A rapid review of the effectiveness of smoking cessation interventions for people with anxiety and/or depression living within the community

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Abstract

The Welsh Government aims to reduce smoking prevalence from the current rate of 13% to below 5% of the population by 2030. People with mental health conditions have a higher rate of smoking prevalence and are less likely to access smoking cessation services. Evidence shows that smoking cessation in this population decreases symptoms, improves positive mood and quality of life. This rapid review aimed to identify and synthesise the evidence for the effectiveness of smoking cessation interventions in people with anxiety and/or depression living in the community.

Results

The literature searches were conducted in March 2024, the included study reports were published between 2008 and 2023, nine were published since 2019. Eleven primary studies from 15 reports were included in the rapid review: 10 RCTs, two of which were pilot RCTs, and one quasi-experimental pilot study. Studies were conducted in the USA (n=6), Spain (n=1), France (n=1), Netherlands (n=1), and two studies were conducted across the EU and USA.

Research Implications and Evidence Gaps

No UK studies were identified therefore it is unclear whether findings are generalisable to the UK. No studies applying interventions at critical touchpoints within smoking cessation or mental health services were identified. Only one study assessed the cost-effectiveness of a smoking cessation intervention. Only one study assessed a smoking cessation intervention in participants with anxiety. Most studies included in this review were judged to be of low quality. Most studies recruited participants from the general population, therefore it is unclear whether participants were engaged with mental health services. Further high-quality UK-based research is needed to better understand the effectiveness of smoking cessation interventions for people with anxiety and depression.

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EXECUTIVE SUMMARY

Report number: RR0025 Date (July 2024)

What is a Rapid Review?

Our rapid reviews use a variation of the systematic review approach, abbreviating or omitting some components to generate the evidence to inform stakeholders promptly whilst maintaining attention to bias.

Who is this Rapid Review for?

The research question was suggested by Welsh Government Health Improvement.

Background / Aim of Rapid Review

The Welsh Government aims to reduce smoking prevalence from the current rate of 13% to below 5% of the population by 2030. People with mental health conditions have a higher rate of smoking prevalence and are less likely to access smoking cessation services. Evidence shows that smoking cessation in this population decreases symptoms, improves positive mood and quality of life. This rapid review aimed to identify and synthesise the evidence for the effectiveness of smoking cessation interventions in people with anxiety and/or depression living in the community.

Results

Recency of the evidence base

- The literature searches were conducted in March 2024, the included study reports were published between 2008 and 2023, nine were published since 2019.

Extent of the evidence base

- Eleven primary studies from 15 reports were included in the rapid review: 10 RCTs, two of which were pilot RCTs, and one quasi-experimental pilot study.
- Studies were conducted in the USA (n=6), Spain (n=1), France (n=1), Netherlands (n=1), and two studies were conducted across the EU and USA.
- Studies investigated pharmacological (Varenicline, Bupropion, nicotine replacement therapy), psychological (behavioural activation, contingency management, mood management, smoking cessation counselling), and aerobic exercise interventions. Most interventions were conducted in-person, with two studies using remote delivery via mobile applications or telephone.
- Outcomes included various measures of smoking cessation, mental health symptoms, adverse events and cost-effectiveness.

Key findings and certainty of the evidence

- Overall, the evidence of effectiveness of smoking cessation interventions for those with anxiety and depression appears to be inconsistent.
- Taking into account the overall methodological quality, variability of outcome measures used and consistency of study findings, it was difficult to make direct comparison between the different studies included. Therefore, we have very low certainty across all the outcome measures identified. This means that the true effect is probably different from the estimated effect.

- There is some evidence to suggest that psychological smoking cessation interventions can increase abstinence in people with depression, however the impact on mental health outcomes appeared to be mixed.
- There is some evidence to suggest that pharmacological smoking cessation interventions can increase abstinence. However, they appeared to have no impact on mental health outcomes and no consistent impact on adverse events for people with anxiety and depression.
- Evidence shows the impact of exercise interventions had mixed findings on abstinence rates and no impact on mental health outcomes in people with depression.
- There is some evidence suggesting multicomponent pharmacological and psychological smoking cessation interventions can increase abstinence rates and reduce adverse events in people with depression. However, the impact on mental health outcomes appears mixed.
- There is limited evidence supporting the effectiveness of multicomponent exercise and psychological smoking cessation interventions but no impact on abstinence rates or mental health outcomes in people with depression.
- There is very limited evidence suggesting psychological smoking cessation interventions for people with depression may be cost-effective.

Research Implications and Evidence Gaps

- No UK studies were identified therefore it is unclear whether findings are generalisable to the UK.
- No studies applying interventions at critical touchpoints within smoking cessation or mental health services were identified.
- Only one study assessed the cost-effectiveness of a smoking cessation intervention.
- Only one study assessed a smoking cessation intervention in participants with anxiety.
- Most studies included in this review were judged to be of low quality.
- Most studies recruited participants from the general population, therefore it is unclear whether participants were engaged with mental health services.
- Further high-quality UK-based research is needed to better understand the effectiveness of smoking cessation interventions for people with anxiety and depression.

Policy and Practice Implications

- There is limited high quality evidence on smoking cessation interventions for those with anxiety or depression, therefore cautious consideration of findings is required if this evidence is used to inform future interventions.
- Although low quality evidence supports the use of pharmacological, psychological, and multicomponent pharmacological and psychological smoking cessation interventions to increase abstinence in people with depression.
- This review identified (limited/low quality) Varenicline as potentially effective for smoking cessation in the population group of interest. In light of recent All Wales Medicine Strategy Group recommendations to allow Cytosine, which has similar action to Varenicline, this may be of particular interest.

Economic considerations

- Smoking is a considerable public health issue that incurs significant economic costs. The estimated economic cost of smoking in people with mental health disorders in the UK is £3.5 billion per annum.
- There is limited economic evidence on the impact of implementing smoking cessation interventions for individuals living with depression and/or anxiety.

A summary of findings and the certainty of evidence has been assessed using an approach adapted from the GRADE evidence profile (Guyatt et al, 2011), which has been adapted for the purpose of this review.

Disclaimer: The views expressed in this publication are those of the authors, not necessarily Health and Care Research Wales. The Health and Care Research Wales Evidence Centre and authors of this work declare that they have no conflict of interest.

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Abbreviations

Acronym	Full Description
BDI-II	Beck Depression Inventory version 2
CBT	Cognitive behavioural therapy
CES-D	Centre for Epidemiological Studies Depression scale
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders-IV
EAGLES	Evaluating Adverse Events in a Global Smoking Cessation Study
HADS	Hospital Anxiety and Depression scale
ISRCTN	International Standard Randomised Controlled Trial Number
MADRS	Montgomery-Asberg Depression Rating Scale
MHRA	Medicines and Healthcare products Regulatory Agency
MINI	Mini International Neuropsychiatric Interview
NRT	Nicotine replacement therapy
PHQ 8/9	Patient Health Questionnaire versions 8/9
PPA	Point prevalence abstinence
RCT	Randomised controlled trial

1. BACKGROUND

1.1 Who is this review for?

This Rapid Review was conducted as part of the Health and Care Research Wales Evidence Centre Work Programme. The research question was formulated by Welsh Government Health Improvement to inform the Welsh Government delivery plan for 2024-2026.

1.2 Background and purpose of this review

Smoking remains a significant public health concern in Wales. It is the leading cause of preventable death in Wales and costs the Welsh NHS an estimated £302 million annually (Welsh Government 2022). The Welsh Government has published a long-term plan towards a smoke-free Wales, with the aim of reducing smoking prevalence from the current rate of 13%, to below 5% of the population by 2030 (Welsh Government 2022).

People with mental health conditions, including those with anxiety and depression, have significantly higher smoking rates compared to the general population; in Wales, 35% of adults aged 16 and over who report having a long-standing mental health condition are smokers (Welsh Government, 2023a). This is over double the rate of smokers in the general population of Wales (13%) (Welsh Government 2023b). These populations are also less likely to access smoking cessation services (National Institute for Health and Care Excellence, 2021). Furthermore, the life expectancy of people with poor mental health is on average 10 to 20 years less than the general population, with smoking being the biggest cause of this difference (Public Health England, 2020).

Anxiety and depression together are the most prevalent common mental health disorders (NHS Digital, 2016). According to the most recent Adult Psychiatric Morbidity Survey, 5.9% and 3.3% of adults aged 16 years and over meet the diagnostic criteria for anxiety or depression, respectively (NHS Digital 2016). Additionally, recent data collected by the Office for National Statistics (2021), showed 16% of adults in Great Britain reported they were experiencing depressive symptoms, and 16% were also likely to be experiencing some form of anxiety.

A range of smoking cessation interventions have been shown to be effective in the general population. According to two Cochrane systematic reviews, these include behavioural interventions such as counselling and guaranteed financial incentives (Hartmann-Boyce et al, 2021), and pharmacological interventions like Varenicline, Bupropion, cytosine, nicotine replacement therapy (NRT), and nicotine e-cigarettes (Lindson et al, 2023). It is unclear if these interventions would also be effective in people with anxiety and depression. Wales' national smoking cessation service, Help Me Quit, currently offers six weeks of behavioural support and 12 weeks of NRT to people who smoke however its effectiveness among people with anxiety and depression is largely unknown. Research suggests that people with mental health disorders are likely to have a better quality of life and feel more positive and calmer after quitting smoking (NHS, 2024). The beneficial effects of giving up smoking on anxiety and depression symptoms is said to equal that of taking anti-depressant medication (NHS, 2024). There is therefore a need to identify the most effective smoking cessation interventions for this population group.

This rapid review focuses on primary studies and aims to identify and synthesise the evidence for the effectiveness of smoking cessation interventions for people with anxiety and/or depression living in the community.

2. RESULTS

2.1 Overview of the Evidence Base

Eleven studies (15 reports) were eligible for inclusion in this rapid review. Eligibility was restricted to comparative primary studies assessing the effectiveness of smoking cessation interventions for adult smokers with anxiety or depression living in the community (see section 5.1 for full eligibility criteria). Ten of the 11 studies were randomised controlled trials (RCTs), two of which were pilot studies. One study was a quasi-experimental uncontrolled before and after pilot study. Studies were conducted in a range of countries, including USA (n=6), Spain (n=1), France (n=1), Netherlands (n=1), and two studies were conducted across multiple countries across the EU and USA. Sample sizes varied across the 15 identified reports, ranging from 17 to 6,653, and 11 reports included more than 100 participants. Reports were published between 2008 and 2023, nine since 2019.

A protocol for a UK-based study investigating the acceptability and impact of a smoking cessation intervention for mental health service users with depression, alongside routine psychological therapy was also identified during searching. This study may be particularly useful for informing smoking cessation interventions for people with anxiety and/or depression as it is UK based and is incorporated into existing psychological therapy for mental health service users. We were informed by the corresponding author that the study report is currently under consideration with the Addiction Journal. The protocol is registered on the International Standard Randomised Controlled Trial Number (ISRCTN); ISRCTN99531779 (https://doi.org/10.1186/ISRCTN99531779).

All of the studies included participants who had depression (n=11), one of which also included people with anxiety. A range of diagnostic tools were used to identify study participants with depression and anxiety at study entry. This included the Structured Clinical Interview for axis I disorders of the DSM-IV, the Beck Depression Inventory-II (BDI-II), the neuropsychiatric interview, the Centre for Epidemiological Studies Depression (CES-D) scale, the Patient Health Questionnaire (PHQ) versions 8/9, and the Hospital Anxiety and Depression Scale (HADS).

For the synthesis of results, studies have been grouped into five categories according to the type of intervention(s) being assessed: psychological (n=3), pharmacological (n=3), exercise-based (n=2), multicomponent pharmacological and psychological (n=2), and multicomponent exercise and psychological interventions (n=1). Greater detail of the specific interventions being investigated is shown in Table 1, which also outlines the current treatment used in Wales. All intervention components only received by participants in the experimental group are highlighted in green (an Asterix is also given for readers with difficulty distinguishing colours). In most studies (n=8), the interventions being assessed were an addition to existing smoking cessation treatment which was also received by participants in the control group. The smoking cessation treatment components received by all participants (intervention and control groups) are highlighted in yellow in Table 1 (or X without an Asterisk).

Interventions were delivered at clinical trials centres or outpatient clinics (n=3), research clinics (n=2), a hospital (n=1), and remotely via a mobile phone application, text messaging programme, or telephone (n=2). Three studies did not state the intervention setting. Intervention durations ranged from six weeks to three months. Details of the interventions can be seen in Table 2; a summary of the findings can be found in Table 3, and a more detailed summary of the included studies can be seen in section 6.2 (Table 5).

Outcome measures identified included smoking abstinence-related outcomes; 7-day point prevalence abstinence (PPA), quit rates, continuous or prolonged abstinence, smoking reduction outcomes; quit attempts, number of cigarettes smoked per day, and cigarette demand, anxiety or depressive symptoms, adverse events, and cost-effectiveness. Data collection methods included self-reported smoking and abstinence rates, validated questionnaires, and tests for biochemical verification were performed in all studies except two (Dahne et al, 2012; van der Meer et al, 2010).

The methodological quality of included studies was assessed using the appropriate Joanna Briggs Institute (JBI) critical appraisal tool for RCTs or quasi-experimental studies. All reports were judged to have some risk of bias, often because of poor reporting of methods. Of the 14 RCT reports, 11 were considered low quality, one was considered moderate quality, and two were considered high quality. Concerns which increased the risk of bias of RCTs included uncertainty about measurement reliability in 11 reports, no description or analysis of loss to follow-up in 11 reports, absence of power calculations stated in 11 reports, and no details about blinding of assessors in 10 reports. The quasi-experimental uncontrolled before and after pilot study was considered low quality due to the absence of a control group and power calculation, therefore it was unclear whether it was sufficiently powered to measure intervention effectiveness. Further details of the quality appraisal can be found in section 6.3.

Multiple reports presented findings from three studies (Anthenelli et al, 2013; Anthenelli et al, 2016; Weidberg et al, 2018), which were included because they provided additional, unique results relevant to the research question. Reports of the same study were identified by trial registration numbers and grouped accordingly. Doran et al (2019) conducted a secondary analysis of the international study reported by Anthenelli et al (2013) (trial number: NCT01078298). Both Ayers et al (2019) and Cinciripini et al (2022) were secondary analyses of the international Evaluating Adverse Events in a Global Smoking Cessation Study (EAGLES) (NCT01456936) (Anthenelli et al, 2016). However, Ayers et al (2019) compares the findings for participants with and without anxiety disorders, whereas Cinciripini et al (2022), compared the findings for participants with and without depression. Anthenelli et al (2016) was not eligible for inclusion because smoking cessation outcomes were not reported specifically for participants with either anxiety or depression. González-Roz et al (2021), Weidberg et al (2018), and Secades-Villa et al (2019), all report findings from the same Spanish study (NCT03163056), although Weidberg et al (2018) report findings from a smaller sample of participants. For the synthesis and summary of study findings (Table 3), reports of the same study have been grouped together.

Table 1. Intervention components and smoking cessation treatments received by participants in the included studies and the current treatment used in Wales

	Psychological					Pharmacological			Exercise
Study	Cognitive behavioural therapy	Cessation counselling	Behavioural activation	Contingency management	Mood management	Nicotine replacement therapy	Varenicline	Bupropion	Aerobic exercise
Help Me Quit Service (Wales) [β]	X					X			
Abrantes et al (2023)		X				X			X*
Anthenelli et al (2013) Doran et al (2019)		X					X*		
Ayers et al (2019) Cinciripini et al (2022)		X				X*	X*	X*	
Bernard et al (2015)		X*				X	X		X*
Dahne et al (2023)			X*			X*			
Evins et al (2008)	X					X		X*	
Heffner et al (2019) [¥]			X						
Hitsman et al (2023)		X*	X*				X*		
Patten et al (2017)		X				X			X*
Van der Meer et al (2010)		X			X*				
Weidberg et al (2018) González-Roz et al (2021) Secades-Villa et al (2019)	X		X	X*					

X* Smoking cessation treatment received by intervention group only (i.e. the intervention being evaluate as part of the study).

X Smoking cessation treatment received by all participants.

[β]The Help Me Quit Service has been added to illustrate similarities and differences between included studies and existing smoking cessation treatment pathways used in Wales.

[¥] Heffner et al (2019) was an uncontrolled before and after study.

2.2 Impact of psychological interventions

Five reports of three studies (González-Roz et al, 2021; Heffner et al, 2019; Secades-Villa et al, 2019; van der Meer et al, 2010; Weidberg et al, 2018) were examining the effect of psychological interventions for improving smoking cessation and mental health outcomes in smokers with depression. Three of the five reports (González-Roz et al, 2021; Secades-Villa et al, 2019; Weidberg et al, 2018) were analyses of the same smoking cessation study conducted in Spain. The remaining studies were conducted in the Netherlands (van der Meer et al, 2010), and USA (Heffner et al, 2019). All studies were RCTs except for one quasi-experimental before and after pilot study (Heffner et al, 2019). One RCT was considered high quality (van Der Meer et al, 2010), the remaining studies were considered low quality. All studies focused on participants with depression. The findings of studies evaluating the effectiveness of psychological smoking cessation interventions was mixed.

2.2.1 Contingency management

Weidberg et al (2018), Secades-Villa et al, (2019), and González-Roz et al, (2021), all reported findings from the same study where both groups received CBT combined with behavioural activation, and the intervention group received additional contingency management comprising of a voucher-based abstinence reinforcement element. Both interventions were implemented in a group-based format of a maximum of four patients over an 8-week period. Individuals received one therapy session per week and were also asked to attend midweek sessions (“b” sessions) to collect biochemical measures.

Smoking abstinence

- Weidberg et al, (2018), assessed smoking status by measuring urine cotinine values, and results showed they were **lower among participants who received CBT with behavioural activation and contingency management compared to those who received only CBT with behavioural activation. Significant differences by group were found in sessions 2b, 3, 3b, 4, 4b, 5 and 6 (all p values <0.05)**. The percentage of participants presenting cotinine levels <80 ng/ml was higher in the CBT with behavioural activation and contingency management group than in the group without contingency management, although differences were only significant in session 5 (p=0.038).

- Secades-Villa et al (2019) reported that **the odds of a point prevalence abstinence in the group receiving CBT combined with behavioural activation and contingency management were 2.42 times higher [β =0.88, standard error (SE)=0.42, p=0.036, Yule’s Q= 0.42] than that of the control group at 1-month follow-up**. In addition, **continuous abstinence was significantly higher at each time-point up to 6-months follow-up in the group receiving CBT combined with behavioural activation and contingency management (all p values<0.05)**.

- González-Roz et al (2021) reported that CBT with behavioural activation and contingency management (53.3%; 32/60) was more effective in facilitating 1-year abstinence compared with treatment without contingency management (23.3%; 14/60), however significance values were not reported. **The odds of a favourable response in terms of point prevalence were 1.16 (SE= 0.067, p=0.010) times higher in CBT with behavioural activation and contingency management participants**. Days of **continuous abstinence ranged from 0 to 418 days (CBT with behavioural activation = 97.14 days [SD = 160.70] vs. CBT with behavioural**

activation and contingency management = 187.28 days [SD = 182.35], p=0.013), and weeks of longest duration of abstinence were also greater in patients allocated to CBT with behavioural activation and contingency management (25.94 weeks [SD = 24.27] vs. 13.97 weeks [SD = 20.61], p=0.004, d=0.53).

