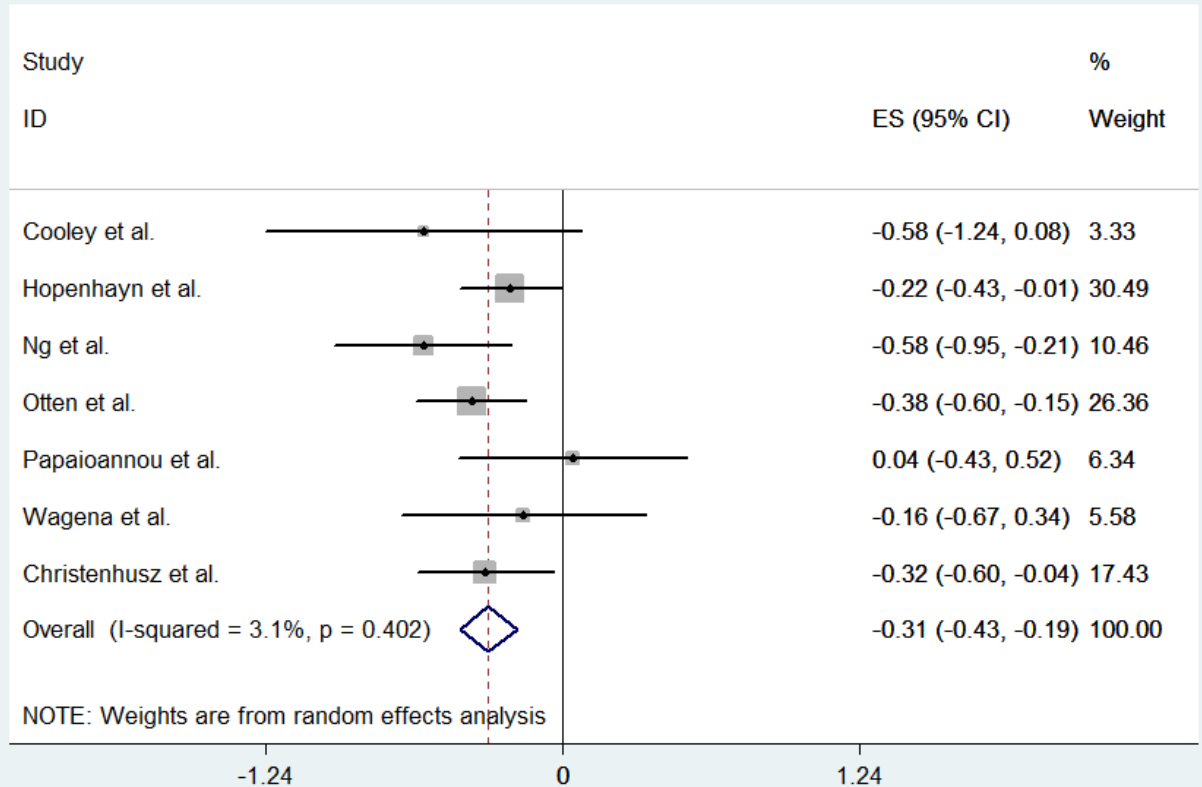


Figure 2: Forest plot of the impact of baseline depression on subsequent smoking cessation

Table 1: Included prospective studies reporting an association between baseline depression and subsequent smoking cessation

Author (Country)	Sample Description	Sample Size: Baseline, Follow-Up	Longest(Mean /Median) Follow-Up Duration	Depression Measure	Smoking Outcome Measure (Continuation / Cessation)	Results	CCAT Quality score	Comments
Christenhusz et al. ³² (The Netherlands)	Chronic obstructive pulmonary disease (COPD)	225, 163	1 year	Beck Depression Inventory (continuous)	Self-report abstinence, confirmed by salivary cotinine values (<20 ng/ml)	Multivariate OR=0.97, (95% CI 0.90-1.05, p=0.48)	52.5%	Data from one arm of randomized trial (SmokeStopTherapy), results for other arm not reported. Salivary cotinine confirmation at 6 and 12 months for all participants.
Cooley et al. ³³ (United States)	Non-Small Cell Lung Cancer (NSCLC)	230, 165	6 months	Center for Epidemiological Studies Depression Scale (>15 =Depressed)	Self-report (continuation) and biochemical variation with urinary cotinine	Crude OR=3.9 (95% CI 1.32-11.49, p=0.014); Multivariate: OR= 2.85, (95% CI 0.85-9.54, p=.088)	72.5%	Observational study. Biochemical confirmation for all participants at 1 st and 2 nd interviews.

