1-1-2014

Systematic review and meta-analysis of the impact of depression on subsequent smoking cessation in patients with coronary heart disease: 1990-2013

Frank Doyle
Royal College of Surgeons in Ireland, fdoyle4@rcsi.ie

Daniela Rohde
Royal College of Surgeons in Ireland, danielamrohde@rcsi.ie

Aleksandra Rutkowska
Royal College of Surgeons in Ireland

Karen Morgan
Royal College of Surgeons in Ireland, kmorgan@rcsi.ie

Grainne Cousins
Royal College of Surgeons in Ireland, gcousins@rcsi.ie

See next page for additional authors

Citation

Doyle F, Rohde D, Rutkowska A, Morgan K, Cousins G, McGee H. Systematic review and meta-analysis of the impact of depression on subsequent smoking cessation in patients with coronary heart disease: 1990-2013. Psychosomatic Medicine. 2014;76(1):44-57.

Authors
Frank Doyle, Daniela Rohde, Aleksandra Rutkowska, Karen Morgan, Grainne Cousins, and Hannah McGee

Systematic review and meta-analysis of the impact of depression on subsequent smoking cessation in patients with coronary heart disease: 1990–2013

Running title: Impact of depression on smoking in CHD

Frank Doyle PhD, Daniela Rohde MSc, Aleksandra Rutkowska MSc, Karen Morgan PhD, Grainne Cousins PhD, Hannah McGee PhD

Division of Population Health Sciences (Psychology), Royal College of Surgeons in Ireland, Dublin, Ireland

Corresponding author:

Frank Doyle, PhD

Department of Psychology, Division of Population Health Sciences, Royal College of Surgeons in Ireland, 123 St Stephen's Green, Dublin 2, Ireland

Email: fdoyle4@csi.ie, Tel: + 353 1 4022718, Fax: + 353 1 4022764

Word count (including tables/figures and references, excluding appendices): 6964

Tables: 2, Figures: 2

Author addresses

Division of Population Health Sciences (Psychology), Royal College of Surgeons in Ireland, Dublin, Ireland (FD, DR, AR)

PU-RCSI School of Medicine, Malaysia (KM)

School of Pharmacy (GC), Royal College of Surgeons in Ireland, Dublin, Ireland

Faculty of Medicine and Health Sciences, Royal College of Surgeons in Ireland (HM)

Conflicts of interest and sources of funding

None

Abstract

Objective:

Smoking cessation is crucial for patients with coronary heart disease (CHD), yet depression may impede cessation success. We systematically reviewed the longitudinal association between depression and subsequent smoking cessation in individuals with CHD in order to quantify this effect.

Methods:

Electronic databases (PsychInfo, PubMed, CINAHL) were searched for prospective studies of CHD patients which measured depression at baseline (scales, diagnostic interview or antidepressant prescription) and reported smoking continuation/cessation at follow-up. Inclusive dates were 1st January 1990 to 22nd May 2013. Standardized mean differences (SMD) and associated 95% confidence interval (CI) were estimated using random effects meta-analysis. Sensitivity analysis explored the impact of limiting meta-analysis to studies using different depression measures (validated scales, diagnostic interviews, antidepressant prescription), different durations of follow-up, or higher quality studies.

Results:

From 1451 citations retrieved, 28 relevant articles were identified. Meta-analysis of all available data from 20 unique datasets found that depressed CHD patients were significantly less likely to quit smoking at follow-up (SMD=-.39, 95% CI -.50 to -.29; I^2=51.2%, p=.005). Estimates remained largely unchanged for each sensitivity analysis, except for two studies that used antidepressants, which showed a much larger effect (SMD=-.94, -1.38 to -.51; I^2=57.7%, p=.124).

Conclusions:

CHD patients with depressive symptoms are significantly less likely to quit smoking than their non-depressed counterparts. This may have implications for cardiovascular prognosis, and CHD smokers may require aggressive depression treatment to enhance their chances of quitting.

Keywords: Depression; coronary heart disease; health behaviors; smoking; smoking cessation

Acronyms:

ACS = acute coronary syndrome,

BDI (II) = Beck Depression Inventory (II),

BDI-FS = Beck Depression Inventory Fast Screen,

CAD = coronary artery disease,

CCAT = Crowe Critical Appraisal Tool,

CES-D = Center for Epidemiological Studies Depression Scale,

CHD = coronary heart disease,

CI = confidence interval

HADS = Hospital Anxiety and Depression Scale,

MI = myocardial infarction,

MOSSAS = Medical outcomes Study Specific Adherence Scale,

OR = odds ratio,

obs = observational study

RCT = randomised controlled trial

PHQ = Patient Health Questionnaire,

PRIME-MD = Primary Care Evaluation of Mental Disorders,

SMD = Standardized mean difference

Introduction

While smoking cessation should be recommended to all patients (1-3), recent reviews have highlighted the importance of smoking in patients with coronary heart disease (CHD) (4-6). Smoking cessation is associated with 36-50% reduction in morbidity and mortality in CHD patients, with the benefits of quitting smoking outperforming those related to other preventive strategies such as blood pressure or cholesterol control (2, 3). Cessation is especially crucial in this population, as continuing to smoke renders such secondary prevention interventions less efficacious (7, 8), therefore smokers are not deriving the full benefit from preventive therapies. For example, when comparing 4424 treated hypertensives, those who smoked had higher levels of suboptimal diastolic blood pressure 90mmHg or more (33% vs. 25%), along with higher rates of microalbuminuria. Men from the same sample also had higher rates of elevated systolic blood pressure of 140mmHg or more (73% vs. 69%), higher left ventricular hypertrophy, and microalbuminuria, whereas women smokers had higher cholesterol (8). Similarly, Milionis et al. (7) have demonstrated how smokers in primary and secondary prevention statin trials have failed to glean full benefits from these lipid lowering drugs, with smokers having an extra 23-86% increased risk of a cardiovascular event. While having an acute coronary event can motivate smokers to quit, the majority of smokers continue to smoke or resume smoking within 6 months after such events (6), therefore identifying factors that predict relapse is of significant value for clinicians.

The prevalence of depression in patients with coronary heart disease (CHD) is elevated in comparison to general population samples (9, 10). Tobacco use has a long-established relationship with depression. Those who smoke have a higher incidence of depressive symptoms, and those with depressive symptoms are less likely to quit smoking and are more likely to relapse if they do (4-6). For example, secondary analysis of a randomised trial on smoking cessation showed that a greater number of nicotine withdrawal symptoms experienced by depressed smokers, as opposed to non-depressed smokers, mediated the effect of depression on smoking continuation 3-months later. Indeed, this was estimated to account for 27% of the effect of depression on cessation outcomes (11). It also appears that treating depression in patients with MI may not increase cessation rates (12), and it is unclear whether quitting smoking leads to an improvement in or worsening of depressive symptoms (13).