Smoking reduction

- Weidberg et al (2018) measured smoking demand through a cigarette purchase task at the end of treatment. There was no significant effect of treatment condition on cigarette demand (Model D: all p values ≤0.32), suggesting that the differential effect of the contingency management component was not significant for this outcome.

Mental health

- Secades-Villa et al (2019) measured change in depressive symptoms using the BDI-II scale over a 6-month period. Depressive symptoms significantly reduced amongst all participants, $F(5,116) = 57.19$, $p<0.0001$, but there was no significant difference between participants who received the addition of contingency management compared to participants in the control who did not, $F(1,111)= 0.53$, $p=0.4665$.

Cost-effectiveness.

- González-Roz et al (2021) estimated the incremental cost-effectiveness of adding contingency management in relation to abstinence outcomes for a CBT and behavioural activation intervention. **The average cost per patient was €208.85 (US$236.57) for CBT with behavioural activation, and €410.64 (US$465.14) for CBT+BA+CM, p<0.001. The incremental cost of using contingency management to enhance 1-year abstinence by one extra longest duration of abstinence week was €18 (US$20.39) (95% CI 17.75 to 18.25)**.

2.2.2 Behavioural activation & smoking cessation mobile application

Heffner et al (2019) described the development and preliminary evaluation of Actify!-a Behavioural Activation Treatment for Depression (BAT-D) smoking cessation mobile health app (native app on an iOS Apple device) for depressed smokers in a pilot study. Participants received daily messages for 6-weeks, which increased in frequency on and around the quit date.

Smoking abstinence

- The findings reported by Heffner et al (2019) showed that the 7-day point prevalence abstinence (PPA) rate at 6-week follow-up was 31% (5/16), and the 30-day PPA at 6-week follow-up fell to 19% (3/16). However, no inferential statistics were reported to support these findings, and the study did not appear to have been powered to detect significant differences.

Mental health

- Heffner et al (2019) also measured change in depressive symptoms using the PHQ-9 scale. After the 6-week intervention, **depression scores significantly reduced from baseline (mean –4.5, 95% CI –7.7 to –1.3, p=0.01), which was also a clinically significant change from moderate to mild symptoms**.

Adverse events

- Heffner et al (2019) was the only study of a behavioural psychological smoking cessation intervention to record adverse events. During the 6-week intervention, no adverse events were reported by participants from either group.

2.2.3 Mood management

van der Meer et al (2010) investigated whether the mood management component as an adjunct to the Dutch national smoking cessation Quitline (telephone smoking cessation counselling) improved smoking abstinence rates and prevented recurrence of depressive symptoms. The mood management intervention consisted of a tailored self-help mood management manual, as well as two additional counselling sessions, whereas the control group received eight telephone counselling sessions.

Smoking abstinence

- Results showed that **prolonged abstinence rates at 6- and 12-month follow-up were significantly higher for participants in the experimental group, 30.5% and 23.9%, respectively, vs 22.3% and 14.0%. At 6-months: OR 1.60 (95% CI 1.06 to 2.42) and at 12-months: OR 1.96 (95% CI 1.22 to 3.14)**. However, although 7-day PPA rates at 6- and 12-month follow-up were higher for participants in the experimental group, 37.4% and 27.6%, respectively, vs 31.0% and 24.0%, this was not statistically significant at 6-months: OR 1.38 (95% CI 0.94 to 2.02) or 12-months: OR 1.23 (95% CI 0.81 to 1.86).

Mental health

- van der Meer et al (2010) measured changes in depressive symptoms using the CES-D scale. There were no significant differences between groups at 6- and 12-months; scores reduced by a mean of 1.1 and 0.6 respectively for participants in the intervention group, and by 2.0 and 0.1 in the control ($p>0.05$).

2.2.4 Bottom line results for psychological interventions

Overall, there is very low certainty evidence that suggests psychological interventions may be effective for improving smoking cessation in people with depression. Certainty is limited because of the small number of studies, which were mostly of low-quality. The only study to suggest psychological interventions improve mental health symptoms, was a small, low-quality quasi-experimental pilot study without a control group. There was no evidence to suggest psychological interventions result in fewer adverse events, however, none of the interventions appeared to cause greater harm. There was limited evidence to suggest that psychological smoking cessation interventions may be cost-effective. However, as these outcomes were reported by single studies which were of low quality, firm conclusions cannot be made. The evidence supporting the use of psychological interventions for improving mental health outcomes in smokers with depression appears inconsistent.

2.3 Impact of pharmacological interventions

Five reports were examining three different studies exploring the effect of pharmacological interventions on smoking cessation and mental health outcomes (Anthenelli et al, 2013; Ayers et al, 2019; Cinciripini et al, 2022; Doran et al, 2019; Evins et al, 2008). Four reports were of two studies two studies conducted internationally across the EU and USA (Anthenelli et al, 2013; Anthenelli et al, 2016), and one study was conducted in the USA alone (Evins et al, 2008). One study was considered high quality (Anthenelli et al, 2013), while the remaining

studies were considered low quality. Four reports focused on participants with depression, and one on participants with anxiety (Ayers et al, 2019). Findings in relation to the effectiveness of the interventions appear mixed.

2.3.1 Varenicline

The effect of Varenicline on smoking cessation was assessed by two studies reported by four reports. Anthenelli et al (2013) and Doran et al (2019) both evaluated smoking abstinence and changes in mood and anxiety levels in smokers with depression treated with Varenicline versus placebo. All participants received smoking cessation counselling, however the effects of Varenicline were compared to a control group which received a placebo. A dose of 1mg of Varenicline was taken twice daily, or placebo, over 12-weeks.

Ayers et al (2019) and Cinciripini et al (2022), reported findings from the EAGLES trial (Anthenelli et al, 2016) comparing the safety and efficacy of Varenicline, Bupropion, NRT, and placebo over 12-weeks. The study administered a dose of 1mg of Varenicline twice daily, 150mg of Bupropion twice daily, or transdermal nicotine patch (NRT) at a dose of 21 mg/day with taper, plus weekly cessation counselling for 12 weeks. The outcomes for each pharmacological intervention were compared with participants in a control group who received smoking cessation counselling and a placebo.

Smoking abstinence

- Results reported by Anthenelli et al (2013) showed **7-day point prevalence abstinence (PPA) rates were higher for participants who received Varenicline compared to placebo across all time points; week 12; 46.1% vs. 20.1% (OR 3.82, 95% CI 2.53 to 5.78, p<0.001), week 24; 31.3% vs. 18.2% (OR 2.16 95% CI, 1.40 to 3.33, p<0.001), and week 52; 28.5% vs. 17.5% (OR 1.98, 95% CI 1.28 to 3.08, p=0.002)**. In addition, **continuous abstinence rates were also higher at every time point for those in the Varenicline group compared to placebo; weeks 9 to 12; 35.9% vs. 15.6% (OR 3.35, 95% CI 2.16 to 5.21, p<0.001), weeks 9 to 24; 25.0% vs. 12.3% (OR 2.53, 95% CI 1.56 to 4.10, p<0.001), and weeks 9 to 52; 20.3% vs. 10.4% (OR 2.36 95% CI 1.40 to 3.98, p<0.001)**.

- Doran et al (2022) was a secondary analysis of Anthenelli et al (2013) and sought to assess the impact of baseline depressive symptoms on abstinence. The results showed at the mean level of baseline depressive symptoms, **participants who received Varenicline were nearly four times more likely to achieve continuous abstinence than those who received the placebo at weeks 9-12 (OR 3.91, 95% CI 2.54% to 6.34%, p<0.001)**. In addition, higher baseline symptoms of depression were associated with significantly lower likelihood of abstinence for the placebo group (OR 0.91, 95% CI 0.85% to 0.97%, p=0.004), but not the Varenicline group (OR 0.99, 95% CI 0.95% to 1.03%, p=0.568). For PPA outcomes, between 13-52 weeks measurement, significant treatment (z= 5.88, p<0.001) and treatment by time (z = −3.28, p=0.001) effects indicated an initial advantage of Varenicline which faded over the 52-weeks, however, PPA rates remained greater in the Varenicline group compared to placebo throughout.

- Ayers et al (2019) reported findings from a subgroup analysis of participants with anxiety from the EAGLES trial (Anthenelli et al, 2016). The results showed **7-day PPA rates were higher for participants with anxiety who received Varenicline compared to placebo at week 12 (OR 4.65, 95% CI 1.95 to 1.11), and week 24**

(OR 3.13, 95% CI 1.28 to 7.62). **Seven-day PPA rates were also higher for participants with anxiety who received Varenicline compared to Bupropion (OR 2.80, 95% CI 1.22 to 6.44), and NRT (OR 2.32, 95% CI 1.04 to 5.17) at week 12**, but there was no significant difference at week 24. **Continuous abstinence rates at weeks 9-12 were also greater for participants with anxiety who received Varenicline compared to placebo (OR 4.53, 95% CI 1.20 to 17.10)**. There were no significant effects in favour of Bupropion or NRT in any comparisons for participants with anxiety.

- Cinciripini et al (2022) reported findings from a subgroup analysis of participants with depression versus those without a psychiatric disorder from the EAGLES trial (Anthenelli et al, 2016). The results showed that **compared to placebo, continuous abstinence rates were higher for participants with depression who received Varenicline at weeks 9-12 (OR 3.004, 95% CI 2.081 to 4.336) and weeks 9-24 (OR 2.396, 95% CI 1.561 to 3.678). Compared to Bupropion, odds of continuous abstinence were greater for Varenicline at weeks 9-12 (OR 1.551, 95% CI 1.118 to 2.152)** but not at weeks 9-24 (OR 1.295, 95% CI 0.888 to 1.890). **compared to NRT, odds of continuous abstinence were greater for Varenicline at weeks 9-12 (OR 1.589, 95% CI 1.146 to 2.202) and weeks 9-24 (OR 1.574, 95% CI 1.066 to 2.325)**.

Mental health

- Anthenelli et al (2013) measured changes in anxiety and depression symptoms amongst participants and found no significant differences between groups. Both groups saw similar changes which trended toward a slight improvement, but values were not given within the study. Furthermore, there were no clinically relevant differences between groups in suicidal ideation or behaviour, and there was no worsening of anxiety or depression.

Adverse events

- Anthenelli et al (2013) reported treatment-emergent adverse events, defined as events which occurred either during treatment, or up to 30-days post-treatment. Adverse events included sleep, anxiety, depression and mood, personality and behaviour, physical activity, and suicide and self-harm events. Adverse events occurred in 72.3% of Varenicline participants and 66.9% of placebo participants, most were rated as mild or moderate, the most frequent adverse event was nausea (Varenicline, 27.0%; placebo, 10.4%). Adverse events led to treatment discontinuation in 6.3% and 7.8% of Varenicline and placebo participants, respectively, however, inferential statistics were not reported within the study to determine whether these differences were statistically significant.

2.3.2 Bupropion

Evins et al (2008) sought to determine if Bupropion improved abstinence rates when added to transdermal NRT and group CBT. The intervention was delivered over 13-weeks, and comparison were made with a control consisting of the same NRT and CBT with a placebo. Cinciripini et al (2022), compared the findings for participants who received Bupropion compared to those who received the placebo control in the EAGLES trial (Anthenelli et al, 2016). The comparisons were made in a subgroup analysis of participants with depression versus those without a psychiatric disorder.

Smoking abstinence

- Results reported by Evins et al (2008) showed that the 7-day PPA rate was higher for participants who received Bupropion in addition to CBT and NRT compared to the control group, but the difference was not statistically significant; 36% (37/97), vs 31% (32/102), p=0.49.

- Results reported by Cinciripini et al (2022) showed that **compared to placebo, odds of continuous abstinence were also greater for participants with depression who received Bupropion at weeks 9-12 (OR 1.936, 95% CI 1.321 to 2.838) and weeks 9-24 (OR 1.85 95% CI 1.188 to 2.881),**

2.3.3 Nicotine replacement therapy

As well as comparing the effect of Varenicline and Bupropion compared to placebo, Cinciripini et al (2022) also reported the effect of NRT compared to placebo in a sub-group analysis of participants with depression versus those without a psychiatric disorder from the EAGLES trial (Anthenelli et al, 2016).

Smoking abstinence

- The results reported by Cinciripini et al (2022) showed that **compared to placebo, odds of continuous abstinence for participants who received NRT were only significantly greater at weeks 9-12 (OR 1.891, 95% CI 1.291 to 2.770), but not** weeks 9-24 (OR 1.522, 95% CI 0.967 to 2.396)**.**

Adverse events

- Anthenelli et al (2013) reported treatment-emergent adverse events as part of the EAGLES trial, defined as events which occurred either during treatment, or up to 30-days post-treatment. Adverse events included sleep, anxiety, depression and mood, personality and behaviour, physical activity, and suicide and self-harm events. Adverse events occurred in 72.3% of Varenicline participants and 66.9% of placebo participants, most were rated as mild or moderate, the most frequent adverse event was nausea (Varenicline, 27.0%; placebo, 10.4%). Adverse events led to treatment discontinuation in 6.3% and 7.8% of Varenicline and placebo participants respectively, however, inferential statistics were not reported within the study to determine whether these differences were statistically significant.

- Ayers et al (2019) also reported adverse events from the EAGLES trial (Anthenelli et al, 2016) and the results showed that participants with generalised anxiety disorder had an increased incidence of moderate-to severe neuropsychiatric adverse events compared to non-psychiatric smokers (5.4% vs 2.1%, p=0.0012), but there were no significant differences in moderate to severe neuropsychiatric adverse events between treatment groups.

- Cinciripini et al (2022) also reported adverse events from the EAGLES trial (Anthenelli et al, 2016), and the results showed that the risk of neuropsychiatric adverse events did not differ by medication in participants with depression (p>0.05).

Bottom line results for pharmacological interventions

There is very low certainty evidence to suggest that pharmacological interventions may be effective at improving smoking cessation outcomes, although the evidence was mostly low

quality. Most of the available evidence focuses on interventions for people with depression, as only one study analysed the effects in participants with anxiety disorders. Each study that evaluated the impact of interventions which used Varenicline reported statistically significant improvements in cessation outcomes, and some of the evidence suggests Bupropion and NRT were also effective, although the evidence was mixed, and particularly limited for NRT.

The evidence supporting the use of pharmacological interventions for improving mental health symptoms in smokers is lacking. It is worth noting that this outcome was examined by only one study. In addition, there was no evidence to suggest that pharmacological interventions resulted in fewer adverse events, but neither was there any evidence to suggest they cause greater harm.

2.4 Impact of aerobic exercise-based interventions

Two studies assessed the impact of aerobic exercises of varying intensities on smoking cessation and mental health (Abrantes et al, 2023; Patten et al, 2017). Both studies were RCTs conducted in the USA and included participants with depression. One study was considered high quality (Abrantes et al, 2023), while the other was considered low quality. Findings in relation to the impact of the interventions appear mixed.

Smoking abstinence

- Abrantes et al (2023) tested the efficacy of a 12-week moderate intensity aerobic exercise intervention compared to a health education contact as an adjunct to standard smoking cessation treatment in individuals with depression. Study findings reported no significant differences in 7-day point prevalence abstinence (PPA) between groups at follow up (OR 0.78; 95% CI 0.32 to 1.94; p=0.60).

- Patten et al (2017) conducted a pilot study to evaluate the potential role of supervised vigorous exercise as a smoking cessation intervention for depressed female smokers. Study participants were randomly assigned to 12 weeks of thrice weekly exercise or health education, with both groups receiving behavioural smoking cessation counselling and NRT. The study found that **after 12 weeks, smoking abstinence rates were significantly higher for participants who received the exercise intervention compared to the health education group (73% [11/15]) vs 33% [5/15]); $\chi 2 = 4.821$, df= 1, p=0.028)**. At 6-months follow-up, there was no statistically significant differences in abstinence rates between groups (27% [4/15] for the exercise condition vs.40% [6/15] for health education; $\chi 2 = .600$, df= 1, p=0.439).

Mental health

- Abrantes et al (2023) measured changes in depressive symptoms using the CES-D scale and reported no significant differences between participants who received the aerobic exercise intervention and those who received health education (b = -0.84; 95% CI −3.25 to 1.57; p=0.49).

- Patten et al (2017) measured change in depressive symptoms using the PHQ-9 scale and reported no significant differences at 12 weeks between groups receiving either the exercise intervention or health education (p=0.90).

2.4.1 Bottom line results for exercise-based interventions

There is very low certainty evidence that suggests exercise interventions as adjuncts to standard smoking cessation treatments in individuals with depression may not be effective. Only two studies evaluating exercise interventions were identified, both of which had contrasting findings in relation to smoking abstinence, and neither study was of high quality. Exercise interventions did not demonstrate any positive impact on alleviating depressive symptoms.

2.5 Impact of multicomponent interventions comprising of pharmacological and psychological components

Two studies investigated the effect of a combination of pharmacological and psychological interventions on smoking cessation and mental health outcomes (Dahne et al, 2023; Hitsman et al, 2023). Both studies were RCTs conducted in the USA and recruited participants with depression. Findings appear to be in support of the interventions.

2.5.1 Behavioural activation mobile phone application with nicotine replacement therapy

Dahne et al (2023) assessed the efficacy of the Goal2Quit intervention, a behavioural activation-based self-directed mobile phone application for treating depression and quitting smoking. This was combined with a two-week course of NRT, including 14mg nicotine patches and 4mg nicotine lozenges. The control group received digital copy of the National Cancer Institute's "Clearing the Air: Quit Smoking Today" booklet.

Smoking abstinence

- The study findings reported by Dahne et al (2023) showed that **both 7-day point prevalence abstinence (PPA) and floating abstinence were significantly higher for Goal2Quit participants at 4- 8- and 12-weeks follow-up compared to control**. **At 12-weeks**, **the 7-day PPA rate was 16% vs 2% (p=0.02), and the floating abstinence rate was 24% vs 4% (p=0.003)**.

Smoking reduction

- Dahne et al (2023) measured self-reported 24-hour quite attempts, and number of cigarettes smoked per day. **Goal2Quit participants were more likely to have made a 24-hour quit attempt during the first 4- (17% vs 2%; p=0.01), 8- (24% vs 4%; p=0.003), and across all 12- (29% vs 6%; p=0.002) weeks follow-up**. Participants in the **Goal2Quit group also reported smoking less cigarettes per day than the treatment as usual group (difference of mean 1.97, SE 0.93 CPD less; p=0.03)**.

Mental health

- Dahne et al (2013) measured change in depressive symptoms using the BDI-II scale and reported that depressive symptoms decreased in both groups, but **the Goal2Quit group reported significantly lower average depressive symptoms compared to the treatment as usual group (difference of mean 3.72, SE 1.37 points less for Goal2Quit; p=0.01)**. In comparison to 14 participants from the treatment as usual group, 23 Goal2Quit participants reported worsening mood over the course of the treatment, but four participants of the Goal2Quit group endorsed suicidality, compared to seven in the treatment as usual group. Inferential statistics were not given to determine whether they were statistically significant.