Hopenhagen et al. ³⁴ (United States)	Lung cancer (stage I, II, IIIA cases)	179, 89	1 year	Hospital Anxiety and Depression Scale (Depression >10)	Self-report (continuation & cessation)	Multivariate: RR (Poisson)= 1.48, (95% CI 1.00- 2.17, p=<0.05)	72.5%	Observational study. Adjusted Poisson estimates used instead of raw numbers for multivariate estimate. Crude estimate obtained from reported raw numbers.
Ng et al. ³⁵ (Singapore)	COPD	376, 275	1 year	Hospital Anxiety and Depression Scale (>7 as depressed)	Self-report (continuation)	Crude OR=2.08 (95% CI 1.20- 3.60, p=0.009); Multivariate: OR= 2.85, (95% CI 01.17-4.52, p=.02)	85%	Observational study. Multivariate estimate adjusted for 10 other factors, including anxiety.
Otten et al. ³⁶ (The Netherlands)	Asthma	372, 372	22-24 Months	Depressive Mood List (>21.8 = depressed)	Self-Report (continuation)	Adjusted OR=1.98 (95% CI 1.31-3.00, p<0.01)	57.5%	Population observational study of adolescents. Estimate used is from entire sample, however authors stated relationship between depressive feelings and smoking was similar for adolescents with or without asthma.

								Analysis adjusted for age, sex, education.
Papaoiou et al. ³⁷ (Greece)	COPD	241, 230	1 Year	Beck Depression Inventory (≥19 = moderate or severe depressive symptoms)	Self-report (continuation)	Results not reported in paper. (23/26 depressed; 44/49 non-depressed smoking at follow-up)	85%	Observational study of patients without prior diagnosis of depression. Results obtained by email. No biochemical verification was used.

Wagena et al. ³⁸ (The Netherlands)	At risk for COPD or with COPD	255,255	26 Weeks	Beck Depression Inventory Score (≥ 15 = depressed)	Self-report (cessation), confirmed by urinary cotinine ≤ 60 ng/mL at wk 4, 12 and 26 after target quit date (TQD)	Association not reported in paper, but calculated from raw data reported in study (17/19 depressed versus 59/70 non- depressed were smoking at follow-up)	67.5%	Data from randomized trial of bupropion hydrochloride and nortriptyline hydrochloride, but control group only (n=89) used to calculate estimates.
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Table 2: Sensitivity analyses

<u>Sensitivity analysis</u>	<u>SMD</u>	<u>95% CI</u>	<u>I²</u>	<u>p-value</u>
<1 year follow-up (n=2)	-.32	-.72 to .08	0%	.327
≥1 year follow-up (n=5)	-.31	-.44 to -.18	7.7%	.362
CCAT≥60% (n=5)	-.29	-.48 to -.10	16.8%	.308
CCAT<60% (n=2)	-.35	-.53 to -.18	0%	.756
Adjusted estimates (n=5)+	-.34	-.46 to -.21	0%	.471
Unadjusted estimates (n=5)+	-.38	-.61 to -.14	23.2%	.267
Objectively measured cessation (n=3)	-.32	-.55 to -.09	0%	.619
Self-report cessation (n=4)	-.31	-.49 to -.14	30.8%	.228

+note – these analyses add to more than 7 studies as some studies provided both an unadjusted and adjusted estimate

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Appendix A - Sample searches:**MEDLINE on PubMed**

depressi*[MeSH Terms] OR depressi*[Title/Abstract] OR antidepress*[Title/Abstract] OR mood disorders[Title/Abstract] OR Mood disorders[MeSH Terms]

AND

smok*[MeSH Terms] OR smok*[Title/Abstract] OR tobacco[MeSH Terms] OR tobacco[Title/Abstract]

OR cigarette[Title/Abstract] OR cigar*[Title/Abstract] OR nicotine[Title/Abstract] OR nicotine[MeSH Terms] OR bupropion[Title/Abstract] OR bupropion[MeSH Terms] OR varenicline[Title/Abstract]

AND

lung diseases, obstructive[MeSH Terms] OR obstructive lung disease* [Title/Abstract] OR pulmonary disease[Title/Abstract] OR Pulmonary Disease, Chronic Obstructive[MeSH Terms] OR Bronchitis, Chronic[MeSH Terms] OR bronchitis[Title/Abstract] OR asthma[MeSH Terms] OR bronchiectasis[MeSH Terms] OR bronchiectasis[Title/Abstract] OR Emphysema[MeSH Terms] OR