Therefore, the effect of depression on subsequent cessation may be profound, however, this has not been subject to systematic review or meta-analysis. The American Academy of Family Physicians have described the research on the impact of depression on lifestyle modifications as “low quantity medium to low quality evidence”, and they suggest that further investigation is required (14). Meta-analysis should provide a more precise effect estimate than single studies alone. We quantified the effects of depression on subsequent smoking in patients with CHD. However, as depression is defined in different ways, the potential for misclassification error is high which has the potential to distort estimates of the exposures effect (depression) on the outcome (smoking), thus resulting in biased estimates of the effect of depression.

Similarly, the impact of depressive symptoms may fluctuate over time, or study quality could be heterogeneous. We planned a number of sensitivity analyses to address these potential biases.

Methods

This systematic review with meta-analysis was performed according to recommended principles (15).

Search strategy

A systematic literature search of PubMed, CINAHL and PsychInfo was conducted in May 2013. Searches used subject headings and keywords. A PubMed example is as follows: ((("Depression"[Mesh] OR "Depressive Disorder"[Mesh] OR "Depressive Disorder, Major"[Mesh] OR "Adjustment Disorders"[Mesh])) AND "Myocardial Ischemia"[Mesh]) AND ("Smoking"[Mesh] OR Smok*)). This search was supplemented by handsearching references of retrieved articles. Studies dating from the 1st January 1990 to May 2013 were included in the analysis.

Study selection and data extraction

Studies were included if they met the following eligibility criteria: CHD samples, published in 1990 or later, prospective, measure of depression at baseline (i.e. diagnostic interview, questionnaire, antidepressant prescription, single-item questions), measure of smoking at follow-up. We included control groups from (non)randomized trials, or combined intervention and control groups from (non)randomized trials (where

data for the control groups could not be obtained). We excluded papers which had samples exclusively enrolled in cardiac rehabilitation (CR) programs for two main reasons. Such programs may have intense behavior modification elements, and should have standard measurements of depression and smoking at baseline and outcome. Thus, a large body of data exists, but is not necessarily reported in each paper on CR. Furthermore, CR participants are not representative of general CHD patients for many reasons: not all CHD patients are referred to CR; not all referred patients attend CR; those who do attend often drop out; and depression has been shown to predict non-attendance and drop-out, which may bias estimates (16-18). Two reviewers independently completed the first screening of abstracts/titles (DR, AR). Studies that were considered eligible for inclusion were read in full and suitability for inclusion was independently determined by DR and AR. Disagreements were managed by consensus or discussed with a third reviewer (KM or FD). Data were extracted on the basis of study setting, % men, length of follow up, depression measures, smoking status (or relevant results). Authors were contacted to provide further information when there was insufficient data provided in the published paper.

Quality assessment

The quality of the studies was assessed using the Crowe Critical Appraisal Tool (CCAT) (19-21), which was developed based on existing tools, general research methods theory and reporting guidelines. It has exhibited a good degree of construct validity (19) and reliability (21), and is reported to be simple to implement and suitable for all research designs in health. The CCAT consists of eight categories corresponding to various

aspects of a study, including introduction, design, sampling, data collection, ethical matters, results and discussion. Each category contains a number of items, which are marked as present, absent, or not applicable, with only those items that are applicable to a specific research design being included in the appraiser's score. Each category is also scored on a scale from 0 (no evidence) to 5 (highest evidence). Scoring is thus not based solely on a checklist, but allows for a combined objective (tick boxes) and subjective scoring of each category (19). The authors recommend publishing individual category scores along with total scores so that weak scores in a category are not obscured. Total scores for each study (ranging from 0-40) are presented as a percentage.

Statistical analysis

Smoking status at follow up was the primary outcome of interest. As some studies used multiple measures of depression, these were considered in the following hierarchical manner: diagnostic interview, validated scale, current prescription of antidepressants, history of depression, single-item (unvalidated) measure. Due to differential measurement and reporting of smoking status (e.g. current/former/ex-smoker; smoking at least 20 cigarettes in a year) and depression (e.g. scoring above threshold on a scale; mean and SD of depression scale for continued smokers and quitters), the unadjusted standardized mean difference between depressed and non-depressed samples was the primary measure of effect. This was estimated for all included studies using the *metaeff* (22) command in Stata 12.1, and estimated using the random effects model (23, 24). The I^2 test was used to assess the percentage of variability in the effect

estimates that can be attributed to heterogeneity (variation in effect estimates arising from methodological or clinical differences between studies) rather than chance. Pre-planned sensitivity analysis included examining the impact of differential depression assessment (validated scales, diagnostic interviews, antidepressant prescription), different durations of follow-up (categorized as <1 year versus ≥1 year), or higher quality studies (≥60%) (24). We also assessed whether study design, or the use of adjusted or unadjusted estimates affected results. Formal statistical testing for publication bias or small study effects was conducted using the Egger's test which is a sensitive regression asymmetry test. Bias is detected by determining whether the intercept deviates significantly from zero in a regression of standardized effect estimates against their precision.

Results

Study identification

A flow diagram of the search strategy is presented in Figure 1. The search yielded 1185 papers of which 1165 were excluded. Twenty-eight explored the association between depression and subsequent smoking (11, 12, 25-50). Nine more were omitted (four repeat publications (38, 44-46), unavailable data (12, 47, 48, 50), one had too few smokers to provide an estimate (49) - see Appendix A). McGee et al. (37) was treated as two studies, as two depression scales were used in independent groups to predict smoking. This left 20 datasets from 19 articles for analysis.

Fig 1 here

Characteristics of included studies are displayed in Table 1, with studies listed in alphabetical order of first author.

Table 1 here

Study Characteristics

Patients were recruited in hospital settings across 9 countries. Sample sizes at follow-up ranged from 20–1276. The majority of samples are from patients who presented with acute CHD, with the remainder consisting of two studies including both acute and chronic CHD patients, two studies with CHD outpatients, and one study being unclear (those diagnosed with coronary artery disease after angiography). Length of follow-up varied from 1 month to 13 years. Various methods were used to assess depressive symptoms, with six studies (30, 31, 33, 37, 41, 43) utilizing more than one measure. Two studies used diagnostic interviews (41, 43), 17 used validated scales (11, 26, 27, 29-37, 39-43), two used antidepressant prescription (25, 30), and one used a single-item measure of mood (28). Quality appraisals are available in Appendix B.

Meta-analysis

Using the depression measure hierarchy outlined in the Methods, the forest plot using the best estimate from individual studies is displayed in Fig 2.

_____

Fig 2 here

_____

Overall, there is a small effect of depression on cessation across the 20 datasets (SMD=-.39, 95% CI -.50 to -.29). There was statistically significant heterogeneity evident (I^2=51.2%, p=.005). There was no evidence of funnel plot asymmetry indicating that the effect of depression on smoking identified in smaller studies was not different to larger studies (p=.071 for Egger's test of asymmetry; see Appendix C for funnel plot).

Sensitivity analyses

Summary estimates for each of the sensitivity analyses are displayed in Table 2 (and Appendix D):

_____

Table 2 here

_____

Estimates were largely unchanged for each of the above conditions. Two studies that used anti-depressants demonstrated an effect size that was between 2-3 times larger than the other estimates (25, 30). One of these studies contributed to significant heterogeneity in the overall estimate and other sensitivity estimates (25), as when it was omitted the overall effect remained similar but the heterogeneity was no longer significant (SMD=-.34, -.42 to -.26, I^2=21.9%, p=.19). The best estimate from the other study was the depression scale so this was adopted for the other analyses (30).