2.5.2 Behavioural activation with Varenicline

Hitsman et al (2023) measured the efficacy and safety of combining 12-weeks of behavioural activation for smoking cessation and Varenicline for smokers with depression. There were four comparator groups: behavioural activation for smoking cessation with Varenicline or a placebo, and standard behavioural treatment and Varenicline or a placebo.

Smoking abstinence

- Results reported by Hitsman et al (2023) showed **that abstinence rates at 27-weeks were higher in participants in the two groups who received Varenicline compared to placebo, rate ratio (RR) 2.16 (95% CI 1.08 to 4.30, p=0.0277)**. Continuous abstinence rates were similar between groups, however, prolonged abstinence over 14- and 27-weeks favoured the Varenicline arms, although significance values were not reported.

Mental health

- Hitsman et al (2023) measured changes in depressive symptoms using the BDI-II scale, and results showed no statistically significant differences in depression levels among treatment arms at any of the follow-up timepoints (p>0.05).

Adverse events

- Hitsman et al (2023) reported adverse events and resulted showed that **at 6 weeks, statistically significant differences were reported with the placebo group experiencing more sleep problems (p=0.035) than those receiving Varenicline. At 14-weeks statistically significant differences were also reported with the placebo group experiencing increased rates of dry mouth (p=0.009) and anxiety (p=0.023**).

2.5.1 Bottom line results for multicomponent interventions (pharmacological and psychological)

There is very low certainty evidence to suggest that multicomponent interventions comprising of pharmacological and psychological components may be effective at improving smoking cessation outcomes in people with depression. However, the evidence supporting the use of these interventions in improving depressive symptoms and adverse events is limited, in particular for adverse events which was only reported by a single study.

2.6 Impact of multicomponent interventions comprising of exercise and psychological intervention components

One study examined the use of a multicomponent intervention comprising of an exercise and behavioural component (Bernard et al, 2015). This study was a pilot RCT conducted in France and focused on smokers with depression. It was considered low quality, and the findings did not favour the intervention.

Smoking abstinence

- Bernard et al (2015) sought to estimate the effects of adding exercise and counselling to standard smoking cessation treatment (consisting of NRT or Varenicline), for smokers with depressive disorders, compared to a health education control. The study results showed that although at 12-weeks from baseline continuous abstinence rates were higher in the experimental group (48.5% (17/35) vs 28.5% (10/35); $\chi 2(7) = 2.95$, p=0.08), there was no statistically significant difference

between groups at any time-point, and no significant differences in continuous abstinence rates were detected.

Smoking reduction

- Bernard et al (2015) measured the number of self-reported cigarettes smoked per day and found no significant between-group differences in the number of cigarettes smoked per day between participants who received exercise and counselling intervention, compared to participants in the control group**.**

Mental health

- Bernard et al (2015) measured change in depressive and anxiety symptoms at weeks 8, 12, 24 and 52 using the HADS scale, but there were no significant differences in depressive or anxiety symptoms at any time point.

2.6.1 Bottom line results for multicomponent interventions (exercise and psychological)

There is very low certainty evidence that suggest multicomponent interventions comprising of exercise and psychological interventions may not be effective at improving smoking cessation in individuals with depression. However, the evidence is limited as only one, low quality study (a pilot RCT) was identified, and this did not show any significant differences for smoking cessation or mental health outcomes.

Table 2. Summary of interventions

Citation (Country)	Name and type of intervention/control	Intervention characteristics
Psychological interventions (n=3 studies from n=5 reports)		
Heffner et al, (2019) **USA**	**Intervention:** Actify!, a Behavioural Activation Treatment for Depression (BAT-D) app along with SmokefreeTXT (a text messaging programme) **Control:** No control, comparisons with baseline scores	**Setting:** Not stated **Mode of delivery:** The frequency and duration of use of the app was up to the participants, follow-up was conducted over 6 weeks **Duration:** 6 weeks
Weidberg et al, (2018), Secades-Villa et al, (2019), González-Roz et al, (2021) **Spain**	**Intervention:** Cognitive Behavioural Therapy (CBT) and Behavioural Activation (BA) and Contingency Management (CM). CM patients received a voucher-based abstinence reinforcement intervention. **Control:** CBT and BA	**Setting:** Research clinics **Mode of delivery:** All treatment conditions were delivered in groups of maximum four patients, over eight continuous weeks. **Duration:** 8 Weeks
van der Meer et al (2010) **Netherlands**	**Intervention:** A mood management intervention (consisting of CBT) and telephone counselling **Control:** Telephone counselling.	**Setting:** Remote Dutch national smoking cessation Quitline. **Mode of delivery:** remote telephone calls **Duration:** 3 months
Pharmacological interventions (n=3 studies from n=5 reports)		
Anthenelli et al, (2013) **Doran et al, (2019)** **Multi-national (8 countries)**	**Intervention:** Varenicline with smoking cessation counselling **Control:** Placebo with smoking cessation counselling	**Setting:** Academic clinical trial centres and smoking cessation clinics **Mode of delivery:** Varenicline, 1 mg twice daily, or placebo for 12 Weeks. Clinic visits every week during treatment and at weeks 13, 16, 24, 32, 40 and 52 during follow-up, Telephone visits occurred at weeks 14, 20, 28, 36, 44 and 48 during follow-up. **Duration:** 12 weeks
Ayers et al, (2019) **Cinciripini et al (2022)** **Multi-national (16 countries)**	**Intervention:** EAGLES trial. Participants received either Varenicline 1 mg twice daily, Bupropion 150 mg twice daily, or transdermal nicotine patch (NRT) 21 mg/day with taper, plus weekly cessation counselling for 12 weeks. **Control:** Placebo with counselling for 12 weeks.	**Setting:** follow-up done at 140 centres (clinical trial centres, academic centres, and outpatient clinics) **Mode of delivery:** Treatment was administered in a double-blind, triple-dummy fashion (i.e., participants received one active and two placebo medications, or three placebo medications). **Duration:** 12 weeks
Evins et al, (2008) **USA**	**Intervention:** Pharmacological (Bupropion) added to NRT and CBT **Control:** Placebo added to NRT and CBT	**Setting:** Not stated **Mode of delivery:** All subjects received 13 sessions of group CBT, 8 weeks of NRT and 12 weeks of either Bupropion-SR or identical placebo during the 13-week acute treatment phase. **Duration:** 13 weeks
Exercise interventions (n=2)		
Abrantes et al, (2023)	**Intervention:** Aerobic exercise (AE) plus smoking cessation counselling and NRT	**Setting:** Not stated where the interventions or smoking cessation counselling was delivered.

USA	**Control:** Health education contact plus smoking cessation counselling and NRT	**Mode of delivery:** 12 weekly AE group sessions supervised by an exercise physiologist plus a home-based exercise prescription or 12 weekly group education sessions facilitated by a postdoctoral level clinician. **Duration:** 12 weeks
Patten et al (2017) **USA**	**Intervention:** Exercise and cessation counselling **Control:** Health education and cessation counselling	**Setting:** In-person screening at clinic. The exercise intervention was mainly implemented in a community YMCA setting, 4 sessions were conducted at a worksite fitness centre. **Mode of delivery:** The 12-week programme comprised three 30–40-minute individual-based sessions per week delivered by wellness coaches. At one session each week for 12 weeks, participants received 15–20 minutes of smoking cessation counselling delivered by their health education or exercise wellness coach. **Duration:** 12 weeks
Multicomponent (pharmacological and psychological interventions) (n=2)		
Dahne et al, (2023) **USA**	**Intervention:** Behavioural Activation-based self-directed mobile app intervention (Goal2Quit), a mobile app providing behavioural strategies for treating depression and quitting smoking. Paired with a mailed 2-week sample of NRT of 14 mg nicotine patches and 4 mg nicotine lozenges. **Control:** Treatment as usual (TAU) participants received a digital copy of the National Cancer Institute's "Clearing the Air: Quit Smoking Today" booklet.	**Setting:** All study procedures were delivered fully remotely. **Mode of delivery:** participants completed follow-up assessments in REDCap (Research Electronic Data Capture) weekly for 8 weeks with an additional final follow-up at 12 weeks. **Duration:** 8 weeks
Hitsman et al, (2023) **USA**	**Intervention: 2x2 design** Behavioural activation for smoking cessation (BASC) and Varenicline BASC and placebo Standard behavioural treatment (ST) and Varenicline **Control:** ST and placebo	**Setting:** Research clinics at Northwestern University, Chicago. **Mode of delivery:** 8 45-minute sessions between weeks 1 and 12, occurring weekly for the first 4 weeks and every other week for the last 8 weeks. Except for sessions 1 and 3 TQD (target quit date), treatment was delivered by telephone. Participants submitted their completed between-session assignments to study therapists using web-based forms, by e-mail/fax or by telephone. **Duration:** 14 weeks
Multicomponent (exercise and psychological interventions) (n=1)		
Bernard et al, (2015) **France**	**Intervention:** standard smoking cessation treatment (nicotine replacement therapy or Varenicline) plus exercise and counselling **Control:** standard treatment (nicotine replacement therapy or Varenicline) plus a time-to-contact control intervention on health education	**Setting:** Montpellier University Hospital in France. **Mode of delivery:** Both programs involved 10 group sessions over 8 weeks. **Duration:** 8 weeks

Table 3. Summary of the evidence*

Intervention *Outcome* [No. of studies]	Findings	Limitations	Imprecision	Indirectness	Inconsistency	Certainty
		Risk of bias from critical appraisal checklist	Eg precision of results, width of confidence interval	Do majority of studies address PICO directly	Variation in findings across studies (eg CIs don't overlap	⊕⊖⊖⊖ very low ⊕⊕⊖⊖ low ⊕⊕⊕⊖ moderate ⊕⊕⊕⊕ high
Smoking cessation						
Psychological interventions *Smoking abstinence* [3 studies from 5 reports]	Positive (González-Roz 2021, Secades-Villa 2019, Weidberg 2018)*, Heffner 2019** Neutral van der Meer 2010***	Four low quality (González-Roz 2021, Heffner 2019, Secades-Villa 2019, Weidberg 2018 One high quality van der Meer 2010	Similar outcome measures, only one study provided CIs	Yes	Findings generally favoured the interventions, but one study was uncontrolled, and another had inconsistent findings	⊕⊖⊖⊖ very low
Psychological interventions *Smoking reduction* [1]	Neutral Weidberg 2018	One low quality Weidberg 2018	One outcome measure, no CIs provided	Yes	Limited evidence and findings did not favour the intervention	⊕⊖⊖⊖ very low
Pharmacological interventions *Smoking abstinence* [3 studies from 5 reports]	Positive (Anthenelli 2013 & Doran, 2019) (Ayers 2019 & Cinciripini 2022) Neutral Evins 2008	Four low quality Ayers 2019, Cinciripini 2022, Doran 2019, Evins 2008 One high quality Anthenelli 2013	Similar outcomes, CIs provided for all studies except one; provided for all studies showing positie effect	Yes	Outcomes mostly favoured the interventions and were mostly statistically significant	⊕⊖⊖⊖ very low
Exercise-based interventions *Smoking abstinence* [2]	Positive Patten 2017**** Neutral Abrantes 2023	One low quality Patten 2017 One moderate quality Abrantes 2023	Similar outcome measures, CIs provided for one study	Yes	Findings did not favour the intervention, except for shorter-term follow-up in one study	⊕⊖⊖⊖ very low
Pharmacological and psycological interventions *Smoking abstinence* [2]	Positive Dahne 2023, Hitsman 2023	Two low quality Dahne 2023, Hitsman 2023	Similar outcome measures, CIs provided by one study	Yes	Similar outcomes and findings favoured the intervention and were statistically significant	⊕⊖⊖⊖ very low
Pharmacological and psycological interventions *Smoking reduction* [1]	Positive Dahne 2023	One low quality Dahne 2023	One outcome measure, no CIs provided	Yes	Limited evidence but findings favoured the intervention and were statistically significant	⊕⊖⊖⊖ very low
Exercise and psycological interventions *Smoking abstinence* [1]	Neutral Bernard 2015	One low quality Bernard 2015	One outcome measure, CIs provided	Yes	Limited evidence and findings did not favour the intervention	⊕⊖⊖⊖ very low

Exercise and psychological interventions *Smoking reduction* [1]	Neutral Bernard 2015	One low quality Bernard 2015	One outcome measure, no CIs provided	Yes	Limited evidence and findings did not favour the intervention	⊕⊖⊖⊖ very low
Mental health						
Psychological interventions *Depressive symptoms* [3]	Positive Heffner 2019 Neutral Secades-Villa 2019, van der Meer 2010	Two low quality Heffner 2019, Secades-Villa 2019 One high quality van der Meer 2010	Similar outcome measures, one study provided CIs	Yes	Findings from one small pre-post study reported positive effects, but findings did not support intervention effectiveness in 2 RCTs	⊕⊖⊖⊖ very low
Pharmacological interventions *Depressive symptoms* [1]	Neutral Anthenelli 2013	One high quality Anthenelli 2013	One outcome measure, no CIs provided	Yes	Limited evidence and findings did not favour the intervention	⊕⊖⊖⊖ very low
Pharmacological interventions *Anxiety symptoms* [1]	Neutral Anthenelli 2013	One high quality Anthenelli 2013	One outcome measure, no CIs provided	Yes	Limited evidence and findings did not favour the intervention	⊕⊖⊖⊖ very low
Exercise-based interventions *Depressive symptoms* [2]	Neutral Abrantes 2023, Patten 2017	One low quality Patten 2017 One moderate quality Abrantes 2023	Similar outcomes, CIs provided by one study	Yes	Similar outcome measures, but findings did not favour the intervention	⊕⊖⊖⊖ very low
Pharmacological and psycological interventions *Depressive symptoms* [2]	Positive Dahne 2023 Neutral Hitsman 2023	Two low quality Dahne 2023, Hitsman 2023	Similar outcome measures, no CIs provided	Yes	Similar outcome measures but findings were mixed, favouring the intervention in one but not the other	⊕⊖⊖⊖ very low
Exercise and psychological interventions *Depressive symptoms* [1]	Neutral Bernard 2015	One low quality Bernard 2015	One outcome measure, no CIs provided	Yes	Limited evidence but findings did support intervention effectiveness	⊕⊖⊖⊖ very low
Exercise and psycological interventions *Anxiety symptoms* [1]	Neutral Bernard 2015	One low quality Bernard 2015	One outcome measure, no CIs provided	Yes	Limited evidence and findings did not favour the intervention	⊕⊖⊖⊖ very low
Adverse events						
Psychological interventions *Adverse events* [1]	Neutral Heffner 2019	One low quality Heffner 2019	One outcome, no CIs provided	Yes	Limited evidence and findings did not favour the intervention	⊕⊖⊖⊖ very low
Pharmacological interventions *Adverse events* [2 studies from 3 reports]	Neutral Anthenelli 2013, (Ayers 2019, Cinciripini 2022)	Two low quality Ayers 2019, Cinciripini 2022 One high quality Anthenelli 2013	A range outcomes from mild to severe adeverse events, no CIs provided	Yes	A range of outcomes, most findings did not favour the intervention, one RCT showed fewer adverse	⊕⊖⊖⊖ very low

					events favouring the intervention	
Pharmacological and psycological interventions [1]	Positive Hitsman 2023	One low Hitsman 2023	A range of adverse events, no CIs provided	Yes	Limited evidence, but findings were statistically significnat and favoured the intervention	⊕⊖⊖⊖ very low
Cost-effectiveness						
Psychological interventions *Cost-effectiveness* [1]	Positive González-Roz 2021	One low quality González-Roz 2021	One outcome measure	Yes	Limited evidence but findngs support intervention cost-effectiveness	⊕⊖⊖⊖ very low

*This table is based on the GRADE evidence profile (Guyatt et al, 2011), which has been adapted for the purpose of this review.

Footnotes:
*Reports presenting findings from the same study are grouped in brackets
** Neutral for 7-day PPA at 6- and 12-months, but positive for prolonged abstinence
*** Neutral for abstinence rates at 6-months follow-up
**** In favour of the intervention but the study was uncontrolled
Abbreviations:
CI Confidence interval; N/A Not applicable; PICO Population, Intervention, Comparison and Outcomes

3. DISCUSSION

3.1 Summary of the findings

This rapid review aimed to identify and synthesise the evidence for the effectiveness of smoking cessation interventions in people with anxiety or depression living in the community. There is some, mostly low quality, evidence to suggest that smoking cessation interventions may be effective at improving a range of smoking cessation and mental health outcomes in people with depression. Only one study was identified assessing smoking cessation interventions in people with anxiety meaning conclusions about the evidence of effectiveness cannot be drawn. Psychological interventions may increase abstinence in smokers with depression, but results were mixed regarding their impact on mental health outcomes. Pharmacological interventions, particularly Varenicline, appear effective for smoking cessation in people with depression and anxiety. However, evidence for Bupropion and NRT is limited and mixed. Findings generally did not support the effectiveness of exercise interventions for smoking cessation, and no sustained benefits or improvements in depressive symptoms were identified. Although the evidence was limited, none of the studies suggested that the interventions caused greater harm than the smoking cessation treatment received by the control group. Delivering interventions as part of a multicomponent approach may be beneficial, but methodological limitations and variation in intervention types and outcome measures across studies compromise the applicability of these findings. Further research with rigorous methodologies is needed to provide clearer guidance on effective smoking cessation strategies for this population.

3.2 Strengths and limitations of the available evidence

A strength of the available evidence is the identification of a wide range of smoking cessation interventions. However, the considerable heterogeneity across studies makes it difficult to compare interventions directly and limits the overall certainty of the evidence base.

Variation in recruitment strategies raises questions about the similarities of participants across the included studies. Furthermore, inconsistency in diagnostic tools and cut-offs scores for inclusion hinders comparisons of depression severity and intervention effectiveness across studies.

The rapid review identified limited, low-quality evidence for smoking cessation interventions in individuals with anxiety or depression. Most studies lacked methodological rigor and were poorly reported. Only two RCTs were deemed high quality, while industry funding and involvement in five studies raised concerns about potential bias. Although 11 studies were identified, three were small pilot studies. These pilot studies, while potentially valuable for informing future research directions, were not powered sufficiently to detect intervention effectiveness due to their limited sample sizes. Additionally, seven reports were secondary analyses of three primary studies. Although secondary analyses may provide data from original studies with greater relevance to the research question (e.g., depression sub-group analysis), they may not be sufficiently powered and there is potential for overlap of participants across reports. If multiple reports draw data from the same original study population, this can inflate the overall sample size but not necessarily represent new data or a broader participant pool. Furthermore, data is limited by the original studies' research questions and data collection methods. These limitations might mean the data wasn't specifically collected to answer questions related to smoking cessation interventions for individuals with anxiety or depression.

Several studies included in this rapid review involved interventions being assessed as an addition to existing smoking cessation treatment which was received by all participants. It is important to consider that the relative effect of the intervention compared to the control may be diminished due to the underlying smoking cessation treatment received by all participants. While examining the effect of an intervention as an addition to existing treatment allows for an assessment of specific intervention components, the underlying treatment received by all participants likely affects the overall findings.

