RESEARCH

Change in mental health after smoking cessation: systematic review and meta-analysis

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Abstract

Objective To investigate change in mental health after smoking cessation compared with continuing to smoke.

Design Systematic review and meta-analysis of observational studies.

Data sources Web of Science, Cochrane Central Register of Controlled Trials, Medline, Embase, and PsycINFO for relevant studies from inception to April 2012. Reference lists of included studies were hand searched, and authors were contacted when insufficient data were reported.

Eligibility criteria for selecting studies Longitudinal studies of adults that assessed mental health before smoking cessation and at least six weeks after cessation or baseline in healthy and clinical populations.

Results 26 studies that assessed mental health with questionnaires designed to measure anxiety, depression, mixed anxiety and depression, psychological quality of life, positive affect, and stress were included. Follow-up mental health scores were measured between seven weeks and nine years after baseline. Anxiety, depression, mixed anxiety and depression, and stress significantly decreased between baseline and follow-up in quitters compared with continuing smokers: the standardised mean differences (95% confidence intervals) were anxiety −0.37 (95% confidence interval −0.70 to −0.03); depression −0.25 (−0.37 to −0.12); mixed anxiety and depression −0.31 (−0.47 to −0.14); stress −0.27 (−0.40 to −0.13). Both psychological quality of life and positive affect significantly increased between baseline and follow-up in quitters compared with continuing smokers 0.22 (0.09 to 0.36) and 0.40 (0.09 to 0.71), respectively). There was no evidence that the effect size differed between the general population and populations with physical or psychiatric disorders.

Conclusions Smoking cessation is associated with reduced depression, anxiety, and stress and improved positive mood and quality of life compared with continuing to smoke. The effect size seems as large for those with psychiatric disorders as those without. The effect sizes are equal or larger than those of antidepressant treatment for mood and anxiety disorders.

Introduction

Tobacco is the leading global cause of preventable death, estimated to cause more than five million deaths a year, and this is predicted to rise.[1] The worldwide cost of healthcare from tobacco use has been estimated within the billion dollar range.[2] Smoking is a major risk factor for the development of cancers and cardiovascular and respiratory diseases[3]; stopping smoking substantially reduces these health risks.[4 5] The association between smoking and mental health, however, is less clear cut. Although most smokers report wanting to quit,[6] many continue as they report that smoking provides them with mental health benefits. Both quantitative and qualitative analyses indicate that regular smokers report smoking cigarettes to alleviate emotional problems and feelings of depression and anxiety, to stabilise mood, and for relaxation as well as relieving stress.[7-13] This pattern of behaviour occurs in smokers with and without diagnosed mental disorders.[9-13] Unsurprisingly, views about smoking predict whether or not people attempt to quit[14] and whether or not they are successful.[15]

Although smokers think that smoking offers mental health benefits, there is a strong association between smoking and poor mental health, and smokers with mental health disorders tend

to be heavier smokers and more dependent.[16 17] Three broad explanations have been proposed to explain these associations: smoking and poor mental health might have common causes[18]; people with poor mental health smoke to regulate feelings such as low mood and anxiety[19]; or smoking might cause or exacerbate mental health problems.[20] Although smokers with and without mental disorders think that smoking provides mental health benefits, they might be misattributing the ability of cigarettes to abolish nicotine withdrawal as a beneficial effect on mental health. Smokers experience irritability, anxiety, and depression when they have not smoked for a while,[21 22] and these feelings are reliably relieved by smoking[20] thus creating the perception that smoking has psychological benefits, while in fact it is smoking that caused these psychological disturbances in the first place.

Whatever the cause, the association between smoking and poor mental health warrants attention. Smokers might be less likely to stop if they believe their mental health will suffer, and health professionals might be reluctant to intervene with some smokers because they believe that this might be detrimental to their mental health.[23 24] As a result, people with mental health disorders have a life expectancy eight years less than the general population,[25] and much of this difference could be because of smoking.[17] For these reasons, we conducted a systematic review and meta-analysis of observational data to examine the difference in change in mental health between people who stop smoking and people who continue to smoke. Our hypothesis was that smokers who gave up would experience an improvement in mental health as a result because they would no longer experience multiple episodes of negative affect induced by withdrawal.

Methods

This study followed PRISMA[26] and MOOSE reporting guidelines.[27] There was no previously published protocol.

Eligibility criteria

We used broad eligibility criteria to capture all potentially relevant data and then used sensitivity and subgroup analyses to investigate clinical and methodological heterogeneity. Eligibility was decided on based on the following criteria:

- Population—studies of smokers in the general population or any that had selected smokers from populations defined by the presence of a clinical diagnosis

- Exposure—studies that reported data on those who had continued smoking and those who had quit smoking during the study period

- Outcome—any study that had measured mental health immediately before quitting and at least six weeks after quitting.

- Language—no exclusions were made based on language

- Study design— only longitudinal studies (that is, randomised controlled trials and cohort studies).

When data on change in mental health were available from different follow-ups within a single study we took the longest. Any type of measure of mental health was included (such as self report and clinician scored). We included studies that provided sufficient data to calculate the standardised mean difference (SMD) and its variance in change in mental health score from baseline to follow-up between quitters and continuing smokers. The standardised mean difference is the difference in change in mental health between baseline and follow-up divided

by the standard deviation (SD) of the change. It is used to overcome the issue that depression, for example, can be measured by different questionnaires with different scoring systems. The questionnaires all measure depression but the different scoring means that they cannot be combined by using a simple mean. An SMD of 1 represents a difference in change in depression score of 1 SD. About 4 SD encompasses 95% of the population.[28]

Information sources and searches

We used searched Web of Science, Cochrane Central Register of Controlled Trials, Medline, Embase, and PsycINFO for studies published from inception to April 2012. We contacted study authors to obtain relevant missing data. We also searched reference lists of included studies. All non-English language studies were translated.

We used a combination of text words and indexed terms related to "mental health," "smoking cessation," and "smoking reduction" (see appendix 1).

Study selection

Our aim was to maximise sensitivity by including studies in initial screens even if data directly relevant to our question were not presented in the abstract. One researcher screened titles of retrieved studies for eligibility. The abstracts of eligible titles were screened twice for inclusion. The researchers met after independently screening abstracts to discuss inclusion/exclusion of each article. If there were disagreements, two researchers obtained and read the full text article.

Data collection process

Two researchers piloted the data extraction form, and appropriate changes were then made. The same two researchers independently extracted data from each paper and agreed on final data extraction in the case of disagreement. The corresponding authors of studies were contacted for additional data when necessary. Studies were excluded only if we could not obtain data on the change in mental health and its variance.

Data items

Participants—We recorded tobacco dependence and number of cigarettes smoked a day, age, sex, and motivation to quit, all at baseline.

Exposure—We extracted data on classification and bioverification of abstinence.

Comparator—The same data items were extracted for continuing smokers.

Outcomes—We extracted data on the change in mental health between baseline and follow-up. When such data were not available, we extracted data to calculate this (see statistical methods). To categorise the mental health outcomes we examined each measure's key reference and questionnaire to determine what it was designed to measure. We extracted the change in mental health unadjusted for confounding and adjusted for confounding using multivariable techniques.

