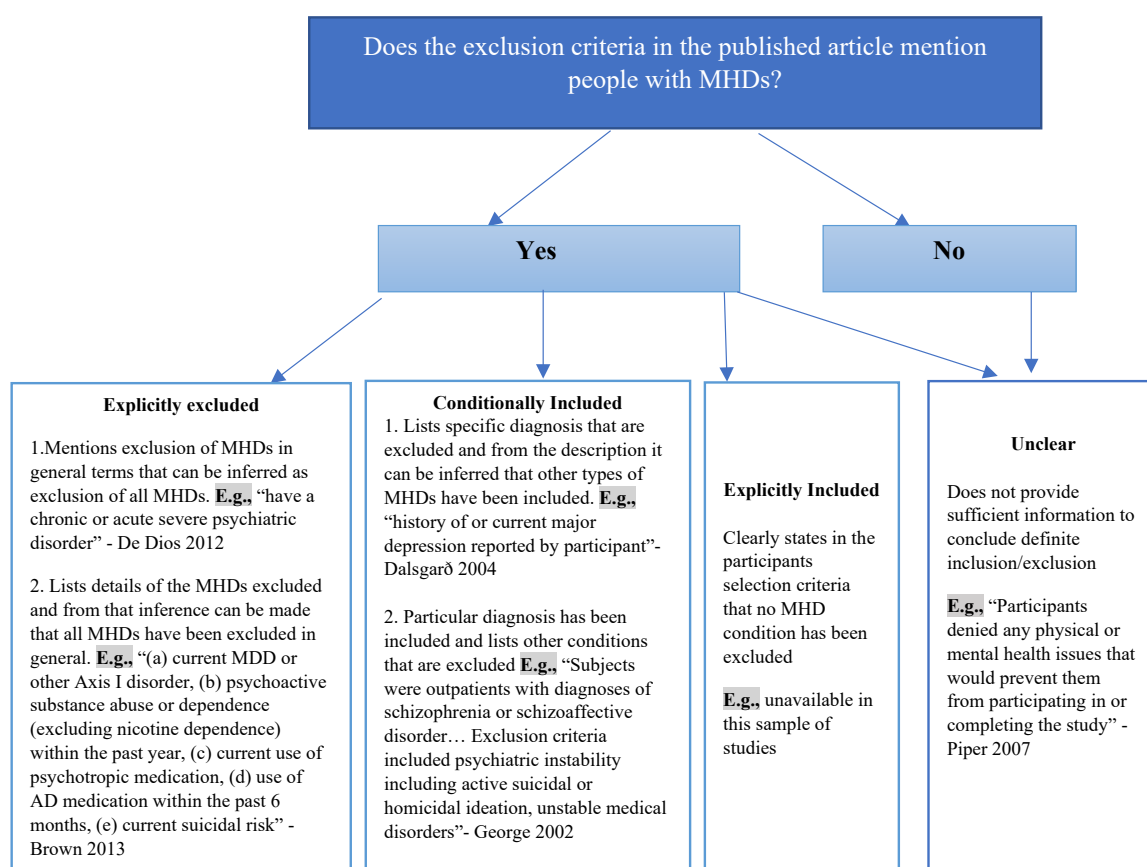


## Inequity in Smoking Cessation Clinical Trials Testing Pharmacotherapies: Exclusion of Smokers with Mental Health Disorders

Saki R. Talukder<sup>a\*</sup>, Julia M. Lappin<sup>b,ii</sup>, Veronica C. Boland<sup>l</sup>, Hayden McRobbie<sup>l</sup>, Ryan J. Courtney<sup>i</sup>

### Supplementary material

Contents	Page number
Figure 1. Decision tree to guide MHD population exclusion/inclusion data extraction	1
Search strategy	2
Table 1: Smoking cessation medication contraindications and warnings/precautions relating to mental illness	2-4
Table 2: Cochrane reviews included in this review to identify RCTs on smoking cessation using pharmacotherapies and RCTs within the Cochrane reviews	4-5
Table 3: Number of included RCTs by the medication being tested	5
Table 4: RCTs included in this review grouped by medication type	6-24



**Figure 1:** Decision tree to guide MHD population exclusion/inclusion data extraction

**Search strategy**

- Identifying all Cochrane reviews on smoking cessation: following search terms were used to identify reviews only on the Cochrane Database of Systematic Reviews without any time limits or filters
  - “quit smoking”, “smoking cessation”, “smoking cessation treatment”, “smoking abstinence”, “smoking abstinence”, “cigarette smoking”, “tobacco use cessation”
- This search identified 506 reviews, 371 duplicated were removed, and further 62 were excluded as “smoking cessation” was not the focus of review. Based on literature pharmacotherapies used for smoking cessation were identified (table 2 in this document), and 60 reviews were excluded as they were not specifically on any of the identified pharmacotherapies for smoking cessation.
- RCTs included within the remaining 13 Cochrane Reviews were checked against the inclusion/exclusion criteria of this review and out of 356 RCTs 279 were included. The PRISMA flow diagram (Figure 1 in main document) provides further details.

Table 1: Smoking cessation medication contraindications and warnings/precautions relating to mental illness

Group of medication	Name of medication	Contraindications and/or warnings and precautions listed in product summary that relate to mental illness
Antidepressants (Atypical antidepressants)	Bupropion	<p>Contraindications</p> <ul style="list-style-type: none"> <li>• Undergoing abrupt withdrawal of alcohol or other medicinal products that are associated with an increased risk of seizure on withdrawal (e.g., benzodiazepines)</li> <li>• Current or previous diagnosis of bulimia or anorexia nervosa</li> <li>• Concomitant use of monoamine oxidase inhibitors</li> <li>• History of bipolar disorder</li> </ul> <p>Special warnings</p> <ul style="list-style-type: none"> <li>• Bupropion should be used with caution in people taking medication that are known to lower seizure threshold. This includes most antidepressant and antipsychotic medications</li> <li>• Care should be taken when using bupropion in people with a history of mental illness, due to the greater possibility of neuropsychiatric events</li> </ul> <p>Source: <a href="https://www.medicines.org.uk/emc/medicine/2948/#gref">https://www.medicines.org.uk/emc/medicine/2948/#gref</a></p>
Antidepressants (Atypical antidepressants)	Venlafaxine	<p>Contraindications</p> <ul style="list-style-type: none"> <li>• None reported</li> </ul> <p>Special warning</p> <ul style="list-style-type: none"> <li>• Venlafaxine should be used with caution in people who have a history of, or if someone in their family has had, mania or bipolar disorder, aggressive behaviour</li> </ul> <p>Source: <a href="https://www.medicines.org.uk/emc/product/4487/pil#gref">https://www.medicines.org.uk/emc/product/4487/pil#gref</a></p>
Antidepressants Selective serotonin reuptake inhibitors (SSRIs)	Fluoxetine	<p>Contraindications</p> <ul style="list-style-type: none"> <li>• Concomitant use of non-selective monoamine oxidase inhibitors</li> </ul> <p>Special warnings</p> <ul style="list-style-type: none"> <li>• Fluoxetine should be taken with caution in people who suffer from epilepsy or had a fit in the past, as it may increase the likelihood of an epileptic fit</li> <li>• Care should be taken when using fluoxetine in people with a history of mental illness known as mania or hypomania</li> </ul> <p>Source: <a href="https://www.medicines.org.uk/emc/files/pil.5787.pdf">https://www.medicines.org.uk/emc/files/pil.5787.pdf</a></p>
Antidepressants Selective serotonin reuptake inhibitors (SSRIs)	Paroxetine	<p>Contraindications</p> <ul style="list-style-type: none"> <li>• Concomitant use of monoamine oxidase inhibitors or have taken them at any time within the last two weeks.</li> <li>• Concomitant use of anti-psychotic medicines called thioridazine or pimozide.</li> </ul> <p>Special warnings:</p> <ul style="list-style-type: none"> <li>• Paroxetine should be taken with caution in people who have epilepsy or history of fits or seizures</li> <li>• Care should be taken in people with history of mania or having a treatment for severe depression called electro convulsive therapy (ECT)</li> <li>• Caution should be followed if taking medicines that may increase the risk of bleeding, including antipsychotics such as perphenazine or clozapine, tricyclic antidepressants, such as clomipramine</li> </ul> <p>Source: <a href="https://www.medicines.org.uk/emc/files/pil.8486.pdf">https://www.medicines.org.uk/emc/files/pil.8486.pdf</a></p>
Antidepressants Selective serotonin reuptake inhibitors (SSRIs)	Sertraline	<p>Contraindications</p> <ul style="list-style-type: none"> <li>• Concomitant use of monoamine oxidase inhibitors</li> <li>• Concomitant use of monoamine oxidase inhibitors called pimozide (a medicine for mental disorders such as psychosis)</li> </ul> <p>Special warnings:</p> <ul style="list-style-type: none"> <li>• Caution should be taken in people with epilepsy (fit) or a history of seizures</li> <li>• Sertraline should be used with caution in people who have suffered from manic depressive illness (bipolar disorder) or schizophrenia. Also, among people have or have previously had suicidal ideation</li> </ul> <p>Source: <a href="https://www.medicines.org.uk/emc/files/pil.4348.pdf">https://www.medicines.org.uk/emc/files/pil.4348.pdf</a></p>