Discussion

Overall, the results of this review suggest that depression is consistently associated with significantly reduced likelihood of subsequently quitting smoking in CHD patients. This is problematic for CHD patients for two reasons. Firstly, smoking cessation benefits CHD patients. Secondly, smoking continuation has a significant negative impact on therapies that reduce hypertension and cholesterol (7, 8). Therefore, it is possible that depressive symptoms may be contributing to higher cardiovascular risk in smokers by reducing the probability of cessation.

Size of effect

According to guidelines (24), the effect sizes reported here is 'small' for all analyses except when analysis is confined to studies defining depression using antidepressant prescription. However, even the small estimate is likely to be a clinically significant effect, and for example is of similar magnitude to a reduction in post-MI depression post-intervention (51). That large effects were demonstrated for antidepressant

prescription may seem counter-intuitive, as bupropion SR has been shown to increase likelihood of quitting in depressed cardiac patients (11, 52). It is possible that this classification may simply reflect those who have more severe depression and are thus less likely to quit, but more likely to come to clinicians' attention for depression and receive antidepressants. Furthermore, as antidepressants can be prescribed for other problems (pain, other psychiatric conditions, etc.) in those who may not have depression, it is possible that such conditions also affect smoking behavior. Another explanation is that the classification as depressed for those using antidepressants or sedatives in one of these studies (25) may have significantly inflated the depression category, and possibly lead to an overly-large effect size for that study. However, caution should be used when interpreting these sensitivity analyses, as there were very studies in some categories.

Study quality

Any conclusions drawn from such meta-analyses must be cognizant of the quality of the literature reviewed (24). While critical appraisal of primary studies is an essential feature of systematic reviews, the lack of a 'gold standard' appraisal method has been acknowledged (53, 54) with many tools lacking information on development, evaluation of validity or testing reliability (19). Assuming the CCAT ratings were appropriate, this had little effect on our results in sensitivity analyses, and indicates the findings are consistent across studies.

However, other indicators of quality could be considered. Studies largely relied on self-report data, which could be considered a weakness, despite the fact that such data has excellent sensitivity and specificity for smoking behavior (55). The severity of smoking addiction, or number of cigarettes smoked were also typically omitted. Possibly more problematic was that studies differed somewhat in their classifications of smokers, or did not report the precise criteria used to categorize smokers and non-smokers. Furthermore, studies largely did not adjust for other potentially confounding factors when reporting the associations of interest, which means that the present results may be over-estimates. Similarly, the measurement of depression was heterogeneous. Differential measurement of depression can lead to starkly contrasting results when predicting prognosis (56, 57). Reassuringly, sensitivity analyses demonstrated similar effect estimates for all measures, with the exception of anti-depressants. It is crucial that future research adopts recommended definitions of smokers (58), and wherever possible incorporates biochemical measures of smoking, and measures of addiction severity.

Treatments and hospitalization

As depression is typically episodic, and chronic, it is possible that the impact of depression on subsequent smoking fluctuates, with the highest influence during more severe depressive episodes (5). However, sensitivity analysis did not show any major effect of follow-up duration on the present results. Given that nicotine is so addictive (and smoking is typically an everyday activity) any hypothesized fluctuating effects may actually be more important for non-addictive behaviors, such as physical activity.

Furthermore, it is possible that depression may have a stronger effect on smoking initiation than cessation (59).

While cessation counseling with more than 1-month follow-up has been shown to be effective for cardiac patients (1), and can even reduce post-discharge mortality when combined with pharmacotherapy (60), no randomized trials have assessed smoking interventions in depressed cardiac patients specifically. Available data is limited to post-hoc analyses, albeit pre-planned (6, 12). Similarly, trials have not examined the safety of nicotine replacement therapies (NRT) in acute cardiac patients, and as nicotine has direct effects on the cardiovascular system, RCTs for acute patients are needed to establish safety (6). These deficiencies in the literature somewhat limit the recommendations that can be made regarding specifically targeting depressed CHD patients who smoke.

In contrast, nicotine replacement therapy (NRT) has been approved for stable CHD patients, and is recommended for selected MI patients as they are being discharged. NRT acts on withdrawal symptoms, so may be especially important for depressed CHD patients who tend to report higher rates of such symptoms (11). Bupropion SR has been shown to be well-tolerated in patients with acute CVD, and to increase subsequent quit rates in those with elevated depressive symptoms compared to those without (19% v 3%), although this was non-significant (p=.07) probably due to limited sample size (11). Although varenicline has demonstrated effectiveness in increasing cessation rates in stable cardiac patients, caution is needed when prescribing this therapy in those with

depression and CHD, due to reported increases in depressed mood and even suicidality, and intensive monitoring would be required (6).

Unfortunately, despite hospitalization being a teachable moment for smoking cessation, healthcare professionals advise patients to quit less often than they should (1, 61, 62). While the results of the present review suggest that depressed CHD patients may require more intensive intervention, the use of systematic programs on cessation seem to be effective, even when controlling for depression (29, 62). Hospitals should implement such systematic programs, and consider screening for depression in smokers to target those in need of more intensive intervention (6).

Future research

The present findings suggest that further, more sophisticated research is required on the interactions between depression and smoking. Adding multiple follow-up phases with measures of depression and smoking at each phase would provide more detail on the effects of depression over time (4). While many studies adjust for smoking status at baseline (10), they typically do not account for the number of cigarettes smoked, or whether people quit post event, and therefore the full effects of smoking may not be assessed properly. Such research may also inform the literature on potential behavioral mechanisms linking depression with poorer prognosis in those with coronary heart disease (63, 64), as our results suggest that smoking may be a mediating factor in the depression-prognosis link (65). As results were largely unadjusted, it is possible that other factors account for the depression-smoking association seen here. Depressed

CHD patients have higher cravings, lower confidence in quitting, greater withdrawal symptoms, lower sense of coherence, lower social support than non-depressed smokers (11, 12, 26, 38, 39), and future research should determine the potential interacting effects of these variables. Furthermore, novel therapies such as behavioural activation may need to be investigated, as the efficacy for talk therapies appears to be mixed for depressed patients (4, 12), and our results highlight the need for establishing the best treatments for cessation in depression CHD patients.. Finally, although we studied the association between depression and cessation in CHD patients, future research should establish whether the effects seen here are similar for other populations.