Other items—We also extracted additional data to investigate clinical and methodological heterogeneity within and across studies (see sensitivity analyses for justification and methods). These items included study design, study quality score (Newcastle-Ottawa scale[29]), evidence of outcome reporting bias, follow-up length, covariates adjusted for, mental health management used in the intervention, and number of participants analysed at baseline and follow-up.

Statistical methods

Data extraction

The summary measure was the standardised mean difference (SMD) in change in mental health from baseline to follow-up between continuing smokers and people who managed to stop. Some studies reported either the difference in change or the standardised difference in change between continuing smokers and quitters, and hence data extraction of the effect estimate was straightforward. In some cases, studies presented the mean change for each group and we calculated the differences. In other cases, studies reported the mean at baseline and at follow-up for each group. We calculated change and its variance using a standard formula,[30] imputing a correlation coefficient taken from one of the largest studies included in the review (see appendix 1). In all cases, we also extracted the variance. If the variance was not presented we calculated it from P values, confidence intervals, or F values following standard formula as recommended by the Cochrane Collaboration.[28]

Meta-analysis method

We used a generic inverse variance random effects model to pool the standardised mean difference (SMD) between change in mental health in quitters and continuing smokers, from baseline to follow-up. We chose a random effects model as it incorporates heterogeneity both within and between studies. Statistical heterogeneity was assessed with τ^2 and I^2 tests. We used RevMan5 to conduct the meta-analyses and sensitivity and subgroup analyses.

Studies' effect estimates (SMD) were pooled by using the following outcome categories: anxiety, depression, mixed anxiety and depression, positive affect, psychological quality of life, and stress. We used SMD because the scales used to measure each outcome varied within category. This is standard practice for meta-analyses as outlined within the Cochrane Collaboration Handbook of Systematic Reviews and Meta-Analyses,[28] and as used in other high quality meta-analyses of continuous mental health outcomes.[31-33]

We also combined studies with different follow-up periods. We combined each study's longest follow-up period, as suggested by the Cochrane Collaboration. Heterogeneity between studies' follow-up length was accounted for by use of a random effects model. This is standard practice as outlined by the Cochrane Collaboration,[28] and as used in other high-quality meta-analyses of continuous mental health, with varying follow-up periods.[31-33]

Quality assessment

We assessed the quality of the evidence in each study on the association of change in smoking status with change in mental health using the Newcastle-Ottawa quality scale,[29] adapted for this study (see appendix 1). This assesses the quality of evidence based on the selection of the comparison groups, the comparability of the groups, and the quality of the measurement of exposure and outcome. The adapted scale rated studies from 0 to 5, and we deemed studies with a rating of 3 or lower as at higher risk of bias.

Assessment of publication and outcome reporting bias

We examined funnel plots for evidence of asymmetry and conducted Egger tests for evidence of small study bias using Stata 13.[34]

In some studies, data on change in mental health were presented incidentally and the aim was to report on other data. In others, the aim of the report was to present data on change in mental health, therefore the decision to publish might have been contingent on the results. We compared effect estimates between studies in which mental health was the primary outcome and those in which it was not to assess if there was evidence of publication bias.

When studies had relevant data on change in mental health but did not report sufficient data for meta-analysis, we attempted to estimate the direction of association and compare this with those included as this could indicate reporting bias.

Sensitivity analyses and assessment of risk of bias within and across studies

We conducted multiple sensitivity analyses to examine if the pooled effect estimate was influenced by including studies in which the risk of bias was greater or was influenced by characteristics of the study design or population. We either performed subgroup analyses or removed studies presenting a risk of bias and compared the pooled estimates with and without the excluded studies.

Adjustment for covariates

It is possible that change in mental health could be confounded by other differences between continuing smokers and quitters. To account for this, some studies adjusted their data for covariates thought to be associated with change in smoking status. We conducted a subgroup analysis to compare the effect estimate between studies that presented adjusted and unadjusted data.

Loss to follow-up

Some studies reported on change in mental health only in participants who were followed up, thus eliminating from the analysis those who were lost-to-follow-up. Other studies reported data on all participants who were present at baseline and the smaller number present at follow up; thus possibly creating spurious changes in mental health through loss to follow-up. The convention in smoking cessation studies is to regard participants who are lost to follow-up as smokers, so loss to follow-up selectively affects the continuing smoker group. We recorded whether or not studies reported data from a different number of participants at baseline and follow-up.

Ascertainment of smoking status

Some studies might misclassify exposure by using point prevalence smoking abstinence. This could include participants who had been abstinent for only a week in the group we classed as having been abstinent for at least six weeks, though most smokers who are point prevalent abstinent for a week have in truth been abstinent for longer.[35 36] Recently abstinent smokers are likely to experience withdrawal symptoms including low mood.[16] Thus, we recorded whether studies used a measure of prolonged or continuous abstinence (when misclassification could not have occurred) or if they used a point prevalence measure of abstinence. Likewise, particularly in smoking cessation trials, there is a danger that participants claim abstinence when this is not the case; therefore it best practice to bioverify smoking status.[35] Accordingly, we recorded whether or not self reported abstinence was biologically verified.

Motivation to quit

Our hypothesis was that cessation improved mental health, but our outcome measure was the difference in change in mental

health between those who stopped smoking and those who continued. It could be that such a difference would be evident if those who continued smoking had a worsening in mental health rather than those who stopped experiencing an improvement. Trying and failing to quit could worsen mental health, and some studies in the review derived data from smoking cessation trials. In these trials, all continuing smokers had tried but failed to achieve abstinence, and this disappointment could lead to worse mental health. In population cohorts, however, many continuing smokers would not have tried to achieve abstinence and therefore not have experienced this failure. We therefore classified studies as selected or not selected by motivation to quit. Populations in which participants were not selected by motivation to quit were less likely to create this spurious difference between quitters and continuing smokers.

Psychotherapeutic component within cessation intervention

Having a psychotherapeutic intervention can improve mental health. Some smoking cessation interventions include mood management. Successful quitters often attend smoking cessation clinics, while relapsers cease attending, meaning that one group might have had more counselling than the other. We searched for the trial protocols and main report of the outcomes of all smoking cessation intervention trials in which counselling had taken place to assess whether mood management was part of this.

Additional analyses

Clinical population comparison

The studies included in the review enrolled the general population, pregnant women, or patients who were postoperative, had a chronic physical condition, a psychiatric condition, or chronic psychiatric or physical conditions. We examined whether there was evidence of a difference in effect size between these populations.

Study design

Our hypothesis was that stopping smoking improved mental health but any association between cessation and improved mood could be caused by reverse causation—that is, that improved mood caused successful cessation. The studies in this review fell into two groups: those recruiting a general population of smokers and those in which all participants were enrolled in smoking cessation trials. In trials, all participants attempted to quit and therefore the decision to quit was not contingent on mood. Secondary analyses from trials therefore exclude reverse causation.

Length of follow-up

We also examined whether there was evidence of a difference in effect estimate between studies in which change in mental health was assessed from six weeks to six months or more than six months after baseline.