Several evidence gaps were identified. Notably, none of the included studies were conducted within the UK. This absence of recent UK-based research limits our understanding of how these interventions might translate to the specific healthcare system and cultural context of the Wales. Although no published UK studies met our criteria, a protocol for a UK-based smoking cessation intervention for smokers with depression was identified. This study, currently under review for publication in the Addiction journal (ISRCTN99531779; https://doi.org/10.1186/ISRCTN99531779), is especially pertinent to this rapid review as it explores smoking cessation support integrated into routine psychological care within the UK. Additionally, the review identified gaps relating to barriers and facilitators to smoking cessation interventions, and the populations studied. Only one study focused on participants with anxiety disorders. No studies reported co-existing mental health conditions, which would have provided a more nuanced understanding of intervention effectiveness within this population. These limitations suggest a need for caution when generalising the findings to broader populations.

This rapid review found no evidence on equity factors and intersectionality. Included studies did not consider how socioeconomic factors, ethnicity, or social capital affect access and success of interventions. Understanding these complexities is essential for developing inclusive and equitable smoking cessation programs.

Additionally, the rapid review found no studies investigating harm reduction approaches, and limited research reporting interventions applied at critical touchpoints within healthcare systems and smoking cessation services (where targeted interventions could reach the review's included population), or interventions that integrate with existing healthcare pathways or mental health services.

This rapid review identified no studies evaluating the effectiveness and safety of e-cigarettes as a smoking cessation or harm reduction tool for people with anxiety or depression. This highlights an absence of research on e-cigarettes as a smoking cessation or harm reduction aid in our population of interest. E-cigarettes have become a popular alternative to traditional cigarettes, potentially offering a route to harm reduction or smoking cessation for smokers with depression or anxiety. Despite their potential benefits, the rising prevalence of e-cigarette use among non-smokers, particularly children and young people, raises concerns which requires further investigation.

Only one study included in this rapid review analysed intervention cost-effectiveness, which investigated the one-year cost-effectiveness of adding contingency management to cognitive-behavioural treatment and behavioural activation for quitting smoking in smokers with depression in Spain. Despite reporting positive outcomes however, we cannot comprehensively assess the cost-effectiveness of such interventions due to insufficient evidence.

3.3 Strengths and limitations of this Rapid Review

The studies included in this rapid review were systematically identified through an extensive search of electronic databases and grey literature. The review was also based on an abbreviated systematic review approach, following established guidelines for conducting rapid reviews in an attempt to capture all relevant publications with minimal risk of bias in a timely manner.

Due to the short timeframe to complete this rapid review, as well as the large number of references initially identified from literature searches, most reports were screened by a single reviewer at title and abstract level. However, 558 references (14%) were double screened to assess consistency. The remaining stages of the review process included consistency checking by at least one other reviewer, with issues being discussed and resolved within the team.

A key strength of this rapid review is its focus on using rigorous participant selection criteria for identifying relevant studies. Studies were only considered eligible if they recruited participants using validated measurement tools for depression and anxiety, and specific cut-off points, depending on the tool used. This approach enabled us to include people with a clinical diagnosis already within the healthcare system, and those who should be but are not currently in the system. Although these two groups may have different needs and respond differently to smoking cessation interventions, we were able to capture a more comprehensive picture of the effectiveness of these interventions within a population accessing the healthcare system.

However, limitations exist. It is important to note that many studies excluded participants who were currently prescribed medication for depression or anxiety. This exclusion may have inadvertently left out individuals who are currently within the healthcare system and who may have responded differently to the intervention than those included in the study.

We excluded primary studies that investigated intervention effectiveness by comparing those with anxiety or depression with a non-psychiatric group (see Appendix 2). This was because our rapid review focussed on people with anxiety and depression, therefore we wanted to compare effectiveness in this population only. However, including these studies may have provided a more detailed understanding of intervention effectiveness.

Furthermore, the review excluded studies relying solely on self-reported depression, potentially missing individuals who experience symptoms but lack a formal diagnosis – a potential hard-to-reach group likely to have been of interest to our stakeholders. Second, studies focusing on anxiety sensitivity were also excluded. While anxiety sensitivity is often related to anxiety disorders, we excluded studies focused on this population to maintain focus on interventions specifically targeting people with anxiety or depression, ensuring our findings provide clear conclusions relevant to these populations. Finally, the rapid review did not include studies investigating mixed mental health populations unless they provided separate analyses for participants meeting specific criteria for anxiety or depression. These limitations restrict the generalisability of the findings to a broader population struggling with co-occurring mental health challenges and potentially experiencing symptoms that fall outside the strict diagnostic categories employed in the rapid review.

3.4 Implications for policy and practice

This rapid review identified a lack of high-quality evidence assessing the effectiveness of smoking cessation interventions for individuals with anxiety or depression. However, despite this, findings identified could help to inform future intervention development and delivery in this underserved population. It is, however, important to consider the context in which the interventions outlined here were evaluated and the uncertainty of the findings as outlined in table 3.

The rapid review identified Varenicline as a potentially effective smoking cessation medication. Varenicline was manufactured by Pfizer, who withdrew it from the market in 2021. More recently, another manufacturer applied for approval from the Medicines and Healthcare products Regulatory Agency (MHRA) for a generic Varenicline. Additionally, as of 09/07/2024, a different treatment with similar action to Varenicline called Cytosine, has been recommended for use in the general population by the All Wales Medicine Strategy Group, and is expected to be available on prescription within two months.

3.5 Implications for future research

Our rapid review identified a paucity of UK-based research in this area, indicating a need for future investigations within the UK to comprehensively assess the effectiveness and generalisability of interventions, particularly within the Welsh context.

While several RCTs were identified, the risk of bias assessment revealed considerable methodological limitations. Future research should prioritise conducting high-quality research with robust methodologies to minimise bias and improve the overall certainty of the evidence base.

There is a notable gap in research on interventions for individuals with predominant anxiety disorders. Future studies should focus on tailored interventions for this population group. Additionally, our review excluded those self-reporting depression or anxiety in order to

identify a population most similar to those engaged with mental health services. Studies which included populations with mixed mental health conditions were also excluded from our review if no sub-group analyses was conducted specifically in participants with either anxiety and/or depression. However, most studies with mixed mental health populations did not perform such analyses. Therefore, future research that includes participants with a range of mental health conditions should conduct analyses to identify the effectiveness of interventions for participants with specific mental health conditions, as it is likely that their needs for support to aid quitting smoking, and the effectiveness of interventions, will vary. This will help to provide greater insight to inform policy for people with specific mental health conditions.

While the rapid review identified various interventions for smoking cessation in individuals with depression, translating efficacy trials into real-world practice remains challenging. Prioritising effectiveness trials within real-world settings is crucial for developing impactful interventions tailored to the Welsh context. In particular, policymakers need evidence-based approaches that can be incorporated into the current system in Wales, enabling them to leverage existing resources.

To strengthen research on smoking cessation interventions for individuals with depression or anxiety, standardised measurement using validated diagnostic tools is essential. Transparent reporting of eligibility criteria will facilitate comparisons to real world settings and build a more robust evidence base. Future research should also include full economic evaluations or cost-effectiveness analyses to provide insights into the financial implications of implementing these interventions within healthcare systems.

3.6 Economic considerations*

- The total economic cost of smoking in people with mental health disorders in the UK is estimated at £3.5 billion** per annum. Of this total cost, £1.1 billion** is attributed to smoking-related healthcare treatment, £1.2 billion** to absenteeism and productivity losses and £1.2 billion** to premature mortality (Wu et al., 2015).
- There is limited economic evidence on the impact of implementing smoking cessation interventions for individuals living with depression and/or anxiety.
- Economic modelling evidence suggests tailored smoking cessation interventions combining behavioural and pharmaceutical support for individuals with severe mental illness can be cost-effective compared to usual care. Severe mental illness in this study concerned any mental illness causing significant functional impairment and limits on major life activities (Mattock, Owen & Taylor, 2023).

**This section has been completed by the Centre for Health Economics & Medicines Evaluation (CHEME), Bangor University*

** Figures have been inflated to May 2024 prices using the Bank of England Inflation Calculator. These figures assume no difference in observed patterns since the original calculation.

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5. RAPID REVIEW METHODS

We searched for primary sources to answer the review question: what is the effectiveness of smoking cessation interventions for people with anxiety and/or depression living in the community.

5.1 Eligibility criteria

Table 4. Eligibility criteria

	Inclusion criteria	Exclusion criteria
Participants	Adults aged ≥18 with a current diagnosis, awaiting a diagnosis, or who met the diagnostic criteria of anxiety or depression using a validated screening tool, living in the community who smoke tobacco. Those with another mental health condition, including substance use disorder, will be included if co-occurring with anxiety or depression.	People aged <18 years. Pregnant or breastfeeding women. People with any other mental health condition, if not co-occurring with anxiety or depression. Any inpatients within mental health or other clinical settings.
Settings	Community, home, primary care, or community mental health team settings.	Any setting which isn't within the community.
Intervention / exposure	Tobacco smoking cessation interventions or harm reduction approaches delivered to people with anxiety or depression living within the community. This could include: • Interventions that are effective in the general population • Interventions that have been modified to better suit the population of interest • Interventions specifically designed for the population of interest	Interventions or harm reduction approaches which aren't delivered to people with anxiety or depression living within the community.
Control or counter intervention	No intervention, alternative population, alternative interventions, usual care.	
Outcome measures	Any outcome relating to smoking cessation or reduction, anxiety and depression, or cost-effectiveness. Facilitators and barriers if they were included as part of an evaluation.	
Study design	Clinical-effectiveness: Primary research studies which use comparative designs. Cost-effectiveness: Full economic evaluations	Primary studies which aren't comparative, qualitative studies, secondary/tertiary research.
Countries	OECD countries.	Non-OECD countries.
Language of publication	English language only.	Any other language.
Publication date	Published between 2007 and 2024.	Published before 2007.
Publication type	Published and preprint (preprint only if limited published research identified).	Commentaries, editorials, letters, conference abstracts

5.2 Literature search

A search was conducted of the electronic bibliographic databases: Medline, Embase, Scopus, and CINAHL Plus with Full Text. A search for ongoing and completed trials was conducted in Clinicaltrials.gov, and WHO International Clinical Trials Registry Platform (ICTRP). A search for grey literature was conducted of the Action on Smoking and Health (ASH) website. Citation tracking from secondary sources identified during the preliminary stages was also undertaken. All searches were conducted between 15/03/2024 and 21/03/2024. Search concepts and keywords included smoking cessation, stop smoking, smoking reduction, depression, anxiety, and terms to reflect the study designs of interest. Searches were limited to items published after 2007 – the year the smoke free legislation was introduced in Wales, and to those published in the English language.

5.3 Study selection process

All studies were uploaded to the systematic reviewing platform Rayyan for screening. For title and abstract screening, titles were screened by a single reviewer. An online random number generator was used to select a sample of 10% (n=387) of all titles, which were screened by a second reviewer to assess consistency with the first reviewer. An additional 171 titles which the first reviewer was unsure whether to include/exclude were screened by a second reviewer, therefore in total, 14% of all titles were double screened at title and abstract.

5.4 Data extraction

Data extracted was conducted by a single reviewer and was consistency checked by a second reviewer. Information extracted includes:

- Reference (author, year, country)
- Study design
- Study aim
- Intervention details (including type of intervention/duration/delivery method/setting)
- Comparator intervention/ control
- Data collection methods and dates
- Outcomes
- Sample size
- Participants
- Anxiety and/or depression diagnosis and classification method
- Smoking abstinence outcomes
- Mental health
- Adverse events outcomes
- Observation/ notes

5.5 Study design classification

A study classification algorithm was not necessary for this rapid review.

5.6 Quality appraisal

The JBI critical appraisal checklists for quasi-experimental studies (updated 2024 version) and RCTs were used to assess the methodological quality of each included study. These checklists are not designed to assign an overall score to each study.

Quality assessment was undertaken in duplicate by two independent reviewers. Any discrepancies were discussed and resolved between reviewers. The quality assessment of individual studies can be seen in section 6.3.

5.7 Synthesis

Data was synthesised narratively to provide a collective interpretation of the evidence.

5.8 Assessment of body of evidence

To assess the body of evidence, findings for each category of interventions were grouped into smoking abstinence outcomes, smoking reduction outcomes, mental health outcomes, adverse events, and cost-effectiveness. The overall quality of studies reporting each outcome was considered in addition to the consistency of study findings in favour of the intervention, to assess whether the certainty of the evidence was considered very low, low, moderate or high.

6. EVIDENCE

6.1 Search results and study selection

A total of 7,778 records were retrieved which were managed in Endnote 20. Following deduplication, 3,867 records remained. The search strategy for Medline is available in appendix 1. A total of 140 articles were screened at full text by two independent reviewers, and any conflicts were discussed and resolved within the team. A visual representation of the flow of studies throughout the review can be found in Figure 1.

Eleven studies reported in 15 publications (reports) were include in the rapid review. Ten of the 11 studies were RCTs, and one was a quasi-experimental uncontrolled before and after pilot study.

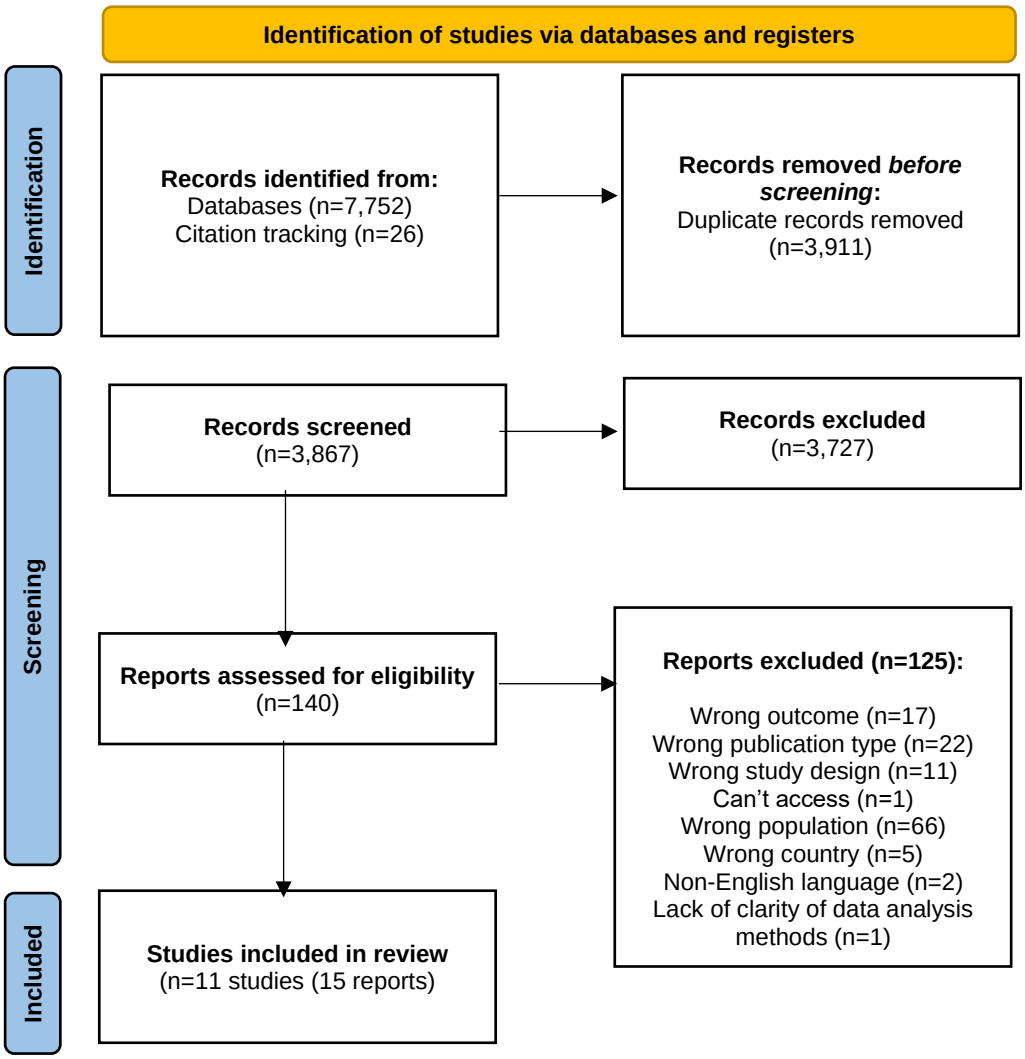

Figure 1. PRISMA flow diagram

6.2 Data extraction

Table 5. Summary of included studies

Citation (Country)	Study Details	Participants & setting	Key findings	Observations/notes
Abrantes et al (2023) Randomized Controlled Trial of Aerobic Exercise for Smoking Cessation among Individuals with Elevated Depressive Symptoms, *Nicotine Tob Res*; ntad201. USA	**Study Design:** Randomised controlled trial. **Study aim:** To test the efficacy of a 12-week moderate-intensity aerobic exercise intervention compared to a health education contact control as an adjunct to standard smoking cessation treatment in individuals with elevated depression. **Type of intervention [*exposure*]:** Moderate-intensity aerobic exercise (30 min/session) supervised by an exercise physiologist plus a home-based exercise prescription. Participants aimed for 2–4 sessions/week, tracked in weekly exercise logs. Pre-session group discussions (20 min) on cognitive-behavioural topics for motivation and adherence. Incentives included monetary and prizes. **Comparator intervention or control:** A health education contact control intervention which included 12 weekly group sessions focused on smoking-relevant health topics. The same monetary and prize incentives used. **Smoking cessation**: Smoking cessation counselling was delivered by a postdoctoral level	**Sample size:** 231 (intervention group: *n*= 119, control group: *n*= 112). **Participants:** Participants were recruited through online, radio, and newspaper adverts, and eligibility included: aged 18-65, smoked at least 10 cigarettes a day, at least mild depression, and low active but able to walk 1 mile on a treadmill. Excluded start or change in antidepressant medication in the past 3 months current smoking cessation treatment. **Diagnosis and classification method:** To be eligible, participants had to score ≥6 on the Center for Epidemiological Studies Depression Scale [CES-D], and the International Neuropsychiatric Interview was used for screening/eligibility and to determine lifetime major depressive disorder diagnosis. **Setting:** Not stated where the interventions or smoking cessation counselling was delivered.	**Smoking cessation outcomes:** Effects on confirmed 7-day PPA during follow-up: The treatment × time interaction for confirmed 7-day PPA was not significant (Wald $\chi2 = 2.66$, df = 2, p = .27), indicating that the effect of intervention did not vary by month of follow-up assessment. Adjusting for covariates, the estimated effect was not significant (OR = 0.78; 95% CI 0.32, 1.94; p = .60) Smoking abstinence at 6- and 12-months: The odds of confirmed smoking abstinence were lower at both 6 (OR = 0.33, p = .004) and 12 months (OR = 0.39, p = .02) than at 3 months. There were no significant differences in smoking cessation outcomes between the aerobic exercise and health education control groups. **Mental health outcomes:** The effect of intervention on CES-D scores (Wald $\chi2 = 0.57$, df = 2, p = .75) did not vary by month of assessment. The main effect of treatment was not significant for any secondary outcome: depression (b = -0.84; 95% CI −3.25, 1.57; p = .49). There were no significant differences in depressive symptom outcomes between the aerobic exercise and health education control groups.	*Fidelity ratings were conducted and overall adherence to CBEX topics ranged from 78% to 100% with a mean adherence of 97%.*