Strengths and Limitations

The results should be interpreted in the context of the limitations relating to the original studies. Although the methodological quality of the included studies was reasonable, eight were rated below the threshold of 60%. However, accounting for quality of the included studies in a sensitivity analysis did not change the pooled effect. In addition, our meta-analysis was restricted to the pooling of unadjusted estimates, thereby failing to account for potential confounders. However, the adjusted estimates did not differ greatly. Furthermore, although we were able to consider the effect of misclassification bias due to different depression measures, we were unable to account for the potential influence of different measures of smoking. However, despite the wide variation in smoking measures, the results across the individual studies are quite consistent as displayed in the forest plot, and when the antidepressant studies are removed, the

heterogeneity is no longer significant, thus suggesting the effect is quite robust. There is the possibility that some chance findings are being submitted, or that studies, including those which measure multiple behaviors, are only reporting those with significant associations, and this was supported by some evidence of publication bias. Data were pooled from six different countries, enhancing the generalizability of the findings. Omission of CR programs also weakens the findings.

Conclusion

Depression reduces the likelihood of quitting smoking in cardiac patients**, and this** effect remains after adjustment for other factors. Clinicians should consider screening for depression in smoking patients with CHD, and provide intensive cessation help. It is vital to establish the cessation methods that are most efficacious for depressed CHD smokers.

References

1. Rigotti NA, Clair C, Munafo MR, Stead LF. Interventions for smoking cessation in hospitalised patients. Cochrane Database Syst Rev. 2012;5:CD001837.

2. Pipe AL, Papadakis S, Reid RD. The role of smoking cessation in the prevention of coronary artery disease. Curr Atherosclerosis Rep. 2010;12:145-50.

3. Wilson K, Gibson N, Willan A, Cook D. Effect of smoking cessation on mortality after myocardial infarction: meta-analysis of cohort studies. Arch Intern Med. 2000;160:939-44.

4. Busch AM, Borrelli B, Leventhal AM. The Relationship between Smoking and Depression Post-Acute Coronary Syndrome. Curr Cardiovasc Risk Rep. 2012;5:510-8.

5. Freedland KE, Carney RM, Skala JA. Depression and smoking in coronary heart disease. Psychosom Med. 2005;67 Suppl 1:S42-6.

6. Thorndike AN, Rigotti NA. A tragic triad: coronary artery disease, nicotine addiction, and depression. Curr Opinion Cardiol. 2009;24:447-53.

7. Milionis HJ, Rizos E, Mikhailidis DP. Smoking diminishes the beneficial effect of statins: observations from the landmark trials. Angiology. 2001;52:575-87.

8. Journath G, Nilsson PM, Petersson U, Paradis BA, Theobald H, Erhardt L. Hypertensive smokers have a worse cardiovascular risk profile than non-smokers in spite of treatment--a national study in Sweden. Blood Press. 2005;14:144-50.

9. Centers for Disease Control and Prevention. QuickStats: Prevalence of Current Depression* Among Persons Aged ≥12 Years, by Age Group and Sex—United States,

National Health and Nutrition Examination Survey, 2007-2010. National Center for Health Statistics, 2012 Jan 6.

10. Meijer A, Conradi HJ, Bos EH, Anselmino M, Carney R, Denollet J, Doyle F, Freedland KE, Grace SL, Hosseini SH, Lane DA, Pilote L, Parakh K, Rafanelli C, Sato H, Steeds RP, Welin C, de Jonge P. Adjusted prognostic association of post-myocardial infarction depression with mortality and cardiovascular events: an individual patient data meta-analysis. Br J Psychiat. 2013;203:90-102.

11. Thorndike AN, Regan S, McKool K, Pasternak RC, Swartz S, Torres-Finnerty N, Rigotti NA. Depressive symptoms and smoking cessation after hospitalization for cardiovascular disease. Arch Intern Med. 2008;168:186-91.

12. Trockel M, Burg M, Jaffe A, Barbour K, Taylor C. Smoking behavior postmyocardial infarction among ENRICHD trial participants: Cognitive behavior therapy intervention for depression and low perceived social support compared with care as usual. Psychosom Med. 2008;70:875-82.

13. Hughes JR. Depression during tobacco abstinence. Nicotine Tobacco Res. 2007;9:443-6.

14. AAFP. AAFP guideline for the detection and management of post-myocardial infarction depression. Annals of family medicine. 2009;7:71-9.

15. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, Moher D, Becker BJ, Sipe TA, Thacker SB. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA. 2000;283:2008-12.

16. Ades PA, Waldmann ML, McCann WJ, Weaver SO. Predictors of cardiac rehabilitation participation in older coronary patients. Arch Intern Med. 1992;152:1033-5.

17. Clark AM, King-Shier KM, Duncan A, Spaling M, Stone JA, Jaglal S, Angus J. Factors influencing referral to cardiac rehabilitation and secondary prevention programs: a systematic review. Eur J Prev Cardiol. 2013;20:692-700.

18. Clark AM, King-Shier KM, Spaling MA, Duncan AS, Stone JA, Jaglal SB, Thompson DR, Angus JE. Factors influencing participation in cardiac rehabilitation programmes after referral and initial attendance: qualitative systematic review and meta-synthesis. Clin Rehabil. 2013;27:948-59.

19. Crowe M, Sheppard L. A general critical appraisal tool: an evaluation of construct validity. Int J Nurs Stud. 2011;48:1505-16.

20. Crowe M, Sheppard L, Campbell A. Comparison of the effects of using the Crowe Critical Appraisal Tool versus informal appraisal in assessing health research: a randomised trial. Int J Evidence-Based Health. 2011;9:444-9.

21. Crowe M, Sheppard L, Campbell A. Reliability analysis for a proposed critical appraisal tool demonstrated value for diverse research designs. J Clin Epidemiol. 2012;65:375-83.

22. Kontopantelis E, Reeves D. METAEFF: Stata module to perform effect sizes calculations for meta-analyses. 24 March 2011 ed2009. http://econpapers.repec.org/software/bocbocode/s457072.htm.

23. Sterne JAC. Meta-Analysis in Stata: An Updated Collection from the Stata Journal. College Station, TX: Stata Press; 2009.

24. Tak LM, Meijer A, Manoharan A, de Jonge P, Rosmalen JG. More than the sum of its parts: meta-analysis and its potential to discover sources of heterogeneity in psychosomatic medicine. Psychosom Med. 2010;72:253-65.

25. Attebring MF, Hartford M, Hjalmarson A, Caidahl K, Karlsson T, Herlitz J. Smoking habits and predictors of continued smoking in patients with acute coronary syndromes. J Adv Nurs. 2004;46:614-23.

26. Berndt N, Bolman C, Mudde A, Verheugt F, de Vries H, Lechner L. Risk groups and predictors of short-term abstinence from smoking in patients with coronary heart disease. Heart Lung. 2012;41:332-43.

27. Berndt N, Hayes AF, Verboon P, Lechner L, Bolman C, de Vries H. Self-efficacy mediates the impact of craving on smoking abstinence in low to moderately anxious patients: results of a moderated mediation approach. Psychol Addict Behav. 2012;27:113-24.

28. Brummett BH, Babyak MA, Mark DC, Williams RB, Siegler IC, Clapp-Channing N, Barefoot JC. Predictors of smoking cessation in patients with a diagnosis of coronary artery disease. J Cardiopulm Rehabil. 2002;22:143-7.

29. Dawood N, Vaccarino V, Reid KJ, Spertus JA, Hamid N, Parashar S. Predictors of smoking cessation after a myocardial infarction: the role of institutional smoking cessation programs in improving success. Arch Intern Med. 2008;168:1961-7.