Antidepressants Tricyclic antidepressants (TCAs)	Nortriptyline	<p>Contraindications</p> <ul style="list-style-type: none"> <li>Suffering from mania (abnormally raised mood)</li> <li>Concomitant use, or have taken in the last two weeks, monoamine oxidase inhibitors</li> </ul> <p>Special warnings:</p> <ul style="list-style-type: none"> <li>Nortriptyline should be taken with caution in people who are suicidal or aggressive, are agitated, overactive or suffer from schizophrenia, and have a history of epilepsy</li> <li>Caution should be followed in people who are undergoing electroconvulsive therapy and had an allergic reaction to another tricyclic antidepressant in the past</li> </ul> <p>Source: <a href="https://www.medicines.org.uk/emc/files/pil.2423.pdf">https://www.medicines.org.uk/emc/files/pil.2423.pdf</a></p>
Antidepressants Monoamine oxidase inhibitors (MAOIs)	Selegiline	<p>Contraindications</p> <ul style="list-style-type: none"> <li>Taking any antidepressants. Antidepressants should be stopped a number of weeks before taking Eldepryl,</li> <li>taking any monoamine oxidase (MAO) inhibitors e.g., the antibiotic linezolid</li> </ul> <p>Special warnings:</p> <ul style="list-style-type: none"> <li>Selegiline (Eldepryl) should be taken with caution if patient is being treated for any mental illness, anxiety or sleep problems</li> <li>Care should be taken in people taking Levodopa, as it can cause agitation and uncontrollable movements.</li> <li>Caution should be followed in people with history of any unusual urges and/or behaviours (such as excessive gambling or excessively sexual behaviour)</li> </ul> <p>Source: <a href="https://www.medicines.org.uk/emc/files/pil.2251.pdf">https://www.medicines.org.uk/emc/files/pil.2251.pdf</a></p>
Antidepressants Monoamine oxidase inhibitors (MAOIs)	Moclobemide	<p>Contraindications</p> <ul style="list-style-type: none"> <li>Suffering from a severe mental problem that may make you confused, lose contact with reality or become unable to think and judge clearly.</li> <li>Concomitant use or have recently stopped taking any other medicines to treat depression or anxiety, such as fluoxetine, paroxetine or clomipramine.</li> </ul> <p>Special warnings:</p> <ul style="list-style-type: none"> <li>Moclobemide (Manerix) should be taken with caution in people suffering from bipolar disorder or manic depression, or have ever had suicidal ideation</li> </ul> <p>Source: <a href="https://www.medicines.org.uk/emc/files/pil.6661.pdf">https://www.medicines.org.uk/emc/files/pil.6661.pdf</a></p>
Antidepressants Extracts of St. John's wort	St. John's wort	<p>Contraindications</p> <ul style="list-style-type: none"> <li>Diagnosis of depression</li> </ul> <p>Source: <a href="https://www.medicines.org.uk/emc/files/pil.9038.pdf">https://www.medicines.org.uk/emc/files/pil.9038.pdf</a></p>
Antidepressants Dietary supplement	S-Adenosyl-L-Methionine (SAME)	<p>Contraindications</p> <ul style="list-style-type: none"> <li>Diagnosis of bipolar disorder, as SAME may worsen symptoms of mania)</li> </ul> <p>Special warnings:</p> <ul style="list-style-type: none"> <li>Precautions must be followed among people who are taking Levodopa to treat Parkinson's disease, taking antidepressants, as SAME increase levels of serotonin</li> </ul> <p>Source: <a href="https://files.nccih.nih.gov/s3fs-public/SAMe_08-11-2015.pdf">https://files.nccih.nih.gov/s3fs-public/SAMe_08-11-2015.pdf</a></p>
nAChR partial agonist	Cytisine	<p>Contraindications</p> <ul style="list-style-type: none"> <li>None reported</li> </ul> <p>Special warnings:</p> <ul style="list-style-type: none"> <li>Cytisine (Desmoxan) should be taken with caution in people suffering from schizophrenia and epilepsy</li> </ul> <p>Source: <a href="https://ndarc.med.unsw.edu.au/sites/default/files/ndarc/resources/Desmoxan.pdf">https://ndarc.med.unsw.edu.au/sites/default/files/ndarc/resources/Desmoxan.pdf</a></p>
nAChR partial agonist	Varenicline	<p>Contraindications</p> <ul style="list-style-type: none"> <li>None reported</li> </ul> <p>Special warnings:</p> <ul style="list-style-type: none"> <li>Champix should be taken with caution, as there have been reports of depression, suicidal ideation and behaviour and suicide attempts in patients taking this medication. If someone develops agitation, depressed mood, changes in behaviour after taking CHAMPIX or develop suicidal thoughts or behaviours, should stop taking Champix and contact the doctor immediately for treatment assessment.</li> <li>Care should be taken among people who have experienced seizures or have epilepsy</li> </ul> <p>Source: <a href="https://www.medicines.org.uk/emc/files/pil.266.pdf">https://www.medicines.org.uk/emc/files/pil.266.pdf</a></p>
NRT	Nicotine Gum	<p>Contraindications</p> <ul style="list-style-type: none"> <li>None reported</li> </ul> <p>Special warnings:</p> <ul style="list-style-type: none"> <li>None reported</li> </ul> <p>Source: <a href="https://www.aafp.org/dam/AAFP/documents/patient_care/tobacco/pharmacologic-guide.pdf">https://www.aafp.org/dam/AAFP/documents/patient_care/tobacco/pharmacologic-guide.pdf</a></p>
NRT	Nicotine Lozenges and Transdermal Patch	<p>Contraindications</p> <ul style="list-style-type: none"> <li>None reported</li> </ul> <p>Special warnings:</p> <ul style="list-style-type: none"> <li>None reported</li> </ul> <p>Source: <a href="https://www.aafp.org/dam/AAFP/documents/patient_care/tobacco/pharmacologic-guide.pdf">https://www.aafp.org/dam/AAFP/documents/patient_care/tobacco/pharmacologic-guide.pdf</a></p>
NRT	Nasal Spray	<p>Contraindications</p> <ul style="list-style-type: none"> <li>None reported</li> </ul> <p>Special warnings:</p> <ul style="list-style-type: none"> <li>None reported</li> </ul> <p>Source: <a href="https://www.aafp.org/dam/AAFP/documents/patient_care/tobacco/pharmacologic-guide.pdf">https://www.aafp.org/dam/AAFP/documents/patient_care/tobacco/pharmacologic-guide.pdf</a></p>

NRT	Oral Inhaler	Contraindications <ul style="list-style-type: none"> <li>None reported</li> </ul> Special warnings: <ul style="list-style-type: none"> <li>None reported</li> </ul> Source: <a href="https://www.aafp.org/dam/AAFP/documents/patient_care/tobacco/pharmacologic-guide.pdf">https://www.aafp.org/dam/AAFP/documents/patient_care/tobacco/pharmacologic-guide.pdf</a>
Opioid antagonist	Naltrexone	Contraindications <ul style="list-style-type: none"> <li>Receiving opioid analgesics, currently dependent, in acute opioid withdrawal</li> </ul> Special warnings: <ul style="list-style-type: none"> <li>Precautions must be followed while taking naltrexone in patients with substance abuse with or without concomitant depression, as it may increase the risk of suicide. This risk is not abated by treatment with naltrexone hydrochloride</li> </ul> Source: <a href="https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&amp;id=CP-2013-PI-01168-1">https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&amp;id=CP-2013-PI-01168-1</a>
Cannabinoid receptor antagonist	Rimonabant	Contraindications <ul style="list-style-type: none"> <li>Suffering from major depressive illness and/or taking anti-depressive treatment</li> </ul> Special warnings: <ul style="list-style-type: none"> <li>Rimonabant (Acomplia) should be taken with caution in people with a history of depressive disorders/mood alterations, uncontrolled psychiatric illness, and seizures</li> </ul> Source: <a href="https://www.ema.europa.eu/en/documents/product-information/acomplia-epar-product-information_en.pdf">https://www.ema.europa.eu/en/documents/product-information/acomplia-epar-product-information_en.pdf</a>
Anxiolytics	Buspirone Beta-blockers Oxprenolol Metoprolol	Contraindications <ul style="list-style-type: none"> <li>Epilepsy</li> </ul> Special warnings: <ul style="list-style-type: none"> <li>Should be taken with caution in people taking benzodiazepine e.g., nitrazepam or temazepam or another common sedative or hypnotic medicine, or have had drug dependence</li> </ul> Source: <a href="https://www.medicines.org.uk/emc/files/pil.5735.pdf">https://www.medicines.org.uk/emc/files/pil.5735.pdf</a>
	Diazepam	Contraindications <ul style="list-style-type: none"> <li>Phobic or obsessional states; chronic psychosis, hyperkinesia (paradoxical reactions may occur)</li> <li>depression or those with anxiety and depression as suicide may be precipitated in such patients.</li> </ul> Special warnings: <ul style="list-style-type: none"> <li>Should be taken with caution in people taking alcohol and/or CNS depressants</li> <li>Extreme caution should be used in prescribing diazepam to patients with personality disorders</li> </ul> Source: <a href="https://www.medicines.org.uk/emc/product/4524/smpc#gref">https://www.medicines.org.uk/emc/product/4524/smpc#gref</a>
Nicotine acetylcholine receptor antagonist	Mecamylamine	Contraindications <ul style="list-style-type: none"> <li>None reported</li> </ul> Special warnings: <ul style="list-style-type: none"> <li>None reported</li> </ul> Source: <a href="https://www.emedicinehealth.com/drug-mecamylamine/article_em.htm">https://www.emedicinehealth.com/drug-mecamylamine/article_em.htm</a>
Alpha-agonist hypotensive	Clonidine	Contraindications <ul style="list-style-type: none"> <li>None reported</li> </ul> Special warnings: <ul style="list-style-type: none"> <li>Should be taken with caution, as sudden cessation of clonidine treatment has, in some cases, resulted in symptoms such as nervousness, agitation, headache, and tremor accompanied or followed by a rapid rise in blood pressure and elevated catecholamine concentrations in the plasma</li> </ul> Source: <a href="https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/017407s034lbl.pdf">https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/017407s034lbl.pdf</a>

Table 2: Cochrane reviews included in this review to identify RCTs on smoking cessation using pharmacotherapies and RCTs within the Cochrane reviews

Treatment	1st Author	Review Year	Title of Review	Number of RCTs included in each Cochrane review (n = 359)	Number of RCTs included in this review from each Cochrane review (n= 279)
Antidepressants	Hughes, J. R.	2014	Antidepressants for smoking cessation	90	80
Anxiolytics	Hughes, J. R.	2000	Anxiolytics for smoking cessation	7	5
Clonidine	Gourlay, S. G.	2004	Clonidine for smoking cessation	6	4
Electronic cigarettes	Hartmann-Boyce, J.	2016	Electronic cigarettes for smoking cessation	24	2
Lobeline	Stead, L. F.	2012	Lobeline for smoking cessation	0	0

Mecamylamine	Lancaster, T.	1998	Mecamylamine (a nicotine antagonist) for smoking cessation	2	2
Nicobrevin	Stead, L. F.	2006	Nicobrevin for smoking cessation	0	0
Nicotine receptor partial agonists	Cahill, K.	2016	Nicotine receptor partial agonists for smoking cessation	44	39
Nicotine vaccines	Hartmann-Boyce, J.	2012	Nicotine vaccines for smoking cessation	4	4
Nicotine Replacement Therapy	Hartmann-Boyce, J.	2018	Nicotine replacement therapy versus control for smoking cessation	136	120
Opioid antagonists	David, S. P.	2013	Opioid antagonists for smoking cessation	8	7
Rimonabant	Cahill, K.	2011	Cannabinoid type 1 receptor antagonists for smoking cessation	3	3
Silver acetate	Lancaster, T.	2012	Silver Acetate for Smoking Cessation	2	2
<b>Search updated in December 2020</b>					
Antidepressants	Howes, S.	2020	Antidepressants for smoking cessation	33	11

Table 3: Number of included RCTs by the medication being tested

Group of treatment	Name of Medication	Number of RCTs (n = 279)
Antidepressants	Bupropion	65
	Fluoxetine	6
	Paroxetine	1
	Venlafaxine	1
	Sertraline	1
	Nortriptyline	7
	Selegiline	5
	Moclobemide	1
	St John's-wort	3
	S-Adenosyl methionine (SAME)	1
nAChR partial agonist	Dianicline	1
	Cytisine	4
	Varenicline	34
NRT	Single NRT product	111
	Combination/choice of NRT products	9
Other	Rimonabant	3
	Silver acetate	2
	Buspirone	3
	Clonidine	4
	Diazepam	1
	Mecamylamine	2
	Beta-blockers	1
	Naltrexone	7
	NEC (nicotine EC)	2
	Nicotine vaccine	4