	clinician blinded to treatment condition. All participants were provided 8 weeks of the Nicoderm CQ 24-hour transdermal nicotine patches. **Data collection methods and dates:** Participants recruited between February 2014 and February 2018. Data was collected from a combination of self-reported validated questionnaires, biochemical verification at 3-, 6- and 12-months. **Outcomes (relevant):** - 7-day point prevalence abstinence (verified with exhaled carbon monoxide ≤6ppm) - 6- and 12-month abstinence - Depressive symptoms (CES-D)			
Anthenelli et al (2013) Effects of varenicline on smoking cessation in adults with stably treated current or past major depression: A randomized trial. *Ann Intern Med*; 159, 6, 390-400. Multi-national (8 countries)	**Study Design:** Randomised controlled trial. **Study aim:** To evaluate smoking abstinence and changes in mood and anxiety levels in smokers with depression treated with varenicline versus placebo. **Type of intervention [*exposure*]:** Varenicline, 1 mg twice daily for 12 weeks following a titration schedule. **Comparator intervention or control:** Placebo **Smoking cessation:** Both groups received smoking cessation counselling at each clinic visit or telephone assessment. Sessions were one-on-one, lasted up to 10 minutes and was based on US Agency for Healthcare Research and Quality Guidelines.	**Sample size:** 525 (intervention group: *n*= 256, control group: *n*= 269) **Participants:** People recruited from investigators' own practice and from the general population using media and advertising campaigns who met current or past criteria for unipolar major depressive disorder without psychotic features and were motivated to quit smoking. Baseline MADRS score was 7.8 indicative of remitted or the normal range. 26% scored > 11, the midpoint between remitted and mildly depressed. Excluded use of bupropion, nortriptyline, medications for mania or psychosis, and investigational drugs (<30 days before baseline) during the study or previous use of varenicline was prohibited.	**Smoking cessation outcomes:** Varenicline-treated participants had higher continuous abstinence rates versus placebo at weeks 9 to 12 (35.9% vs. 15.6%; odds ratio [OR], 3.35 [95% CI, 2.16 to 5.21]; p<0.001), weeks 9 to 24 (25.0% vs. 12.3%; OR, 2.53 [CI, 1.56 to 4.10]; p<0.001), and weeks 9 to 52 (20.3% vs. 10.4%; OR, 2.36 [CI, 1.40 to 3.98]; p<0.001). 7-day PPA rates were higher for the varenicline group than the placebo group at week 12 (46.1% vs. 20.1%; OR, 3.82 [CI, 2.53 to 5.78]; p<0.001), week 24 (31.3% vs. 18.2%; OR, 2.16 [CI, 1.40 to 3.33]; p<0.001), and week 52 (28.5% vs. 17.5%; OR, 1.98 [CI, 1.28 to 3.08]; p=0.002). **Mental health outcomes:** Over time, both treatment groups had a similar change in depression and anxiety rating scores from baseline to week 16 (values not reported) and rating trajectories trended toward slight improvement. There were no clinically relevant differences between groups in suicidal ideation or behaviour and no overall worsening of depression or anxiety in either group.	*Trial number: NCT01078298* Pfizer funded the study and was involved in study design and in collection, analysis, and interpretation of data with the authors.

	Data collection methods and dates: The study, conducted from 25 March 2010 to 13 June 2012, required clinic visits at screening, baseline, weekly during treatment, and routinely in follow-up. Telephone visits occurred on most non-visit weeks during follow-up. Abstinence was measured via biochemical verification (CO-confirmed ≤10 ppm), with depressive symptoms and adverse events assessed through MADRS questionnaires and Neuropsychiatric Adverse Event Interviews. **Outcomes (relevant):** - Continuous abstinence rates - 7-day point prevalence abstinence - Depressive symptoms - Anxiety - Adverse events	**Diagnosis and classification method:** The diagnosis was confirmed by the Structured Clinical Interview for Axis I Disorders (Research Version, Patient Edition) of the *Diagnostic and Statistical Manual of Mental Disorders* administered by trained mental health professionals. Participants also had been receiving an antidepressant treatment for major depressive disorder at a stable dose (at least 2 months without dosing changes anticipated during study treatment) and/or had had a successfully treated major depressive episode in the past 2 years. **Setting:** Study sites (n=38) were academic clinical trial centres and smoking cessation clinics providing outpatient services.	**Adverse events** Treatment-emergent adverse events (that is, those occurring during treatment and < 30 days thereafter) occurred in 72.3% of varenicline participants and 66.9% of placebo participants, with most being rated as mild or moderate. Treatment discontinuations due to adverse events occurred in 6.3% and 7.8% of varenicline and placebo participants, respectively. The most frequent adverse event was nausea (varenicline, 27.0%; placebo, 10.4%). Intentional self-injury or a possible suicide attempt occurred on day 73 of treatment in a placebo participant. One death by overdose occurred in the varenicline group during follow-up, 76 days after the last dose of study treatment. A possible suicide could not be ruled out.	
Doran et al (2019) Effects of varenicline, depressive symptoms, and region of enrolment on smoking cessation in depressed smokers, *Nicotine Tob Res*; 21(2): 156–162.	(*Secondary analysis of Anthenelli et al 2013, see above for full details*) **Study Design:** Randomised controlled trial. **Study aim:** To evaluate whether the effects of varenicline and depression symptoms on cessation differed by region (United States vs. Europe). **Type of intervention [*exposure*]:** Varenicline **Comparator intervention or control:** Placebo	**Sample size:** 525 (intervention group: *n* = 256, control group *n*= 269) • Intervention group: (USA *n*= 126, EU *n*= 130) • Control group: (USA *n*= 129, EU *n*= 140). **Participants:** Smokers with current stable or past major depression. 37% of participants were male. EU participants were significantly more likely to be male, and tended to have lower baseline depression scores than their US counterparts. US participants in the placebo group	**Smoking cessation outcomes:** *Continuous abstinence rates (weeks 9-12):* There were significant effects of treatment group (OR = 3.91 [2.54% to 6.34%], p< .001) and MADRS × treatment group (OR = 1.08 [1.00% to 1.17], p= .043). Given that the MADRS × treatment group interaction was retained in the model, the treatment group main effect indicates that, at the mean level of baseline depressive symptoms, those randomized to varenicline were nearly four times more likely to achieve continuous abstinence than were those randomised to placebo. *Point prevalence abstinence (weeks 13-52):* There were significant treatment (z= 5.88, p< .001) and treatment × time (z = −3.28, p= .001) effects, indicating an initial advantage of varenicline that faded over time; however, treatment with varenicline retained a substantial	*This is a secondary analysis of* Anthenelli et al 2013 *comparing data from the USA and Europe.*

Multi-national (8 countries)	**Data collection methods and dates:** See Anthenelli et al, 2013 **Outcomes (relevant):** - Continuous abstinence - Past week 7-day point prevalence abstinence	smoked significantly fewer cigarettes per day than those in the EU placebo group, but neither was significantly different from the US or EU varenicline groups. **Diagnosis and classification method:** See Anthenelli et al, 2013 **Setting:** See Anthenelli et al, 2013	advantage over placebo, particularly in the EU. In the US model, treatment effects mirrored those of the full model, with significant treatment (z= 3.15, p= .002) and treatment × time (z= −2.19, p= .028) effects indicating an initial advantage of varenicline versus placebo that weakened over time. The EU model yielded the same pattern of results for treatment group, with an advantage of varenicline at week 13 (z = 5.12, p< .001) that decreased over time (z= −2.74, p= .006).	
Ayers et al (2019) Efficacy and safety of pharmacotherapies for smoking cessation in anxiety disorders: Subgroup analysis of the randomized, active- and placebo-controlled EAGLES trial, *Depress Anxiety*; 37, 3, 247-260. 16 countries including USA, and selected countries in Europe, South and Middle Americas	**Study Design:** Randomised controlled trial (post-hoc subgroup analysis). **Study aim:** To compare the safety and efficacy of varenicline, bupropion, nicotine-replacement therapy (NRT), and placebo across anxiety disorder sub-cohorts, and compare clinical characteristics and rates of clinically significant neuropsychiatric adverse events and cessation in smokers with anxiety disorders versus a cohort of smokers without psychiatric disorders. **Type of intervention [*exposure*]:** Participants received either varenicline 1 mg twice daily, bupropion 150 mg twice daily, transdermal nicotine patch (NRT) 21 mg/day with taper, or placebo along with weekly smoking-cessation counselling for 12 weeks. **Comparator intervention or control:** Varenicline, bupropion, NRT, placebo **Smoking cessation:** All groups received smoking cessation counselling at each clinic visit or telephone assessment. Sessions were	**Sample size:** 4740 (anxiety subcohort: *n*= 712, non-psychiatric cohort: *n*= 4028). • *Varenicline*: generalised anxiety disorder *n*= 64, panic disorder *n*= 69, non-psychiatric cohort *n*= 1005 • *Bupropion*: generalised anxiety disorder *n*= 56, panic disorder *n*= 77, non-psychiatric cohort *n*= 1001 • *NRT*: generalised anxiety disorder *n*= 58, panic disorder *n*= 77, non-psychiatric cohort *n*= 1013 • *Placebo*: generalised anxiety disorder *n*= 65, panic disorder *n*= 61, non-psychiatric cohort *n*= 1009 **Participants:** Eligible participants were adults aged 18–75 years who smoked an average of ≥10 cigarettes/day with an exhaled carbon monoxide >10 ppm at screening and wanted to stop smoking. Anxiety disorder sub-cohort included primary panic disorder (with/without agoraphobia; n = 277), PTSD (n = 192), or generalised anxiety disorder (n =	**Smoking cessation outcomes:** *Continuous abstinence rates:* Among smokers with generalised anxiety disorder and panic disorder, varenicline demonstrated superior efficacy to placebo (OR= 4.53; 95% CI= 1.20–17.10; and OR= 8.49; 95% CI= 1.57–45.78, respectively). Additionally, among smokers with panic disorder, NRT significantly improved quit rates versus placebo (OR= 7.42; 95% CI= 1.37–40.35) but this significant improvement was not apparent for the generalised anxiety disorder cohort (OR= 2.44; 95% CI= 0.58–10.34). Bupropion did not significantly improve continuous abstinence rates for the panic disorder or generalised anxiety disorder groups (OR= 3.33; 95% CI= 0.56–19.26; and OR= 2.43; 95% CI= 0.57–10.31, respectively) Smokers with panic disorder were significantly less likely to quit than non-psychiatric cohort smokers (odds ratio [OR]= 0.53; 95% CI= 0.31–0.88). *7-day PPA:* Varenicline showed superior efficacy to placebo on 7-day PPA at week 12 in smokers with generalised anxiety disorder (OR 4.65; 95% CI= 1.95 - 1.11) and panic disorder (OR 4.08; 95% CI= 1.52 - 10.97). This effect remained at week 24 among smokers with generalised anxiety disorder (OR= 3.13; 95% CI= 1.28 – 7.62) but not in those with panic disorder (OR= 2.16; 95% CI= 0.81 – 5.17). In addition, among smokers with panic disorder, NRT was superior to placebo for 7-day PPA at both weeks 12 (OR= 4.34; 95% CI 1.62 – 11.62) and 24 (OR= 2.70; 95% CI 1.04 – 7.01).	*This study is a secondary analysis of EAGLES (Evaluating Adverse Events in a Global Smoking Cessation Study, NCT01456936), a 24-week randomised, double-blind, triple-dummy, placebo- and active-controlled trial characterising the neuropsychiatric safety and efficacy of varenicline and bupropion.* *In this study, PTSD, generalised anxiety disorder, and panic disorder are treated as sub-categories of anxiety disorders. However, PTSD is now classified under trauma and stressor-related disorders in the DSM-5. Consequently, PTSD-related data have been*

	one-on-one, lasted up to 10 minutes and was based on US Agency for Healthcare Research and Quality Guidelines. **Data collection methods and dates:** No data collection dates were provided; the primary EAGLES trial was published in 2016. Continuous abstinence was defined by self-report of no smoking, with expired CO ≤10 ppm. 7-day PPA rates at weeks 12 and 24 were evaluated. Anxiety and depression were assessed using the Hospital Anxiety and Depression Scale. Neuropsychiatric adverse events were assessed with open-ended questions, observation, a 25-item interview, family reports, and the Columbia Suicide Severity Rating Scale. **Outcomes (relevant):** - Continuous abstinence rates - 7-day PPA - Neuropsychiatric adverse events	243). Anxiety disorder participants must have been considered psychiatrically stable as evidenced by no exacerbations of their psychiatric condition in the prior 6 months and if on pharmacotherapy, to have been on a stable dose for ≥3 months. **Diagnosis and classification method:** Psychiatric diagnoses were evaluated using SCID-I and -II. Diagnosis was confirmed by the Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID-I) **Setting:** Study sites included clinical trial centres, academic centres, and outpatient clinics treating patients with and without psychiatric disorders.	**Adverse events:** There was a significant anxiety disorder sub-cohort effect (p= 0.0012), with smokers in the anxiety disorder sub-cohorts (generalised anxiety disorder, 5.4% and panic disorder, 6.2%) having an increased incidence of moderate-to severe neuropsychiatric adverse events versus NPC smokers (2.1%). There were no significant differences in the incidence of moderate to severe neuropsychiatric adverse events by treatment group. Smokers with PD were significantly more prone to experience moderate to severe neuropsychiatric adverse events versus non-psychiatric cohort smokers (RD= 4.0; 95% CI= 0.34–7.65). Across anxiety disorder sub-cohorts the rates of treatment discontinuation due to neuropsychiatric adverse events were similar, generalised anxiety disorder= 1.3%; panic disorder 1.5%; non-psychiatric cohort= 0.4%.	*removed from our review analyses.* *This is an efficacy trial, i.e. not measured under 'real life' conditions* *The EAGLES study was sponsored by Pfizer and GlaxoSmithKline. Sponsors contributed to data analysis, interpretation, and approval of the manuscript.*
Cinciripini et al (2022) The effects of varenicline, bupropion, nicotine patch, and placebo on smoking cessation among smokers with major depression: A randomized	*This is a secondary analysis of Anthenelli et al 2016 which has not been included in our rapid review, see Ayers et al 2019 for further intervention details.* **Study Design:** Randomised controlled trial (secondary analysis) **Study aim:** To evaluate the comparative safety and efficacy of smoking cessation pharmacotherapy (varenicline, bupropion, NRT) and placebo in	**Sample size:** 6653 (primary diagnosis of major depressive disorder: *n*= 2635, non-psychiatric cohort: *n*= 4028) • *Varenicline*: major depressive disorder *n*= 657, non-psychiatric *n*= 990 • *Bupropion*: major depressive disorder *n*= 632, non-psychiatric *n*= 989 • *NRT*: major depressive disorder *n*= 649, non-psychiatric *n*= 1006	**Smoking cessation outcomes:** *Continuous abstinence rates:* Within the major depressive disorder cohort, comparisons with placebo for weeks are significant for varenicline and bupropion at both timepoints but only at weeks 9-12 for NRT: Varenicline (week 9-12: OR= 3.004; 95% CI= 2.081, 4.336; week 9-24 OR= 2.396; 95% CI= 1.561, 3.678) Bupropion (week 9-12: OR= 1.936; 95% CI= 1.321,2.838; week 9-24 OR= 1.850; 95% CI= 1.188, 2.881) NRT (week 9-12: OR= 1.891; 95% CI= 1.291,2.770; week 9-24 OR= 1.522; 95% CI= 0.967, 2.396). Varenicline, at weeks 9-12 was found to be superior to bupropion (OR= 1.551; 95% CI= 1.118,2.152) and NRT	*This study is a secondary analysis of EAGLES (Evaluating Adverse Events in a Global Smoking Cessation Study), a 24-week randomised, double-blind, triple-dummy, placebo- and active-controlled trial characterising the neuropsychiatric safety and efficacy of*

clinical trial, *Depress Anxiety*; 39, 5, 429-440. 16 countries including USA, and selected countries in Europe, South and Middle Americas	smokers with clinically stable major depressive disorder versus those with no psychiatric disorder. A secondary aim was to explore differential responses to these medications in smokers with recurrent versus single episode major depressive disorder. **Type of intervention [*exposure*]:** **Comparator intervention or control:** Varenicline, bupropion, NRT or placebo. **Data collection methods and dates:** See Ayers et al, 2022 **Outcomes (relevant):** - Neuropsychiatric adverse event - Continuous abstinence rates	• *Placebo*: major depressive disorder *n*= 664, non-psychiatric *n*= 999 **Participants:** Community volunteers 18-75 years of age; smoke 10+ cigarettes/day; with clinically stable major depressive disorder from 140 sites in 16 countries. Major depressive disorder participants must have been considered psychiatrically stable as evidenced by no exacerbations of their psychiatric condition in the prior 6 months and if on pharmacotherapy, to have been on a stable dose for ≥3 months. **Diagnosis and classification method:** See Ayers et al, 2022 **Setting:** See Ayers et al, 2022	at both timepoints (week 9-12: OR= 1.589; 95% CI= 1.146,2.202; week 9-24 OR= 1.574; 95% CI= 1.066, 2.325) in the major depressive disorder cohort. The major depressive disorder cohort reported lower abstinence when combining all treatments compared to non-psychiatric cohort (week 9-12: OR= 0.903; 95% CI= 0.799,1.020; week 9-24 OR= 0.831; 95% CI= 0.722, 0.957). **Adverse events:** Risk of neuropsychiatric adverse events did not differ by medication for major depressive disorder. The major depressive disorder cohort was at significantly higher risk ($p<0.0001$) for the occurrence of an neuropsychiatric adverse events than the non-psychiatric cohort (risk difference= 0.032 (95% CI: 0.023, 0.042) but no differences were observed between the three medications and placebo.	*varenicline and bupropion.* *This is an efficacy trial, i.e. not measured under 'real life' conditions* *The EAGLES study was sponsored by Pfizer and GlaxoSmithKline. Sponsors contributed to data analysis, interpretation, and approval of the manuscript.*
Bernard et al (2015) Exercise and counseling for smoking cessation in smokers with depressive symptoms: A randomized controlled pilot trial, *J Dual Diag*; 11, 3, 2015-216. France	**Study Design:** Pilot randomised controlled trial. **Study aim:** To estimate the effects of adding an exercise and counselling intervention to standard smoking cessation treatment for smokers with depressive disorders. **Type of intervention [*exposure*]:** The exercise consisted of both supervised group exercise and unsupervised home exercise. Group counselling sessions goals were to (a) to increase one's level of physical activity in the long term, (a) to use short bouts of exercise in response to	**Sample size:** 70 (intervention group: *n* = 35, control group: *n* = 35) **Participants:** Smokers with current depressive disorders recruited from the general population. Thirty-eight participants (54.3%) had sub-threshold depressive symptoms and 32 (45.7%) met diagnostic criteria for major depressive disorder or dysthymia. Participants were able to but did not regularly participate in physical activity and were not currently receiving smoking cessation pharmacotherapy, mood stabilisers or antipsychotics.	**Smoking cessation outcomes:** Twelve weeks after the beginning of the intervention, 48.5% (17/35) of the exercise participants and 28.5% (10/35) of the control participants had remained continually abstinent from smoking; $\chi^2(7) = 2.95$, p=.08. No statistically significant difference in abstinence was found at week 8 (IG: 57.1%,20/35; CG: 13/35, 37.1%), week 24 (IG: 12/35, 34.3%; CG: 8/35, 22.9%) or week 52 (IG; 7/35, 20%; CG: 4/35, 11.4%). Logistic regression analyses also did not reveal any significant difference in continuous abstinence rates by treatment group. No significant between-group differences were established for cigarettes per day or expired CO (ppm). **Mental health outcomes:** No significant between-group differences were found for HADS-D scores across all time points in the study (week	*This study was a pilot study and does not appear to have been powered to detect significant differences in depressive symptoms or smoking cessation.* *Following trial ended because of recruitment challenges.*

	negative affect and craving, (c) to develop skills for managing withdrawal symptoms, and (d) to develop skills for becoming and remaining an ex-smoker. **Comparator intervention or control:** The participants assigned to the health education control condition received information on a variety of health prevention topics including sleep hygiene, nutrition, stress, and health screening tests for cancer prevention. **Smoking cessation:** Both groups received an initial brief counselling session and a 12-week prescription for nicotine replacement therapy or varenicline. Interventions consisted of a 10-session, 8-week group program, with biweekly meetings for weeks 1 and 2 and weekly meetings for weeks 3 through 8. **Data collection methods and dates:** Participants were recruited over a 17-month period (between October 2010 and May 2012). Continuous abstinence since the quit date and anxiety and depression was assessed at week 8 (end of the intervention) and at 12-, 24-, and 52-week follow-ups. The subjects were considered to be continuously abstinent if they had not smoked after the quit day, as confirmed by a carbon monoxide concentration of 10 ppm or less. Anxiety and depression were assessed using HADS. **Outcomes (relevant):** - Continuous abstinence, - Cigarettes/day	**Diagnosis and classification method:** Participants were included if they scored ≥8 on the Depression subscale of the Hospital Anxiety and Depression Scale when screened for eligibility to the study. **Setting:** The selection, inclusion, and treatment of participants, as well as the collection of data, were performed at Montpellier University Hospital in France.	8: IG: 5.92 ± 4.41, CG: 5.36 ± 3.38; week 12: IG: 5.25 ± 4.87, CG: 5.63 ± 3.51; week 24: IG: 6.50 ± 4.96, CG: 6.66 ± 4.56; week 52: IG: 3.87 ± 2.89, CG: 4.83 ± 3.78). **Additional findings:** At week 8, no statistical difference was found in adherence to group sessions, with 82% (8.2 of 10) attendance in the exercise and counselling intervention and 75% (7.5 of 10) in the control intervention; Z=−1.44, p=.14. However, participants in the exercise intervention self-reported adhering to only 63% (3.7 of 6) of the home-based exercise sessions. Length of smoking cessation medication treatment did not differ significantly between groups. For exercise and control intervention subjects, respectively, the mean length of the nicotine replacement therapy was 105.5 days (*SD* = 64.3) and 102.0 days (*SD* = 53.5), and that of the varenicline treatment was 91.7 days (*SD* = 42.6) and 89.8 days (*SD* = 67.0).	