30. Gravely-Witte S, Stewart DE, Suskin N, Grace SL. The association among depressive symptoms, smoking status and antidepressant use in cardiac outpatients. J Beh Med. 2009;32:478-90.

31. Holtrop JS, Stommel M, Corser W, Holmes-Rovner M. Predictors of smoking cessation and relapse after hospitalization for acute coronary syndrome. J Hosp Med. 2009;4:E3-9.

32. Huijbrechts IP, Duivenvoorden HJ, Deckers JW, Leenders IC, Pop GA, Passchier J, Erdman RA. Modification of smoking habits five months after myocardial infarction: relationship with personality characteristics. J Psychosom Res. 1996;40:369-78.

33. Jones DA, West RR. Psychological rehabilitation after myocardial infarction: multicentre randomised controlled trial. BMJ. 1996;313:1517-21.

34. Kronish IM, Rieckmann N, Halm EA, Shimbo D, Vorchheimer D, Haas DC, Davidson KW. Persistent depression affects adherence to secondary prevention behaviors after acute coronary syndromes. J Gen Intern Med. 2006;21:1178-83.

35. Ladwig KH, Roll G, Breithardt G, Budde T, Borggrefe M. Post-infarction depression and incomplete recovery 6 months after acute myocardial infarction. Lancet. 1994;343:20-3.

36. Mayou RA, Gill D, Thompson DR, Day A, Hicks N, Volmink J, Neil A. Depression and anxiety as predictors of outcome after myocardial infarction. Psychosom Med. 2000;62:212-9.

37. McGee HM, Doyle F, Conroy RM, De La Harpe D, Shelley E. Impact of briefly-assessed depression on secondary prevention outcomes after acute coronary syndrome: a one-year longitudinal survey. BMC Health Serv Res. 2006;6:9.

38. Gerber Y, Koren-Morag N, Myers V, Benyamini Y, Goldbourt U, Drory Y. Long-term predictors of smoking cessation in a cohort of myocardial infarction survivors: a longitudinal study. Eur J Cardiovasc Prevention Rehab. 2011;18:533-41.

39. Myers V, Gerber Y, Benyamini Y, Goldbourt U, Drory Y. Post-myocardial infarction depression: increased hospital admissions and reduced adoption of secondary prevention measures--a longitudinal study. J Psychosom Res. 2012;72:5-10.

40. Pedersen SS, Deckers JW, van Os F, Erdman RAM. A multifactorial smoking cessation programme for patients with coronary artery disease: experiences and preliminary results. Neth Heart J. 2002;10:48-53.

41. Perez GH, Nicolau JC, Romano BW, Laranjeira R. Depression: a predictor of smoking relapse in a 6-month follow-up after hospitalization for acute coronary syndrome. Eur J Cardiovasc Prev Rehabil. 2008;15:89-94.

42. Taylor D, Barber K, McIntosh B, Khan M. The impact of post acute myocardial infarction (AMI) depression on patient compliance and risk factor modification. Psychol Health Med. 1998;3:439-42.

43. Ziegelstein RC, Fauerbach JA, Stevens SS, Romanelli J, Richter DP, Bush DE. Patients with depression are less likely to follow recommendations to reduce cardiac risk during recovery from a myocardial infarction. Arch Int Med. 2000;160:1818-23.

44. Romanelli J, Fauerbach JA, Bush DE, Ziegelstein RC. The significance of depression in older patients after myocardial infarction. J Am Geriatric Soc. 2002;50:817-22.

45. Fogel J, Fauerbach JA, Ziegelstein RC, Bush DE. Quality of life in physical health domains predicts adherence among myocardial infarction patients even after adjusting for depressive symptoms. J Psychosom Res. 2004;56:75-82.

46. Kuhl EA, Fauerbach JA, Bush DE, Ziegelstein RC. Relation of Anxiety and Adherence to Risk-Reducing Recommendations Following Myocardial Infarction. Am J Cardiol 2009 103(12):1629-34.

47. Brummett BH, Babyak MA, Siegler IC, Mark DB, Williams RB, Barefoot JC. Effect of smoking and sedentary behavior on the association between depressive symptoms and mortality from coronary heart disease. Am J Cardiol. 2003;92:529-32.

48. Stafford L, Jackson HJ, Berk M. Illness beliefs about heart disease and adherence to secondary prevention regimens. Psychosom Med. 2008;70:942-8.

49. Ramaekers BL, Janssen-Boyne JJ, Gorgels AP, Vrijhoef HJ. Adherence among telemonitored patients with heart failure to pharmacological and nonpharmacological recommendations. Telemedicine and e-Health. 2009;Vol.15:pp.

50. Nikolic G, Samardzic L, Jovanovic T. Changes in psychological parameters and health behavior of coronary and non-coronary patients following hospitalization - a six month follow-up.Acta Medica Medianae. 2012;51:12-9.

51. The ENRICHD Investigators. Effects of treating depression and low perceived social support on clinical events after myocardial infarction: the Enhancing Recovery in Coronary Heart Disease Patients (ENRICHD) Randomized Trial. JAMA. 2003;289:3106-16.

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

53. Katrak P, Bialocerkowski AE, Massy-Westropp N, Kumar S, Grimmer KA. A systematic review of the content of critical appraisal tools. BMC Med Res Method. 2004;4:22.

54. Moja LP, Telaro E, D'Amico R, Moschetti I, Coe L, Liberati A. Assessment of methodological quality of primary studies by systematic reviews: results of the metaquality cross sectional study. BMJ. 2005;330:1053.

55. Patrick DL, Cheadle A, Thompson DC, Diehr P, Koepsell T, Kinne S. The validity of self-reported smoking: a review and meta-analysis. Am J Public Health 1994;84:1086-93.

56. Doyle F, Conroy R, McGee H. Differential Predictive Value of Depressive Versus Anxiety Symptoms in the Prediction of 8-Year Mortality After Acute Coronary Syndrome. Psychosom Med. 2012;74:711-6.

57. Doyle F, Conroy R, McGee H. Challenges in reducing depression-related mortality in cardiac populations: cognition, emotion, fatigue or personality? Health Psychol Rev. 2007;1:137-72.

58. West R, Hajek P, Stead L, Stapleton J. Outcome criteria in smoking cessation trials: proposal for a common standard. Addiction. 2005;100:299-303.

59. Patton GC, Carlin JB, Coffey C, Wolfe R, Hibbert M, Bowes G. Depression, anxiety, and smoking initiation: a prospective study over 3 years. Am J Public Health. 1998;88:1518-22.

60. Mohiuddin SM, Mooss AN, Hunter CB, Grollmes TL, Cloutier DA, Hilleman DE. Intensive smoking cessation intervention reduces mortality in high-risk smokers with cardiovascular disease. Chest. 2007;131:446-52.

61. Bartels C, Abuhaliga AR, McGee H, Morgan K, McElvaney NG, Doyle F. A survey of the prevalence of smoking and smoking cessation advice received by inpatients in a large teaching hospital in Ireland. Ir J Med Sci. 2012;181:445-9.