Table 4: RCTs included in this review grouped by medication type

Author & Year	Treatment group	Medication type	Comparison group	Exclusion criteria related to mental illness	Does the exclusion criteria mention Population with MHDs?	Reviewers' Decision on MHDs exclusion/inclusion based on information provided in published article
Ahluwalia 2002	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>current use of psychoactive medication</li> <li>in drug treatment during the past 6 months</li> <li>being treated for depression</li> </ul>	Yes	Conditionally include
Aubin 2004	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>diagnosis of anorexia nervosa or bulimia, bipolar affective disorder, panic disorder or psychosis</li> <li>recent history of alcohol severe problems</li> <li>substance abuse or dependence</li> <li>current major depression</li> </ul>	Yes	Conditionally include
Aveyard 2008	Antidepressants	Nortriptyline	Placebo	<ul style="list-style-type: none"> <li>a contraindication or caution to nortriptyline or contraindication to nicotine replacement therapy and those taking a drug that interacted with nortriptyline</li> </ul>	Yes	Conditionally include
Berlin 1995	Antidepressants	Moclobemide	Placebo	<ul style="list-style-type: none"> <li>DSM-III-R criteria for psychoactive substance use disorders: alcohol dependence or abuse or drug dependence or abuse (with the exception of nicotine dependence)</li> <li>actual episodes of major depression, dysthymia, anxiety disorders, or psychotic episodes; or if they took antidepressants, anxiolytics</li> </ul>	Yes	Conditionally include
Biberman 2003	Antidepressants	Selegiline	Placebo	<ul style="list-style-type: none"> <li>major physical or mental disorder</li> <li>abuse of alcohol or use of illegal drug within the preceding year</li> </ul>	Yes	Conditionally include
Blondal 1999	Antidepressants	Fluoxetine	Placebo + NRT	<ul style="list-style-type: none"> <li>current and past (in the preceding 2 years) treatment with an antidepressant were excluded</li> <li>current abuse of alcohol</li> </ul>	Yes	Conditionally include
Brown 2007	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>current Axis I disorder according to the 4th edition</li> <li>DSM-IV diagnosis of past-year psychoactive substance abuse or dependence</li> <li>current use of psychotropic medication or medication that may interact adversely with bupropion</li> <li>current weekly (or more frequent) psychotherapy</li> <li>eating disorder; or panic disorder."</li> </ul>	Yes	Explicitly exclude
Brown 2013	Antidepressants	Fluoxetine	No Placebo	<ul style="list-style-type: none"> <li>current MDD or other Axis I disorder</li> <li>psychoactive substance abuse or dependence (excluding nicotine dependence) within the past year</li> <li>current use of psychotropic medication,</li> <li>use of AD medication within the past 6 months</li> <li>current suicidal risk</li> </ul>	Yes	Explicitly exclude
Cinciripini 2005	Antidepressants	Venlafaxine	Placebo	<ul style="list-style-type: none"> <li>currently taking psychoactive medication</li> <li>current substance abuse, or other psychiatric disorders</li> </ul>	Yes	Explicitly exclude
Cinciripini 2013	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>currently taking psychotropic medication</li> <li>lifetime history of a psychotic disorder</li> </ul>	Yes	Explicitly exclude

				<ul style="list-style-type: none"> <li>psychiatric hospitalization within the last year</li> <li>current psychiatric disorder (including substance abuse except for smoking)</li> <li>scoring moderate or higher on the suicidality subscale of the Mini-International Neuropsychiatric Interview</li> <li>contraindications to the use of varenicline (e.g., severe renal impairment) or bupropion SR (e.g., history of seizures).”</li> </ul>		
Collins 2004	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>currently used psychotropic medications</li> <li>history of Diagnostic and Statistical Manual of Mental Disorders Axis I psychiatric disorder</li> <li>contraindications for bupropion</li> </ul>	Yes	Explicitly exclude
Covey 2002	Antidepressants	Sertraline	Placebo	<ul style="list-style-type: none"> <li>use of a psychotropic medication</li> <li>major depression, alcohol or drug dependence, panic disorder, posttraumatic stress disorder, anorexia nervosa, or bulimia nervosa within the past 6 months</li> <li>lifetime diagnosis of bipolar disorder, antisocial or schizotypal personality disorder, severe borderline personality disorder, obsessive-compulsive disorder, or psychosis including schizophrenia</li> </ul>	Yes	Conditionally include
Covey 2007	Antidepressants	Bupropion	Placebo + NRT	<ul style="list-style-type: none"> <li>use of psychoactive medications</li> <li>psychiatric conditions including current major depressive disorder</li> <li>dependence on alcohol or drugs within the past year</li> <li>life-time history of bipolar disorder or any psychotic illness</li> </ul>	Yes	Conditionally include
Cox 2012	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>use of psychoactive medications</li> <li>history of alcohol or substance abuse within the past year; current drinking of 14 or more alcoholic drinks per week and/or drinking five or more drinks on one occasion two or more times in the past month</li> <li>history of bulimia or anorexia nervosa</li> </ul>	Yes	Conditionally include
Croghan 2007	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>history of bulimia/anorexia nervosa</li> <li>chemical dependence on any drug other than nicotine in the past year</li> <li>use of antipsychotics, antidepressants</li> </ul>	Yes	Conditionally include
Da Costa 2002	Antidepressants	Nortriptyline	Placebo	<ul style="list-style-type: none"> <li>mental deficiency</li> </ul>	Yes	Conditionally include
Dalsgarð 2004	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>history of or current major depression reported by participant</li> </ul>	Yes	Conditionally include
Eisenberg 2013	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>use of anti-depressants, anti-psychotics</li> <li>current diagnosis of major depression (requiring medication), bipolar disease, or dementia</li> <li>history of suicidal events (previous suicide attempt, suicidal ideation) or family history of suicide; History of anorexia nervosa or bulimia</li> <li>use of any illegal drugs in the past year (e.g., opiates, cocaine, heroin)</li> </ul>	Yes	Conditionally include
Evins 2001	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>acute exacerbation of psychosis</li> <li>active co-morbid substance abuse, or bulimia</li> <li>current but not past major depressive episode</li> </ul>	Yes	Conditionally include
Evins 2005	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>unstable symptoms and an unstable dose of antipsychotic medication for 30 days</li> <li>meet Diagnostic and Statistical Manual of Mental Disorders</li> <li>history of bulimia, and history of mania or substance abuse disorder other than nicotine or caffeine within 6 months of enrolment</li> </ul>	Yes	Conditionally include
Evins 2007	Antidepressants	Bupropion	Placebo + NRT	<ul style="list-style-type: none"> <li>unstable psychiatric symptoms and antipsychotic dose for 30 days or more</li> </ul>	Yes	Conditionally include

				<ul style="list-style-type: none"> <li>• current major depressive disorder</li> <li>• substance use disorder other than nicotine or caffeine within 6 months of screening</li> <li>• bulimia</li> </ul>		
Fossati 2007	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>• use of antidepressants and antipsychotics</li> <li>• a medical history of eating disorders</li> </ul>	Yes	Conditionally include
Gariti 2009	Antidepressants	Bupropion	Placebo + NRT	<ul style="list-style-type: none"> <li>• not in reasonably good health, including being psychiatrically unstable</li> <li>• history of psychosis, mania (Bipolar 1), eating disorder</li> <li>• substance abuse/dependence within the past 6 months or current use of cocaine</li> <li>• current use of an anti-depressant was also exclusionary</li> <li>• Severe anxiety disorders and depressive disorders</li> </ul>	Yes	Conditionally include
George 2002	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>• unstable schizophrenia or schizoaffective disorder</li> <li>• not on stable doses of their antipsychotic drugs for at least one month prior to randomization and continued antipsychotic treatment during the trial</li> <li>• evidence of alcohol or illicit drug abuse or dependence in the 3 months prior to screening evaluation</li> <li>• psychiatric instability including active suicidal or homicidal ideation, unstable medical disorders and inability to give informed consent</li> </ul>	Yes	Conditionally include
George 2003	Antidepressants	Selegiline	Placebo	<ul style="list-style-type: none"> <li>• lifetime history of schizophrenia, bipolar disorder, panic disorder, and posttraumatic stress disorder were excluded from the trial</li> <li>• past history of major depression</li> <li>• use of antidepressant medications or sympathomimetic agents (e.g., phenylephrine, methylphenidate)</li> <li>• history of alcohol/drug abuse or dependence (except nicotine or caffeine) in the 6 months before study enrolment</li> </ul>	Yes	Conditionally include
George 2008	Antidepressants	Bupropion	Placebo + NRT	<ul style="list-style-type: none"> <li>• positive urine drug screen, or evidence of alcohol or illicit drug abuse or dependence in the 3 months prior to screening evaluation</li> <li>• history of seizure disorders</li> <li>• psychiatric instability including active suicidal or homicidal ideation, unstable medical disorders and inability to give informed consent</li> </ul>	Yes	Conditionally include
Gonzales 2001	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>• history of bulimia or anorexia nervosa</li> <li>• had a current diagnosis of major depression</li> </ul>	Yes	Conditionally include
Grant 2007	Antidepressants	Bupropion	Placebo + NRT	<ul style="list-style-type: none"> <li>• history of schizophrenia or bipolar affective disorder</li> <li>• current use of any of the following medications: tricyclic antidepressants, monoamine oxidase inhibitors, fluoxetine, antipsychotics, benzodiazepines, protriptyline, theophylline or any investigational drug in the previous four weeks</li> </ul>	Yes	Conditionally include
Haggström 2006	Antidepressants	Bupropion & Nortriptyline	Placebo	<ul style="list-style-type: none"> <li>• serious or unstable clinical or psychiatric disorders (including history of severe depression)</li> <li>• alcohol or any other drug abuse</li> </ul>	Yes	Conditionally include
Hall 1998	Antidepressants	Nortriptyline	Placebo	<ul style="list-style-type: none"> <li>• met the criteria for MDD within 3 months of the baseline were excluded and referred for depression treatment</li> <li>• use of prescribed psychotropic drugs</li> </ul>	Yes	Conditionally include
Hall 2002	Antidepressants	Bupropion & Nortriptyline	Placebo	<ul style="list-style-type: none"> <li>• bulimia</li> <li>• bipolar disease, current major depressive disorder (MDD)</li> </ul>	Yes	Conditionally include