	- Anxiety and depression (HADS)			
Dahne et al (2023) Behavioral Activation–Based Digital Smoking Cessation Intervention for Individuals With Depressive Symptoms: Randomized Clinical Trial, *J Med Internet Res*; 1:25:e49809. USA	**Study Design:** Randomised controlled trial (RCT) **Study aim:** To examine the usability and uptake of a Behavioral Activation-based self-directed mobile app intervention (Goal2Quit) among adult smokers with depressive symptoms as well as its efficacy for improving depression and promoting smoking cessation. **Type of intervention [*exposure*]:** Goal2Quit – a mobile app providing behavioural strategies for treating depression and quitting smoking based on Behavioural Activation Treatment for Depression. Participants also received a 2-week sample of combination NRT including 14 mg nicotine patches and 4 mg nicotine lozenges. **Comparator intervention or control:** Treatment as usual (TAU) participants received a digital copy of the National Cancer Institute's "Clearing the Air: Quit Smoking Today" booklet – a self-help booklet which provides evidence-based strategies for quitting smoking but is not tailored for depression. **Data collection methods and dates:** Participants were enrolled between June 25, 2020, and February 23, 2022. They completed baseline and weekly follow-up assessments for 8 weeks, with a final follow-up at 12 weeks via Research Electronic Data Capture. Depression was self-reported using the Patient Health Questionnaire-8 at	**Sample size:** 150 (intervention group: *n*= 103, control group: *n*= 47) **Participants:** Participants were English-speaking adults who currently smoked (self-report of ≥5 cigarettes per day for at least 25 out of the last 30 days for at least the last 6 months) and had elevated depressive symptoms (Patient Health Questionnaire-8 score ≥10). **Diagnosis and classification method:** Researchers screened participants for depressive symptoms at entry to the study using the Participant Health Questionnaire- 8 (PHQ-8 score ≥ 10). Participants had been seen by a primary care provider in the last year. **Setting:** All study procedures were delivered fully remotely.	**Smoking cessation outcomes:** Across time points, all cessation outcomes favoured Goal2Quit. Goal2Quit participants were more likely to have made a 24-hour quit attempt during the first 4 (17% vs 2%; p=0.01), first 8 (24% vs 4%; p =0.003), and across all 12 (29% vs 6%; p =0.002) weeks of follow-up. Both floating and 7-day point prevalence abstinence were significantly higher for Goal2Quit participants relative to TAU at week 4 (Floating abstinence: 14% vs 0%; p =0.01 and 7-day PPA: 11% vs 0%; p=0.02), week 8 (floating abstinence: 19% vs 2%; p=.001 and 7-day PPA: 12% vs 0%; p=0.02), and week 12 (Floating abstinence: 24% vs 4%; p=0.003 and 7-day PPA: 16% vs 2%; p=0.02). Overall, both groups decreased their cigarettes per day over the course of the study (difference of mean 4.71, SE 0.42 cigarettes per day less by week 12; p<0.001), but the Goal2Quit group reported smoking less cigarettes per day than the TAU group (difference of mean 1.97, SE 0.93 CPD less; p=0.03). Within the Goal2Quit group, total time spent using the app was significantly related to abstinence at week 12, with the odds of reporting 7-day PPA increasing 7% for every 5-minute increase in app use (odds ratio [OR] 1.07, 95% CI 1.01-1.13; p=0.02). **Mental health outcomes:** On average, after adjusting for covariates and baseline BDI score, both groups showed a decrease in depressive symptoms over time (difference of mean 8.57, SE 0.86 points from week 1 to week 12; p<0.001), but the Goal2Quit group reported lower average depressive symptoms over the course of the trial as compared to the TAU group (difference of mean 3.72, SE 1.37 points less for Goal2Quit; p=0.01). Regarding worsening depression over time, 37 participants reported worsening mood, defined as an increase of 10 or more points on the BDI-II since	*Goal2Quit uptake and usability scores were measured however these outcomes were non-comparative and therefore not reported.* *Participants were compensated up to US $140 via electronic gift codes for completion of all assessments.* *Smoking cessation outcomes were based on self-report and were not biochemically verified.*

	screening and the Beck Depression Inventory-II at baseline and throughout the study. At each follow-up, participants reported the number of cigarettes smoked per day over the last 7 days (also at baseline) and the incidence of quit attempts lasting at least 24 hours since the prior assessment. Data collection dates are not provided. **Outcomes (relevant):** - Depression - Cigarettes/day - Floating abstinence - 7-day PPA - 24-hour quit attempts		baseline, at some point during the study duration (23 Goal2Quit, 14 TAU) and 11 participants endorsed suicidality (4 Goal2Quit, 7 TAU). **Additional findings:** NRT use was high with 76% (n=78) of Goal2Quit participants reporting use during the 12-week study period compared to only 17% (n=8) of the TAU group (p<0.001), NRT was not provided to the TAU group as part of the study.	
Evins et al (2008) A controlled trial of bupropion added to nicotine patch and behavioral therapy for smoking cessation in adults with unipolar depressive disorder, *J Clin Psychopharmacol*; 28(6):660-6. USA	**Study Design:** Randomised controlled trial. **Study aim:** To determine if bupropion improves abstinence rates and abstinence-associated depressive symptoms when added to transdermal nicotine replacement therapy (NRT) and group cognitive behavioural therapy (CBT) in smokers with unipolar depressive disorder. **Type of intervention [*exposure*]:** Bupropion-SR (150 mg per day for 3 days then 150 mg bid) added to transdermal NRT (21 mg per day from study weeks 2–6, 14 mg per day for study weeks 7 and 8, and 7 mg per day for study weeks 9 and 10) and 13 weekly group CBT meetings that used a multi-component group therapy approach. **Comparator intervention or control:**	**Sample size:** 199 (intervention group: *n*= 97, control group: *n*= 102) **Participants:** Adult smoker with current (n=90) or past (n=109) unipolar depressive disorder. Of the 90 subjects with current unipolar depressive disorder, 76% (68/90) met criteria for major depressive disorder, 16% (14/90) for minor depressive disorder and 11% (10/90) for dysthymia. Excluded those using psychotropic medications, including antidepressant medications, or behavioral smoking cessation treatments. **Diagnosis and classification method:** Participants were screened prior to enrolment and met DSM-IV criteria for lifetime diagnosis of a unipolar depressive disorder (major	**Smoking cessation outcomes:** 7-day point prevalence abstinence rates at the end of the trial were 36% (37/97) in the bupropion + NRT + CBT group and 31% (32/102) in the placebo + NRT + CBT group, Chi^2=0.49, non-significant. Lifetime anxiety disorder diagnosis was associated with failure to attain abstinence at the end of treatment: 23% (18/79) of participants with an anxiety disorder achieved abstinence at the end of treatment vs. 41% (49/120) of those without an anxiety disorder (Chi^2= 6.9, p<0.01). Due to the high number of drop-outs, a second exploratory analysis used the last observation carried forward (LOCF) method to impute missing data, including abstinence status at drop-out. 48% of participants (90/199) met the criteria for 7-day point-prevalence abstinence at endpoint. 56% (54/97) of those in the bupropion group and 41% (42/102) on placebo met criteria for 7-day point prevalence abstinence at end of trial, Chi2=4.18, p=0.04. Among those with current unipolar depressive disorder, 56% (25/45) of those on bupropion and 44% (20/45) of those on placebo attained 7-day point prevalence abstinence. Among those with past unipolar depressive disorder, 56% (29/52) of those	*Fifty percent of those who entered randomized treatment dropped out before the end of the 13-week intervention. There was a trend for those randomized to bupropion to remain in the trial longer (mean= 6.5 weeks, SD=3.4) than those on placebo (mean=5.3 weeks, SD=3.6), t=1.57, p<0.12.* *Because of the high rate of drop-out in the 12-month follow-up period of this trial, researchers were unable to assess long term abstinence rates or the risk of relapse to*

	Participants in the comparator group received a placebo and the same transdermal NRT dose and number of group CBT sessions. **Data collection methods and dates:** Abstinence was determined using self-report and expired air CO concentration (<9 ppm) at study week 13. The 6-item Hamilton Rating Scale for Depression (HAM-D-6) was performed at baseline and each week. Dates not stated. **Outcomes (relevant):** - 7-day point prevalence abstinence - Depression status	depression, minor depression, or dysthymic disorder), according to the Structured Clinical Interview for DSM-IV-Axis I Disorders/Patient Edition (SCID-I/P). **Setting:** Not stated.	on bupropion and 39% (22/57) of those on placebo met abstinence criteria at endpoint, Chi^2=3.22, p<0.072. **Mental health outcomes:** Bupropion was not protective against abstinence-associated increase in depression symptoms as 50% (17/34) of those on bupropion vs. 62% (18/29) of those on placebo who entered the trial with HAMD-6 ≤4 and achieved abstinence reported a subsequent roughening of depressive symptoms as evidenced by HAM-D-6 score >4, Chi^2=0.923, p=0.34. **Qualitative findings:** A scripted follow-up telephone interview was conducted with participants who were abstinent at drop-out to assess duration of abstinence and reasons for drop-out. Sixty-three percent reported remaining abstinent for ≥6 months. Participants cited time demands, increased work responsibilities, or scheduling conflicts as reasons for dropping out. No participants reported dropping out due to negative experiences or adverse events.	*major depressive disorder.*
Heffner et al (2019) A behavioral activation mobile health app for smokers with depression: Development and pilot evaluation in a single-arm trial, *JMIR Form Res*; 3(4):e13728. USA	**Study Design:** Pilot before and after study **Study aim:** To develop a Behavioural Activation Treatment for Depression (BAT-D) mobile health app with great potential for high reach and determine its feasibility, acceptability, and preliminary effects on theory-based behavioural processes of behavioural activation, depressive symptomatology reduction, and the primary outcome of smoking cessation. **Type of intervention [*exposure*]:** Actify! - a Behavioural Activation Treatment app for depressed smokers (BAT-D) along with SmokefreeTXT (a text messaging program from the US National Cancer Institute (NCI)).	**Sample size:** 17 **Participants:** Adult smokers, averaging at least 5 cigarettes per day for the last 30 days, that screened positive for mild to moderate current depressive symptoms (9-item Patient Health Questionnaire [PHQ-9] score 5-19). **Diagnosis and classification method:** Participants screened positive for mild to moderate current depressive symptoms (9-item Patient Health Questionnaire [PHQ-9] score 5-19) at entry to the study. Excluded individuals currently using a depression app or receiving other treatment for depression, including	**Smoking cessation outcomes:** The CO-confirmed 7-day PPA rate at 6-week follow-up was 31% (5/16), and the 30-day PPA at 6-week follow-up was 19% (3/16). In a post hoc sensitivity analysis using a conservative cutoff for CO levels indicative of abstinence (3 ppm or less), the findings were unchanged. **Mental health outcomes:** Average change in depression on the PHQ-9 was a 5-point decrease from baseline (mean –4.5, 95% CI –7.7 to –1.3), which was a statistically significant improvement in symptoms (p=0.01) as well as a clinically significant change from moderate symptoms to mild symptoms. Average change in BADS overall scale scores and activation subscale scores (BAT-D's theory-based change mechanism) were not statistically significant but were in the hypothesized direction: BADS total scores increased by 14 points (mean 14.4, 95% CI –2.6 to 31.3; p =0.09) and activation subscale scores increased by 4 points (mean 3.6, 95% CI –1.7 to 8.9; p =0.17	*This study was a pilot study and does not appear to have been powered to detect significant differences in depressive symptoms or smoking cessation.* *Participants were compensated $30 for the baseline visit and $70 for the six-week follow-up visit.* *Participants must have owned an iPhone to take part in the study.*

	Participants accessed this app and service for six-weeks. **Comparator intervention or control:** Six-week follow-up data was compared to baseline. **Data collection methods and dates:** Data collection dates were not explicitly stated; however, the trial was completed between November 2017 and June 2018. The 6-item Fagerström Test for Nicotine Dependence (FTND) assessed nicotine dependence. Efficacy for reducing depression symptoms was assessed via changes in PHQ-9 scores. Efficacy for increasing behavioral activation was assessed using the 25-item Behavioral Activation for Depression Scale (BADS). Efficacy for smoking cessation was measured by CO-confirmed 7-day PPA and 30-day PPA at 6 weeks post-enrolment. Smoking outcomes were assessed using the smoking timeline follow-back (TLFB). Expired-air CO levels were taken at baseline and at the follow-up visit to biochemically verify smoking self-report. **Outcomes (relevant):** • Depressive symptoms • 7-day PPA • 30-day PPA	psychotherapy or medication and those receiving other treatment for smoking cessation. **Setting:** The follow-up visit was in-person, location not stated.		
Hitsman et al (2023) Efficacy and safety of combination behavioral activation for smoking	**Study Design:** Randomised controlled trial. **Study aim:** To measure the efficacy and safety of 12 weeks of behavioural activation for smoking cessation (BASC), varenicline	**Sample size:** 300 (178 attended week-14 and were included in the primary analysis). • Standard treatment and placebo: *n*=68	**Smoking cessation outcomes:** No significant interaction was detected between behavioural treatment and pharmacotherapy at 27 weeks ($\chi2(1) = 0.19$, $P = 0.67$). BASC and ST did not differ ($\chi2(1) = 0.43$, $P = 0.51$). Significant differences in ITT abstinence rates ($\chi2(1) = 4.84$, $P = 0.03$) emerged among pharmacotherapy arms (16.2% for varenicline, 7.5% for placebo), with results favouring varenicline over	*Use of antidepressant medication and educational level differed significantly among treatment arms.*

cessation and varenicline for treating tobacco dependence among individuals with current or past major depressive disorder: A 2 × 2 factorial, randomized, placebo-controlled trial, *Addiction*; 118(9), 1710-1725. USA	and their combination, for individuals with major depressive disorder. **Type of intervention [*exposure*]:** Participants received 12 weeks of varenicline and behavioural activation. Pharmacological treatment followed FDA-approved labelling for varenicline: days 1–3 (0.5 mg once daily); days 4–7 (0.5 mg twice daily); days 8–84 (1.0 mg twice daily). Behavioural treatment included 8 counselling sessions (a mix of in-person and telephone visits) over 12 weeks. Behavioural activation focused on increasing engagement in rewarding activities as alternatives to smoking by reducing avoidance, withdrawal, and inactivity. **Comparator 2:** Placebo and behavioural activation. **Comparator 3:** Varenicline and standard counselling. Standard counselling was based on the U.S. Public Health Service guidelines for smoking cessation treatment. **Comparator 4:** Placebo and standard counselling. **Data collection methods and dates:** Recruitment and treatment took places between June 2015 and March 2020. Assessments included in this analysis were conducted at baseline (Week 0) and end of treatment (Week 14) and included self-report questionnaires, biochemical verification of abstinence (CO levels ≤6 ppm) physical examination, and blood draw. Assessments of medication side	• Behavioural Activation for Smoking Cessation and placebo*: n*=68 • Standard treatment and varenicline: *n*=81 • Behavioural Activation for Smoking Cessation and varenicline: *n*=83 **Participants:** Adult smokers (≥1 cigarette/day) with lifetime (current or past) major depressive disorder with an interest in quitting smoking, recruited from targeted print and electronic advertisements, presentations at and referrals from local primary care and mental health clinics, and electronic health record identification. Excluded current or recent (past 14 days) participation in smoking cessation treatment or use of cessation pharmacotherapy, or current cognitive or behavioural therapy for depression. **Diagnosis and classification method:** Participants were eligible and classified as having major depressive disorder based on the Mini International Neuropsychiatric Interview (MINI) 7.0, validated for the Diagnostic and Statistical Manual of Mental Disorders 5th edition. **Setting:** Research clinics at Northwestern University, Chicago.	placebo (rate ratio = 2.16, 95% confidence interval = 1.08, 4.30). Continuous abstinence rates remained steady at 2.9% for ST + placebo and 1.8% for BASC + placebo between weeks 14 and 27 but declined further to 5.6% for ST + varenicline and 2.4% for BASC + varenicline during this period. Differences in time to prolonged abstinence failure were significant over 14 weeks ($\chi 2$ (3) = 15.5, P = 0.001) and remained highly significant over 27 weeks ($\chi 2$ (3) = 11.1, P = 0.01). Prolonged abstinence rates at week 14 were 6.8% for ST + placebo, 5.6% for BASC + placebo, 21.7% for ST + varenicline and 14.1% for BASC + varenicline. Prolonged abstinence rates also remained steady at 6.8% for ST + placebo and 5.6% for BASC + placebo between weeks 14 and 27, but showed declines to 9.0% for ST + varenicline and 9.4% for BASC + varenicline during this period. **Mental health outcomes:** There were no statistically significant differences in depression levels among treatment arms at baseline or any of the follow-up timepoints (Ps > 0.05). **Adverse events:** At week 1, which occurred 1 week before starting medication, there were no statistically significant differences between varenicline and placebo arms in adverse events rates. At week 6, adverse events rates differed between varenicline and placebo only for sleep problems (p= 0.035). At week 14, rates of dry mouth (p= 0.009) and anxiety (p= 0.023) differed significantly between varenicline and placebo arms. At weeks 6 and 14, all statistically significant adverse events were higher for placebo than for varenicline. Regarding blood pressure, there were no significant differences between medication arms in rates of hypertension across treatment (p > 0.05). Both varenicline- and placebo-treated participants showed reductions in hypertension between baseline and week 14. The same pattern was observed for suicide risk between and within medication arms. Only one serious adverse event rate differed significantly between varenicline and placebo across the	