Results

Study selection

The database and reference list searches resulted in 13 050 references. After initial screening we assessed 219 full text articles for eligibility, of which 166 were excluded before data extraction. Twenty seven were then excluded during data extraction (see tables B and C in appendix 1 for details), 15 of which provided sufficient descriptions to include in a narrative synthesis of the direction and/or significance of change in mental health. We included 26 studies in the meta-analyses and for six of these studies authors supplied additional data (fig 1⇓) (the full reference list is in appendix 1).

Outcome categories

The included studies examined six different measures of mental health: anxiety, depression, mixed anxiety and depression, positive affect, psychological quality of life, and stress (appendix 2).

Extraction

Several studies presented data on more than one outcome. Sixteen effect estimates were calculated from groups' mean mental health scores, which were reported at both baseline and follow-up. Seven were calculated from studies that presented each groups' mean change in mental health score from baseline to follow-up. Two were calculated from a non-standardised difference in change. Three were extracted from other types of effect estimates.

Study characteristics

Eleven of the studies were cohort studies, 14 were secondary analyses of cessation interventions, and one was a randomised trial. Study enrolment included the general population (14 studies), populations living with a chronic physical condition (three), pregnant women (two), postoperative patients (one), people with either a chronic physical and/or psychiatric condition (two), and people with psychiatric conditions (four). The median age was 44, and on average 48% were men. On average, participants smoked 20 cigarettes a day and scored 5.4 on the Fagerström test for nicotine dependence, indicating moderate dependence. The median length of follow up was six months (appendix 2 and 3).

In 11 studies, abstinence was measured as continuous abstinence from a point soon after baseline assessment, and in 18 studies abstinence was biologically verified. In seven studies participants received a psychological intervention as part of the cessation intervention. In 17 studies participants were motivated to quit (appendix 4).

Study quality

Twenty studies had high quality scores on the Newcastle-Ottawa scale, and five had medium to low scores; for one study there was insufficient information to determine a score (conference abstract).

Results of meta-analyses

Anxiety

Four studies reported change in anxiety from baseline to follow-up, with follow-ups ranging from seven weeks to 12 months (median six months). Compared with continuing to smoke, quitting smoking was associated with a significant decrease in anxiety from baseline to follow-up (standardised mean difference (SMD) −0.37, 95% confidence interval −0.70 to −0.03; P=0.03). There was substantial statistical heterogeneity between studies (I²=71%; fig 2⇓).[28]

Mixed anxiety and depression

Five studies reported change in mixed anxiety and depression from baseline to follow-up, with follow-up ranging from three months to six years (median six months). Compared with continuing to smoke, quitting smoking was associated with a significant decrease in mixed anxiety and depression from baseline to follow-up (SMD −0.31, 95% confidence interval −0.47 to −0.14; P<0.001; I^2=0%; fig 2⇓).

Depression

Ten studies reported change in depression from baseline to follow-up, with follow-up ranging from 11 weeks to five years (median 12 months). Compared with continuing to smoke, quitting smoking was associated with a significant decrease in depression from baseline to follow-up (SMD −0.25, 95% confidence interval −0.37 to −0.12; P<0.001; I^2=30%; fig 2⇓).

Stress

Three studies reported change in stress from baseline to follow-up, with follow-up ranging from six months to six years (median 12 months). Compared with continuing to smoke, quitting smoking was associated with a significant decrease in stress (SMD −0.27, 95% CI −0.40 to −0.13; P<0.001) from baseline to follow-up (I^2=0%; fig 2⇓).

Psychological quality of life

Eight studies reported change in psychological quality of life from baseline to follow-up, with follow-ups ranging from two months to nine years (median 12 months). Compared with continuing to smoke, quitting smoking was associated with a significant improvement in psychological quality of life from baseline to follow-up (SMD 0.22, 95% confidence interval 0.09 to 0.36; P<0.001). There was moderate statistical heterogeneity between studies (I^2=63%; fig 3⇓).[28]

Positive affect

Three studies reported change in positive affect from baseline to follow-up, with follow-ups ranging from three months to four years (median 12 months). Compared with continuing to smoke, quitting smoking was associated with a significant increase in positive affect from baseline to follow-up (SMD 0.40, 95% confidence interval 0.09 to 0.71; P=0.01; I^2=49%; fig 3⇓).

Sensitivity and subgroup analyses

We conducted numerous sensitivity and subgroup analyses to investigate clinical and methodological heterogeneity and to investigate risk of bias within and across studies.

Study quality

Removal of studies with medium to low scores on the Newcastle-Ottawa scale did not greatly change the summary estimates (table 1⇓).

Publication and outcome reporting bias

There were sufficient studies to create funnel plots for anxiety, depression, mixed anxiety and depression, and psychological quality of life. The plots were symmetrical for depression, anxiety, and mixed anxiety and depression and asymmetrical for psychological quality of life. Egger tests indicated that small studies measuring psychological quality of life provided larger effect estimates than studies with larger samples (P=0.017). Seven out of eight of the pooled studies, however, had sample

sizes ranging from 34 to 323. Thus, the result of the Egger test is likely influenced by the only large study (Sarna 2008, see appendix 1), which analysed data from 11 809 participants, and accounted for 25.7% of the pooled effect estimate. There was no evidence of small study bias for studies that measured anxiety (P=0.184), depression (P=0.064), mixed anxiety and depression (P=0.307), positive affect (P=0.179), or stress (P=0.705).

In 20 of the 26 studies, the main aim was to report on change in mental health and the decision to publish could have been contingent on the strength or significance of the finding (appendix 4). The main aim of the six other studies was to report on other outcomes, and they reported only psychological quality of life and positive affect. Subgroup analysis showed no evidence of a difference in effect between studies that did not primarily report on change in mental health and those that did so for psychological quality of life (P=0.19) and positive affect (P=0.14). One of the 26 studies showed evidence of multiple testing and selectively reported the only significant result (appendix 4).

Results of narrative synthesis

We excluded 15 studies because there were insufficient data to extract an effect size or its variance, despite contact with the authors (see table C in appendix 1). Nine of the 15 studies reported on the significance of the difference in change between quitters and continuing smokers (see table D in appendix 1): three reported no significant difference, five favoured quitters, and one study showed a difference favouring continuing smoking. Of the nine studies, seven reported that mental health improved in quitters, one showed no change, and one showed a worsening in mental health for quitters. Five of nine studies reported information on change in mental health for continuing smokers; three studies reported that mental health had worsened at follow-up and two reported that it had improved.

Adjustment for covariates

Two studies supplying estimates for three outcomes (anxiety, depression, and positive affect) provided effect sizes of the difference in change in mental health both unadjusted and adjusted for confounders. The confounders included demographics, information pertaining to tobacco consumption, and/or treatment allocation. Comparison of these estimates indicates that adjustment did not greatly change the results (table 2⇓).

We also compared the summary effect estimates from studies that supplied only unadjusted effect estimates with studies that supplied only adjusted effect estimates. Studies adjusted for several potential confounders. For anxiety one study adjusted for covariates, for depression four studies adjusted for covariates, for psychological quality of life five studies adjusted for covariates, for positive affect two studies adjusted for covariates, and for stress and mixed anxiety and depression no studies adjusted for covariates. The effect sizes were similar for studies that did and did not adjust for covariates for all outcomes except anxiety. Studies that adjusted for covariates showed a significantly bigger difference between quitters and smokers than those that did not adjust (table 3⇓).