				<ul style="list-style-type: none"> <li>• treatment for alcohol or other drug use within 6 months</li> <li>• psychiatric hospitalization within 1 year</li> <li>• use of any psychiatric medication</li> <li>• suicidal or psychotic symptoms</li> </ul>		
Hall 2004	Antidepressants	Nortriptyline	Placebo	<ul style="list-style-type: none"> <li>• bulimia</li> <li>• bipolar disease, current major depressive disorder (MDD)</li> <li>• treatment for alcohol or other drug use within 6 months</li> <li>• psychiatric hospitalization within 1 year</li> <li>• use of any psychiatric medication</li> <li>• suicidal or psychotic symptoms</li> </ul>	Yes	Conditionally include
Hall 2011	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>• lifetime bipolar disorder, current major depression disorder</li> <li>• current use of any psychiatric medication</li> <li>• suicidal or psychotic symptoms</li> <li>• treatment of drug or alcohol use within the prior 6 months</li> <li>• psychiatric hospitalization within the prior year</li> </ul>	Yes	Conditionally include
Hatsukami 2004	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>• eating disorders</li> <li>• concurrent drug therapy (e.g., psychoactive drugs, theophylline)</li> <li>• symptoms of depression at the time of enrolment (Beck Depression Inventory score 7 and verified by clinical impression)</li> <li>• history or current diagnosis of other serious psychiatric illness (e.g., panic disorder, psychosis, bipolar disorder)</li> <li>• history of alcohol or other substance abuse in the year before enrolment.”</li> </ul>	Yes	Conditionally include
Hays 2001	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>• history or current diagnosis of anorexia nervosa or bulimia</li> <li>• presence of an unstable medical or psychiatric condition</li> <li>• current use of psychotropic medications</li> <li>• current use of any behavioural therapy for smoking cessation</li> <li>• current major depression</li> </ul>	Yes	Conditionally include
Hays 2009	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>• current diagnosis of anorexia nervosa or bulimia</li> <li>• presence of an unstable medical or psychiatric condition</li> <li>• current use of psychotropic medications</li> <li>• current (within the past 3 months) DSM - IV diagnosis of a major depressive disorder</li> </ul>	Yes	Conditionally include
Hertzberg 2001	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>• use psychotropic medication or an unstable psychotropic regimen (same dosage and drug for at least 6 months before the study).”</li> </ul>	Yes	Conditionally include
Holt 2005	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>• anorexia or bulimia</li> <li>• pregnant or lactating; history of alcohol or drug abuse</li> </ul>	Yes	Conditionally include
Hurt 1997	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>• history or current diagnosis of anorexia nervosa or bulimia</li> <li>• presence of an unstable medical or psychiatric condition</li> <li>• history of dependence on alcohol or a non-nicotine substance within the past year</li> <li>• current use of psychotropic medications</li> <li>• current depression as assessed by the physician</li> </ul>	Yes	Conditionally include
Hurt 2003	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>• current (1 month) major psychiatric disorder or use of major psychiatric medications</li> <li>• active alcoholism or drug dependence</li> </ul>	Yes	Conditionally include

				<ul style="list-style-type: none"> <li>• history of anorexia or bulimia</li> </ul>		
Jorenby 1999	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>• current diagnosis of major depressive episode or a history of panic disorder, psychosis, bipolar disorder, or eating disorders</li> <li>• abuse of alcohol or a non-nicotine-containing drug within the preceding year</li> <li>• use of a psychoactive drug within the week before enrolment</li> </ul>	Yes	Conditionally include
Jorenby 2006	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>• contraindications for use of bupropion (diagnosis of eating disorder)</li> <li>• serious or unstable disease within the previous 6 months</li> <li>• history of alcohol or other drug abuse or dependence in the previous 12 months (nicotine excepted)</li> <li>• treatment for major depression in the previous 12 months</li> <li>• history of or current panic disorder, psychosis, or bipolar disorder</li> </ul>	Yes	Conditionally include
Kahn 2012	Antidepressants	Selegiline	Placebo	<ul style="list-style-type: none"> <li>• current diagnosis of major depressive disorder or other neuropsychiatric disorders that required current contraindicated pharmacological treatment</li> </ul>	Yes	Conditionally include
Kalman 2011	Antidepressants	Bupropion	Placebo + NRT	<ul style="list-style-type: none"> <li>• diagnosis of schizophrenia</li> <li>• current psychotic episode</li> </ul>	Yes	Conditionally include
Killen 2000	Antidepressants	Paroxetine	Placebo + NRT	<ul style="list-style-type: none"> <li>• history of bipolar disorder, schizophrenia</li> <li>• receiving active treatment for or reported current depression or substance abuse</li> <li>• taking antidepressants, psychotropics, or other drugs that could interact with paroxetine resulting in potentially adverse consequences</li> </ul>	Yes	Conditionally include
Killen 2004	Antidepressants	Bupropion	Placebo + NRT	<ul style="list-style-type: none"> <li>• potential participants received a comprehensive history and physical exam conducted by a study physician and an assessment of past and current depression and current drug use. No further details provided</li> </ul>	No	Unclear
Killen 2006	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>• bipolar disorder, schizophrenia</li> <li>• receiving active treatment for or reporting current depression or substance abuse</li> </ul>	Yes	Conditionally include
Killen 2010	Antidepressants	Selegiline	Placebo	<ul style="list-style-type: none"> <li>• bipolar disorder, schizophrenia</li> <li>• active treatment for or reporting current depression or substance abuse</li> <li>• use of medications contraindicated for use with selegiline</li> </ul>	Yes	Conditionally include
Levine 2010	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>• current major depressive disorder or suicidality</li> <li>• drug or alcohol dependence within the past year</li> <li>• psychotic disorders</li> <li>• use of medications contraindicated with bupropion</li> </ul>	Yes	Conditionally include
McCarthy 2008	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>• bipolar disorder, psychosis, current depression</li> <li>• contraindications to bupropion SR use</li> <li>• history of eating disorders</li> <li>• current heavy drinking</li> </ul>	Yes	Conditionally include
Muramoto 2007	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>• history or current diagnosis or treatment of panic disorder, psychosis, bipolar disorder, or eating disorder</li> <li>• substance abuse or dependence in the 3 months preceding the study</li> <li>• current clinical depression or ADHD</li> <li>• any psychoactive drug treatment within 4 weeks of the study treatment phase</li> </ul>	Yes	Conditionally include
Myles 2004	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>• any medical condition or drug therapy that was considered likely to interact with bupropion</li> </ul>	Yes	Conditionally include

				<ul style="list-style-type: none"> <li>major depression or psychosis</li> <li>alcoholism or substance abuse</li> </ul>		
Niaura 2002	Antidepressants	Fluoxetine	Placebo	<ul style="list-style-type: none"> <li>use of psychotropic medication or current psychiatric illness</li> <li>alcohol or drug abuse in the past year</li> <li>suicidal ideation</li> <li>history of bipolar disorder</li> </ul>	Yes	Explicitly exclude
Parsons 2009	Antidepressants	St John's-wort	Placebo	<ul style="list-style-type: none"> <li>history of an eating disorder</li> <li>severe mental illness</li> <li>regular use of illegal drugs or alcohol dependence within the past 6 months</li> <li>currently depressed or taking antidepressant medication</li> </ul>	Yes	Conditionally include
Piper 2007	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>any mental health issues that would prevent them from participating in or completing the study. No further details provided</li> </ul>	No	Unclear
Planer 2011	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>clinical depression or was prescribed antidepressants</li> <li>had been diagnosed as having anorexia nervosa and/or bulimia</li> </ul>	Yes	Conditionally include
Prochazka 1998	Antidepressants	Nortriptyline	Placebo	<ul style="list-style-type: none"> <li>current major depression or other significant psychiatric disorder</li> <li>alcohol or drug dependence</li> <li>contraindication or allergy to nortriptyline</li> </ul>	Yes	Conditionally include
Prochazka 2004	Antidepressants	Nortriptyline	Placebo	<ul style="list-style-type: none"> <li>current major depression or other significant psychiatric disorder</li> <li>alcohol or drug dependence</li> <li>contraindication or allergy to nortriptyline</li> </ul>	Yes	Conditionally include
Richmond 2013	Antidepressants	Nortriptyline	Placebo	<ul style="list-style-type: none"> <li>mental illness (major depressive disorder, bipolar disorder; threats of suicide or repeated deliberate self-harm; current psychotic disorder)</li> <li>current use of antidepressant or antipsychotic medication</li> <li>current major depression</li> </ul>	Yes	Conditionally include
Rigotti 2006	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>contraindication to bupropion</li> <li>heavy alcohol use (3 drinks/day)</li> <li>major depression, psychosis</li> </ul>	Yes	Conditionally include
Rovina 2009	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>history or current diagnosis of anorexia nervosa or bulimia</li> <li>presence of an unstable medical or psychiatric condition</li> <li>history of dependence on alcohol or a non-nicotine substance within the past year</li> <li>current use of psychotropic medications, fluoxetine, clonidine, buspirone or doxepin</li> <li>current depression, as assessed by the psychiatrist of the program</li> </ul>	Yes	Conditionally include
Saules 2004	Antidepressants	Fluoxetine	Placebo	<ul style="list-style-type: none"> <li>acute psychiatric crisis</li> <li>met criteria for a psychiatric disorder within the past six months</li> <li>currently taking psychiatric medications</li> </ul>	Yes	Explicitly exclude
Schmitz 2007	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>anorexia nervosa, or bulimia</li> <li>presence of a current psychiatric disorder or serious medical condition</li> <li>dependence on alcohol or other illicit substances</li> <li>concurrent drug therapy or psychotherapy for smoking cessation</li> </ul>	Yes	Explicitly exclude
Schnoll 2010	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>Axis I psychiatric conditions and medical conditions</li> </ul>	Yes	Explicitly exclude
Siddiqi 2013	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Simon 2004	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>contraindications to bupropion or NRT</li> <li>serious psychiatric illnesses, including major depression</li> </ul>	Yes	Conditionally include

				<ul style="list-style-type: none"> <li>recent history of alcohol abuse within the prior 3 months</li> </ul>		
Simon 2009	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>contraindications to bupropion</li> <li>serious unstable psychiatric illness (defined by frequent mental health visits or changing psychiatric medication regimens)</li> <li>history of drug abuse within the prior 3 months</li> </ul>	Yes	Conditionally include
Smith 2009	Antidepressants	Bupropion	NRT	<ul style="list-style-type: none"> <li>bipolar disorder, psychosis, bulimia, or anorexia nervosa</li> <li>serious thoughts of self-harm in the previous 2 weeks</li> <li>drug or alcohol dependence in the past 6 months</li> </ul>	Yes	Conditionally include
Sood 2010	Antidepressants	St John's-wort	Placebo	<ul style="list-style-type: none"> <li>met diagnostic criteria for current major depressive disorder</li> <li>lifetime history of bipolar disorder or schizophrenia</li> <li>currently (past 30 days) using antipsychotic or antidepressant medicines</li> <li>a recent history (past 3 months) of alcohol abuse or dependence</li> <li>a recent history of drug abuse</li> <li>currently taking medications known to interact with SJW including all serotonergic drugs (serotonin reuptake inhibitors, tricyclic antidepressants, tramadol, venlafaxine, tryptophan, and buspirone)</li> </ul>	Yes	Conditionally include
Sood 2012	Antidepressants	S-Adenosyl methionine (SAME)	Placebo	<ul style="list-style-type: none"> <li>clinically significant levels of current depression</li> <li>lifetime diagnosis of bipolar disorder, schizophrenia, or dementia</li> <li>an unstable medical condition</li> <li>currently (past 30 days) using antipsychotics or antidepressants</li> <li>recent history (past 3 months) of alcohol abuse or dependence</li> <li>had a recent history (past 3 months) of drug abuse</li> </ul>	Yes	Conditionally include
Spring 2007	Antidepressants	Fluoxetine	Placebo	<ul style="list-style-type: none"> <li>lifetime history of MDD or as having at least one past episode of MDD</li> <li>currently depressed or an MDD episode within the past 6 months</li> <li>current episode of Axis I disorder (other than nicotine dependence)</li> <li>history of seizures, psychosis, or bipolar disorder</li> <li>use of psychotropic medication within the past month</li> <li>medically unstable conditions</li> </ul>	Yes	Conditionally include
Stapleton 2013	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>contraindication to bupropion or NRT according to the summary of product characteristics (SpC)</li> </ul>	Yes	Conditionally include
Swan 2003	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>current use of medications contraindicated for use with bupropion SR or known to lower seizure threshold</li> <li>history of or current diagnosis of anorexia nervosa or bulimia</li> <li>current depression</li> <li>recent high frequency or binge drinking, abuse of other substances including recreational/street drugs</li> </ul>	Yes	Conditionally include
Tashkin 2001	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>any serious or unstable medical disorders for which bupropion SR was contraindicated</li> <li>current diagnosis of major depression</li> </ul>	Yes	Conditionally include
Tonnesen 2003	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>psychiatric disease</li> <li>currently depressed, or had a history or current diagnosis of bulimia, anorexia nervosa, panic disorder, psychosis or bipolar disorder</li> </ul>	Yes	Conditionally include
Tonstad 2003	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>history or current diagnosis of bulimia or anorexia nervosa</li> <li>history or current diagnosis of panic disorder, psychosis, or bipolar disorder</li> <li>current depression</li> </ul>	Yes	Conditionally include