	effects, mood, and suicidality also occurred. **Outcomes (relevant):** - 7-day point-prevalence abstinence at 14 and 27 weeks - Continuous abstinence - Depressive symptoms - Adverse events, (AEs) including serious adverse events (SAEs), between varenicline and placebo arms		three time-points: suicidal ideation (p= 0.032), which was higher for varenicline than placebo at week 1 before medication was started. None of the nominally significant p-values survived multiplicity adjustment.	
Patten et al (2017) Supervised, vigorous intensity exercise intervention for depressed female smokers: A pilot study, *Nicotine Tob Res*; 19(1):77-86. USA	**Study Design:** Pilot randomised controlled trial. **Study aim:** To evaluate the potential role of supervised vigorous exercise as a smoking cessation intervention for depressed females. **Type of intervention [*exposure*]:** 12-week vigorous intensity exercise intervention comprising of three 30–40 minute individual-based sessions per week delivered by wellness coaches. **Comparator intervention or control:** 12 weeks of thrice weekly health education. **Smoking cessation:** Both groups received a nicotine patch and behavioural smoking cessation counselling (weekly 15 – 20 minutes of smoking cessation counselling). **Data collection methods and dates:** Study start date: September 2013; Study end date: December 2015.	**Sample size:** 30 (intervention group: *n*= 15, control group: *n*= 15) **Participants:** Participants were female, aged 18-55 years, smoked at least 10 cigarettes/day for at least the past year, willing to make a quit attempt, currently depressed, not currently meeting the American College of Sports Medicine (ACSM) guidelines of moderate intensity exercise for at least 30 minutes on at least 5 days/week or vigorous exercise for at least 20 minutes on at least 3 days/week, willing and able to participate in all aspects of the study. Excluded participants who had a change in anti-depressant medication in past 3 months, or those attending other smoking cessation medication/ behavioural treatment. **Diagnosis and classification method:** Participants were recruited by provider referrals and flyers	**Smoking cessation outcomes:** Based on intent-to-treat analysis, the exercise condition was associated with significantly higher biochemically verified smoking abstinence rates (73% [11/15]) compared to health education (33% [5/15]) at Week 12; $\chi 2$ =4.821, df= 1, p= 0.028. No statistically significant differences between groups were detected at 6-month follow-up (27% [4/15] for the exercise condition vs. 40% [6/15] for health education); $\chi 2$= .600, df= 1, p= 0.439. When adjusted for PHQ-9 score and antidepressant medication use, p= 0.035 at Week 12 and p= 0.48 at 6-month follow-up. **Mental health outcomes:** No statistically significant differences between groups were detected at week 12 for PHQ-9 score (p=0.90). **Qualitative outcomes:** Satisfaction with the counselling provided by the coach was high for both treatment groups (mean Consultation and Relational Empathy score = 38.0 ± 4.0 [range 30–40] for health education vs. 39.0 ± 3.0 [range 30–41] for the exercise condition, p= .52). **Adherence:** Treatment adherence was high in both groups. Health education participants completed a mean (SD) = 24.0 (10.0) sessions (range 5–36) and the exercise condition	*This study was a pilot study. The study authors sought to obtain estimates of the intervention effect toward planning a definitive trial.* *Participants received $25 for completing the baseline assessment and $50 after completing each follow-up. All participants received a free 6-month YMCA membership (health education participants received this after the final assessment).*

	Seven-day PPA, self-reported cigarette smoking status was obtained at Week 12 and at 6-month follow-up. A saliva sample was collected at each time point for cotinine analysis. The PHQ-9 was used to assess depressive symptoms at baseline and at Week 12. **Outcomes (relevant):** • 7-day PPA • Depressive symptoms	posted in the clinic and radio and newspaper advertisements. Initial screening was completed by telephone and current depression was classified by a clinical cutoff score of at least 16 on the 10-item Center for Epidemiological Studies Depression Scale corresponding to moderate–severe depression (CES-D). Eligible women were asked to complete an in-person screening assessment. Participants were stratified according to current depression severity (baseline Patient Health Questionnaire [PHQ-9]. **Setting:** In-person screening at clinic. The exercise intervention was mainly implemented in a community YMCA setting, 4 sessions were conducted at a worksite fitness centre.	participants completed a mean of 26.0 (10.0) sessions (range 5–36), p= .55. The average proportion of sessions attended was 66% for health education participants and 72% for the exercise condition. NRT adherence was low in both groups with only 13% (2/15) of health education participants and 27% (4/15) of women in the exercise condition completing the recommended 8 weeks of nicotine patch. Reasons for nonadherence were relapse to smoking, skin irritation, patch falling off, or participants not feeling that they needed it.	
van der Meer et al (2010) Effectiveness of a mood management component as an adjunct to a telephone counselling smoking cessation intervention for smokers with a past major depression: A pragmatic randomized	**Study Design:** Randomised controlled trial. **Study aim:** To assess whether the addition of a mood management component to telephone counselling produces higher abstinence rates in smokers with past major depression and helps to prevent recurrence of depressive symptoms. **Type of intervention [*exposure*]:** The mood management intervention was an integration of the control intervention with a mood management component. This component consisted of a self-help mood management manual, two more preparatory proactive telephone counselling	**Sample size:** 485 (intervention group: *n*= 243, control group: *n*= 242) **Participants:** Daily smokers, aged between 18 and 65 years, who wanted to quit smoking within 1 month (preparation stage) or between 1 month and 6 months (contemplation stage) and had a major depression according to the DSM-IV in the period longer than 1 month ago. Excluded those currently using antidepressant medication or receiving or on a waiting list for treatment of psychological problems.	**Smoking cessation outcomes:** Prolonged abstinence rates at 6- and 12-month follow-up for the experimental condition were 30.5% and 23.9%, respectively, and for the control condition were 22.3% and 14.0%. The 6-month odds ratio (OR) was 1.60 [95% confidence interval (CI) 1.06–2.42] and the 12-month OR was 1.96 (95% CI 1.22–3.14). Seven-day point prevalence abstinence rates at 6- and 12-month follow-up for the experimental condition were 37.4% and 27.6%, respectively, and for the control condition were 31.0% and 24.0%. The 6-month OR was 1.38 (95% CI 0.94–2.02) and the 12-month OR was 1.23 (95% CI 0.81–1.86). The biochemical validation (saliva cotinine) confirmed that 24 (96.0%) of the 25 included participants were non-smokers. **Mental health outcomes:** In the experimental condition, the mean differences for change in depressive symptoms were 1.1 and 0.6 from 0	*Excluded patients with a DSM-IV diagnosis of depression within a month of the study, unclear the reason why and what impact this would have.*

controlled trial, *Addiction*; 105(11), 1991-1999. Netherland	sessions and supplementary homework assignments and advice. **Comparator intervention or control:** The control intervention consisted of eight sessions of proactive telephone counselling. **Data collection methods and dates:** Participants were recruited between July 2003 and July 2005. The final sample consisted of 25 participants (27.2% of 92) who were prolonged abstinent according to the 12-month follow-up questionnaire. During the interview, a research assistant collected saliva samples from these participants. Saliva cotinine levels were tested using the validated NicAlertTM assay. Depressive symptoms were assessed using the Center for Epidemiological Studies Depression Scale (CES-D). **Outcomes (relevant):** - Self-reported prolonged abstinence without biochemical verification - 7-day point prevalence - Depressive symptoms	**Diagnosis and classification method:** Past depression was confirmed during screening for eligibility for the study. Past and current major depression according to the DSM-IV, as determined by the Composite International Diagnostic Interview (CIDI, Dutch version). Telephone screenings were conducted by 10 trained psychology students, who underwent 27 hours of certified training as well as weekly supervision. **Setting:** Dutch national smoking cessation quitline.	to 6 months and from 6 to 12 months, respectively. For the control condition, the mean differences for change in depressive symptoms were 2.0 and 0.1. Subgroup analyses by smoking–quit pattern (S–Q) showed that quitting was associated with improvements in depressive symptoms, particularly from 0 to 6 months for the S–Q-Q subgroup compared to the subgroup that did not quit. Additionally, there appeared to be no intervention effect on the change of depressive symptoms. A regression analysis with 12-month prolonged abstinence as the dependent variable and change in depressive symptoms × intervention as the effect modifier also suggested that there was no intervention effect on the change of depressive symptoms. **Additional findings:** Counsellor adherence to protocol was 90.4% (55 deviations total/570 items total) in the mood management condition and 92.6% (36 deviations total/486 items total) in the control condition. There was no significant difference between both conditions. Participants took part in an average of 7.8 telephone calls (SD = 3.0) in the mood management condition and 6.3 calls (SD = 2.5) in the control condition. No difference was found between the experimental condition and control condition on using pharmacotherapy aids for cessation: 50.0% of the participants used no pharmacotherapy aids, 38.2% used nicotine replacement therapy, 8.9% used bupropion or nortriptyline and 3.0% used nicotine replacement therapy combined with bupropion or nortriptyline.	
Weidberg et al (2018) In-treatment cigarette demand among treatment-seeking smokers with depressive	**Study Design:** Randomised controlled trial **Study aim:** To examine the differential effect of cognitive behavioural treatment (CBT) with behavioural activation (BA) compared to CBT with BA and contingency management (CM), on cigarette demand among treatment	**Sample size:** 92 (intervention group: *n*= 45, control group: *n*= 47) **Participants:** Adults meeting the diagnostic criteria for nicotine dependence according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) assessed by the structured	**Smoking cessation outcomes:** Cotinine values were lower across the intervention among participants who received CBT+BA+CM when compared to those who received CBT+BA. Significant differences by group were found in sessions 2b, 3, 3b, 4, 4b, 5 and 6 (all p values <.048). The percentage of participants presenting cotinine levels<80 ng/ml was higher in the CBT+BA+CM condition than in the CBT+BA, although differences were only significant in session 5 (p=.038). There was no significant effect of	

symptoms, *Addict Behav*; 82:35-43. Spain	seeking smokers with depressive symptoms. **Type of intervention [*exposure*]:** *CBT+BA+CM* Individuals in this treatment condition received the same CBT+BA intervention, with the addition of a CM component reinforcing abstinence. The number of sessions and collection of cotinine samples were the same as in the CBT+BA condition. From the fifth session onward (the first session requiring abstinence), patients were given vouchers upon proof of abstinence (cotinine levels ≤80 ng/ml). The reinforcement followed an escalating schedule, with maximum possible earnings of 175€ (US$190) and an average of 112.11€ (US$137.47) earned in vouchers. **Comparator intervention or control:** *CBT + BA* This intervention combined CBT and behavioural activation strategies for smoking cessation and depression management. It included nicotine fading, where participants gradually reduced their nicotine consumption, and psychoeducation about the link between smoking and depression. The intervention also focused on identifying meaningful activities in various life areas and creating a supportive network through contracts during cessation efforts. **Data collection methods and dates:** Data was collected over eight weeks, the specific timepoints at which data was collected include the intake visit and seven midweek sessions.	Clinical Interview for DSM-IV who smoked ≥10 cigarettes/day for the previous year, and who met the criteria for current unipolar major depressive disorder. Exclude those receiving other smoking cessation treatment. **Diagnosis and classification method:** Current unipolar major depressive disorder according to DSM-IV-TR and/or scoring ≥14 on the Beck Depression Inventory (BDI). **Setting:** Addictive Behaviours Clinic of the University of Oviedo, Spain.	treatment condition on cigarette demand (Model D: all p values≤.32), suggesting that the differential effect of the CM component was not significant. The group x time interaction was not significant for any cigarette demand index, with the exception of intensity (Model D: β4intensity=−0.32, p=0.004). as time passes, the intervention that includes CM significantly reduces the intensity index when compared to the intervention that does not include such a component. Although not significant, this trend can be observed for the remaining demand indices.	

	Validated questionnaires and biochemical verification, dates not stated. **Outcomes (relevant):** - Urine cotinine levels using a BS-120 chemistry analyser (≥80 ng per milliliter) - Cigarette demand using a cigarette purchase task (CPT)			
Secades-Villa et al (2019) Additive effectiveness of contingency management on cognitive behavioural treatment for smokers with depression: Six-month abstinence and depression outcomes, *Drug Alcohol Depen*; 204(107495). Spain	*This report is linked to Weidberg et al (2018). See Weidberg et al (2018) for full details.* **Study Design:** **Study aim:** To compare the effectiveness of cognitive behavioural treatment (CBT) combined with behavioural activation (BA) and the same treatment protocol plus contingency management (CM). **Type of intervention [*exposure*]:** See Weidberg et al, 2018 **Comparator intervention or control:** See Weidberg et al, 2018 **Data collection methods and dates:** Recruitment occurred between January 2015 and July 2018. After treatment completion, participants attended four follow-up visits at 1, 2, 3, and 6 months to assess long-term outcomes in smoking abstinence and depression. CO and cotinine samples were collected at intake, therapy sessions, and follow-up visits to confirm abstinence (CO ≤4 ppm, cotinine ≤80 ng/ml). Depression-related changes were evaluated using the BDI-II.	**Sample size:** 120 adult smokers (intervention group: *n*= 60, control group: *n*= 60) **Participants:** Aged 18+, self-report using ≥10 cigarettes on a daily basis, meeting current criteria for nicotine dependence as per the Diagnostic and Statistical Manual of Mental Disorders, and obtaining a score ≥ 14 on the Beck Depression Inventory. 70.8% of the included participants were female. Excluded those using pharmacotherapy and/or psychological treatment for smoking cessation or receiving psychotherapy for depression at the intake assessment. Those meeting the criteria for substance use disorders other than nicotine were also excluded and referred to other quitting services **Diagnosis and classification method:** See Weidberg et al, 2018 **Setting:** See Weidberg et al, 2018	**Smoking cessation outcomes:** *Point-prevalence abstinence:* Among participants, the overall point-prevalence abstinence rate at post-treatment (8 weeks) was 69.2% (83/120). Of the different tested mixed-effects model repeated measures models based on residual pseudo likelihood estimation method, Model B was retained as the best-fitting one and showed a significant main effect of time [F(4,395)= 12.04, p< 0.0001], and group by time interaction [F (4,394)= 2.47, p= 0.0442]. This indicates that the effect of treatment conditions on point-prevalence abstinence differed over time. Specifically, the odds of a favourable response in terms of point prevalence abstinence in the group receiving CBT + BA + CM were 2.42 times higher [β =0.88, standard error (SE)= 0.42, p= 0.036, Yule's Q= 0.42] than that of CBT + BA at 1-month follow-up. Of the tested covariates, nicotine dependence severity measured in the intake [F (1,130) = 5.99, p= 0.0158] and the longitudinal covariate (i.e., depressive symptoms) [F(1,487)= 9.06, p= 0.0027 were inversely related to point prevalence abstinence. *Continuous abstinence:* The results obtained from residual maximum likelihood based mixed-effects model repeated measures analysis indicated that there was a significant main effect of group [F(1,155)= 9.55, p= 0.0024], time [F(4,96) = 7.93, p< 0.0001], and group by time interaction [F(4,96) = 6.12, p= 0.0002], which indicates that the effect of treatment conditions on continuous abstinence days differed by group and time-frame assessment. Simple effect comparisons of group by time least-squares means for smoking abstinence	*Trial number: NCT03163056*

	Outcomes (relevant): - Point-prevalence abstinence - Continuous abstinence - Depression		indicated that continuous abstinence at 1-, 2-, 3-, and 6-month follow-up was significantly higher in CBT+BA+CM compared to CBT+BA. Lastly, both the longitudinal covariate (i.e., depressive symptoms) [F(1,186) = 4.11, p= 0.0439] and nicotine dependence [F(1,110) = 4.98, p = 0.0277] were found to be main effects in predicting days of continuous abstinence, thus indicating a relationship between higher levels of depression and nicotine dependence severity and lower treatment effects on continuous abstinence. **Mental health outcomes:** Effects of treatment conditions on depression: There was a significant decrease in depressive symptoms across time [F(5,116) = 57.19, p< 0.0001] that did not differ by treatment condition [F(1,111)= 0.53, p= 0.4665]. The non-significant group by time interaction indicated that treatment groups were similarly associated with a sustained reduction in depression at each of the follow-up visits [F(5,110) = 1.73, p= 0.1332]. Effects of smoking abstinence on depression: The residual maximum likelihood based mixed-effects model repeated measures results for the depression data adjusted for days of continuous abstinence showed that the latter variable was negatively related to depressive symptoms scores [β= -.02, standard error (SE)= .007, t= -3.18, p= 0.0019], thus indicating that a greater number of days of continuous abstinence promotes lower depressive symptoms across time.	
González-Roz et al (2021) <u>One-Year Efficacy and Incremental Cost-effectiveness of Contingency Management</u>	(*Secondary analysis of Secades-Villa et al 2019, see above for full details*) **Study Design:** Cost-effectiveness analysis of a randomised controlled trial. **Study aim:** To examine the 1-year cost-effectiveness of adding contingency management (CM) to cognitive-	**Sample size:** see Secades-Villa et al, 2019 **Participants:** see Secades-Villa et al, 2019). **Diagnosis and classification method:** See Weidberg et al, 2018 **Setting:**	**Smoking cessation outcomes:** The overall point-prevalence rate at 12-month follow-up was 38.3% (46/120). CBT+BA+CM (53.3%; 32/60) was more effective in facilitating 1-year abstinence compared with CBT+BA (23.3%; 14/60). Continuous abstinence ranged from 0 to 418 days (CBT+BA = 97.14 [SD = 160.70] vs. CBT+BA+CM = 187.28 [SD = 182.35], p= .013).	

for Cigarette Smokers with Depression, *Nicotine Tob Res*; 23(2):320-326. Spain	behavioural treatment (CBT) and behavioural activation (BA) for quitting smoking in smokers with depression. **Type of intervention [*exposure*]:** See Weidberg et al, 2018 **Comparator intervention or control:** See Weidberg et al, 2018 **Data collection methods and dates:** Smoking abstinence rates, point prevalence at one-year was determined by self-report of 7-days and verified by carbon monoxide (≤4 ppm) and cotinine-free urine samples (≤80 ng/mL). Longest duration of abstinence was defined as the longest span of consecutive weeks that patients remained continuously abstinent throughout the entire study period. Severity of depressive symptoms was also assessed using the BDI-II. **Outcomes (relevant):** - Smoking abstinence, point prevalence at one-year - Continuous abstinence - Longest duration of abstinence (LDA) at 1-year (longest span of consecutive weeks that patients remained continuously abstinent throughout the entire study period) - Cost-effectiveness	See Weidberg et al, 2018	Weeks of longest duration of abstinence (25.94 [SD = 24.27] vs. 13.97 [SD = 20.61], p= .004, d= .53) were also superior in patients allocated to CBT+BA+CM. The adjusted generalised estimated equations model showed a significant effect of time by group interaction (β= 0.149, 95% CI: 0.035 to 0.262, p= .010). This indicated that the odds of a favourable response in terms of point prevalence were 1.16 (SE= 0.067, p= .010) times higher in CBT+BA+CM than in CBT+BA. **Mental health outcomes:** In regard to BDI-II scores, there was a main effect of abstinence (β= 10.54, 95% CI: 8.87 to 12.22, p< .0001) and time (β= 0.327, 95% CI: −2.04 to 0.76, p< .0001) that did not differ significantly by treatment arm at 12-month follow-up (CBT+BA= 15.23 [SD= 14.07] vs. CBT+BA+CM = 11.33 [SD= 9.17], p= .107). **Cost effectiveness:** The incremental cost-effectiveness ratio for extending the longest duration of abstinence by 1 week was €18 (95% CI: 17.75 to 18.25). At €30, CBT+BA+CM would be 96% likely to be cost-effective, while at €170, the increase in cost-effectiveness would be minimal (0.03%). Above a threshold value of €170, there would be no change in cost-effectiveness. Contingency management is cost-effective with a minimum investment of €20 (US$22.66) (incremental net benefit: €38/US$43.06). As willingness to pay increased, CM net benefit also increased. At an actual cost of €410.64/US$465.14, the net benefit is estimated at €4704 (US$5344.80). The area under the receiving operating characteristic for CM was 0.95 (95% CI: 0.89 to 0.99), indicating an optimum cost per patient of €272.50 (US$308.75) that maximizes the proportion of correctly classified abstinent patients (sensitivity: 81.3%; specificity: 100%).	