Loss to follow-up

Twelve of the 26 studies reported means at baseline on a larger number than contributed to the mean at follow-up. Removal of these 12 did not greatly change the effect estimates (table 4⇓).

Ascertainment of smoking status

Eleven studies did not report continuous abstinence, classification of smoking status was not clear in four studies, and eight did not biochemically confirm abstinence; exclusion of these did not change the results (table 5⇓).

Motivation to quit

In a subgroup analysis we compared the 16 studies in which participants were all attempting to quit with the 10 studies in which participants were not selected by motivation to quit. There was no evidence of subgroup differences (table 6⇓, suggesting that deterioration in mental health as a reaction to failing to quit was an unlikely cause of the difference between quitters and continuing smokers.

Psychotherapeutic component within cessation intervention

Seven studies included a psychotherapeutic element in the cessation intervention to help participants manage symptoms of anxiety or low mood. Removal of these studies did not greatly change the summary estimate (table 7⇓).

Additional analyses

Comparison of clinical population

Fourteen studies enrolled smokers from the general population, four enrolled patients with psychiatric disorders, three enrolled patients with chronic physical conditions, two enrolled patients with either psychiatric or physical conditions, two enrolled pregnant women, and one enrolled patients after surgery. There was no evidence that the effect size differed across these different clinical populations (table 8⇓).

We were especially interested in the population with psychiatric disorders, and data were available on change in depression, mixed anxiety and depression, and positive affect. The effect estimates for this subgroup compared with the general population were −0.39 (95% confidence interval −0.63 to −0.14) versus −0.30 (−0.48 to −0.12) for depression; −0.21 (−1.07 to 0.65) versus −0.32 (−0.53 to −0.11) for mixed anxiety and depression; 0.40 (−0.03 to 0.83) versus 0.15 (−0.01 to 0.30) for psychological quality of life; and 0.68 (0.24 to 1.12) versus 0.16 (−0.14 to 0.46) for positive affect.

Study design

Eleven studies were cohort studies, 14 were secondary analyses of cessation interventions, and one was a randomised trial. There was no evidence of subgroup differences between these study designs (table 9⇓).

Length of follow-up

The effect sizes were similar for studies that assessed mental health between six weeks and six months and those with follow-ups longer than six months (table 10⇓). We also ordered studies according to follow-up length in forest plots (figures 2 and 3[2]⇓), which indicated no clear chronological pattern in effect estimates.

Discussion

There is consistent evidence that stopping smoking is associated with improvements in depression, anxiety, stress, psychological quality of life, and positive affect compared with continuing to smoke. The strength of association is similar for both the general population and clinical populations, including those with mental health disorders. There is no evidence that methodological heterogeneity or short comings explained these associations nor is there substantial evidence of publication bias.

Strength of the study

The strengths of this study lay in the broad search terms that we used to retrieve literature, including hand searching to avoid missing available literature and also checking reference lists of included studies. We also contacted authors and calculated data from papers in which, in most cases, the data were not provided in a directly usable form.

In most included studies, the quality of measurement of exposure status—smoking—was adequate. Nearly half of the studies reported prolonged or continuous abstinence that was biologically verified; this removed the threat of misclassification of exposure. Sensitivity analysis showed no evidence that studies that assessed smoking in other ways could have altered the results. Inclusion of such studies would, in general, underestimate the true strength of the association. Likewise, assessment of outcome was good, with participants completing validated self reported mental health questionnaires before they stopped smoking and at follow-up. Assessors were, in that sense, blind to exposure status, and no study was set up primarily to investigate change in mental health on cessation.

Confounding is usually a major threat to the validity of most associations based on observational data. In this case, there was limited scope for confounding because we compared change within individuals between groups. Confounders associated with mental health at baseline and at follow-up will not affect the validity of association. Confounding will occur only if the strength or direction of association changes between baseline and follow-up and that change differs by exposure group (quitters and continuing smokers). The latter case is not so plausible. In support of this, adjustment for potential confounders, which were mostly factors associated with propensity to achieve cessation, had only small effects in the studies that reported such data. We consider that the data within each study are robust and the association is unlikely to arise through bias or confounding.

The validity of the review rests on whether the search retrieved appropriate literature. We aimed to retrieve a large number of cohort studies that might have contained data, even when this was not readily apparent. Doing so, we uncovered several studies that would have been missed if we had confined the search to studies that seemed to be about smoking cessation and mental health. In all cases, the data were derived from secondary analyses of studies investigating other hypotheses (for example, secondary analyses of cessation interventions, population cohorts). It could be that authors of similar studies analysed the data in the same way but found no association so might have chosen not to publish the data. We found one example when a study reported quantitative data only for the significant (and presumably stronger) association and did not report other non-significant associations. Other studies that reported on the association but not completely enough for us to assess quantitatively, however, seemed to give similar results to those in which the data were more clearly presented. Overall, we found little evidence of publication bias, but this cannot be excluded.

Possible interpretations

We believe that the data are valid and propose three possible explanations for the association. The first is that smoking cessation causes the improvement in mental health, the second

is that improving mental health causes cessation, and the third is that a common factor explains both improved mental health and cessation. Observational data can never prove causality, but almost all we know about the harms of smoking and the benefits of cessation derive from observational studies as randomised trials to examine this have insurmountable ethical and practical difficulties.

Could a common factor explain both cessation and improved mental health? This supposes that a single factor—such as positive life events—can cause people to attempt or achieve cessation and improve mental health. As far as we know, there is no evidence that positive life events lead to sustained cessation. In addition, mental health outcomes were assessed anywhere from seven weeks to nine years after baseline, and it seems implausible that such events are associated with positive mental health changes during this entire period.

An obvious explanation for the association is that improvements in mental health prompt people to attempt cessation and that this explains the association. This is contradicted by the data, however. Over half the studies were secondary analyses of randomised trials. In these studies everyone attempted cessation and therefore the decision to quit was not contingent on change in mental health. Subgroup analyses that split data by whether they were derived from such trials or from population cohorts showed no evidence of a difference and a significant difference in change in smokers who quit compared with those who continued in the trial based analyses. Further data support the notion that cessation improves mood. In some but not all of the studies we could calculate the change in mental health in quitters and continuing smokers, rather than just the difference in the change as we have presented. We calculated the weighted mean change for both groups, though formal statistical analysis was not possible to compare groups (data available on request). These data indicate little change in mental health from baseline to follow-up in continuing smokers, while smokers who quit showed reductions in adverse mental health symptoms and improvements in positive affect and quality of life. One of the studies in the review was a trial in which participants were randomised to continue smoking or quit. Obviously adherence to this instruction was not absolute, but analysis of the data by trial arm showed a modest benefit of cessation compared with continuing to smoke. The trial was not powered to detect this difference and it was not significant, but it does provide further evidence to support the notion that stopping smoking leads to improvements in mental health.

Data from a systematic review of randomised trials support the notion that cessation improves mental health. Banham and Gilbody systematically reviewed eight trials of smoking cessation interventions in people with severe mental illnesses.[37] All trials that assessed psychological function typically used several scales at multiple times. Most showed no difference between active and control groups, but the two studies that reported significant differences favoured the intervention groups. Another study reported after this review randomised people with serious mental illness to cessation support or usual care. It showed that cessation support reduced readmissions for worsening mental illness.[38] These data do not directly estimate the effect of cessation on mental health because most people who were randomised to the intervention did not quit. But these findings, in people with serious mental illness, support the findings in our review that psychological outcomes improve on cessation.