Wagena 2005	Antidepressants	Bupropion & Nortriptyline	Placebo	<ul style="list-style-type: none"> <li>• use of psychoactive medication at the time of assessment</li> <li>• any serious or unstable medical disorders for which bupropion SR or nortriptyline was contraindicated</li> </ul>	Yes	Conditionally include
Weinberger 2010	Antidepressants	Selegiline	Placebo	<ul style="list-style-type: none"> <li>• evidence of alcohol or other drug abuse or dependence in the previous 6 months</li> <li>• met DSM-IV criteria for a current diagnosis of major depressive disorder, panic disorder or post-traumatic stress disorder</li> <li>• met DSM-IV criteria for a current or past diagnosis of bipolar disorder or schizophrenia</li> <li>• unstable medical disorders</li> <li>• inability to give informed consent</li> <li>• use of antidepressant medication, or other medications (e.g., meperidine) which might interact with SEL</li> </ul>	Yes	Conditionally include
Wittchen 2011	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>• current diagnosis of major depressive episode</li> <li>• history of panic disorder, psychosis, bipolar disorder, or eating disorder</li> <li>• abuse of alcohol or a non-nicotine containing drug within the preceding year</li> <li>• concurrent use of tricyclics, selective serotonin re-uptake inhibitors (SSRIs), serotonin- norepinephrine re-uptake inhibitors (SNRIs), neuroleptics or monoamine oxidase (MAO) inhibitors</li> </ul>	Yes	Conditionally include
Zellweger 2005	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>• history or current diagnosis of bulimia, anorexia nervosa, panic disorder, psychosis, or bipolar disorder</li> <li>• current depression</li> </ul>	Yes	Conditionally include
Cinciripini 1995 L + H	Other	Bupirone	Placebo	<ul style="list-style-type: none"> <li>• current history of a psychiatric disorder or use of psychotropic medications</li> </ul>	Yes	Explicitly exclude
Dow 1984	Other	Beta-blockers 1. Oxprenolol 2. Metoprolol	Placebo	<ul style="list-style-type: none"> <li>• not reported</li> </ul>	No	Unclear
Hao 1988	Other	Diazepam	Placebo	<ul style="list-style-type: none"> <li>• not reported</li> </ul>	No	Unclear
Hilleman 1994	Other	Bupirone	NRT	<ul style="list-style-type: none"> <li>• history of psychiatric illness, alcoholism or drug addiction</li> </ul>	Yes	Explicitly exclude
Schneider 1996	Other	Bupirone	Placebo	<ul style="list-style-type: none"> <li>• use of psychoactive drugs, or a history of diagnosed anxiety and depression</li> </ul>	Yes	Conditionally include
Glassman 1988	Other	Clonidine	Placebo	<ul style="list-style-type: none"> <li>• drug or alcohol abuse, schizophrenia, and current major depression</li> </ul>	Yes	Conditionally include
Glassman 1993	Other	Clonidine	Placebo	<ul style="list-style-type: none"> <li>• drug or alcohol abuse, schizophrenia, and current major depression</li> <li>• current use of any antidepressant drug</li> <li>• history of major depressive disorder had to have been free of symptoms for at least 6 months and to have taken no antidepressant medication for at least 6 weeks</li> </ul>	Yes	Conditionally include
Hilleman 1993	Other	Clonidine	Placebo	<ul style="list-style-type: none"> <li>• unstable disease states</li> <li>• history of psychiatric illness, alcoholism, or drug addiction</li> </ul>	Yes	Explicitly exclude
Niaura 1996	Other	Clonidine	Placebo	<ul style="list-style-type: none"> <li>• current treatment for a psychiatric disorder (excluding nicotine dependence)</li> </ul>	Yes	Explicitly exclude
Bullen 2013	Other	NEC (nicotine EC)	Placebo	<ul style="list-style-type: none"> <li>• not reported</li> </ul>	No	Unclear
Caponnetto 2013a	Other	NEC (nicotine EC)	Placebo	<ul style="list-style-type: none"> <li>• regular psychotropic medicine use</li> <li>• current or past history of alcohol abuse</li> </ul>	Yes	Conditionally include
Rose 1994	Other	Mecamylamine + Nicotine patch	Placebo + NRT	<ul style="list-style-type: none"> <li>• alcohol or drug abuse</li> <li>• use of psychotropic medications</li> </ul>	Yes	Explicitly exclude

Rose 1996	Other	Mecamylamine	Placebo + NRT	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Scharfenberg 1971	nAChR partial agonist	Cytisine	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Vinnikov 2008	nAChR partial agonist	Cytisine	Placebo	<ul style="list-style-type: none"> <li>serious or unstable disorders</li> <li>contraindication for cytisine use</li> <li>schizophrenia</li> </ul>	Yes	Conditionally include
West 2011	nAChR partial agonist	Cytisine	Placebo	<ul style="list-style-type: none"> <li>diagnosis of a current psychiatric disorder or a medical condition that was contraindicated according to the cytisine label</li> </ul>	Yes	Explicitly exclude
Walker 2014	nAChR partial agonist	Cytisine	NRT	<ul style="list-style-type: none"> <li>schizophrenia</li> </ul>	Yes	Conditionally include
Tonstad 2011	nAChR partial agonist	Dianicline	Placebo	<ul style="list-style-type: none"> <li>current psychotic disorder or major depressive episode based on DSM-IV</li> </ul>	Yes	Conditionally include
Anthenelli 2013	nAChR partial agonist	Varenicline	Placebo	<ul style="list-style-type: none"> <li>current or past diagnosis of dementia, schizophrenia, schizoaffective disorder, or other psychotic disorder, bipolar I disorder, bipolar II disorder</li> <li>antisocial, schizotypal, or any other personality disorder severe enough to compromise their ability to comply with the study requirement</li> </ul>	Yes	Conditionally include
Aubin 2008	nAChR partial agonist	Varenicline	NRT	<ul style="list-style-type: none"> <li>diagnoses of or treatment for depression or other psychological disorder</li> <li>drug or alcohol dependence within the previous 12 months</li> </ul>	Yes	Explicitly exclude
Baker 2016	nAChR partial agonist	Varenicline	NRT	<ul style="list-style-type: none"> <li>prior suicide attempts within the last 5 years or current suicidal ideation</li> <li>diagnosis of or treatment for psychoses within the last 10 years</li> <li>moderately severe depression via the Patient Health Questionnaire 18</li> <li>current use of bupropion</li> </ul>	Yes	Explicitly exclude
Bolliger 2011	nAChR partial agonist	Varenicline	Placebo	<ul style="list-style-type: none"> <li>diagnosis of, or treatment for, depression during the previous 12 months</li> <li>history of or current psychosis, panic disorder, or bipolar disorder</li> <li>use of bupropion, clonidine, or nortriptyline within the previous 6 months</li> </ul>	Yes	Conditionally include
Carson 2014	nAChR partial agonist	Varenicline	No Placebo	<ul style="list-style-type: none"> <li>acute or pre-existing psychiatric illnesses including depression uncontrolled with medication</li> <li>past history psychosis or suicidal ideation</li> </ul>	Yes	Conditionally include
Chengappa 2014	nAChR partial agonist	Varenicline	Placebo	<ul style="list-style-type: none"> <li>history of psychiatric emergency room visits or hospitalization, suicidal attempts, or aggressive or violent acts</li> <li>Comorbid psychiatric condition diagnosed within the last three months was excluded.”</li> </ul>	Yes	Conditionally include
Cinciripini 2013	nAChR partial agonist	Varenicline	Placebo	<ul style="list-style-type: none"> <li>currently taking psychotropic medication</li> <li>lifetime history of a psychotic disorder</li> <li>psychiatric hospitalization within the last year</li> <li>current psychiatric disorder (including substance abuse except for smoking)</li> <li>scoring moderate or higher on the suicidality subscale of the Mini-International Neuropsychiatric Interview</li> <li>contraindications to the use of varenicline (e.g., severe renal impairment) or bupropion SR (e.g., history of seizures).”</li> </ul>	Yes	Explicitly exclude
De Dios 2012	nAChR partial agonist	Varenicline	Placebo	<ul style="list-style-type: none"> <li>history of a suicide attempt/s</li> <li>chronic or acute severe psychiatric disorder that will interfere with participation</li> <li>substance dependence other than nicotine dependence.”</li> </ul>	Yes	Explicitly exclude
Ebbert 2015	nAChR partial agonist	Varenicline	Placebo	<ul style="list-style-type: none"> <li>history of a suicide attempt or suicidal behaviour in the previous 2 years</li> </ul>	Yes	Conditionally include