62. Reid RD, Mullen KA, Slovinec D'Angelo ME, Aitken DA, Papadakis S, Haley PM, McLaughlin CA, Pipe AL. Smoking cessation for hospitalized smokers: an evaluation of the "Ottawa Model". Nicotine Tobacco Res. 2010;12:11-8.

63. Freedland KE, Carney RM. Depression as a risk factor for adverse outcomes in coronary heart disease. BMC Med. 2013;11:131.

64. Meijer A, Zuidersma M, Jonge P. Depression as a non-causal variable risk marker in coronary heart disease. BMC Med. 2013;11:130.

65. Skala JA, Freedland KE, Carney RM. Coronary heart disease and depression: a review of recent mechanistic research. Can J Psychiat. 2006;51:738-45.

Table 1: Prospective studies reporting an association between baseline depression and subsequent smoking

Author, Country	**Study design**	**Sample, % Men**	**Sample size: baseline, follow-up**	**Longest** (mean/ median) **follow-up duration**	**Depression measures (measured at follow-up Yes/No)**	**Smoking Outcome measure**	**Results**	**Adjusted or unadjusted**	**Quality score**	**Comments**
Attebring et al. (25), Sweden	**Obs**	ACS, 72%	434, 348	3 months	Sedatives or antidepressants at time of admission (No)	Self-report. Current smokers classified as at least one cigarette/pipe/ cigar per day at time of admission or within month prior to admission Ex-smokers had stopped at least one month prior to admission	Smokers taking antidepressants or sedatives less likely to quit (OR=8.4, 95% CI 2.36-30)	Adjusted for history of cerebrovascular disease, history of cardiac event, cigarette consumption, history of smoking-related pulmonary disease, participation in Cardiac rehabilitation	62.5%	**The classification of depression using both sedatives and antidepressants may have significantly broadened the depression category, and contributed to a higher effect size.** Associations for other outcomes unavailable. Unadjusted estimates used in meta-analysis. Effect size far exceeds other research findings, even in adjusted analysis. This study is a significant source of heterogeneity in the meta-analysis.
Berndt et al., (a) (26), The Netherlands	**Obs**	**Chronic or acute** CHD, 65%	133, 108	1 month	HADS (No)	Self-report plus nurse reports of patients' smoking	Association for depressed v non-depressed or quitters v non-quitters not reported. High risk cluster 1 identified from cognitive variables (pros and cons of non-smoking, self-efficacy etc.), which had highest depression score (mean (SD) 5.77 (3.99) compared to 4.19 (2.97) for cluster 1 and 4.21 (3.59) for cluster 2). Continued abstinence at 1 month was lower among cluster 3 patients (36.1% compared to 68.3% for cluster 1 and 65.2% for cluster 2).	Unadjusted	57.5%	Did not measure disease diagnosis severity. Cluster 3 included cardiac patients with a high risk to resume smoking after discharge. Patients in this cluster were characterised by a history of cardiac disease, high addiction levels, high scores for depression, and low intentions toward non-smoking. Data for meta-analysis obtained via email, predicting continued abstinence
Berndt et al. (b) (27), The Netherlands	**Obs**	**Chronic or acute** cardiac patients	168, 168	6 months	HADS (No)	Self-report	Significant negative correlation between HADS	Unadjusted correlation. Later adjusted for nicotine	70.0%	Unadjusted results provided on email. This is an independent sample from the above Berndt study. **Most conservative adjusted results**

		(majority ACS), 78%					depression score and 7-day smoking abstinence at 6 months (r=-.21, p<.01)	dependence, craving, study hospital, total HADS score, depression and anxiety		**reported that depression accounted for 0.2% of variance in abstinence.**
Brummett et al. (28), United States	**Obs**	CAD, 72%	525, 505	Up to 6 years**, mean 25.5 months**	"How depressed or cheerful have you been during the past month?" (Likert 0-10) (No)	Self-report Classified as smokers if reported at least one cigarette/day for the past 6 weeks	40% of full sample quit without relapse. Those depressed (scoring 1 standard deviation above mean) more likely to continue smoking (OR=1.6, 95% CI 1.12-2.27)	Adjusted for socio-demographic characteristics, disease severity variables, and psychological variables (hostility, concern about health, tension, depression, lack of energy)	45.0%	Results represent an average OR from repeated measures of different follow-up times. Unclear how many completed depression measure. Assumed to be total sample (n=525) for estimation of effect size. Authors unable to provide original data.
Dawood et al. (29), United States	**Obs**	MI, 67%	834, 639	6 months	PHQ-9 (>9 as depressed) (Unclear: not included in analysis)	Self-report Classified as smokers if one puff in past 30 days	Those depressed during hospitalisation were less likely to quit than non-depressed (18% v 31%; OR adjusted, 0.57, 95% CI, 0.36-0.90)	Adjusted for socio-demographic variables, medical history variables (e.g. substance use, diabetes, lung disease etc.), procedures and clinical status on admission, psychosocial variables (depression and social support), referral to CR, smoking cessation counselling, availability of smoking cessation programme at admitting hospital, enrolment site	67.5%	Importantly, association survives adjustment for several potential confounders. Even though adjusted for systematic cessation programmes, depression still predictor of continuation. Referral to cardiac rehabilitation and having a systematic cessation programme on site predicted cessation when adjusting for depression.
Gravely-Witte et al. (30), Canada	**Obs**	CAD **outpatients**, 71%	1498, 1276	9 months	Anti-depressant prescription, BDI-II (Yes)	Self-report. Current smokers – smoking at baseline survey Former smokers had quit prior to first assessment	BDI-II at baseline was associated with smoking status (p<0.01), but not change in smoking status at 9-months. Smokers on antidepressants (n=127) less likely	Adjusted for demographic and clinical differences including age, sex, co morbid conditions, overweight/obesity, index MI, work status,	67.5%	BDI-II results obtained via email.