Possible mechanisms

The hypothesis that cessation improves mood is supported by a plausible biological mechanism. Chronic tobacco smoking is associated with neuroadaptations in nicotinic pathways in the brain. Neuroadaptations in these pathways are associated with occurrence of depressed mood, agitation, and anxiety shortly after a cigarette is smoked.[39-42] This is known as the withdrawal cycle and is marked by fluctuations in a smoker's psychological state throughout the day[40 41] and could worsen mental health.[20] A study reported that the neurological functioning of quitters returned to the same level as non-smokers by three weeks after cessation,[43] consistent with reports that withdrawal symptoms abate after a few weeks.[21] The misattribution hypothesis is that smokers attribute these symptoms as arising from stress or poor mental health and conclude from the ability of cigarettes to ameliorate these symptoms that cigarettes improve mental health.

Not all data, however, support this causal interpretation. An epidemiological study exploiting mendelian randomisation examined the causal link between current smoking and current anxiety and depression.[44] Although there was some evidence that smoking causes anxiety, the results as a whole did not support a causal link between smoking status and current mental health problems. These data argue against the misattribution hypothesis, whereby periods of psychological changes related to withdrawal from smoking are eliminated by neurological adaptation to permanent deprivation of nicotine.

If the associations we found in this review are causal then the effect size is clinically important. Fournier and colleagues meta-analysed trials of selective serotonin reuptake inhibitors and estimated the effect size.[45] For mild to severe depression the effect estimates ranged from −0.17 to −0.11; this is lower than the effect size for smoking cessation. A meta-analysis of 34 randomised controlled trials assessed the effect of antidepressants on generalised anxiety disorder.[46] These effect estimates ranged from −0.23 (−0.43 to −0.13) to −0.50 (−0.77 to −0.23); this is similar to smoking cessation at −0.37. This result is particularly important in view of our findings in patients with psychiatric disorders. There was no evidence that the effect size differed between population subgroups based on clinical diagnosis, and the effect on depression, psychological quality of life, and positive affect was significant in people who had mental disorders. These data should reassure doctors treating patients with mental illness that cessation is unlikely to exacerbate their symptoms and might indeed be therapeutic.

We recommend that future studies investigating the association between stopping smoking and change in mental health should use statistical techniques that can strengthen the causal inferences that could be drawn from observational research. Propensity score matching can be used to balance the distribution of baseline covariates that could influence disposition to group membership (smoking status). In addition, mendelian randomisation can be used as an instrumental variable approach by using genes that have a common association with change in mental health and smoking status.

Conclusions

Whether or not smoking cessation directly causes the observed improvement in mental health, there are direct clinical implications. Smokers can be reassured that stopping smoking is associated with mental health benefits. This could also overcome barriers that clinicians have toward intervening with smokers with mental health problems. Furthermore, challenging

the widely held assumption that smoking has mental health benefits could motivate smokers to stop.

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What is already known on this topic

Many smokers want to stop but continue smoking as they believe smoking has mental health benefits

In addition, health professionals are reluctant to deal with smoking in people with mental disorders in case stopping smoking worsens mental health

What this study adds

Smoking cessation is associated with an improvement in mental health in comparison with continuing to smoke

The effect estimates are equal or larger to those of antidepressant treatment for mood disorders

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Tables

Table 1| **Effect of smoking cessation on mental health. Sensitivity analysis after removal of studies of low quality (medium-low scores on Newcastle-Ottawa scale)**

Outcome	No of studies included	No of studies excluded	Standardised mean difference (95% CI)	
			Effect estimate	Original effect estimate
Anxiety	4	0	−0.37 (−0.70 to −0.03)	−0.37 (−0.70 to −0.03)
Depression	9	1	−0.29 (−0.42 to −0.15)	−0.25 (−0.37 to −0.12)
Mixed anxiety and depression	4	1	−0.36 (−0.58 to −0.14)	−0.31 (−0.47 to −0.14)
Psychological quality of life	4	4	0.17 (−0.02 to 0.35)	0.22 (0.09 to 0.36)
Positive affect	1	2	0.68 (0.24 to 1.12)	0.40 (0.09 to 0.71)
Stress	2	1	−0.23 (−0.39 to −0.07)	−0.27 (−0.40 to −0.13)

Table 2| **Effect of smoking cessation on mental health. Comparison of unadjusted and adjusted estimates from studies in which both were presented**

Study	Covariates adjusted for	Outcome (measure)	Standardised mean difference (95% CI)	
			Unadjusted estimate	Adjusted estimate
Blalock (2008)*	Baseline CO expiration, baseline nicotine withdrawal score, treatment group allocation	Beck's depression inventory	−0.54 (−1.42 to 0.34)	−0.58 (−1.00 to −0.16)
		Positive and negative affect schedule (positive affect subscale)	0.59 (−0.29 to 1.47)	0.68 (0.24 to 1.12)
McDermott (2012)†	Age, nicotine dependence, and daily cigarette consumption	State trait anxiety inventory-6	−0.62 (−0.88 to −0.36)	−0.74 (−1.00 to −0.48)

*Blalock JA, Robinson JD, Wetter DW, Schreindorfer LS, Cinciripini PM. Nicotine withdrawal in smokers with current depressive disorders undergoing intensive smoking cessation treatment. *Psychol Addict Behav* 2008;22:122-8.

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Table 3| Effect of smoking cessation on mental health. Subgroup analysis with comparison of effect estimates between studies that did and did not adjust for covariates

Outcome	Standardised mean difference (95% CI)			Test for subgroup differences
	Original estimate	Adjusted estimate	Unadjusted estimate	
Anxiety*	−0.37 (−0.70 to −0.03) (4 studies)	−0.74 (−1.00 to −0.48) (1 study)	−0.34 (−0.61 to −0.07) (4 studies)	χ^2=4.40, P=0.04
Depression*	−0.25 (−0.37 to −0.12) (10 studies)	−0.41 (−0.65 to −0.17) (4 studies)	−0.15 (−0.27 to−0.03) (7 studies)	χ^2=3.49, P=0.062
Mixed anxiety and depression	−0.31 (−0.47 to −0.14) (5 studies)	No data	−0.31 (−0.47 to −0.14) (5 studies)	Not applicable
Positive affect	0.40 (0.09 to 0.71) (3 studies)	0.28 (−0.02 to 0.57) (2 studies)	0.68 (0.24 to 1.12) (1 study)	χ^2=2.22, P=0.14
Psychological quality of life	0.22 (0.09 to 0.36) (8 studies)	0.24 (0.07 to 0.40) (5 studies)	0.22 (−0.13 to 0.57) (3 studies)	χ^2=0.01, P=0.92
Stress	−0.27 (−0.40 to −0.13) (3 studies)	No data	−0.27 (−0.40 to −0.13) (3 studies)	Not applicable

*Please note that for anxiety and depression some studies provided both adjusted and unadjusted estimates, so these were compared within corresponding subgroup analysis.