Emphysema[Title/Abstract] OR pulmonary fibrosis[MeSH Terms] OR pulmonary fibrosis[Title/Abstract] OR respiratory symptom[Title/Abstract] OR lung neoplasms[MeSH Terms] OR lung neoplasms[Title/Abstract]

PsychINFO on OVID

(depression OR depressive OR antidepressation OR antidepressive OR mood disorders).mp

AND

(smoking OR smoker OR smokers OR tobacco OR cigarette OR cigar OR cigars OR nicotine OR nicotine OR bupropion OR varenicline).mp

AND

(obstructive lung diseases OR pulmonary disease OR Bronchitis OR asthma OR bronchiectasis OR Emphysema OR pulmonary fibrosis OR respiratory symptom OR lung neoplasms).mp

Appendix B

Appendix B: Omitted studies that did not report the association between baseline depression and subsequent smoking

Author	Sample Description	Sample Size: Baseline, Follow-Up	Longest Follow-Up Duration	Depression Measures (Measured at Follow-Up Yes/No)	Smoking Outcome Measures	Results	Comments
Aguiar et al. ¹	Pulmonary disease in 274	526,307	30 Months	A diagnosis of depression, Taking sedative-hypnotics and/or antidepressants	Self-report	No association reported between depression and subsequent smoking cessation	Email sent – Author did not reply by
Arnardottir et al. ²	COPD	60,60	16 weeks	(HADS), higher score indicates worse mental health	Self-report	No association reported between depression and subsequent smoking cessation	Email sent
Attebring et al. ³	ACS, some of sample had pulmonary disease	434,348	3 Months	Sedatives/ Anti-depressants at baseline	Self-report	Being on Sedatives/ Anti-depressants at baseline predicts odds for continued smoking at follow-up (OR=8.40, CI= 2.36-30.0)	Email sent
Berlin et al. ⁴ , West et al. ⁵	Asthma, COPD, Emphysema	2009, ?	2.5 years	2 times or more visits to the doctor due to depression	Self-report	Depression is associated with higher nicotine dependence and urges.	Email sent

Brito-Mutunayagam et al. 6	COPD	4060, 3206	3.5 Years	Center for Epidemiologic Studies Depression Scale (CES-D), ≥ 16 = depressed	Self-report	No association reported between depression and subsequent smoking cessation	Author will provide data after deadline
Bucknall et al. ⁷	COPD	464, 265	12 Months	HADS	Self-report	No association reported between depression and subsequent smoking cessation	Email sent
Coultas et al. ⁸	COPD	217, 151	6 Months	CES-D	Self-report	No association reported between depression and subsequent smoking cessation	Email sent
Garcia-Aymerich et al. ^{9, 10}	COPD	342, ?	8 years	HADS	Self-report	No association reported between depression and subsequent smoking cessation	Email sent
Gudmundsson et al. 11, 12	COPD	416, 406	12 Months	Hospital Anxiety and Depression Scale (HADS-D), ≥ 8 = depressed	Self-report	No association reported between depression and subsequent smoking cessation	Email sent
Hanania et al. ¹³ , Vestbo et al. ¹⁴	COPD	2118, ?	3 Years	Center for Epidemiologic Studies Depression Scale (CES-D), ≥ 16 = depressed. Self-reported depression or use of Anti-depressants	Self-report	Depression has no effect on smoking status. And, No association reported between depression and subsequent smoking	Email sent

				at baseline		cessation	
Hasler et al. ¹⁵	Asthma	591, 367	20 years	Diagnostic interview	Self-report	No association reported between depression and subsequent smoking cessation	Email sent
Jones et al. ¹⁶	COPD	158, 115	?	HADS	Self-report	No association reported between depression and subsequent smoking cessation	Author was emailed on 19/2. They did not respond to previous request for PDF, so unlikely to reply to this data request.
Joseph et al. ¹⁷	Asthma	196, 90	12 months	?	Self-report	No association reported between depression and subsequent smoking cessation	Email sent
Kotz et al. ¹⁸	COPD	228, 228	50 days	(BDI) Beck Depression Inventory and (HADS) Hospital Anxiety and Depression Scale	Self-report	No association reported between depression and subsequent smoking cessation	Email sent
Katz et al. ¹⁹	Asthma	374, 128	36 months	CES-D, the higher scores the more depressed	Self-report	No association reported between depression and subsequent smoking	Email sent