							to quit at follow-up than those not on antidepressants (3 v 18%, p=0.03)	marital status, education and dyslipidemia		
Holtrop et al. (31), United States	**RCT**	ACS, 61%	166, 136	3 and 8 months	Self-report history of depression, CES-D (Unclear – not reported or included in analysis)	Self-report. Classified as smokers if smoking at hospitalisation All others classified as non-smokers	History of depression associated with increased risk of relapse when compared to successful quitters (OR=6.38, 95% CI 2.3–17.3), or those who continued to smoke (OR=2.7, 95% CI 1.02–7.5), but not likelihood of quitting (OR=0.42, 0.16–1.4)	Adjusted for socio-demographic characteristics, co morbidity, intensity of smoking, presence of other smokers in household, intervention group (receiving health behaviour intervention programme, or control)	62.5%	Analyses data from total recruited sample before subsample randomised to controlled trial. Trial arm not a significant predictor of smoking status. Current depression not a predictor of cessation, but data not reported and authors did not respond to email. Unadjusted results used to estimate effect size. **In adjusted results most conservative finding used (likelihood of quitting).**
Huijbrechts et al. (32), The Netherlands	**Obs**	**First** MI, 71%	164, 164	5 months	HADS (Yes)	Self-report	Persistent smokers had higher baseline depressive symptoms than ex-smokers or non-smokers ($p<0.05$) Results estimated from figure	Unadjusted	45.0%	Results difficult to interpret, but appear to be consistent across three mood scales. Used HADS data for effect estimation as it is the only established depression scale.
Jones & West (33), United Kingdom	**RCT**	MI, % men not reported	1128, 568	6 months	DSSI/sAD	Self-report	47% of depressed v 41% of non-depressed smoking at follow-up	Unadjusted	65.0%	Results obtained on email. High dropout rate at follow-up. Sample size refers to smokers only.
Kronish et al. (34), United States	**Obs**	ACS, 59%	560, 492	3 months	BDI (<5 compared to >9, scores of 5-9 omitted) (Yes)	Self-report Classified as smokers if smoked in the last 7 days	Persistent depression was positively associated with smoking continuation.	Adjusted for socio-demographic variables, co morbidity	62.5%	Persistent depression better predictor of outcomes than remitted depression in analyses. Results may be overestimate since those with intermediate levels of depressive symptoms omitted. Results to estimate effect size obtained via email.
Ladwig et al. (35), Germany	**Obs**	MI, 100%	552, 377	6 months	Unclear, but instruments stated to be previously validated. (No)	Self-report	Relative risk for maintenance of smoking habits in depressed compared to non-depressed was 2.63 (95% CI 1.23 to 5.60).	Adjusted for age, social status (blue/white collar), recurrent infarction before baseline, in-hospital rehabilitation, non-fatal cardiac events after index infarction, helplessness,	50.0%	Relative risk was used as an odds-ratio estimate as base rates unavailable and author did not respond to email. This may overestimate effect.

							Multivariate analysis: relapse predicted by major depression (46.3% v 28.9%; OR=2.55, 95% CI 1.52–4.23)	Adjusted for Socio-demographic characteristics, living status, stages of change, cardiac history, cardiac diagnosis, medication use (anxiolytic, anti-depressant), duration of hospitalisation, age of smoking onset, number of quit attempts		
Perez et al. (41), Brazil	**Obs**	ACS, % men not reported	628, 403	6 months	PRIME-MD, BDI (Yes)	Self-report	Depression predicted continued smoking (41% of distressed smokers v 10% of non-distressed at 3-months). at 1 year, the figures were 47% of distressed and 29% of nondistressed (p=0.003)		50.0%	Association also survived multivariate adjustment. Anxiolytic use also predicted relapse. Non-adjusted data used for meta-analysis (rather than adjusted estimates reported (and used in the meta-analysis), as the authors state that the patterns were similar for both HADS anxiety and depression scales. No response to email to obtain depression-specific data.
Mayou et al. (36), United Kingdom	**Obs**	MI, 73%	344, 224	1 year	HADS (HADS-D>10, or summed HADS-A and HADS-D>19) (Yes)	Self-report	Elevated BDI (Mean (SD) BDI: 15.3 (8.3) v 12.84 (7.96); p=0.003)	Unadjusted	65.0%	**Only distressed quitters reported.**
										Unclear if this is cross-sectional or prospective association. Treated as
Taylor et al. (42), United States	**Obs**	MI, 70%	245, 245	3 months	CES-D (Yes)	Self-report	Depression associated with smoking (mean 7.87 vs 5.41, p=0.001).	Unadjusted	40.0%	prospective as this was stated aim of paper. Limited data available. Standard error imputed for median value as base rates unavailable and no response from email request.
McGee et al. (37), Thomas et al. (11), United States	**Obs** **RCT**	ACS, 78% CVD, 71%	598, 447 245, 244	1 year 12 months	HADS-D (>7 as depressed), BDI-FS (>3 as depressed) BDI >15 depressed) (No) (Yes)	Self-report, expired carbon monoxide, saliva cotinine concentration	Depressed smokers more likely to smoke at 4 weeks after discharge (p=.007; incidence rate ratio, 2.40; 95% CI, 1.48–3.78) and 1 year (OR= 1.6, 95% CI=1.1–4.3), but BDI-FS scores did not predict smoking at follow-up for either	Adjusted for site of treatment	82.5% 75.0%	Only study to use objective measure of smoking cessation. Pre-planned post-hoc analysis of randomised trial. Trend for those depressed smokers treated with bupropion SR to be more likely to quit (p=.07), but small sample size. This study contained two independent samples so separate estimates used for HADS and BDI-FS groups.
Ziegelstein et al. (43), Ziegelstein et al. (44), Ziegelstein et al. (38), United States	**Obs** **Obs**	MI, 57% MI, 86%	276, 204 632, ?	13 years 4 (**mean 12.33 ±2.75)**	SCID DSM-III-R, BDI (>5) (No)	**Self-report** Classified as MOSSAS smoker or never smoker	Depressed less likely to stop smoking (MOSSAS score 3.75, CI 0.50-0.94 (2.0)) or BDI groups (Mean (SD) MOSSAS score 2.9 (1.7)] v 3.3 (1.8)] who	Adjusted for age and sex and other various factors depending on model reported	70.0% 60.0%	Raw data received on email to calculate unadjusted effect size. Multiple papers from dataset. Depression not significant in several models, and only becomes significant in adjusted model. Sense of coherence a consistent predictor of cessation. **Adjusted results represent 1-SD increase in depression.**
Pederson et al. (40), The Netherlands	**Obs**	CAD **outpatients**, 61%	28, 20	3 months	HADS (No)	Self-report	Patients who successfully quit scored lower on depression [mean (SD): 5 (3)] than those who continued smoking [mean (SD): 8 (5), p=.10]	Unadjusted	52.5%	Pilot programme with small sample. No report of larger dataset found.

Table 2: Sensitivity analyses

Sensitivity analysis	SMD	95% CI	I^2	p-value
Diagnostic interviews	-.37	-.57 to -.17	0%	.93
Validated depression scales	-.33	-.42 to -.24	20.8%	.21
Antidepressants	-.94	-1.38 to -.51	57.7%	.12
<1 year follow-up	-.43	-.58 to -.28	61.6%	.001
≥1 year follow-up	-.35	-.5 to -.2	1.8%	.40
CCAT≥60%	-.37	-.52 to -.22	61.4%	.002
CCAT<60%	-.41	-.54 to -.28	11.4%	.34
Observational studies	-.40	-.51 to -.28	43.3%	.030
Randomised Trials	-.39	-.74 to -.03	78.7%	.009
Adjusted estimates	-.35	-.47 to -.22	50.9%	.021
Unadjusted estimates	-.37	-.57 to -.17	44.7%	.081