				<ul style="list-style-type: none"> <li>major depressive or anxiety disorder assessed by a physician as severe (lifetime or current) or unstable (ie, medication dose change or exacerbations in the last 6 months)</li> <li>lifetime diagnosis of psychosis, panic disorder, posttraumatic stress disorder, or schizophrenia</li> <li>alcohol or substance abuse in the last 12 months</li> </ul>		
Eisenberg 2016	nAChR partial agonist	Varenicline	Placebo	<ul style="list-style-type: none"> <li>excessive alcohol use, current use of marijuana or noncigarette tobacco products</li> <li>history of neuropsychiatric disorders including suicidal attempts or suicidal ideation, family history of suicide, panic disorder, psychosis, bipolar disorder, dementia, bulimia, anorexia</li> <li>recent or recurring depression</li> </ul>	Yes	Conditionally include
Evens 2014	nAChR partial agonist	Varenicline	Placebo	<ul style="list-style-type: none"> <li>suicidal or homicidal ideation</li> <li>hospitalization for suicidality in the prior 12 months</li> <li>active substance use disorder, or major depressive episode in the prior 6 months</li> </ul>	Yes	Conditionally include
Gonzales 2006	nAChR partial agonist	Varenicline/ Bupropion	Placebo	<ul style="list-style-type: none"> <li>any serious or unstable disease within 6 months</li> <li>major depressive disorder within the past year requiring treatment</li> <li>history of panic disorder, psychosis, bipolar disorder, or eating disorders; alcohol or drug abuse/ dependency within the past year</li> <li>use of clonidine, or nortriptyline within the month prior to enrolment</li> </ul>	Yes	Conditionally include
Gonzales 2014	nAChR partial agonist	Varenicline	Placebo	<ul style="list-style-type: none"> <li>history of a suicide attempt or any suicidal behaviour in the past 2 years or current suicidal ideation</li> <li>self-reported current depression</li> <li>diagnosis of depression or treatment with antidepressants during the previous 12 months recorded in medical history</li> <li>lifetime diagnosis of psychosis, panic disorder, other anxiety disorders, or bipolar disorder</li> <li>active alcohol or substance abuse/dependence (except nicotine) within the past 12 months</li> <li>any severe medical or psychiatric condition or laboratory abnormality that would make the participant inappropriate for the study</li> </ul>	Yes	Conditionally include
Jorenby 2006	nAChR partial agonist	Varenicline	Placebo	<ul style="list-style-type: none"> <li>contraindications for use of bupropion (e.g., history of seizure, diagnosis of eating disorder)</li> <li>use of a monoamine oxidase inhibitor in the prior 14 days</li> <li>serious or unstable disease within the previous 6 months</li> <li>history of alcohol or other drug abuse or dependence in the previous 12 months</li> <li>treatment for major depression in the previous 12 months</li> <li>history of or current panic disorder, psychosis, or bipolar disorder</li> </ul>	Yes	Conditionally include
Nahvi 2014a	nAChR partial agonist	Varenicline	Placebo	<ul style="list-style-type: none"> <li>current major depressive or manic episode</li> <li>current psychotic disorder,</li> <li>past-year suicide attempt or psychiatric hospitalization, or current suicidal ideation with plan or intent</li> </ul>	Yes	Conditionally include
Nakamura 2007	nAChR partial agonist	Varenicline	Placebo	<ul style="list-style-type: none"> <li>neurologic and psychiatric disorder</li> </ul>	Yes	Explicitly exclude

NCT00828113	nAChR partial agonist	Varenicline	Placebo	<ul style="list-style-type: none"> <li>• current or history of psychotic disorder</li> <li>• current major depressive disorder</li> <li>• history of suicidal ideation in the previous 3 months</li> <li>• unstable medical condition</li> </ul>	Yes	Conditionally include
NCT01347112	nAChR partial agonist	Varenicline	Placebo	<ul style="list-style-type: none"> <li>• current moderate or severe depression</li> <li>• current non-specific suicidal thoughts, or have a lifetime history of a suicidal attempt</li> <li>• current (past 30 days) major depressive disorder or has a history of another psychiatric disorder such as psychosis or bipolar disorder</li> </ul>	Yes	Conditionally include
Niaura 2008	nAChR partial agonist	Varenicline	Placebo	<ul style="list-style-type: none"> <li>• history of psychiatric, pulmonary, renal, or cardiovascular disease</li> <li>• history of depression, panic disorder, psychosis, or bipolar disorder</li> <li>• non-nicotine drug or alcohol dependence within 12 months before study enrolment</li> </ul>	Yes	Explicitly exclude
Nides 2006	nAChR partial agonist	Varenicline/ Bupropion	Placebo	<ul style="list-style-type: none"> <li>• active depression requiring treatment</li> <li>• history of panic disorder, psychosis, bipolar disorder, eating disorders</li> <li>• alcohol or drug abuse/dependency within the previous year</li> </ul>	Yes	Conditionally include
Oncken 2006	nAChR partial agonist	Varenicline	Placebo	<ul style="list-style-type: none"> <li>• major depression within the prior year</li> <li>• panic disorder, psychosis, or bipolar disorder</li> <li>• use of bupropion within the previous 3 months</li> <li>• drug or alcohol abuse or dependence within the past year</li> </ul>	Yes	Conditionally include
Rennard 2012	nAChR partial agonist	Varenicline	Placebo	<ul style="list-style-type: none"> <li>• use of bupropion, clonidine, or nortriptyline within the past 3 months</li> <li>• serious or unstable psychiatric disorders in the past 6 months or on the basis of medical history</li> <li>• current depression or depression diagnosed or treated within the past 12 months</li> <li>• history of suicidal ideation or suicidal behaviour in the past 5 years</li> <li>• history of or present psychosis, panic attacks, or anxiety disorders, or bipolar disorder</li> <li>• history of drug (except nicotine) or alcohol abuse/dependence</li> </ul>	Yes	Conditionally include
Rigotti 2010	nAChR partial agonist	Varenicline	Placebo	<ul style="list-style-type: none"> <li>• diagnosis of depression; treatment with antidepressants in the past year</li> <li>• history of psychosis, panic disorder, or bipolar disorder</li> <li>• drug or alcohol abuse or dependence in the past year</li> <li>• use of bupropion, clonidine, or nortriptyline in the past month.”</li> </ul>	Yes	Conditionally include
Rose 2013	nAChR partial agonist	Varenicline /Bupropion	NRT	<ul style="list-style-type: none"> <li>• current psychiatric disease (with the exception of anxiety disorders, OCD and ADHD; Suicidal ideation (within the past 10 years)</li> <li>• lifetime occurrence of attempted suicide</li> <li>• current depression</li> <li>• psychiatric medications including antidepressants, anti-psychotics</li> </ul>	Yes	Conditionally include
Steinberg 2011	nAChR partial agonist	Varenicline	Placebo	<ul style="list-style-type: none"> <li>• mental illness requiring antipsychotic medications</li> <li>• currently using bupropion, nortriptyline</li> <li>• active substance abuse</li> <li>• deemed clinically unstable</li> </ul>	Yes	Conditionally include
Tashkin 2011	nAChR partial agonist	Varenicline	Placebo	<ul style="list-style-type: none"> <li>• unstable or uncontrolled medical conditions</li> <li>• diagnosis of depression or treatment with antidepressants in the past year</li> <li>• drug or alcohol abuse (other than nicotine) in the past year</li> <li>• history of psychosis, panic disorder, or bipolar disorder</li> </ul>	Yes	Conditionally include



Tsai 2007	nAChR partial agonist	Varenicline	Placebo	<ul style="list-style-type: none"> <li>past or present history of a serious or unstable clinical disease requiring treatment including neurologic or psychiatric disorders</li> <li>history of drug (except nicotine) or alcohol abuse</li> </ul>	Yes	Explicitly exclude
Tsukahara 2010	nAChR partial agonist	Varenicline	NRT	<ul style="list-style-type: none"> <li>drug or alcohol dependence</li> <li>psychological disorders</li> </ul>	Yes	Explicitly exclude
Wang 2009	nAChR partial agonist	Varenicline	Placebo	<ul style="list-style-type: none"> <li>diagnosed with, or treated for, depression during the previous 12 months</li> <li>history of psychosis, panic disorder, bipolar disorder</li> </ul>	Yes	Conditionally include
Westergaard 2015	nAChR partial agonist	Varenicline	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Williams 2007	nAChR partial agonist	Varenicline	Placebo	<ul style="list-style-type: none"> <li>use of antidepressants, antipsychotic agents, naltrexone</li> </ul>	Yes	Conditionally include
Williams 2012	nAChR partial agonist	Varenicline	Placebo	<ul style="list-style-type: none"> <li>psychiatric hospitalization</li> <li>serious suicidal ideation/behaviour</li> <li>history of drug or alcohol abuse/dependence</li> </ul>	Yes	Conditionally include
Wong 2012	nAChR partial agonist	Varenicline	Placebo	<ul style="list-style-type: none"> <li>psychiatric disorders.”</li> </ul>	Yes	Explicitly exclude
Cornuz 2008	Other	NIC002 (formerly Nicotine-Qβ)	Placebo	<ul style="list-style-type: none"> <li>current diagnosis or a history of major depressive episodes, of panic attacks, psychosis, bipolar or eating disorders</li> <li>use of bupropion within 6 months before study enrolment or at the time of screening</li> <li>abuse of alcohol or other recreational drugs</li> <li>use of a psychoactive drug (excluding sleeping pills) within one month before enrolment</li> </ul>	Yes	Conditionally include
Hatsukami 2011	Other	NicVAX [3'AmNic-rEPA]	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
NCT00836199 2011	Other	NicVAX [3'AmNic-rEPA]	Placebo	<ul style="list-style-type: none"> <li>history of drug or alcohol abuse or dependence within 12 months</li> <li>psychiatric disease</li> </ul>	Yes	Explicitly exclude
NCT01102114 2010	Other	NicVAX [3'AmNic-rEPA]	Placebo	<ul style="list-style-type: none"> <li>history of drug or alcohol abuse or dependence within 12 months</li> <li>psychiatric disease</li> </ul>	Yes	Explicitly exclude
Abelin 1989	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Ahluwalia 1998	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>self-reported alcohol or drug dependency</li> </ul>	Yes	Conditionally include
Ahluwalia 2006	NRT	Nicotine gum (2 mg),	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Anthenelli (EAGLES) 2016	nAChR partial agonist	Varenicline, Bupropion, Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>clinical exacerbation of psychotic, anxiety, mood disorders, Axis I and Axis II disorders in the prior 6 months</li> <li>not on stable treatment (medication and dose) for ≥ 3 months (if on treatment)</li> <li>judged to be at imminent risk of self-injurious or suicidal behaviour</li> </ul>	Yes	Conditionally include
Areechon 1988	NRT	Nicotine Gum	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Blondal 1997	NRT	Nicotine nasal spray	Placebo	<ul style="list-style-type: none"> <li>current abuse of alcohol or other drugs</li> </ul>	Yes	Conditionally include
Br Thor Society 1983	NRT	nicotine chewing gum	Placebo	<ul style="list-style-type: none"> <li>psychiatric disorder contraindicating smoking withdrawal</li> </ul>	No	Unclear