Table 4| Effect of smoking cessation on mental health. Sensitivity analysis with removal of studies in which different numbers of participants were analysed at baseline and follow-up

Outcome	No of studies included	No of studies excluded	Standardised mean difference (95% CI)	
			Effect estimate	Original effect estimate
Anxiety	4	0	−0.37 (−0.70 to −0.03)	−0.37 (−0.70 to −0.03)
Depression	3	7	−0.30 (−0.67 to 0.07)	−0.25 (−0.37 to −0.12)
Mixed anxiety and depression	3	2	−0.26 (−0.44 to −0.07)	−0.31 (−0.47 to −0.14)
Positive affect	3	0	0.40 (0.09 to 0.71)	0.40 (0.09 to 0.71)
Psychological quality of life	5	3	0.18 (0.02 to 0.33)	0.22 (0.09 to 0.36)
Stress	2	1	−0.27 (−0.42 to −0.12)	−0.27 (−0.40 to −0.13)

Table 5| Effect of smoking cessation on mental health. Sensitivity analyses after ascertainment of smoking status

Removed studies and outcome	No of studies included	No of studies excluded	Standardised mean difference (95% CI)	
			Effect estimate	Original effect estimate
Smoking status not biochemically verified				
Anxiety	4	0	−0.37 (−0.70 to −0.03)	−0.37 (−0.70 to −0.03)
Depression	7	3	−0.32 (−0.50 to −0.13)	−0.25 (−0.37 to −0.12)
Mixed anxiety and depression	3	2	−0.35 (−0.59 to −0.10)	−0.31 (−0.47 to −0.14)
Psychological quality of life	4	4	0.17 (−0.02 to 0.35)	0.22 (0.09 to 0.36)
Positive affect	1	2	0.68 (0.24 to 1.12)	0.40 (0.09 to 0.71)
Stress	2	1	−0.23 (−0.39 to −0.07)	−0.27 (−0.40 to −0.13)
Point prevalence smoking status				
Anxiety	2	1	−0.51 (−1.04 to 0.03)	−0.37 (−0.70 to −0.03)
Depression	6	4	−0.34 (−0.52 to −0.16)	−0.25 (−0.37 to −0.12)
Mixed anxiety and depression	3	2	-0.29 (-0.52 to -0.07)	−0.31 (-0.47 to -0.14)
Psychological quality of life	1	7	0.37 (0.07 to 0.67)	0.22 (0.09 to 0.36)
Positive affect	2	1	0.39 (−0.11 to 0.90)	0.40 (0.09 to 0.71)
Stress	2	1	−0.27 (−0.42 to −0.12)	−0.27 (−0.40 to −0.13)

Table 6| **Effect of smoking cessation on mental health. Subgroup analysis with comparison of studies in which participants were motivated or not motivated to quit**

Population (No of studies)	Standardised mean difference (95% CI)	Test for subgroup differences
Anxiety		
Overall (4)	−0.37 (−0.70 to −0.03)	—
Motivated to quit (3)	−0.41 (−0.81 to −0.00)	χ^2=2.77, P=0.10
Not motivated to quit (1)	−0.19 (−0.68 to 0.30)	
Depression		
Overall (10)	−0.25 (−0.37 to −0.12)	—
Motivated to quit (6)	−0.31 (−0.53 to −0.09)	χ^2=1.16, P=0.28
Not motivated to quit (4)	−0.17 (−0.30 to −0.05)	
Mixed anxiety and depression		
Overall (5)	−0.31 (−0.47 to −0.14)	—
Motivated to quit (3)	−0.35 (−0.59 to −0.10)	χ^2=0.19, P=0.66
Not motivated to quit (2)	−0.27 (−0.50 to −0.04)	
Psychological quality of life		
Overall (8)	0.22 (0.09 to 0.36)	—
Motivated to quit (4)	0.20 (0.03 to 0.38)	χ^2=0.17, P=0.68
Not motivated to quit (4)	0.26 (0.04 to 0.49)	
Positive affect		
Overall (3)	0.40 (0.09 to 0.71)	—
Motivated to quit (2)	0.39 (−0.11 to 0.90)	χ^2=3.95, P=0.11
Not motivated to quit (1)	0.47 (0.04 to 0.90)	
Stress		
Overall (3)	−0.27 (−0.40 to −0.13)	—
Motivated to quit (2)	−0.23 (−0.39 to −0.07)	χ^2=0.74, P=0.39
Not motivated to quit (1)	−0.36 (−0.61 to −0.11)	

Table 7| **Effect of smoking cessation on mental health. Sensitivity analysis after removal of studies with psychological component within cessation intervention**

Outcome	No of studies included	No of studies excluded	Standardised mean difference (95% CI)	
			Effect estimate	Original effect estimate
Anxiety	4	0	−0.37 (−0.70 to −0.03)	−0.37 (−0.70 to −0.03)
Depression	6	4	−0.15 (−0.26 to −0.03)	−0.25 (−0.37 to −0.12)
Mixed anxiety and depression	3	2	−0.28 (−0.46 to −0.10)	−0.31 (−0.47 to −0.14)
Psychological quality of life	5	3	0.15 (−0.01 to 0.31)	0.22 (0.09 to 0.36)
Positive affect	1	2	0.47 (0.04 to 0.90)	0.40 (0.09 to 0.71)
Stress	3	0	−0.27 (−0.40 to −0.13)	−0.27 (−0.40 to −0.13)

Table 8| Effect of smoking cessation on mental health. Subgroup analysis with comparison of effect estimates between different clinical populations

Outcome and population (No of studies)	Effect estimate standardised mean difference (95% CI)	Test for subgroup differences
Anxiety		
Overall	−0.37 (−0.70 to −0.03)	—
General (3)	−0.48 (−0.81 to −0.15)	χ²=2.77, P=0.10
Pregnant (1)	−0.06 (−0.42 to 0.30)	
Depression		
Overall	−0.25 (−0.37 to −0.12)	—
General (5)	−0.30 (−0.48 to −0.12)	χ²=5.86, P=0.053
Psychiatric condition (3)	−0.39 (−0.63 to −0.14)	
Pregnant (2)	−0.07 (−0.23 to 0.09)	
Mixed anxiety and depression		
Overall	−0.31 (−0.47 to −0.14)	—
General (3)	−0.32 (−0.53 to −0.11)	χ²=0.08, P=0.96
Psychiatric condition (1)	−0.21 (−1.07 to 0.65)	
Chronic physical and/or psychiatric condition (1)	−0.29 (−0.57 to −0.01)	
Psychological quality of life		
Overall	0.22 (0.09 to 0.36)	—
General (3)	0.15 (−0.01 to 0.30)	χ²=5.25, P=0.25
Psychiatric condition (1)	0.40 (−0.03 to 0.83)	
Chronic physical and/or psychiatric condition (1)	0.60 (0.17 to 1.03)	
Chronic physical condition (1)	0.16 (−0.11 to 0.43)	
Postoperative (1)	0.62 (−0.27 to 1.51)	
Positive affect		
Overall	0.40 (0.09 to 0.71)	—
Chronic physical and/or psychiatric condition (1)	0.47 (0.04 to 0.90)	χ²=3.95, P=0.11
General (1)	0.16 (−0.14 to 0.46)	
Psychiatric condition (1)	0.68 (0.24 to 1.12)	
Stress		
Overall	−0.27 (−0.40 to −0.13)	—
General (2)	−0.32 (−0.52 to −0.12)	χ²=0.51, P=0·48
Chronic physical condition (1)	−0.22 (−0.40 to −0.04)	