cessation

Laitinen et al. ²⁰	COPD	739, ?	1-3 years, intended to follow-up for 10 years	?	Self-report	No association reported between depression and subsequent smoking cessation	Email sent
Leander et al. ²¹	Asthma	616, 460	13 years	Gothenburg Quality-of-Life Instrument (GQL)	Self-report	No association reported between depression and subsequent smoking cessation	Email sent
LoConte et al. ²²	Non-small cell lung cancer (NSCLC)	96,52	6 Months	CES-D, ≥ 16 = depressed	Self-report	Depression levels were similar in current, ex-, and never smokers. No association reported between depression and subsequent smoking cessation.	Email sent
Loerbroks et al. ²³	Asthma	5114, 4010	8.5 years	Depression scale developed by von Zerssen	Self-report	High depression scores associated with never or current smoking status. No association reported between depression and subsequent smoking cessation	Email sent
Mancuso et al. ²⁴	Asthma	296, 197	1 year	Geriatric Depression Scale ≥ 11 = depressed	Self-report	No association reported between depression and subsequent smoking cessation	Email sent
Myrdal et al. ²⁵	Lung cancer (primary)	194, 132	22.5 months	HADS	Self-report	No association reported between depression and	Email sent

				8-10 = probable depression, ≥ 11 = definite" clinical depression		subsequent smoking cessation	
Neuman et al. ²⁶	Asthma	542, 515	8.6 years	HADS, ≥ 8 = depressed	Self-report	No association reported between depression and subsequent smoking cessation	Email sent
Oga et al. ²⁷	COPD	137, 72	5 years	HADS	Self-report	No association reported between depression and subsequent smoking cessation	Email sent
Pahwa et al. ²⁸	Chronic bronchitis and Asthma	14713, ?	7 years	Distress scale developed by Kessler et al.	Self-report	No association reported between depression and subsequent smoking cessation	Email sent
Ringlever et al. ²⁹	Asthma	10087, 6769	24 months	Depressive Mood List (DML), higher scores imply higher levels of depressive feelings	Non-smokers	Data base in this paper is rejected, however author was e-mailed for extra data	Email sent
Sarna et al. ³⁰	Non-small cell lung cancer (NSCLC)	119, 119	6 months	CES-D, ≥ 16 = depressed	Self-report, confirmed by urinary cotinine at baseline and 3 months	No association reported between depression and subsequent smoking cessation	Email sent

					follow-up		
Sherman et al. ⁴¹	COPD	1914, 1150	12 months	(CES-D), ≥ 10 = depressed	Self-report	Smokers were 47 % likely to be depressed. No association reported between depression and subsequent smoking cessation	
Simmons et al. ³²	Thoracic Cancer	177, 154	12 Months	(CES-D) Center for Epidemiologic Studies Depression Scale + self-reported history use of anti-depressants.	Self-report , a proportion of the sample (n=44) were tested by collecting biochemical conformation of quit state by breath CO	Smoking relapse was predicted by greater depression proneness (p=0.004) or previous depression treatment (p=0.042)	Email sent
Tashkin et al. ³³	COPD	200, 129	6 months	History of depression	University of Wisconsin Center for Tobacco Research and Intervention craving and withdrawal questionnaire	?	Email sent

Uyar et al. ³⁴	Unclear if sample had respiratory disease	131, 131	24 weeks	(BDI) Beck Depression Inventory Score 0-13 minimal depression, 14-19 mild depression, 20-28 moderate depression, and 29-63 severe depression	Mesure CO levels to confirm status levels < 10 ppm confirmed abstinent.	Abstinence rates were higher in individuals with lower levels depression	Email sent
Van Sachayck et al. ³⁵	COPD	255, 214	1 year	BDI	Self-report, confirmed by urinary cotinine values (cut-off point 60 ng/ml)	Depression had no effect on subsequent smoking cessation	Email sent
von Leupoldt et al. ³⁶	COPD	238, 238	3 weeks	HADS, ≥ 8 = depressed	Self-report	No association reported between depression and subsequent smoking cessation	Email sent
Walker et al. ³⁷	Non-small cell lung cancer (NSCLC)	43,	?	Beck Depression Inventory Score (BDI)	Self-report	No association reported between depression and smoking.	Email sent