Buchkremer 1988	NRT	Nicotine patch + behavioural therapy	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Campbell 1987	NRT	Nicotine gum (2 mg)	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Campbell 1991	NRT	Nicotine gum 2 to 4 mg	Placebo	<ul style="list-style-type: none"> <li>organic psychosis</li> <li>drug and alcohol abuse</li> </ul>	Yes	Conditionally include
Campbell 1996	NRT	Nicotine patch (21 mg)	Placebo	<ul style="list-style-type: none"> <li>mental disturbances</li> </ul>	Yes	Explicitly exclude
Cinciripini 1996	NRT	Nicotine patch (21 mg)	No Placebo	<ul style="list-style-type: none"> <li>uncontrolled systemic illnesses</li> <li>recent history (within 1 year) of diagnosed major depression or treatment with antidepressants</li> </ul>	Yes	Conditionally include
Clavel 1985	NRT	Nicotine gum	No Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Clavel-Chapelon 1992	NRT	Nicotine gum	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Coleman 2012	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>chemical or alcohol dependence</li> </ul>	Yes	Conditionally include
Cooper 2005	NRT	Nicotine gum	Placebo	<ul style="list-style-type: none"> <li>currently taking antidepressant medication or receiving psychiatric or alcohol/drug abuse treatment.</li> <li>history of depression still in treatment</li> </ul>	Yes	Conditionally include
Cummins 2016	NRT	Nicotine patch	No Placebo	<ul style="list-style-type: none"> <li>not enough information provided</li> </ul>	No	Unclear
Cunningham 2016	NRT	Nicotine patch	No Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Daughton 1991	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Daughton 1998	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>current use of psychotropic drugs</li> <li>recent history of drug or alcohol abuse (within 1 year of the study)</li> </ul>	Yes	Conditionally include
Davidson 1998	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Ehram 1991	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Fagerström 1982	NRT	Nicotine gum	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Fagerström 1984	NRT	Nicotine gum	No Placebo	<ul style="list-style-type: none"> <li>psychologically imbalanced or in the midst of a crisis</li> </ul>	Yes	Conditionally include
Fee 1982	NRT	Nicotine gum	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Fiore 1994a	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>regular use of psychotropic drugs</li> <li>current symptomatic psychiatric disorder</li> <li>alcohol or other drug abuse</li> </ul>	Yes	Explicitly exclude
Fiore 1994b	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>regular use of psychotropic drugs</li> <li>alcohol or drug abuse; chronic dermatologic disorders</li> <li>current symptomatic psychiatric disorder</li> </ul>	Yes	Explicitly exclude
Fortmann 1995	NRT	Nicotine gum	No Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Fraser 2014	NRT	Nicotine lozenge	No Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Gallagher 2007	NRT	NRT patch	No Placebo	<ul style="list-style-type: none"> <li>acute decompensation/exacerbation of psychiatric symptomatology that precluded the ability to participate,</li> <li>active, significant substance use in the last 30 days</li> </ul>	Yes	Conditionally include
Garvey 2000	NRT	Nicotine gum	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear

Gilbert 1989	NRT	Nicotine gum	No Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Glavas 2003	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>drug dependence</li> <li>major psychiatric disorders</li> </ul>	Yes	Conditionally include
Glover 2002	NRT	Nicotine sublingual tablet	Placebo	<ul style="list-style-type: none"> <li>regular use of psychotropic medication</li> <li>alcohol or any other drug abuse during the previous 12 months</li> </ul>	Yes	Conditionally include
Graham 2017	NRT	Nicotine patch	No Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Gross 1995	NRT	Nicotine gum	No Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Hall 1985	NRT	Nicotine gum	No Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Hall 1987	NRT	Nicotine gum	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Hall 1996	NRT	Nicotine gum	Placebo	<ul style="list-style-type: none"> <li>current major depression</li> </ul>	Yes	Conditionally include
Hand 2002	NRT	Nicotine patch + inhaler	No Placebo	<ul style="list-style-type: none"> <li>alcoholism, drug dependency</li> <li>active psychiatric illness</li> </ul>	Yes	Explicitly exclude
Harackiewicz 1988	NRT	Nicotine Gum	No Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Hasan 2014	NRT	Patch and gum	No Placebo	<ul style="list-style-type: none"> <li>history of substance abuse</li> <li>major psychiatric disorder included schizophrenia, bipolar and personality disorders</li> </ul>	Yes	Conditionally include
Hays 1999	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Herrera 1995	NRT	Nicotine Gum	Placebo	<ul style="list-style-type: none"> <li>use of any psychotropic medications</li> <li>abuse alcohol or any other drugs</li> </ul>	Yes	Conditionally include
Heydari 2012	NRT	Nicotine patch	No Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Heydari 2013	NRT	Patch, Gum and Lozenges	No Placebo	<ul style="list-style-type: none"> <li>mental or physical illness</li> </ul>	Yes	Explicitly exclude
Hjalmarson 1984	NRT	Nicotine gum	Placebo	<ul style="list-style-type: none"> <li>psychosis, mental retardation, and alcohol abuse</li> </ul>	Yes	Conditionally include
Hjalmarson 1994	NRT	Nicotine nasal spray	Placebo	<ul style="list-style-type: none"> <li>current use of any psychotropic medication</li> <li>current abuse of alcohol or any other drug</li> </ul>	Yes	Conditionally include
Hjalmarson 1997	NRT	Nicotine inhaler	Placebo	<ul style="list-style-type: none"> <li>regular treatment with psychotropic drugs</li> <li>abuse of alcohol or any other drugs during the last 12 months</li> </ul>	Yes	Conditionally include
Huber 1988	NRT	Nicotine gum	No Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Hughes 1989	NRT	Nicotine gum	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Hughes 1990	NRT	Nicotine gum	Placebo	<ul style="list-style-type: none"> <li>contraindication to nicotine gum</li> <li>history of drug abuse, drug dependence</li> <li>history of psychiatric disorder</li> </ul>	Yes	Explicitly exclude
Hughes 1999	NRT	Nicotine Patch	Placebo	<ul style="list-style-type: none"> <li>use of psychotropic</li> </ul>	Yes	Conditionally include
Hughes 2003	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>past alcohol dependence but no alcohol or illicit drug intake for last 30 days</li> <li>current major psychiatric disorder and not taking a psychoactive medication</li> </ul>	Yes	Conditionally include
Hurt 1990	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Hurt 1994	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>active chemical dependence on alcohol</li> <li>current psychiatric disorder,</li> <li>current use of clonidine, buspirone hydrochloride, doxepin hydrochloride, or fluoxetine</li> </ul>	Yes	Explicitly exclude
ICRF 1994	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Jamrozik 1984	NRT	Nicotine gum	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Jarvis 1982	NRT	Nicotine gum	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear

Jensen 1991	NRT	Nicotine gum	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Jorenby 1999	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>current diagnosis of major depressive episode</li> <li>history of panic disorder, psychosis, bipolar disorder, or eating disorders</li> <li>abuse of alcohol or a non-nicotine-containing drug within the preceding year</li> <li>use of a psychoactive drug within the week before enrolment</li> <li>clinical depression</li> </ul>	Yes	Conditionally include
Joseph 1996	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>presence of unstable psychiatric illness</li> <li>unstable disorder involving the use of alcohol or controlled substances</li> </ul>	Yes	Conditionally include
Killen 1984	NRT	Nicotine gum	No Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Killen 1990	NRT	Nicotine gum	No Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Killen 1997	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Kornitzer 1995	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>regular use of psychotropic medication</li> <li>abuse of alcohol or any other drug</li> </ul>	Yes	Conditionally include
Kralikova 2009	NRT	Nicotine gum or inhaler	Placebo	<ul style="list-style-type: none"> <li>psychiatric treatment or use of medication</li> <li>alcohol or other drug problems</li> </ul>	Yes	Conditionally include
Leischow 1996	NRT	Nicotine Inhaler	Placebo	<ul style="list-style-type: none"> <li>regular use of psychotropic drugs</li> <li>alcohol or drug abuse</li> </ul>	Yes	Conditionally include
Lerman 2015	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>history of substance misuse treatment</li> <li>current use of cocaine or methamphetamine, or more than 25 alcoholic drinks per week</li> <li>history of DSM-IV Axis 1 psychiatric disorder</li> <li>suicide risk score on the MINI International Neuropsychiatric Interview (MINI) of more than 1</li> <li>current major depression; current use of antipsychotics (e.g., monoamine oxidase inhibitors, tricyclic antidepressants)</li> </ul>	Yes	Conditionally include
Lewis 1998	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>drug and alcohol abuse within 6 month of admission</li> <li>history of major psychiatric illnesses</li> </ul>	Yes	Conditionally include
Malcolm 1980	NRT	Nicotine gum	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
McGovern 1992	NRT	Nicotine gum	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Molyneux 2003	NRT	Choice of NRT	No Placebo	<ul style="list-style-type: none"> <li>admission for psychiatric care</li> <li>history of alcohol and/or illicit drug abuse in the last 12 months</li> </ul>	Yes	Conditionally include
Moolchan 2005	NRT	Nicotine patch + gum	Placebo	<ul style="list-style-type: none"> <li>drug or alcohol dependence other than nicotine</li> <li>current mania, psychosis, and acute depression</li> </ul>	Yes	Conditionally include
NCT00534404	NRT	Nicotine patch	No Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Nebot 1992	NRT	Nicotine gum	No Placebo	<ul style="list-style-type: none"> <li>addiction to legal or illegal drugs</li> </ul>	Yes	Conditionally include
Niaura 1994	NRT	Nicotine gum	No Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Niaura 1999	NRT	Nicotine gum	No Placebo	<ul style="list-style-type: none"> <li>treatment for any psychiatric disorder in the past year</li> <li>using recreational drugs</li> </ul>	Yes	Explicitly exclude
Ockene 1991	NRT	Nicotine gum	No Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Oncken 2007	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>Axis I psychiatric diagnosis that required clinical attention (e.g., current major depression or substance dependence other than nicotine)</li> <li>chronic treatment with bupropion for depression was not exclusionary</li> </ul>	Yes	Conditionally include
Oncken 2008	NRT	Nicotine gum	Placebo	<ul style="list-style-type: none"> <li>evidence of cognitive or mental health problems (e.g., diagnosis of mental disorder in chart or interviewer or support specialist suspected problems)</li> </ul>	Yes	Explicitly exclude