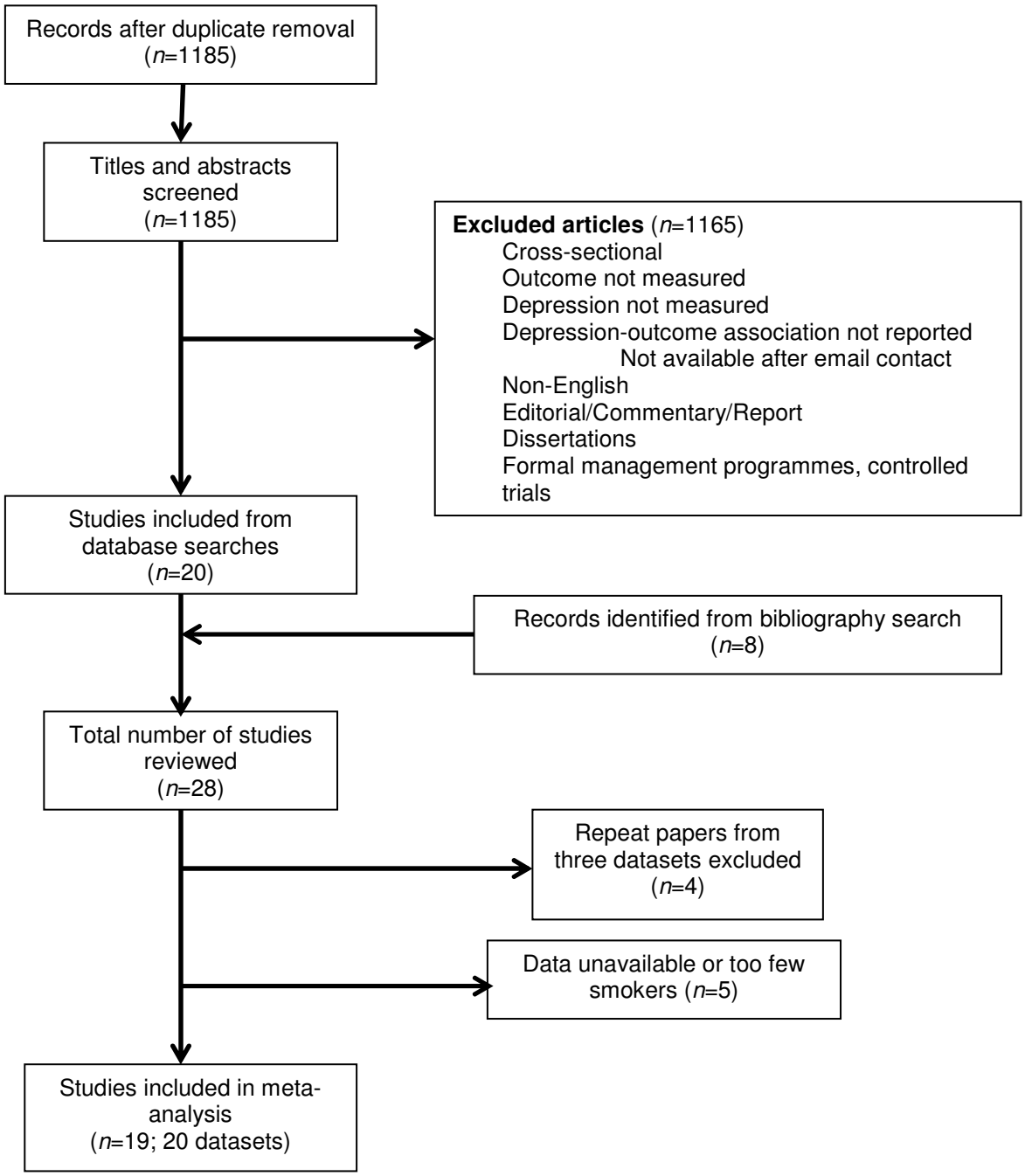

Figure 1: Flowchart of selected articles

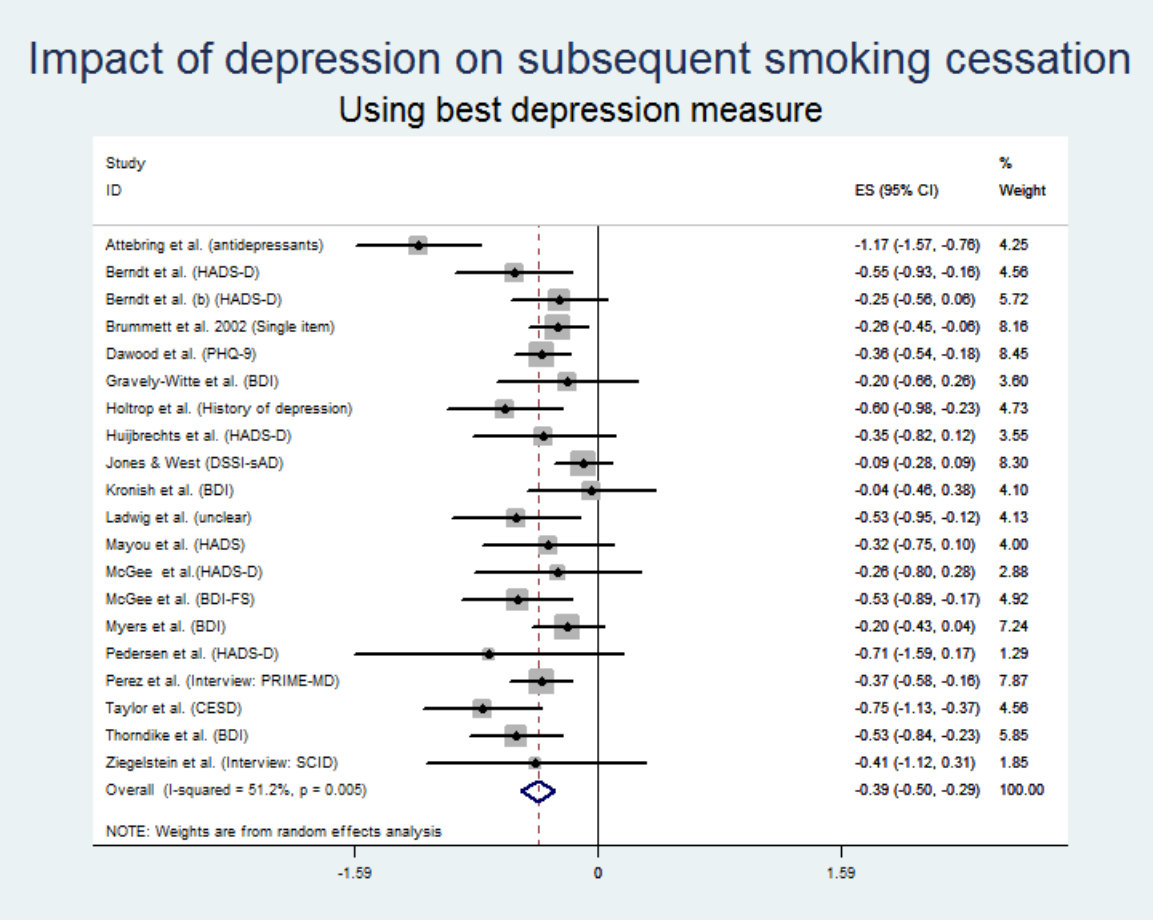

Fig 2. Forest plot of the impact of depression on subsequent smoking cessation