Table 9| Effect of smoking cessation on mental health. Subgroup with comparison of effect estimates between different study designs

Study design *No of studies)	Effect estimate standardised mean difference (95% CI)	Test for subgroup differences
Anxiety		
Overall	−0.37 (−0.70 to −0.03)	—
Cohort (1)	−0.06 (−0.42 to 0.30)	χ²=4.07, P=0.13
Randomised controlled trial (1)	−0.19 (−0.68 to 0.30)	
Secondary analyses of cessation intervention (2)	−0.57 (−0.93 to −0.21)	
Depression		
Overall	−0.25 (−0.37 to −0.12)	—
Cohort (3)	−0.12 (−0.25 to 0.01)	χ²=5.15, P=0.08
Randomised controlled trial (1)	−0.39 (−0.88 to 0.10)	
Secondary analyses of cessation intervention (6)	−0.36 (−0.53 to −0.18)	
Mixed anxiety and depression		
Overall	−0.31 (−0.47 to −0.14)	—
Cohort (3)	−0.28 (−0.46 to −0.10)	χ²=0.76, P=0.38
Secondary analyses of cessation intervention (2)	−0.51 (−0.99 to −0.03)	
Psychological quality of life		
Overall	0.22 (0.09 to 0.36)	—
Cohort (5)	0.28 (0.08 to 0.48)	χ²=0.95, P=0.33
Secondary analyses of cessation intervention (3)	0.15 (−0.04 to 0.33)	
Positive affect		
Overall	0.40 (0.09 to 0.71)	—
Cohort (2)	0.28 (−0.02 to 0.57)	χ²=2.22, P=0.14
Secondary analyses of cessation intervention (1)	0.68 (0.24 to 1.12)	
Stress		
Overall	−0.27 (−0.40 to −0.13)	—
Cohort (1)	−0.36 (−0.61 to −0.11)	χ²=0.74, P=0.39
Secondary analyses of cessation intervention (2)	−0.23 (−0.39 to −0.07)	

Table 10| Effect of smoking cessation on mental health. Subgroup analysis after comparison of effect estimates between studies with follow-up periods from baseline to follow-up between six weeks to six months and studies with follow-ups from baseline to more than six months

Outcome	Standardised mean difference (95% CI)			Test for subgroup differences
	Original estimate	6 weeks to <6 months	>6 months	
Anxiety	−0.37 (−0.70 to −0.03)	−0.35 (−0.83 to 0.12) (3 studies)	−0.37 (−0.72 to −0.02) (1 study)	χ²=0.00, P=0.95
Depression*	−0.25 (−0.37 to −0.12)	−0.18 (−0.31 to −0.05) (8 studies)	−0.23 (−0.41 to −0.06) (5 studies)	χ²=0.25, P=0.62
Mixed anxiety and depression*	−0.31 (−0.47 to −0.14)	−0.37 (−0.58 to −0.15) (4 studies)	−0.27 (−0.50 to −0.04) (2 studies)	χ²=0.34, P=0.56
Positive affect	0.40 (0.09 to 0.71)	0.68 (0.24 to 1.12) (1 study)	0.28 (−0.02 to 0.57) (2 studies)	χ²=2.22, P=0.14
Psychological quality of life*	0.22 (0.09 to 0.36)	0.30 (0.15 to 0.44) (7 studies)	0.23 (0.09 to 0.37) (8 studies)	χ²=0.36, P=0.92
Stress	−0.27 (−0.40 to -0.13)	−0.25 (−0.58 to 0.08) (1 study)	−0.27 (−0.42 to −0.12) (2 studies)	χ²=0.01, P=0.92

*Please note some studies measured outcome at multiple follow-ups, so these were compared within corresponding subgroup analysis
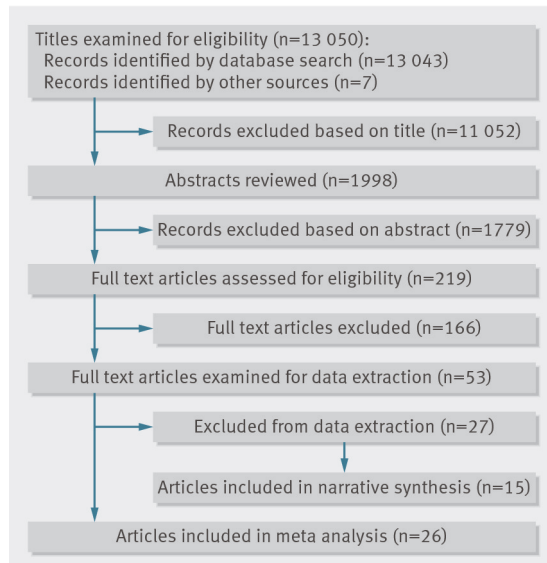
Figures

Fig 1 Flow and identification of studies to include in review of change in mental health after smoking cessation

Study	SE	Standard mean difference (95% CI)	Weight (%)	Standard mean difference (95% CI)
Anxiety				
Solomon 2006	0.19		25	-0.06 (-0.42 to 0.30)
Dawkins 2009	0.25		20	-0.19 (-0.68 to 0.30)
McDermott 2013	0.13		29	-0.74 (-1.00 to -0.48)
Becona 2002	0.18		26	-0.37 (-0.72 to -0.02)
Total			100	-0.37 (-0.70 to -0.03)
Test for heterogeneity: τ^2=0.08, χ^2=10.43, df=3, P=0.02, I^2=71%				
Test for overall effect: z=2.16, P=0.03				
Depression				
Solomon 2006	0.19		9	0.01 (-0.35 to 0.37)
Berlin 2010	0.22		7	-0.30 (-0.72 to 0.12)
Blalock 2008	0.22		7	-0.58 (-1.00 to -0.16)
Dawkins 2009	0.25		5	-0.39 (-0.88 to 0.10)
Kahler 2011	0.21		7	-0.28 (-0.69 to 0.13)
Vazquez 1999	0.17		11	-0.12 (-0.44 to 0.20)
Busch 2011	0.19		9	-0.30 (-0.67 to 0.07)
Kahler 2002	0.20		8	-0.69 (-1.09 to -0.29)
Munafo 2008	0.09		21	-0.09 (-0.27 to 0.09)
Kinnunen 2006	0.11		17	-0.21 (-0.42 to 0.00)
Total			100	-0.25 (-0.37 to -0.12)
Test for heterogeneity: τ^2=0.01, χ^2=12.83, df=9, P=0.17, I^2=30%				
Test for overall effect: z=3.89, P<0.001				
Mixed anxiety and depression				
Blalock 2008	0.44		4	-0.21 (-1.07 to 0.65)
Kahler 2009	0.29		8	-0.64 (-1.22 to -0.06)
Steinberg 2011	0.14		35	-0.29 (-0.57 to -0.01)
Mino 2000	0.26		10	-0.44 (-0.95 to 0.07)
Chassin 2002	0.13		42	-0.23 (-0.48 to 0.02)
Total			100	-0.31 (-0.47 to -0.14)
Test for heterogeneity: τ^2=0.00, χ^2=1.94, df=4, P=0.75, I^2=0%				
Test for overall effect: z=3.61, P<0.001				
Stress				
Manning 2005	0.17		17	-0.25 (-0.58 to 0.08)
Hajek 2010	0.09		55	-0.22 (-0.40 to -0.04)
Chassin 2002	0.13		29	-0.36 (-0.61 to -0.11)
Total			100	-0.27 (-0.40 to -0.13)
Test for heterogeneity: τ^2=0.00, χ^2=0.77, df=2, P=0.68, I^2=0%				
Test for overall effect: z=3.80, P<0.001				