				<ul style="list-style-type: none"> <li>evidence of possible drug or alcohol addiction</li> </ul>		
Ortega 2011	NRT	Nicotine patch or gum	No Placebo	<ul style="list-style-type: none"> <li>pathologies related to psychiatry or neurology</li> </ul>	Yes	Explicitly exclude
Otero 2006	NRT	Nicotine patch	No Placebo	<ul style="list-style-type: none"> <li>lifetime mental disorders</li> <li>alcohol and other drugs dependence</li> </ul>	Yes	Explicitly exclude
Page 1986	NRT	Nicotine Gum	No Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Paoletti 1996	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>past or current history of psychiatric disorders</li> <li>currently taking daily psychiatric medications</li> </ul>	Yes	Explicitly exclude
Piper 2009	NRT	Choice of NRT/Bupropion	Placebo	<ul style="list-style-type: none"> <li>current psychosis or schizophrenia diagnosis</li> <li>contraindications for any of the study medications</li> <li>high alcohol consumption (6 drinks per day on 6 or 7 days of the week)</li> <li>bipolar disorder, an eating disorder</li> </ul>	Yes	Conditionally include
Pirie 1992	NRT	Nicotine Gum	No Placebo	<ul style="list-style-type: none"> <li>substance abuse in the past 6 months</li> </ul>	Yes	Conditionally include
Pollak 2007	NRT	Nicotine patch, gum, lozenge	No Placebo	<ul style="list-style-type: none"> <li>cognitive or mental health problems (e.g., diagnosis of mental disorder in chart or interviewer or support specialist suspected problems)</li> <li>possible drug or alcohol addiction</li> </ul>	Yes	Explicitly exclude
Prapavessis 2007	NRT	Nicotine patch	No Placebo	<ul style="list-style-type: none"> <li>psychological problems"</li> </ul>	Yes	Explicitly exclude
Puska 1979	NRT	Nicotine gum	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Richmond 1993	NRT	Nicotine gum	No Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Richmond 1994	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Russell 1983	NRT	Nicotine gum	No Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Sachs 1993	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>current regular use of psychotropic medications</li> <li>current or past alcohol or other drug abuse</li> </ul>	Yes	Conditionally include
Scherphof 2014	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Schneider 1983a	NRT	Nicotine gum	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Schneider 1983b	NRT	Nicotine gum	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Schneider 1995	NRT	Nicotine nasal spray	Placebo	<ul style="list-style-type: none"> <li>use of psychoactive medication</li> <li>past or current drug abuse</li> <li>psychiatric conditions</li> </ul>	Yes	Explicitly exclude
Schneider 1996	NRT	Nicotine inhaler	Placebo	<ul style="list-style-type: none"> <li>psychiatric conditions or diagnoses</li> <li>psychoactive medication</li> <li>past or current drug abuse</li> </ul>	Yes	Explicitly exclude
Segnan 1991	NRT	Nicotine gum	No Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Shiffman 2002 (2 mg)	NRT	Nicotine lozenge	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Shiffman 2002 (4 mg)	NRT	Nicotine lozenge	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Shiffman 2009 (2 mg)	NRT	Nicotine gum	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Shiffman 2009 (4 mg)	NRT	Nicotine gum	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Stapleton 1995	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>current psychotropic medication</li> </ul>	Yes	Conditionally include

Stein 2013	NRT	Nicotine patch + gum	Placebo	<ul style="list-style-type: none"> <li>self-reported psychiatric history</li> </ul>	Yes	Explicitly exclude
Sutherland 1992	NRT	Nicotine nasal spray	Placebo	<ul style="list-style-type: none"> <li>current use of psychotropic medication</li> <li>current abuse of alcohol or other drugs</li> </ul>	Yes	Conditionally include
Sønderskov 1997	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
TNSG 1991	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Tuisku 2016	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>current drug or alcohol abuse</li> </ul>	Yes	Conditionally include
Tønnesen 1988	NRT	Nicotine gum	Placebo	<ul style="list-style-type: none"> <li>alcohol abuse</li> <li>major psychiatric disorders</li> </ul>	Yes	Conditionally include
Tønnesen 1991	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>regular use of psychiatric drugs</li> <li>alcohol or drug abuse</li> </ul>	Yes	Conditionally include
Tønnesen 1993	NRT	Nicotine inhaler	Placebo	<ul style="list-style-type: none"> <li>regular use of psychotropic drugs</li> <li>abuse of alcohol or any other drugs</li> </ul>	Yes	Conditionally include
Tønnesen 2000	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>regular use of psychotropic drugs</li> <li>abuse of alcohol or any other drugs</li> </ul>	Yes	Conditionally include
Tønnesen 2006	NRT	Nicotine lozenges	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Tønnesen 2012	NRT	Nicotine spray	Placebo	<ul style="list-style-type: none"> <li>suspected alcohol or drug abuse</li> <li>psychiatric condition</li> </ul>	Yes	Explicitly exclude
Wallstrom 2000	NRT	Nicotine lozenges	Placebo	<ul style="list-style-type: none"> <li>use of psychotropic medication</li> </ul>	Yes	Conditionally include
Ward 2013	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Westman 1993	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>major psychiatric disorders requiring medication</li> </ul>	Yes	Conditionally include
Wisborg 2000	NRT	Nicotine patch	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Zelman 1992	NRT	Nicotine gum	No Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Baltieri 2009	Other	Naltrexone	Placebo	<ul style="list-style-type: none"> <li>current diagnosis of dependence or abuse of other substances except nicotine</li> <li>concomitant psychiatric disorders that might require specific drug treatment</li> <li>clinical history of mental retardation</li> </ul>	Yes	Conditionally include
Covey 1999	Other	Naltrexone	Placebo	<ul style="list-style-type: none"> <li>current psychiatric disorder including major depression</li> <li>drugs or alcohol abuse or dependence</li> <li>history of a psychotic illness</li> </ul>	Yes	Conditionally include
King 2006	Other	Naltrexone + Nicotine Patch	Placebo + NRT	<ul style="list-style-type: none"> <li>current or recent past major medical or psychiatric disorder</li> <li>use of psychotropic medications in the previous year</li> </ul>	Yes	Explicitly exclude
King 2012	Other	Naltrexone + Nicotine Patch	Placebo + NRT	<ul style="list-style-type: none"> <li>past-year history of a major medical or psychiatric disorder</li> <li>substance dependence (except nicotine)</li> <li>lifetime diagnosis of opioid abuse or dependence</li> <li>use of opioids psychotropic medications</li> </ul>	Yes	Explicitly exclude
O'Malley 2006	Other	Naltrexone + Nicotine Patch	Placebo	<ul style="list-style-type: none"> <li>past-year history of a major medical or psychiatric disorder</li> <li>substance dependence (except nicotine)</li> <li>lifetime diagnosis of opioid abuse or dependence</li> <li>use of opioids psychotropic medications</li> </ul>	Yes	Conditionally include
Toll 2010a	Other	Naltrexone	Placebo	<ul style="list-style-type: none"> <li>current alcohol or drug dependence other than nicotine dependence</li> <li>serious current neurologic, psychiatric, suicidal risk or medical illness</li> <li>use of any psychotropic drug or on any drug with a psychotropic component [except those who were on a stable dose of a Selective</li> </ul>	Yes	Explicitly exclude

				Serotonin Reuptake Inhibitor for at least 2 months for the indications of Major Depressive Disorder, Premenstrual Syndrome or Premenstrual Dysphoric Disorder]		
Wong 1999	Other	Naltrexone	Placebo	<ul style="list-style-type: none"> <li>contraindication for the use of either naltrexone or nicotine patch therapy</li> <li>history of depression, were currently depressed</li> <li>had other psychiatric conditions requiring medication</li> </ul>	Yes	Conditionally include
STRATUS-EU 2006	Other	(i) Rimonabant 5 mg (ii) Rimonabant 20 mg	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
STRATUS-US 2006	Other	(i) Rimonabant 5 mg (ii) Rimonabant 20 mg	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
STRATUS-WW 2005	Other	(i) Rimonabant 5 mg (ii) Rimonabant 20 mg	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Hymowitz 1996	Other	2.5mg silver acetate lozenge	Placebo	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Jensen 1990	Other	6mg Silver acetate chewing gum, up to six pieces daily	Placebo + NRT	<ul style="list-style-type: none"> <li>not reported</li> </ul>	No	Unclear
Following studies are included after search updated in December 2020						
Barnes 2006	Antidepressants	St John's Wort, 300 mg per day	St John's Wort, 300 mg twice per day	<ul style="list-style-type: none"> <li>history of dependence on alcohol or a non-nicotine substance within the past year</li> <li>current diagnosis of major depressive episode</li> <li>history of panic disorder, psychosis, bipolar disorder or eating disorders</li> <li>current use of antidepressant agents</li> </ul>	Yes	Conditionally include
Benli 2017	Antidepressants	Bupropion	Varenicline	<ul style="list-style-type: none"> <li>current treatment for previously known psychiatric disease</li> </ul>	Yes	Explicitly exclude
Cinciripini 2018	Antidepressants	Bupropion	Varenicline	<ul style="list-style-type: none"> <li>currently taking psychotropic medication</li> <li>having a current psychiatric disorder, psychiatric hospitalization within the last year</li> <li>life-time history of a psychotic disorder</li> <li>scoring moderate or higher on the suicidality scale of the Mini International Neuropsychiatric Interview (MINI)</li> </ul>	Yes	Explicitly exclude
CTRI/2013/07/003830	Antidepressants	Bupropion	No Placebo	<ul style="list-style-type: none"> <li>past psychiatric illness"</li> </ul>	Yes	Conditionally include
Ebbert 2014	Antidepressants	Bupropion	Varenicline	<ul style="list-style-type: none"> <li>history of psychosis, bipolar disorder, bulimia, or anorexia nervosa</li> <li>current depression (moderate or severe)</li> <li>active substance abuse other than nicotine</li> <li>current use (previous 14 days) of antipsychotics, monoamine oxidase inhibitors, or drugs with bupropion SR interactions</li> <li>recent antidepressant dose change (previous 3 months)</li> </ul>	Yes	Conditionally include
Gilbert 2019	Antidepressants	Bupropion	Placebo	<ul style="list-style-type: none"> <li>current use of psychoactive drugs or medications</li> </ul>	Yes	Conditionally include

				<ul style="list-style-type: none"> <li>• alcohol use 28 alcoholic drinks per week</li> <li>• bulimia or anorexia</li> <li>• current diagnoses of a mood, bipolar, or psychotic disorder</li> </ul>		
Moreno-Coutino 2015	Antidepressants	Bupropion	NRT	<ul style="list-style-type: none"> <li>• use or abuse of another psychoactive substance (including psychiatric medications)</li> <li>• diagnosis of mental disorders and conditions</li> <li>• contraindications to bupropion</li> </ul>	Yes	Explicitly exclude
NCT00132821	Antidepressants	Bupropion	NRT	<ul style="list-style-type: none"> <li>• met DSM-IV criteria for dependence on substances other than nicotine and caffeine</li> <li>• substance abuse within the year prior to enrolment</li> <li>• history of DSM-IV diagnosis of schizophrenia, bipolar disorder, obsessive compulsive disorder, or chronic depression</li> <li>• current diagnosis of major depression</li> <li>• currently diagnosed with a sleep disorder, anorexia or bulimia</li> <li>• use of medications contraindicated with bupropion</li> <li>• high frequency alcohol use or binge drinking in the month prior to enrolment</li> </ul>	Yes	Conditionally include
NCT00308763	Antidepressants	Bupropion	NRT	<ul style="list-style-type: none"> <li>• history of substance abuse, including alcohol use in excess of 14 drinks a week</li> <li>• history of anorexia or bulimia</li> <li>• presence of an unstable psychiatric illness</li> <li>• current use of a psychotropic medication, including antidepressant medications</li> </ul>	Yes	Conditionally include
NCT00578669	Antidepressants	Fluoxetine	Placebo	<ul style="list-style-type: none"> <li>• current Axis I disorder, including Major Depressive Disorder</li> <li>• psychoactive substance abuse or dependence within past year</li> <li>• current use of psychotropic medication</li> <li>• use of antidepressant medication within past 6 months</li> <li>• current suicidal risk</li> </ul>	Yes	Explicitly exclude
Rose 2014	Antidepressants	Bupropion	Varenicline	<ul style="list-style-type: none"> <li>• not reported</li> </ul>	No	Unclear