Appendix C – Quality ratings

Author	Preamble	Introduction	Design	Sampling	Data Collection	Ethical Matters	Results/	Discussion	Total Score (%)
Christenhusz et al. ³²	4	5	4	4	2	0	4	4	67.5%
Cooley et al. ³³	3	3	3	1	4	1	4	4	57.5%
Hopenhayn et al. ³⁴	4	5	1	3	3	3	5	5	72.5%
Ng et al. ³⁵	4	5	3	3	3	2	4	5	72.5%
Otten et al. ³⁶	5	5	4	4	4	4	4	4	85%
Papaioannou et al. ³⁷	4	4	3	1	1	4	2	2	52.5%

Wagena et al. ³⁸	5	5	5	4	3	3	4	5	85%
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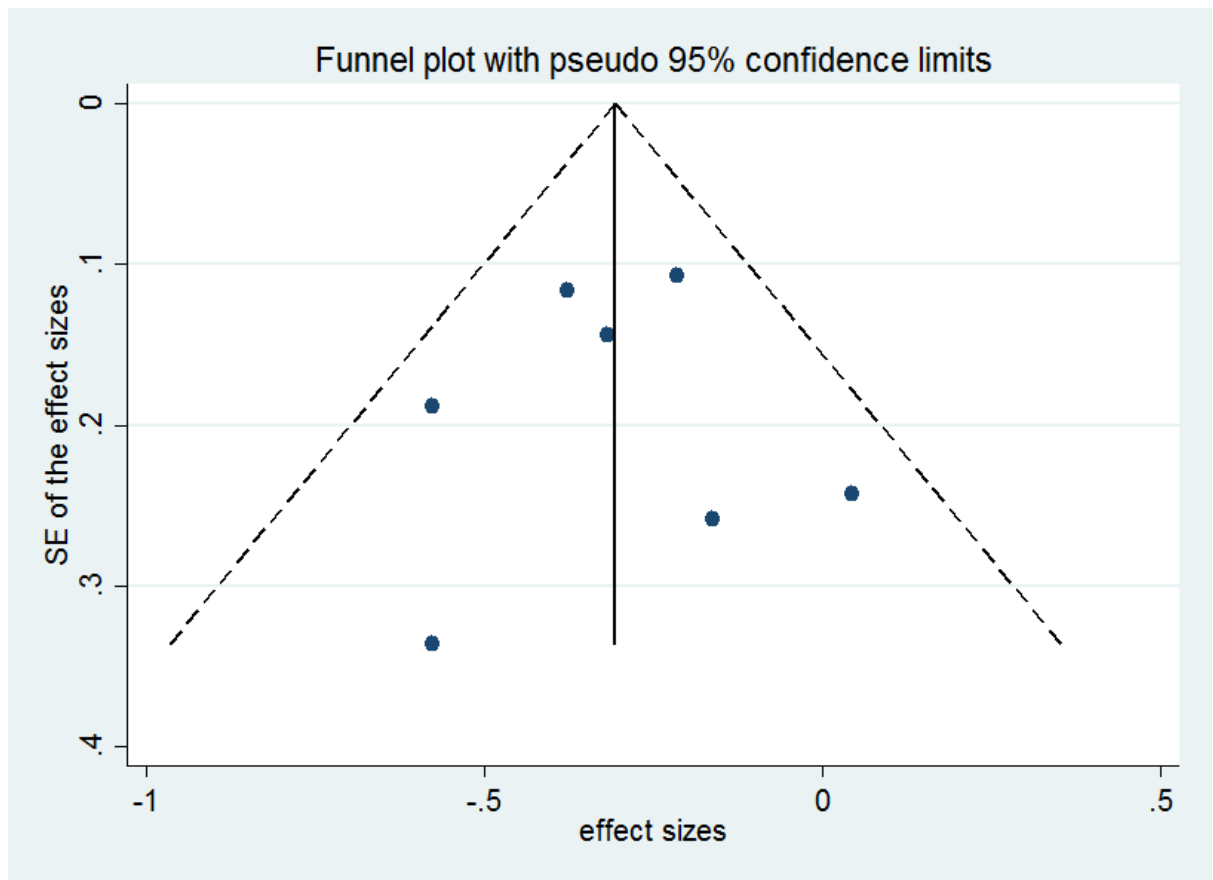
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Appendix D – Funnel plot and test for bias



Egger's test for small-study effects: Regress standard normal deviate of intervention effect estimate against its standard error

Number of studies = 7

Root MSE = 1.111

Std_Eff	Coef.	Std. Err.	t	P>t	[95% Conf.	Interval]
slope	-.2889435	.1847927	-1.56	0.179	-.7639682	.1860811
bias	-.1176586	1.16425	-0.10	0.923	-3.110459	2.875142

Test of H0: no small-study effects P = 0.923