-1   -0.5   0   0.5   1
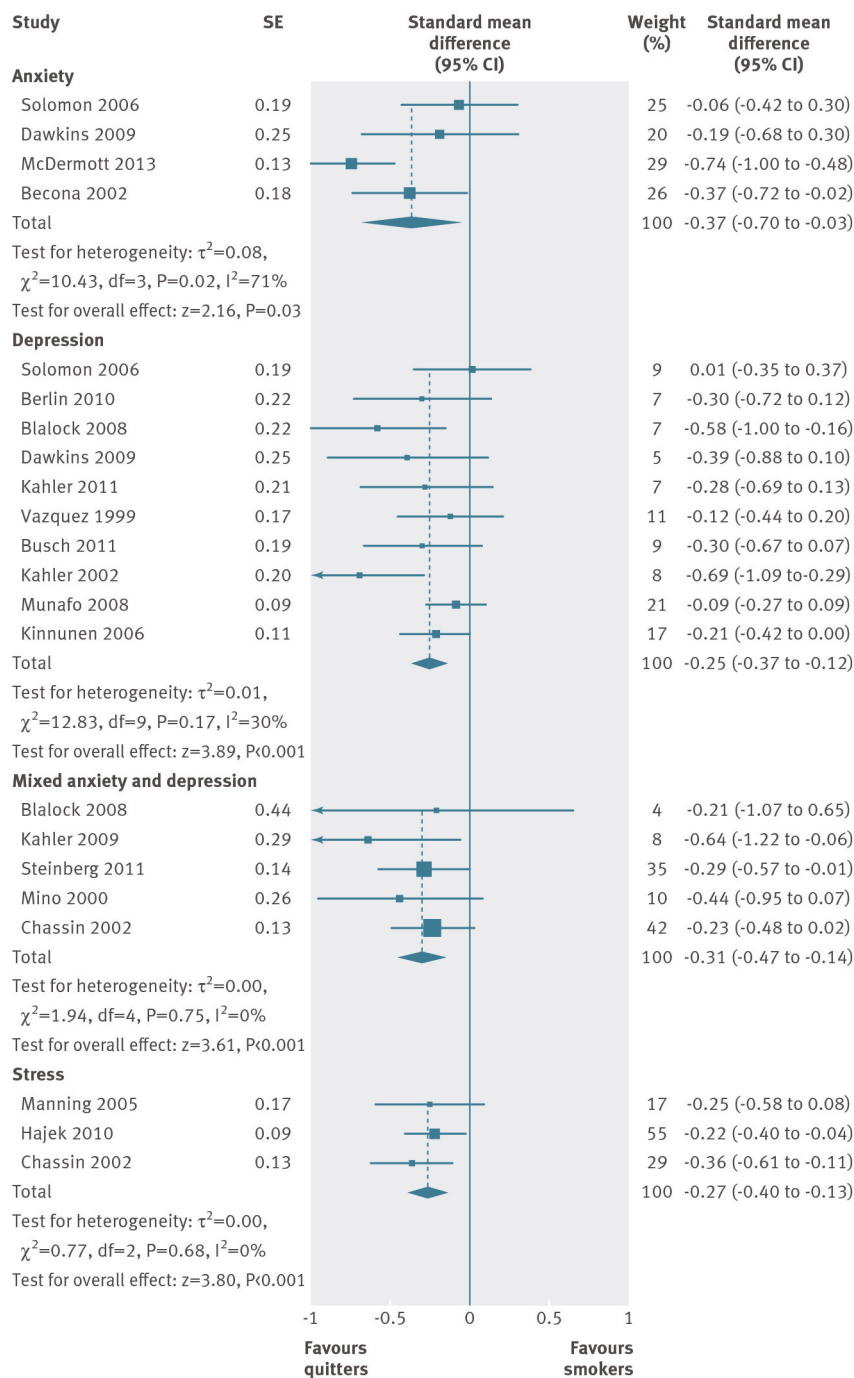
Favours quitters   Favours smokers

Fig 2 Difference between change in mental health outcomes (anxiety, mixed anxiety and depression, depression, stress) from baseline to longest follow-up in people who stopped smoking or continued to smoke. Study by McDermott was in submission during search
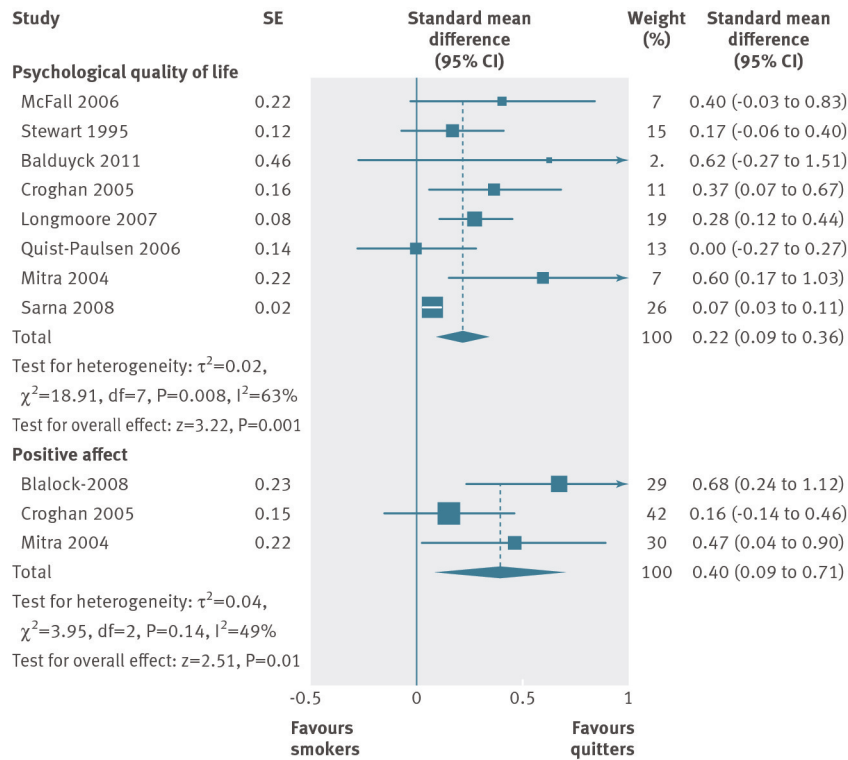
Fig 3 Difference between change in mental health outcomes (positive affect, psychological quality of life) from baseline to longest follow-up in people who stopped smoking or continued to smoke