6.3 Quality appraisal

Table 6. Risk of bias of randomised controlled trials

			INTERNAL VALIDITY Bias related to:													
		Domain	Selection and allocation			Administration of intervention/ exposure			Assessment, detection, and measurement of the outcome			Participant retention	Statistical conclusion validity			Methodological quality
		Question no.	1	2	3	4	5	6	7	8	9	10	11	12	13	
Study	Outcome	Result at follow up														
Abrantes et al (2023)	7-day PPA	3-months	U	U	Y	U	Y	Y	U	Y	U	N	Y	Y	Y	Moderate quality
		6-months										N	Y	Y		
		12-months										N	Y	Y		
	Depression	3-months							U	Y	U	N	Y	Y		
		6-months										N	Y	Y		
		12-months										N	Y	Y		
Anthenelli et al (2013)	Abstinence	Weeks 9-12	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	Y	High quality
		Weeks 9-24										Y	Y	Y		
		Weeks 9-52										Y	Y	Y		
	7-day PPA	12-weeks							Y	Y	U	Y	Y	Y		
		24-weeks										Y	Y	Y		
		52-weeks										Y	Y	Y		
	Depression	9-weeks							Y	Y	N	Y	Y	Y		
		12-weeks										Y	Y	Y		
Ayers et al (2019)	Abstinence	Weeks 9-12	Y	Y	N	Y	Y	Y	Y	Y	U	U	N	N	Y	Low quality
		Weeks 9-24										U	N	N		
Bernard et al (2015)	Abstinence	12-weeks	Y	U	Y	N	U	Y	U	Y	U	U	Y	N	Y	Low quality
		24-weeks										U	Y	N		

		52-weeks										U	Y	N		
	Anxiety	8-weeks							U	Y	U	U	Y	N		
		12-weeks										U	Y	N		
		24-weeks										U	Y	N		
		52-weeks										U	Y	N		
	Depression	8-weeks							U	Y	U	U	Y	N		
		12-weeks										U	Y	N		
		24-weeks										U	Y	N		
		52-weeks										U	Y	N		
Cinciripini et al (2022)	Abstinence	Weeks 9-12	Y	U	U	Y	Y	U	U	Y	U	U	Y	U	Y	Low quality
		Weeks 9-24										U	Y	U		
Dahne et al (2023)	Floating abstinence	Up to 12-weeks	U	U	U	U	U	N	U	Y	U	U	Y	N	Y	Low quality
	7-day PPA	4-week							U	Y	U	U	Y	N		
		8-weeks										U	Y	N		
		12-weeks										U	Y	N		
	Cigarettes/ day	4-week FU							U	Y	U	U	Y	N		
		8-week FU										U	Y	N		
		12-week FU										U	Y	N		
	24-hour quit attempts	4-week FU							U	Y	U	U	Y	N		
		8-week FU										U	Y	N		
		12-week FU										U	Y	N		
Doran et al (2019)	Abstinence	Weeks 9-12	U	U	Y	Y	Y	U	N	Y	U	N	U	N	Y	Low quality
	7-day PPA	13-weeks							N	Y	U	N	U	N		
		14-weeks										N	U	N		
		16-weeks										N	U	N		
		20-weeks										N	U	N		
		24-weeks										N	U	N		

		28-weeks										N	U	N		
		32-weeks										N	U	N		
		36-weeks										N	U	N		
		40-weeks										N	U	N		
		44-weeks										N	U	N		
		48-weeks										N	U	N		
Evins et al (2008)	7-day PPA	4-week	Y	Y	Y	Y	Y	Y	U	Y	U	U	Y	U	Y	Low quality
	4-week continuous abstinence	Week 10-13							U	Y	U	U	Y	U		
	Depression	13-weeks							U	Y	U	U	Y	U		
González-Roz (2021)	Continuous abstinence	12-month follow up	Y	U	Y	U	U	Y	U	Y	U	U	U	N	Y	Low quality
	7-day PPA	12-month follow up							U	Y	U	U	U	N		
	Depression	12-month follow up							U	Y	U	U	U	N		
Hitsman et al (2023)	7-day PPA	14-weeks	U	Y	N	Y	Y	Y	Y	Y	U	Y	Y	N	Y	Low quality
		27-weeks										Y	Y	N		
	Depression	14-weeks							Y	Y	U	Y	Y	N		
Patten et al (2017)	7-day PPA	12-weeks	Y	Y	Y	N	N	Y	U	Y	U	U	Y	N	Y	Low quality
		6-months										U	Y	N		
	Depression	12-weeks							U	Y	U	U	Y	N		
Secades-Villa et al (2019)	7-day PPA	1-month follow up	Y	U	Y	U	U	Y	U	Y	U	U	Y	N	Y	Low quality
		2-month follow up										U	Y	N		
		3-month follow up										U	Y	N		
		6-month follow up										U	Y	N		
	Continuous abstinence	1-month follow up							U	Y	U	U	Y	N		
		2-month follow up										U	Y	N		

		3-month follow up										U	Y	N		
		6-month follow up										U	Y	N		
	Depression	End of treatment							U	Y	U	U	Y	N		
van der Meer et al (2010)	Prolonged abstinence	6-months	Y	Y	Y	N	N	Y	U	U	Y	U	Y	Y	Y	High quality
		12- months										U	Y	Y		
	7-day PPA	6-months							U	Y	Y	U	Y	Y		
		12- months										U	Y	Y		
	Depression	6-months							U	Y	Y	U	Y	Y		
		12- months										U	Y	Y		
Weidberg et al (2018)	Urine cotinine	Week 1	Y	U	Y	U	U	Y	U	Y	N	Y	Y	N	Y	Low quality
		Week 2										Y	Y	N		
		Week 3										Y	Y	N		
		Week 4										Y	Y	N		
		Week 5										Y	Y	N		
		Week 6										Y	Y	N		
		Week 7										Y	Y	N		
	Cigarette demand	End of treatment							U	Y	N	Y	Y	N		

1. Was true randomisation used for assignment of participants to treatment groups?
2. Was allocation to treatment groups concealed?
3. Were treatment groups similar at baseline?
4. Were participants blind to treatment assignment?
5. Were those delivering the treatment blind to treatment assignment?
6. Were treatment groups treated identically other than the intervention of interest?
7. Were outcome assessors blind to treatment assignment?
8. Were outcomes measured in the same way for treatment groups?
9. Were outcomes measured in a reliable way?
10. Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analysed?
11. Were participants analysed in the groups to which they were randomised?

12. Was appropriate statistical analysis used?
13. Was the trial design appropriate and deviations from the standard RCT design accounted for in the conduct and analysis of the trial?

Table 7. Risk of bias of quasi-experimental studies

			INTERNAL VALIDITY Bias related to:								Statistical conclusion validity	Methodological quality
		Domain	Temporal precedence	Selection and allocation	Confounding factors	Administration of intervention/ exposure	Assessment, detection, and measurement of the outcome			Participant retention		
		Question no.	1	2	3	4	5	6	7	8	9	
Study	Outcome	Result										
Heffner et al (2019)	7-day point prevalence	6-weeks	Y	N	Y	Y	Y	Y	N	N	N	Low quality
	30-day point prevalence	6-weeks					Y	Y	N	N	N	
	Depression	6-weeks					Y	Y	N	N	N	

1. Is it clear in the study what is the “cause” and what is the “effect”?
2. Was there a control group?
3. Were participants included in any comparisons similar?
4. Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?
5. Were there multiple measurements of the outcome, both pre and post the intervention/exposure?
6. Were the outcomes of participants included in any comparisons measured in the same way?
7. Were outcomes measured in a reliable way?
8. Was follow-up complete and if not, were differences between groups in terms of their follow-up adequately described and analysed?
9. Was appropriate statistical analysis used?

6.4 Information available on request

The following are available on request: protocol; search strategies.

7. ADDITIONAL INFORMATION

7.1 Conflicts of interest

The authors declare they have no conflicts of interest to report.

7.2 Acknowledgements

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8. APPENDIX

APPENDIX 1:

Ovid MEDLINE(R) ALL <1946 to March 20, 2024>

1 (anxiety or anxious or depression or depressed or depressive).ti,ab. 690559
2 exp Anxiety/ or Anxiety Disorders/ or Depression/ or Anxiety, Separation/ or Panic Disorder/ or exp Phobic Disorders/ 277678
3 1 or 2 749926
4 Smoking Cessation/ or "Tobacco Use Cessation"/ or "Tobacco Use Cessation Devices"/ 34902
5 ("smoking cessation" or "tobacco cessation" or (tobacco adj2 abstain*) or (smok* adj2 abstain*) or (cigar* adj2 abstain*) or (tobacco adj2 abstinence) or (smok* adj2 abstinence) or (cigar* adj2 abstinence) or (stop* adj2 tobacco) or (stop* adj2 smok*) or (stop* adj2 cigar*) or (quit* adj2 tobacco) or (quit* adj2 smok*) or (quit* adj2 cigar*) or (ceas* adj3 tobacco) or (ceas* adj3 smok*) or (ceas* adj3 cigar*) or ("give up" adj2 tobacco) or ("give up" adj2 smok*) or ("give up" adj2 cigar*)).ti,ab. 43148
6 smoking reduction/ 116
7 ("smoking reduc*" or "tobacco reduc*" or (tobacco adj3 "cut down") or (smoking adj3 "cut down") or (cigar* adj3 "cut down")).ti,ab. 1540
8 4 or 5 or 6 or 7 55485
9 3 and 8 3192
10 Clinical Study/ or exp Clinical Trial/ or Clinical Trial Protocol/ or Observational Study/ or Comparative Study/ 2848018
11 (treatment* or approach* or strateg* or intervention* or trial*).ti,ab. 9710019
12 10 or 11 11404694
13 9 and 12 2317
14 limit 13 to (english language and yr="2007 -Current") 1741
15 (case reports or comment or editorial or letter).pt. 4394954
16 exp animals/ not humans/ 5205065
17 15 or 16 9488032
18 14 not 17 1675

APPENDIX 2:

A reference list of smoking cessation studies comparing people with mental health conditions to the general population. These studies were identified by our search and deemed ineligible for this rapid review but may contribute to a broader understanding of the impact of these interventions in this population.

Depression populations

Pharmacological and psychological interventions

McClure, J. B., Swan, G. E., Jack, L., Catz, S. L., Zbikowski, S. M., McAfee, T. A., ... & Javitz, H. (2009). Mood, side-effects and smoking outcomes among persons with and without probable lifetime depression taking varenicline. *Journal of general internal medicine*, *24*, 563-569. Available at: https://link.springer.com/article/10.1007/s11606-009-0926-8

Comparing those with probable lifetime major depression vs no apparent major depression history.

Pharmacological interventions

Minami, H., Kahler, C. W., Bloom, E. L., Strong, D. R., Abrantes, A. M., Zywiak, W. H., ... & Brown, R. A. (2015). Effects of depression history and sex on the efficacy of sequential versus standard fluoxetine for smoking cessation in elevated depressive symptom smokers. *Addictive Disorders & Their Treatment*, *14*(1), 29-39. Available at: https://journals.lww.com/addictiondisorders/fulltext/2015/03000/Effects_of_Depression_History_and_Sex_on_the.3.aspx

Comparing those with no past depressive episode vs recurrent depressive episodes vs single past depressive episode.

Spring, B., Doran, N., Pagoto, S., McChargue, D., Cook, J. W., Bailey, K., ... & Hedeker, D. (2007). Fluoxetine, smoking, and history of major depression: A randomized controlled trial. *Journal of consulting and clinical psychology*, *75*(1), 85. Available at: https://core.ac.uk/reader/17225910

Comparing those with a history of depression vs without history of depression.

Tidey, J. W., Pacek, L. R., Koopmeiners, J. S., Vandrey, R., Nardone, N., Drobes, D. J., ... & Donny, E. C. (2016). Effects of 6-week use of reduced-nicotine content cigarettes in smokers with and without elevated depressive symptoms. *Nicotine & Tobacco Research*, *19*(1), 59-67. Available at: https://academic.oup.com/ntr/article/19/1/59/2631697

Comparing those with vs without elevated depressive symptoms.

Zawertailo, L., Voci, S., & Selby, P. (2015). Depression status as a predictor of quit success in a real-world effectiveness study of nicotine replacement therapy. *Psychiatry research*, *226*(1), 120-127. Available at: https://www.clinicalkey.com/#!/content/playContent/1-s2.0-S0165178114010208?returnurl=null&referrer=null

Participants were divided into four mutually exclusive groups: current/recent depression, recurrent depression, past depression and no depression history.

Zhang, H., Gilbert, E., Hussain, S., Veldhuizen, S., Le Foll, B., Selby, P., & Zawertailo, L. (2023). Effectiveness of bupropion and varenicline for smokers with baseline depressive

symptoms. *Nicotine and Tobacco Research*, *25*(5), 937-944. Available at: https://academic.oup.com/ntr/article/25/5/937/6911424
Compares those with depressive symptoms vs those without.

Mixed mental health populations

Pharmacological and psychological interventions
Carroll, A. J., Mathew, A. R., Leone, F. T., Wileyto, E. P., Miele, A., Schnoll, R. A., & Hitsman, B. (2020). Extended nicotine patch treatment among smokers with and without comorbid psychopathology. *Nicotine and Tobacco Research*, *22*(1), 24-31. Available at: https://academic.oup.com/ntr/article/22/1/24/5095857
Compares those with vs without a psychiatric condition.

Psychological and exercise interventions
Garey, L., Rogers, A. H., Manning, K., Smit, T., Derrick, J. L., Viana, A. G., ... & Zvolensky, M. J. (2020). Effects of smoking cessation treatment attendance on abstinence: The moderating role of psychologically based behavioral health conditions. *Journal of substance abuse treatment*, *109*, 1-7. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6927534/pdf/nihms-1542480.pdf
Compares those with vs without psychologically based behavioural health conditions.

Media campaigns
Prochaska, J. J., Gates, E. F., Davis, K. C., Gutierrez, K., Prutzman, Y., & Rodes, R. (2019). The 2016 tips from former smokers® campaign: associations with quit intentions and quit attempts among smokers with and without mental health conditions. *Nicotine and Tobacco Research*, *21*(5), 576-583. Available at: https://academic.oup.com/ntr/article/21/5/576/5212283?login=true
Compares people living with mental health conditions vs people without mental health conditions.

Quitline
Nair, U. S., Bell, M. L., Yuan, N. P., Wertheim, B. C., & Thomson, C. A. (2018). Associations between comorbid health conditions and quit outcomes among smokers enrolled in a state Quitline, Arizona, 2011-2016. *Public Health Reports*, *133*(2), 200-206. Available at: https://journals.sagepub.com/doi/full/10.1177/0033354918764903
Compares a chronic health condition group (CHC) vs Mental health condition group (MHC), CHC and MHC group, vs no comorbid condition group.

Vickerman, K. A., Schauer, G. L., Malarcher, A. M., Zhang, L., Mowery, P., & Nash, C. M. (2015). Quitline Use and Outcomes among Callers with and without Mental Health Conditions: A 7-Month Follow-Up Evaluation in Three States. BioMed Research International, 2015(1), 817298. Available at: https://onlinelibrary.wiley.com/doi/full/10.1155/2015/817298
Compares users with and without a reported mental health condition.

Psychological interventions
Heffner, J. L., Mull, K. E., Watson, N. L., McClure, J. B., & Bricker, J. B. (2018). Smokers with bipolar disorder, other affective disorders, and no mental health conditions: comparison of baseline characteristics and success at quitting in a large 12-month behavioural intervention randomized trial. *Drug and alcohol dependence*, *193*, 35-41. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6239897/

Compares those with bipolar disorder vs other affective disorders vs no mental health conditions.

Watson, N. L., Heffner, J. L., Mull, K. E., McClure, J. B., & Bricker, J. B. (2019). Comparing treatment acceptability and 12-month cessation rates in response to web-based smoking interventions among smokers who do and do not screen positive for affective disorders: secondary analysis. *Journal of Medical Internet Research*, *21*(6), e13500. Available at: https://www.jmir.org/2019/6/e13500/
Compares a no affective disorder group vs six non-mutually exclusive subgroups: those with depression, posttraumatic stress disorder, panic disorder, generalized anxiety disorder, social anxiety disorder, and more than one affective disorder.

Wen, S., Wiers, R. W., Boffo, M., Grasman, R. P., Pronk, T., & Larsen, H. (2021). Subtypes of smokers in a randomized controlled trial of a web-based smoking cessation program and their role in predicting intervention non-usage attrition: Implications for the development of tailored interventions. *Internet Interventions*, *26*, 100473. Available at: https://www.sciencedirect.com/science/article/pii/S2214782921001135
Compares three clusters of smokers that differed on a broad range of characteristics – none diagnosed as depression and anxiety but relatively high scores on hopelessness, anxiety sensitivity, impulsivity, depression, and alcohol use.

Pharmacological interventions
Wu, A. D., Gao, M., Aveyard, P., & Taylor, G. (2023). Smoking cessation and changes in anxiety and depression in adults with and without psychiatric disorders. *JAMA Network Open*, *6*(5), e2316111-e2316111. Available at: https://jamanetwork.com/journals/jamanetworkopen/article-abstract/2805442
Compares people with and without psychiatric disorders.

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